

Rs.10



J I M A

Volume 67 (RNI) ♦ Number 08 ♦ AUGUST 2023 ♦ KOLKATA

JOURNAL *Of the* INDIAN MEDICAL ASSOCIATION

Official Publication of the Indian Medical Association



Indexed in

INDEX  COPERNICUS
INTERNATIONAL

Scopus®

Volume 121 (JIMA) ♦ Number 08 ♦ August 2023 ♦ KOLKATA



Largest
Circulated
Medical Journal
in India

ISSN 0019-5847

94 TH
YEAR OF
PUBLICATION

Visit us at <https://onlinejima.com>

sanofi



In Allergic Rhinitis

Allegra[®]-M

(Fexofenadine Hydrochloride 120 mg + Montelukast Sodium 10 mg)

The ONLY FEXO & MONTE[^]
brand published in the IJPS for
its bio-equivalence¹

In moderate to severe Allergic Rhinitis,

Allegra[®] nasal spray

(Fluticasone Furoate 27.5 mcg/spray)




**Acts Faster &
Stays Longer²**

ACTS IN  **15 MINS²**

 **For QUICK RELIEF**



In moderate to severe Allergic Rhinitis,

Allegra[®] nasal Duo

Fluticasone Furoate 27.5 mcg & Azelastine HCl 140 mcg

[^]Fexofenadine & Monte ukast

Reference:

1. Walekar A, Chodankar D, Naqvi M, Trivedi C: Assessment of Bioequivalence of Fexofenadine and Montelukast Fixed Dose Combination Tablet Versus Separate Formulations of the Individual Components at the Same Dose Levels. Indian Journal of pharmaceutical sciences, 2016, 78(5), 656-56 2. Kumar R , Kumar D ,Parakh A. Futicasone furoate: A new 'Intranasa corticosteroid. J Postgrad Med 2012;58:79-831.
 Allerga Nasal Spray API : <https://www.sanofi.in/dam/jcr:d0151535-e26e-401f-8bc4-c044d5fd197d/Allegra%20Nasal%20API.pdf>
 Allerga Nasal Duo API : <https://www.sanofi.in/dam/jcr:4cc83095-772a-4324-8d30-9770b3a5f075/Allegra%20Nasal%20Duo%20API.pdf>
 Allegra- M : https://www.sanofi.in/dam/jcr:927c3836-686f-4cc0-9a1e-df6366327510/Allegra%20M_API_Sep%202021.pdf

Believe in the Best

^{Rx} **FlemiClav**

1000
625 | 375
KID DT

Amoxicillin & Potassium Clavulanate Tablets



The Most Economical Brand

FlemiClav[®] 1000

₹ 30 / Tab



FlemiClav[®] 625

₹ 15 / Tab



FlemiClav[®] 228.5
KID DRY SYRUP **mg/5ml**



Vanilla Flavour

FlemiClav[®] 457
FORTE DRY SYRUP **mg/5ml**



Mix Fruit Flavour

FlemiClav[®] I.V. 1.2g
Injection



FDC Limited 142-48, S.V. Road, Jogeshwari (W), Mumbai - 400 102

TEAM IMA (2022-24)



Chief Patron
Past President, WMA, MCI, IMA
Dr Ketan Desai



National President
(2022-23)
Dr Sharad Kumar Agarwal



Imm. Past National President
(2022-23)
Dr Sahajanand Prasad Singh



National President
(2023-24)
Dr R.V. Asokan



Hony. Secretary General
(2022-24)
Dr Anilkumar J Nayak



National Vice President
(2022-23)
Dr. Jayesh M Lele



National Vice President
(2022-23)
Dr Sachchidanand Kumar



National Vice President
(2022-23)
Dr Shailesh H Shah



National Vice President
(2022-23)
Dr Daggumati Shree Harirao



National Vice President
(2023-24)
Dr R Gunasekaran



National Vice President
(2023-24)
Dr. Suresh Gutta



National Vice President
(2023-24)
Dr Ashok Sharda



National Vice President
(2023-24)
Dr Shiv Kumar Utture



Hony. Finance Secretary
(2022-24)
Dr Shitij Bali



Hony. Joint Secretary
from NCR (2022-24)
Dr Munish Prabhakar



Hony. Joint Secretary
from National Capital
Region (2022-24)
Dr. Prakash Lalchandani



Hony. Joint Secretary
from rest of the country
(2022-24)
Dr. M. Venkatachalapathy



Hony. Joint Secretary
stationed at Calcutta
(2022-24)
Dr. Pradeep Kumar Nemani



Hony. Joint Secretary
nominated by National
President (2022-23)
Dr Anand Prakash



Hony. Jt Finance Secretary
from rest of the country
(2022-24)
Dr Mahendra Nath Thareja



Hony. Joint Finance Secretary
stationed at Calcutta
(2022-24)
Dr Sarbari Dutta

IMA College of General Practitioners



Hony. Asstt. Secretary
from NCR (2022-24)
Dr M Thiraviam Mohan



Hony. Asst. Secretary from
rest of the country (2022-24)
Dr Paramjit Singh Maan



Dean, IMA-CGP
(2022-23)
Dr Rayapu Ramesh Babu



Dean, IMA-CGP
(2023-24)
Dr Satyajit Borah



Vice Dean, IMA CGP
(2022-24)
Dr Poonam Singh



Hony. Secretary
IMA CGP (2022-24)
Dr. R Anburajan



Hony. Joint Secretary IMA CGP
from Tamilnadu (2022-24)
Dr M Thiraviam Mohan



Hony. Jt. Secy., IMA CGP
from Tamilnadu (2022-24)
Dr D Senthil Kumar



Hony. Joint. Secy. IMA CGP from
rest of the country (2022-24)
Dr Satish Joshi



Hony. Joint. Secy. IMA CGP from
rest of the country (2022-24)
Dr Sunil Bhikhabhai Chenwala



Hony. Joint. Secy., IMA CGP
from rest of the country (2022-24)
Dr Yeshwant Vasantao Gade



Hony. Joint. Secy. IMA CGP from
rest of the country (2022-24)
Dr Pavankumar N Patil

TEAM IMA (2022-24)

Journal of IMA



Hony. Editor-JIMA (2022-23)
Dr Nandini Chatterjee



Hony. Editor-JIMA (2023-24)
Dr Sanjoy Banerjee



Hony. Associate Editor JIMA (2022-24)
Dr Ranjan Bhattacharyya



Hony. Associate Editor JIMA (2022-24)
Dr Prasanta Kr. Bhattacharyya

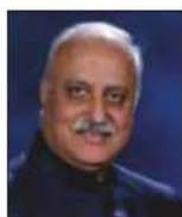


Hony. Secretary JIMA (2022-24)
Dr Sibabrata Banerjee



Hony. Asstt. Secretary JIMA (2022-24)
Dr Meenakshi Ganguly

IMA Academy of Medical Specialities



Chairman, IMA AMS (2022-23)
Dr Pankaj Mutneja



Chairman, IMA AMS (2023-24)
Dr Nomeeta Shiv Gupta



Vice Chairman, IMA-AMS (2022-24)
Dr Nibedita Pani



Hony. Secretary, IMA-AMS (2022-24)
Dr Srirang Abkari

IMA AKN Sinha Institute



Director IMA-AKNSI (2022-23)
Dr G N Prabhakara



Director IMA-AKNSI (2023-24)
Dr Ramneek Singh Bedi



Hony. Executive Secretary IMA-AKNSI (2022-24)
Dr Sanjiv Ranjan Kr. Singh



Hony. Joint Secretary IMA-AKNSI (2022-24)
Dr Deepak Kr. Singh



Hony. Joint Secretary IMA-AKNSI (2022-24)
Dr Parul Vedgama

Your Health of IMA



Hony. Editor Your Health (2022-24)
Dr Kakoli Sen Mandal



Hony. Associate Editor Your Health (2022-24)
Dr Sankar Sen Gupta



Hony. Associate Editor Your Health (2022-24)
Dr Bibartan Saha



Hony. Secretary Your Health (2022-24)
Dr Samrendra Kumar Basu

Apka Swasthya of IMA



Hony. Editor Apka Swasthya (2022-24)
Dr Sudhir Singh



Hony. Associate Editor Apka Swasthya (2022-24)
Dr Anun Kumar Tripathi



Hony. Secretary Apka Swasthya (2022-24)
Dr Ritu Garg



Chairman IMA HBI (2022-24)
Dr A K Ravikumar



Hony. Secretary IMA HBI (2022-24)
Dr Dinesh Bhujangrao Thakare



Treasurer IMA HBI (2022-24)
Dr Rajeev Balkrishna Agarwal

IMA Hospital Board of India

JIMA COMMITTEE 2022-2024



Dr. Sharad Kumar Agarwal
National President, IMA
(2022-23)



Dr. R V Asokan
National President, IMA
(2023-24)



Dr. Anilkumar J Nayak
Hony Secretary General, IMA



Dr. Pradeep Kumar Nemani
Hony. Joint Secretary, Hqs



Dr. Sarbari Datta
Hony. Jt. Finance Secretary, Hqs



Prof (Dr) Nandini Chatterjee
Hony. Editor, JIMA
(2022-23)



Dr Sanjoy Banerjee
Hony. Editor, JIMA
(2023-24)



Dr Ranjan Bhattacharyya
Hony. Associate Editor,
JIMA



Dr Prasanta Kumar
Bhattacharyya
Hony. Associate Editor, JIMA



Dr. Sibabrata Banerjee
Hony. Secretary,
JIMA



Dr. Minakshi Gangopadhyay
Hony. Assistant Secretary,
JIMA



Prof (Dr) Tamas Chaudhuri
Member, JIMA Committee



Dr Debraj Jash
Member, JIMA Committee



Dr Awadhesh Kumar Singh
Member, JIMA Committee



Dr Sekhar Chakraborty
Member, JIMA Committee



Dr. Prakash Chandra Mondal
Member, JIMA Committee



SAROJ GUPTA CANCER CENTRE AND RESEARCH INSTITUTE

MG ROAD, THAKURPUKUR, KOLKATA – 700 063

Website: <https://sgccri.org>

Email:- hr@sgccri.com; Phone:- 033-61234343

Requires immediately:-

1. **Consultant Clinical Haemato Oncologist** preferably with DM / DrNB
2. **Surgical Oncologist:** MCh/DrNB in Surgical Oncology
3. **Full Time /Part time Radiologist:** MD/DNB from recognized institute, working experience in this discipline preferred
4. **Full Time Senior Pathologist:** MD/DNB/DM with experience in Oncopathology
5. **Consultant Radiation Oncologist:** MD/DNB (Radiation Oncology) should have post PG eight years experience in any Oncology institute.

Interested candidates can apply with full bio-data with phone number to:

Director,
SAROJ GUPTA CANCER CENTRE AND RESEARCH INSTITUTE
MG ROAD, THAKURPUKUR, KOLKATA – 700 063

Presenting Once a Day Lincomycin

Rx LYNX[®]-OD

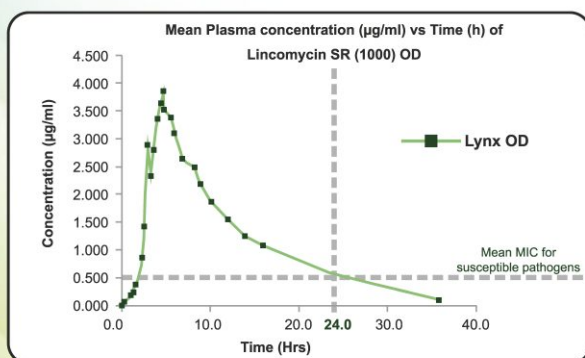
Lincomycin Hydrochloride Sustained Release Tablets 1000 mg

Penetrates... Ensures Success

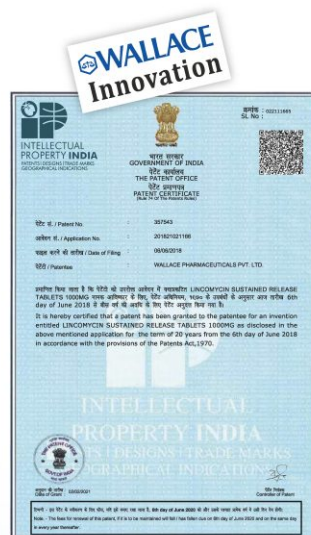
What makes LYNX the ideal 1st line of treatment ?

- High Penetration¹**
 High concentrations in both vascular & avascular tissues like Skin, Scar tissue, Tonsils & Lung tissue
- Low MIC²**
 Very low MIC against most of the gram positive pathogens & anareobes
- Least Resistance**
 Unique mechanism of action & High Susceptibility

Maintains plasma concentration for 24 hours above MIC *



Convenience of OD dose



1. Br J Surg. 1976 Dec;63(12);973-7 2. JAC 7 supplement A: 1981 * Data on file



JIMA Editorial Advisory Board Members (National and International)



Dr. Vedprakash Mishra
Physiology
Maharashtra



Dr. Ravi S. Wankhedkar
General Surgeon
Maharashtra



Dr. T. Nirmal Fredrick
Ophthalmologist
Tamilnadu



Dr. Shiva K. Misra
Minimal Access Surgeon
Uttar Pradesh



Prof Gurpreet S. Wander
Cardiologist
Punjab



Dr. C Palanivelu
Robotic Gastro Surgeon
Coimbatore



Dr Bipin M Patel
Anaesthesiologist
Gujarat



Dr Anil J Nayek
Orthopaedic
Gujarat



Dr Mansukh R Kanani
Paediatrician
Gujarat



Dr Vinay Aggarwal
Physician
New Delhi



Dr Shashank Joshi
Endocrinologist
Mumbai



Dr Jayanta Panda
Medicine
Cuttack, Orissa



Dr D P Singh
Respiratory Medicine
Bhagalpur, Bihar



Dr Surya Kant
Respiratory Medicine
Lucknow



Dr G Narsimulu
Rheumatologist
Hyderabad



Dr Dilip Gode
Minimal Access Surgeon
Nagpur



Dr Apurba Ghosh
Paediatric Medicine
Kolkata



Dr. Tanu Raj Sirohi
Internal Medicine
Uttar Pradesh



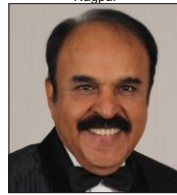
Dr V G Pradeep Kumar
Neurologist
Kozhikode, Kerala



Dr V Amuthan
Emeritus
Cardiologist
Tamil Nadu



Dr V Mohanan Nair
Public Health
Ananthapuri



Dr A Muruganathan
Medicine
Tamil Nadu



Dr Alok Pandit
Neurologist
Kolkata



Dr Deepraj Bhandarkar
Minimal Access Surgeon
Mumbai



Dr C Daniaia
Radiologist
Shillong, Meghalaya



Dr Anju Grewal
Anaesthesiologist
Punjab



Dr Vikram Kate
Gastro Surgeon
Puducherry



Dr Om Tantia
Bariatric Surgeon
Kolkata



Dr Bibhuti Saha
Tropical Medicine
Kolkata



Dr Dinesh Kumar
Microbiology
Patna



Dr Gautamananda Roy
Acute & Stroke Medicine
UK



Dr Colin Robertson
A&E Medicine
UK



Dr Shohael M Arafat
Medicine
Bangladesh



Dr Narimantas E Samalavicius
Robotic Surgeon
Lithuania



Prof Roman Jaeschke
Medicine
Canada



Dr Partha Sarathi Roy
Neurologist
UK



Dr Fazila TN Malik
Cardiologist
Dhaka Bangladesh



Dr. Ricardo Escalante
Colorectal Surgeon
Venezuelan



Dr SM Mostafa Zaman
Cardiologist
Dhaka, Bangladesh



Dr Serene Perkins
Chief Medical Officer
USA



DrWJW Nunoo - Mensah,
Colorectal Surgeon
London



Dr Aminur Rahman
Neurologist
Dhaka, Bangladesh



CELEBRATING LIFE SAVERS

Awards for those who've earned **RESPECT & LOVE** everyday of their life

Doctor's First

Governing Council & Jury of Eminent Doctors and Experts

Award Categories - 2023

Excellence in Medicine and Healthcare Award

INR 50 Lakhs

Emerging Young Leader in Medicine and Healthcare Award

INR 10 Lakhs

Exemplary Leadership in Rural Medicine and Healthcare Award

INR 10 Lakhs

Smt. Gayatri Jaipuria Women's Medicine and Healthcare Excellence Award

INR 10 Lakhs

Shri Ashwini Kumar Lifetime Achievement in Medicine and Healthcare Award*

INR 10 Lakhs

In association with

Ashok Jaipuria & Family

Cosmo First
Ahead Always

COSMO FILMS
Engineered to Enhance

COSMO FERRITES

COSMO SPECIALITY CHEMICALS
We Value Research

zi&ly

Knowledge Partner



*by nominations only.

✉ info@sjfmedicalawards.com

REGISTER NOW

🌐 www.sjfmedicalawards.com



Follow us on



For details & application, log on to website or scan the QR code



$\frac{20}{200}$	A	1
$\frac{20}{100}$	C L	2
$\frac{20}{70}$	E A R	3
$\frac{20}{50}$	V I S I O N	4
$\frac{20}{40}$	O F 25 YEARS	5
$\frac{20}{30}$	A N D T H E	6
$\frac{20}{25}$	J O U R N E Y	7
$\frac{20}{20}$	J U S T B E G A N	8

25 years is not just a milestone for us. It is a commitment to serve the people with advanced eye care, for time immemorial. Like always, we hope to clear visions as well as win the hearts of our patrons in future as well.

The largest eye care provider in Eastern India

DISHA EYE HOSPITALS

www.kolaz.in

Disha Helpline: 033 6636 0000 • appointments@dishaeye.org • www.dishaeye.org
 Barrackpore | Palta | Sheoraphuli | Newtown | Durgapur | Burdwan | Berhampur | Mourigram
 Howrah | Mecheda | Behala | Garlahat | Sinthi | Teghorla | Sillguri | Arambagh | Barasat

DISHA VISION CLINIC Raniganj | Sainthia | Suri | Ukhra



JOURNAL *Of the* INDIAN MEDICAL ASSOCIATION

Volume 121 (JIMA)
Number 08
August 2023
KOLKATA
ISSN 0019-5847

13 Editorial

Online Learning — Boon or Bane
— *Nandini Chatterjee*

15 Original Articles

22 Causality Assessment of Different Set of Variables using time Series Data Analysis — A Prospective Cohort Study — *Mamtarani Verma, J K Kosambiya, Divakar Balusamy, Sachin Mehta*

27 A Clinical Study of Dyselectrolytemia in Patients with Cirrhosis of Liver and its Association with Severity of Disease and Development of Complications — *Bikash Narayan Choudhury, Bhaskar Jyoti Baruah, Nikhil Gandhi, Mallika Bhattacharyya, Utpal Jyoti Deka, Jayanta Nanda, Pallab Medhi, Antara Sen, Preeti Sarma, Biswajit Kalita, Suranjana Jonak Hazarika, Juchidananda Bhuyan*

32 A Study on the Evaluation of Swallowing in Post-CVA Patients — *Anton Dev X, Gauranga Prosad Mondal, Somnath Saha*

37 Implementation of an Interactive Teaching Session using 'Snowball Technique' for Introducing 1st Professional MBBS Students to Clinical Correlation in Biochemistry — *Niket Verma, Kusum Singla, Bishambar Toora, Richa Dixit*

41 Association between Reverse Osmosis Water and Heart Diseases, Back pain and Joint Pain — *Sangita Patel, Rahul Khokhariya, Greenam Tarani, Jagruti Rathod, Deya Ghosh Chatterji, Jesal Patel*

46 Clinical Profile of Drug Induced Parkinsonism in Eastern India — *Praveen Kumar Yadav, Kumud Sahu*

49 Feasibility of WHO Recommended 3 visit fractional dose Intra-dermal Rabies Vaccine Regimen (IPC) and only Wound Infiltration of RIG in Rabies Post Exposure Prophylaxis to 1,84,955 Patients — Evidence from India — *Omesh Kumar Bharti*

54 Clinico-mycological Profile of Dermatophytoses in a Tertiary Care Hospital in Kolkata : A Cross Sectional Study — *Subhendu Sikdar, Suranjan Pal, Reena Ray (Ghosh), Anindita Ballav, Mitali Chatterjee*

Oral and Systemic Symptoms of COVID-19 among Patients Vaccinated and Unvaccinated against SARS-CoV-2 — *Pankaj Goel, Aman Kumar*

Contents



JOURNAL *Of the* INDIAN MEDICAL ASSOCIATION

Volume 121 (JIMA)
Number 08
August 2023
KOLKATA
ISSN 0019-5847

CONTENTS

- 58
Effectiveness of Nursing Care Bundles in Hospitalized Patients with Chronic Obstructive Pulmonary Disease (COPD) — *Smita Roba Tirkey, Rashmi P John, Anuj Kumar Pandey, Ajay Kumar Verma, Surya Kant*
- 64
Study of Cardiac Dysfunction in Non-alcoholic Cirrhotic Patients in a Tertiary Care Hospital — *Antarleena Ray, Manjari Saha, Tanmay Roy, Jayanti Ray, Udas Chandra Ghosh, Soumya Sarathi Mondal*
- 68
Summer Surge of Acute Appendicitis in Adults — *Abdul Razack G S, Harindranath HR, Uday C, Nashwath Kumar KH*
- 71
Post Mortem Renal Pathological Changes in Snake bite Patients and Association with Clinical Features — *Pinaki Mukhopadhyay, Joydeep Khan, Piyali Banerjee, Palas Bhattacharya, Manik Kataruka, Suparna Datta*
- 75
Evaluation of Organoleptic Properties and Compliance with Marketed Cough Syrups : A Cross Sectional Consumer Survey in Indian Patients — *Ketan K Mehta, Akil Contractor, Sanjiv Maniar, Atul Mashru, Manoj Kumar Singh, Atul Gogia, Rohan Mahajan, Harsh Mittal, Monil Yogesh Neena Gala, Mayank R Dhore, Snehal Muchhala, Gauri Dhanaki, Arti Sanghavi, Rahul Rathod, Bhavesh Kotak*
- 81 **Case Series**
- Gossypiboma : Word of Caution for an Unexpected Guest in the Abdomen — A Case Series and a Review of the Literature — *Afzal Anees, Yaqoob Hassan, Shereen Fatima, Surbhi Gupta*
- 86 **Case Report**
- Angina Ludovici — A Rare Case Report — *Ishwariya, Madhan Raja, Jude Vinoth*
- 88 **Commentary**
- Health Care Systems during Pandemic : Role of Government and Regulatory Authorities — *Ankur Gupta, Alok Pandey, Puja Bansal, Anureet Kaur, Pranava Prakash*
- 91 **Image in Medicine**
- *Bhoomi Angirish, Bhavin Jankharia*
- 92 **Letter to the Editor**

Online Learning — Boon or Bane

— Nandini Chatterjee

MD, FRCP (Glasgow), FICP
Professor, Department of Medicine,
IPGME&R and SSKM Hospital, Kolkata 700020 and
Hony Editor, JIMA

Necessity is the mother of invention. The COVID-19 pandemic has presented us with a priceless innovation which has **revolutionized** the ways of learning. The virtual platform has made the world a small place. During lockdowns, the students had no other option but to log in to their computers for online learning. All around the world, educational institutions are taking resort to online learning platforms to disseminate knowledge.

Attractive audiovisual presentation

Virtual teaching learning allows teachers to deliver lessons in innovative ways that make life easier for the students. Various tools, such as videos, animations, podcasts, voting pads and masterful use of artificial intelligence take teaching beyond traditional text books to a higher level of comprehension.

Wherever you are ...

Students are able to attend classes from any location on the globe. This has enabled teachers to reach out to an extensive network of learners, from one corner of the world to another. Moreover, online lectures can be recorded, archived and shared, to be accessed or downloaded in a convenient time. Videos of classes may be repeatedly watched at leisure, though the effectiveness of such an exercise is doubtful.

Less pinch on your pockets..

Online education is more cost effective as compared to physical learning. The expenses involved in transportation, student meals and study materials/books are curtailed. A vast expanse of information is stored online easily available at the click of a button, most often free of cost.

However, the immense potential of virtual learning is riddled with a number of **impediments**. There are also certain inherent disadvantages when compared to one to one traditional teaching.

Distraction

One of the biggest challenges of online learning is to maintain one's concentration and focus on the screen. This happens more frequently if the class is prolonged beyond twenty minutes. Distractions towards social media or other sites or even to

other leisurely activities if one is at home, is a practical problem. It is the onus of the teachers to keep their online classes concise, interesting and interactive to help students stay focused on the lesson.

Technology Hurdles

Internet connectivity is a central issue in virtual learning. A consistent internet connection is mandatory for a continuous, smooth viewing experience and also for sustaining interest. However, students in remote areas may suffer from poor connectivity or slow internet speeds.

The Human Touch

The main drawback of online classes are- minimal physical interactions between students and teachers. The students may feel isolated and less motivated. A peer group is very important for overall development of healthy competition and boosts the level of performance. Even the teachers feel the absence of direct interactions and receptivity of the students. Whether the students are comprehending the topic in question, what is their general mood or reaction to the class, is also very important for the teacher. This is impossible to gauge in an online class.

One **way out** is to maintain various forms of communication between the students, peers, and teachers like online messages, emails and video conferencing that will allow for face-to-face interaction and counteracts the feeling of isolation. Discussions and asking for timely feedback about classes help in addressing the expectations and requirements of the students.

Teacher needs to learn

One prerequisite for the teachers, is to have a basic understanding of digital forms of instruction. Also the necessary resources and tools to conduct online classes needs to be at their disposal. Training of teachers are important so that they are conversant with the technology and logistics of virtual teaching.

Also there might be hidden costs, like specific software, constant electricity, and high-bandwidth internet and other computer applications to support the online classes. The technology used may be difficult to grasp for the teacher and time-consuming.

Digital literacy and awareness among both the teacher and students regarding online communication etiquette and responsibilities is the need of the hour.

Is health at stake?

Another concern is the health hazard potential of **sedentary habits** and continuous screen gazing. Bad posture and its related problems, eye strain, headaches, obesity, anxiety and depression all are the consequences of prolonged in screen time in online learning.

To conclude, online learning has its share of advantages as well as pitfalls. It is capable of imparting an ocean of **knowledge** to anyone who cares to delve into it.

However, **true wisdom comes from experience**, specially in the medical terrains.

It is the "**Parampara**" that needs to be handed down from teacher to student in **face to face** discussions and dialogue.

The greatest teachers of medicine are the **patients**, and—

They need to be heard with empathy and compassion,

They need to be examined with our own hands and
They need to be reassured by us in person.

Thus virtual teaching should be **complementary to classical forms of instruction and guidance** but it **can not and should not** totally replace it unless we are faced with yet another catastrophe like the COVID Pandemic .

FURTHER READING

- 1 Davis, Nicole L, Mimi Gough, Lorraine L. Taylor — Online teaching: Advantages, obstacles and tools for getting it right. *Journal of Teaching in Travel & Tourism* 19.3 (2019): 256-263.
- 2 Mukhtar, Khadijah, *et al* — "Advantages, Limitations and Recommendations for online learning during COVID-19 pandemic era." *Pakistan journal of medical sciences* 36.COVID19-S4 (2020): S27.
- 3 Jayara, Stuty. "The advantages and disadvantages of online teaching in medical education." *Journal of Medical Evidence* 1.2 (2020): 144.

Original Article

Causality Assessment of Different Set of Variables using Time Series Data Analysis — A Prospective Cohort Study

Mamtarani Verma¹, J K Kosambiya², Divakar Balusamy³, Sachin Mehta⁴

Background : As per Targeted Intervention guidelines FSWs have to attend regular medical check-ups and counselling sessions quarterly a year. Go for RPR testing for syphilis and ICTC testing for HIV at least twice a year. STIs detection and treatment is done through Drop-In Centre (DIC) Clinics or Urban Health Centres.

Aims and Objectives : To assess Long-run causality between attendance at counselling sessions and regular medical check-ups. Causality between other pair of variables was also assessed.

Materials and Methods : Study design - Prospective cohort with retrospective comparison. Mix of primary and secondary data analysis was carried. Data was collected prospectively for 2013-14 and it was compared with programme data collected retrospectively for rest of the years. **Study setting -** Two different drop in centre clinics. Data entry and analysis was done using SPSS software and EViews software. Long-run causality assessment between attendance at counselling sessions and ICTC testing, attendance at counselling sessions and RPR testing etc. was done using time series analysis technique. First, Augmented Dickey - Fuller unit root test was done to check stationarity of data ie, whether data have equal mean and variance over a period of time), then Johansen co-integration technique was applied to check integration at same level of stationarity. Then final step of causality assessment was applied.

Results : Correlation between counselling sessions and regular medical check-ups among FSWs each year from 2009 to 2014 was statistically significant with p value <0.05. Correlation between counselling sessions and RPR testing for syphilis among them each year from 2009 to 2014 was statistically significant with p value <0.05.

Conclusion : Our study re-establishes the cause and effect relationship between regular medical check-ups and attendance at counselling sessions, RPR testing and ICTC testing, STD positivity, etc using different steps of time series analysis.

[J Indian Med Assoc 2023; 121(8): 15-21]

Key words : Causality assessment, Targeted Interventions, Time Series Data Analysis, Drop-In Centre (DIC) Clinics.

Targeted interventions among Female Sex Workers bring awareness about health implications of unsafe sex and HIV/AIDS issues. The TIs reduce sex workers vulnerability to STIs and HIV/AIDS, through promotion of STI services, condom use, Behaviour Change Communication (BCC) through peer and outreach, building enabling environment, ownership building in the community and linking prevention to HIV related care and providing continuum of services.¹

All TIs are rights based; they empower the high risk groups. NGOs/CBOs engaged in TIs are networked and linked to general healthcare facilities to ensure that HRGs access them without stigma or discrimination; they are also linked to community care

Department of Community Medicine, Government Medical College, Surat, Gujarat 395001

¹MD (PSM), Assistant Professor and Corresponding Author

²MD (PSM), Professor and Head

³MD (Pharmacology), Assistant Professor, Department of Pharmacology

⁴B Com, Assistant Professor, Department of Commerce, Government Arts and Commerce College, Ahwa, Gujarat 394710

Received on : 14/05/2022

Accepted on : 14/07/2023

Editor's Comment :

- Based on different steps of time series analysis cause and effect relationship between regular medical check-ups and attendance at counselling sessions, RPR testing and ICTC testing, STD positivity is observed.

centres, counselling and testing centres and ART centres. The prevention strategies are thus linked to care and treatment and empower the HRGs against stigma and discrimination¹.

As per Targeted Intervention guidelines FSWs have to attend regular medical check-ups and counselling sessions quarterly a year. Go for RPR testing for syphilis and ICTC testing for HIV at least twice a year. STIs detection and treatment is done through Drop-In Centre (DIC) Clinics or Urban Health Centres. Presumptive treatment is given to those who are detected with new STDs and coming late to Drop-In Centre clinic after 6 months instead of coming regularly.

The targeted intervention project is run by our institute since 1997 and above mentioned services (regular medical check-ups, counselling sessions, RPR testing, ICTC testing, presumptive treatment) are

provided to enrolled beneficiaries. Moreover, other services like Information Education Communication and free condom distribution and other social welfare programmes are also being done. Service provision under this project is maintained through various records.

In our study we want to prove the long term association and causality (one to one cause and effect relationship/ one event leading to happening of other event). If we want to decrease the *RPR positivity for syphilis* and *ICTC positivity for HIV and STDs other than syphilis and HIV* "regular medical check-ups" and "attendance at counselling sessions" is very important. We are trying to identify the interrelationships among these set of variables, whether RPR positivity is leading towards ICTC positivity? We want to see is there any long run association between regular medical check-ups and attendance at counselling sessions, association between STD positivity and RPR positivity, HIV testing and HIV positivity, RPR positivity and HIV positivity etc ?

We have to tried to prove this thing and similar other long term associations with the help of causality assessment using econometric technique, time series data analysis.

AIM AND OBJECTIVES

- To assess Long-run causality between attendance at counselling sessions and regular medical check-ups.
- To assess Long-run causality between attendance at counselling sessions and RPR testing.
- To assess Long-run causality between attendance at counselling sessions and ICTC testing.
- To assess Long-run causality between STD positivity and RPR positivity.
- To assess Long-run causality between STD positivity and HIV positivity.
- To assess Long-run causality between RPR positivity and HIV positivity.
- To assess Long-run causality between ICTC testing and RPR testing.
- To assess Long-run causality between ICTC positivity and ICTC testing.

MATERIALS AND METHODS

Study design-Prospective cohort with retrospective comparison. This was a Prospective cohort study with comparison to existing programme data. Mix of primary and secondary data analysis was carried out among 2193 Female Sex Workers (FSWs) over a period of 5 years from 2009 to 2014. Data was collected prospectively for 2013-14 and it was compared with programme data collected retrospectively from 2009

to 2012. The selected FSWs were beneficiaries of project implemented by Community Medicine Department, Government Medical College under State AIDS Control Society. Permission from State AIDS Control Society and Institutional Ethical Committee was obtained. This data was validated & a tracking sheet was generated from 2009 onwards for 5 years. Study setting- Study was done at two different DIC NGOs/clinics and project field area of Surat City. Study tool and process of data collection- Study tool was designed with the help of records maintained by two Drop in Centre clinics as per National AIDS Control Organization (NACO) guidelines. Thus pre-tested semi-structured questionnaire was used for data collection of both clinics. Tracking sheets are maintained at DIC clinics to track each FSW. Tracking sheet comprised information on socio-demographic profile (age, marital status, education, employment status, alcohol consumption), Regular Medical Check-ups (RMC) (quarter wise and year wise), STDs, syndrome wise STDs, Presumptive Treatment (PT), Rapid Plasma Reagin (RPR testing for syphilis and its positivity), Integrated Counselling and Testing (ICTC and its status) and attendance at counselling sessions (quarter wise and year wise) etc. Data collection for each variable was done for each year from 2009 onwards till 2014. Data entry from different records, data cleaning and merging different variables of both clinics was done with the help of excel software. Information was collected separately for both clinics and later compiled into a single sheet. Combined sheet was used for further analysis. Validation of data was done during field visits and at DIC clinics.

Causality assessment using time series data analysis- This study investigates the Long-run causality between attendance at Counselling sessions and Regular Medical Check-ups (RMCs), attendance at counselling sessions and RPR testing, attendance at counselling sessions and ICTC testing, STD positivity and RPR positivity, STD positivity and HIV positivity, RPR positivity and HIV positivity, ICTC testing and RPR testing, ICTC positivity and ICTC testing. It was done using time series analysis technique.

The following time series econometric techniques were applied, First, Augmented Dickey-Fuller (ADF) unit root test was done to check stationarity of data ie, whether data have equal mean and variance over a period of time, then Johansen co-integration technique was applied to check integration at same level of stationarity ie, whether variables move parallel or not²⁻⁴.

First step : The unit-root test was applied to identify whether a variable is stationary or not. The test also helps in finding the order of integration (at level or at

first difference) at which the variables become stationary. These types of tests are necessary to avoid spurious correlation between variables. Testing for the presence of unit root in the variables is the primary task before attempting cointegration. The augmented Dickey-Fuller unit root has been applied to test stationarity of data both at levels and at their first difference in our study. Variables which were tested for stationarity were Regular Medical Check-ups (RMCs), attendance at Counselling sessions, Presumptive Treatment (PT), STD Positivity (STD +ve), RPR Testing for syphilis (RPR), RPR Positivity (RPR +ve), ICTC Testing for HIV and ICTC positivity for HIV. Variables which are not integrated at order one, I(1) were not considered for further analysis.

Second step : Johansen Test for co-integration between different variables (counselling and regular Medical check-ups, counselling and RPR testing for syphilis, counselling and ICTC testing for HIV, RPR testing for syphilis and ICTC testing for HIV, STD positivity and RPR positivity for syphilis, STD positivity and ICTC positivity, RPR positivity for syphilis and ICTC positivity for HIV) were applied. At this step the pair of variables which showed the integrated relationship were identified and considered for next step of analysis.

Third step : The pairs of variables which showed the one Co-integrating relationship in second step of analysis were considered for final step of analysis ie, - Long run causality test based on Vector Error Correction Model (VECM). On the basis of this final step test uni-directional and bi-directional causality between pair of variables was established.

Statistical Analysis : Data entry and analysis was done using SPSS software version 22 and E Views software 7.0 version.

RESULTS

Results were obtained from analysis of 2193, Female Sex Workers obtaining services from the DIC and Municipal Corporation linked health centres. Mean age of FSWs was 32.48±4.67 years.

Correlation between counselling sessions and regular medical check-ups among FSWs each year from 2009 to 2014 was statistically significant with p value <0.05. Correlation between counselling sessions and RPR testing for syphilis among them each year from 2009 to 2014 was statistically significant with p value <0.05. Year wise correlation between counselling sessions and ICTC testing for HIV among them from 2009

to 2014 was also statistically significant with p value <0.05.

In Table 1, Augmented Dickey-Fuller unit root (ADF test) suggests that all series are integrated of order one, I(1) at their levels except for presumptive treatment (PT). It means all variables have equal mean and variance at the same level except presumptive treatment. For further analysis, series whose order of integration is the same are only retained for empirical analysis. Therefore, *Presumptive Treatment (PT) has not been considered for further analysis.*

Table 2 to Table 8 expresses the results of the co-integration test using “Johansen test for co-integration (Trace Test). Pair of variables which were tested for co-integration at this stage were counselling and regular Medical check-ups, counselling and RPR testing for syphilis, counselling and ICTC testing for HIV, RPR testing for syphilis and ICTC testing for HIV, STD positivity and RPR positivity for syphilis, STD positivity and ICTC positivity, RPR positivity for syphilis and ICTC positivity for HIV.

Null hypothesis - there is no co-integration/no co-integrated equation among the variables.

Alternate Hypothesis - there is co-integration among the variables.

If the value of The Trace-Statistic and maximum Eigen value test statistics comes out to be greater than the critical values 5% levels. We reject the null hypothesis of no co-integration among the variables.

Variables	At Level		At First Difference		Conclusion
	ADF	Sign	ADF	Sign.	
Regular Medical Check-ups (RMCs)	-1.28	0.61	-1.96	0.04	I (1)
Counselling	-1.28	0.61	-1.96	0.04	I (1)
Presumptive Treatment (PT)	-19.82	0.00	-3.34	0.03	I (0)*
STD Positive (STD +ve)	-0.72	0.48	-2.25	0.02	I (1)
RPR Testing for syphilis (RPR)	-1.31	0.60	-13.66	0.00	I (1)
RPR Positive (RPR +ve)	-4.54	0.00	-6.79	0.00	I (1)*
ICTC Testing	-1.23	0.64	-13.92	0.00	I (1)
ICTC positive	-4.42	0.00	-9.07	0.00	I (1)*

*R square value is high for this model

Johansen Test for Co-integration (Trace Test)				
Hypothesized No of CE(s)	Trace Statistic	0.05 Critical Value	Prob.	Conclusion
None (r = 0)	13.63	15.49	0.09	No Co integrating
At most 1 (r > 0)	0.18	3.84	0.67	Relationship
Johansen Test for Co-integration (Maximum Eigen value Test)				
Hypothesized No of CE(s)	Max-Eigen Statistic	0.05 Critical Value	Prob.	Conclusion
None (r = 0)	13.45	14.26	0.06	No Co-integrating
At most 1 (r + 1)	0.18	3.84	0.67	Relationship

Source : Estimated by researcher

We reject the null hypothesis of no co-integration only if both the trace-statistic and maximum Eigen values are greater than the critical values 5% levels and if both the trace-statistic/maximum Eigen values are lesser than the critical values 5% levels we accept the null hypothesis of no-difference.

From Tables 2-8 on the basis of trace-statistic values and maximum Eigen values test statistics results have been expressed.

There is no long run relationship between attendance for counselling sessions at DIC clinics and undergoing Regular Medical Check-ups (RMCs)(Table 2).

There is long run relationship between attendance for counselling sessions at DIC clinics and undergoing RPR testing for Syphilis (Table 3).

There is long run relationship between attendance for counselling sessions at DIC clinics and undergoing ICTC testing for HIV (Table 4).

There is long run relationship between RPR testing for Syphilis among FSWs and their ICTC testing for HIV (Table 5).

There is long run relationship between STD positivity observed among FSWs and their RPR positive status for Syphilis (Table 6).

There is long run relationship between STD positivity observed among FSWs and their ICTC positivity for HIV (Table 7).

There is long run relationship between RPR positivity for Syphilis among FSWs and their ICTC positivity for HIV (Table 8).

The results of the final step in establishing cause and effect relationship between tested variables (Table 9). If the error correction term for co-integrating equation between tested variables is negative and significant we can say there is unidirectional/bi-directional causal relationship between two variables. On the basis of this final step of testing unidirectional/bi-directional causal relationship is established between following variables and results are shown in Table 9.

The result showed that the error correction term for co-integrating equation with RPR testing as the dependent variable is negative and significant and error correction term for co-integrating equation with counselling as the dependent variable is non-negative and significant. It means that there is long run unidirectional causal relationship running from counselling to RPR testing.

Similarly, there is long run unidirectional causal relationship running from counselling to ICTC

Table 3 — Johansen Test for co-integration between counselling and RPR testing for syphilis				
Johansen Test for Co-integration (Trace Test)				
Hypothesized No of CE(s)	Trace Statistic	0.05 Critical Value	Prob.	Conclusion
None (r = 0)	46.14	15.49	0.00	One Co integrating
At most 1 (r > 0)	4.28	3.84	0.03	Relationship
Johansen Test for Co-integration (Maximum Eigen value Test)				
Hypothesized No of CE(s)	Max-Eigen Statistic	0.05 Critical Value	Prob.	Conclusion
None (r = 0)	41.85	14.26	0.00	One Co-integrating
At most 1 (r + 1)	4.28	3.84	0.03	Relationship
Source : Estimated by researcher				

Table 4 — Johansen Test for co-integration between counselling and ICTC testing for HIV				
Johansen Test for Co-integration (Trace Test)				
Hypothesized No of CE(s)	Trace Statistic	0.05 Critical Value	Prob.	Conclusion
None (r = 0)	46.60	15.49	0.00	One Co integrating
At most 1 (r > 0)	4.12	3.84	0.04	Relationship
Johansen Test for Co-integration (Maximum Eigen value Test)				
Hypothesized No of CE(s)	Max-Eigen Statistic	0.05 Critical Value	Prob.	Conclusion
None (r = 0)	42.47	14.26	0.00	One Co-integrating
At most 1 (r + 1)	4.12	3.84	0.04	Relationship
Source : Estimated by researcher				

Table 5 — Johansen Test for co-integration between RPR testing for syphilis and ICTC testing for HIV				
Johansen Test for Co-integration (Trace Test)				
Hypothesized No of CE(s)	Trace Statistic	0.05 Critical Value	Prob.	Conclusion
None (r = 0)	33.07	15.49	0.00	One Co integrating
At most 1 (r > 0)	9.85	3.84	0.00	Relationship
Johansen Test for Co-integration (Maximum Eigen value Test)				
Hypothesized No of CE(s)	Max-Eigen Statistic	0.05 Critical Value	Prob.	Conclusion
None (r = 0)	23.22	14.26	0.00	One Co-integrating
At most 1 (r + 1)	9.85	3.84	0.00	Relationship
Source : Estimated by researcher				

Table 6 — Johansen Test for co-integration between STD positivity and RPR positivity for Syphilis				
Johansen Test for Co-integration (Trace Test)				
Hypothesized No of CE(s)	Trace Statistic	0.05 Critical Value	Prob.	Conclusion
None (r = 0)	36.83	15.49	0.00	One Co integrating
At most 1 (r > 0)	13.07	3.84	0.03	Relationship
Johansen Test for Co-integration (Maximum Eigen value Test)				
Hypothesized No of CE(s)	Max-Eigen Statistic	0.05 Critical Value	Prob.	Conclusion
None (r = 0)	23.75	14.26	0.00	One Co-integrating
At most 1 (r + 1)	13.07	3.84	0.00	Relationship
Source : Estimated by researcher				

Table 7 — Johansen Test for co-integration between STD positivity and ICTC positivity

Johansen Test for Co-integration (Trace Test)				
Hypothesized No of CE(s)	Trace Statistic	0.05 Critical Value	Prob.	Conclusion
None (r = 0)	29.37	15.49	0.00	One Co integrating Relationship
At most 1 (r > 0)	2.36	3.84	0.12	
Johansen Test for Co-integration (Maximum Eigen value Test)				
Hypothesized No of CE(s)	Max-Eigen Statistic	0.05 Critical Value	Prob.	Conclusion
None (r = 0)	27.00	14.26	0.00	One Co-integrating Relationship
At most 1 (r + 1)	2.36	3.84	0.12	

Source : Estimated by researcher

Table 8 — Johansen Test for co-integration between RPR positivity for Syphilis and ICTC positivity for HIV

Johansen Test for Co-integration (Trace Test)				
Hypothesized No of CE(s)	Trace Statistic	0.05 Critical Value	Prob.	Conclusion
None (r = 0)	22.88	15.49	0.00	One Co integrating Relationship
At most 1 (r > 0)	3.72	3.84	0.05	
Johansen Test for Co-integration (Maximum Eigen value Test)				
Hypothesized No of CE(s)	Max-Eigen Statistic	0.05 Critical Value	Prob.	Conclusion
None (r = 0)	19.15	14.26	0.00	One Co-integrating Relationship
At most 1 (r + 1)	3.73	3.84	0.05	

Source : Estimated by researcher

testing, long run unidirectional causal relationship running from RPR testing to ICTC testing, long run bi-directional relationship running between STD positivity and RPR positivity, long run unidirectional causal relationship running from ICTC positivity to STD positivity (Table 9).

DISCUSSION

Importance of Regular Medical Check-ups, attendance at counselling sessions, RPR testing for syphilis and ICTC testing for HIV positivity is established in literature. Under targeted intervention

guidelines high risk group population enrolled under this project have to undergo these tests as per guidelines. We want to improve their testing as much as possible. Usually targets are set to achieve maximum coverage of beneficiaries for undergoing these screening tests so that we can identify health problems at the early stage through screening tests and minimize its further transmission and ensure timely completion of treatment.

Wairiki WMV, *et al* in a systematic review (2012) reported several successful behavioural interventions including interventions to reduce HIV/STI incidence and prevalence, change behaviour, promote condom use, improve condom availability, and increase sexual health knowledge⁵.

Meda N, *et al* in Senegal (1999) reported that regular screening of sex workers regardless of symptoms, regular screening and treatment with high quality diagnostics, where available, can be highly cost-effective, given sex worker's high rates of curable STIs. Clinical services for sex workers that include regular screening coupled with prevention messages have reported increase in condom use and reductions in STI and HIV prevalence. Regular screening and treatment services for sex workers in Senegal have been credited with contributing to low and stable HIV seroprevalence in Senegal (where sex work is legal)⁶.

Services like regular medical check-ups, presumptive treatment, detection of STDs and its syndromic management were provided at DIC clinic while RPR testing and ICTC testing were done at Municipal Corporation linked Health Centres. Peer educators and outreach workers accompanied the sex workers for testing at health centres and reports were collected by outreach workers on given date. If confirmed positive, sex workers were given treatment

Table 9 — Long run causality test based on VECM: Counselling and RPR testing counselling & ICTC testing, ICTC & RPR testing, STD positive & RPR positive, STD positive & ICTC positive.

Direction of Causality	Direction of Causality	ECM _{t-1}	T-Statistic	P-Value	Result
Causality between RPR testing and Counselling	Causality from Counselling to RPR testing	-2.48	-3.23	0.00	Uni directional Causality
	Causality from RPR testing to Counselling	1.02	2.53	0.02	
Causality between ICTC testing and counselling	Causality from counselling to ICTC testing	-2.60	-3.48	0.00	Uni directional Causality
	Causality from ICTC testing to counselling	1.02	2.53	0.02	
Causality between ICTC testing and RPR testing	Causality from RPR testing to ICTC testing	-20.76	-6.20	0.00	Uni directional Causality
	Causality from ICTC testing to RPR testing	5.27	1.14	0.27	
Causality between STD +ve and RPR +ve	Causality from STD +ve to RPR +ve	-0.06	-3.41	0.00	Bi- directional Causality
	Causality from RPR +ve to STD +ve	-1.82	-5.45	0.00	
Causality between ICTC +ve and STD +ve	Causality from STD +ve to ICTC +ve	0.72	3.05	0.00	Uni directional Causality
	Causality from ICTC +ve to STD +ve	-3.06	-8.55	0.00	

Source: Estimated by researcher

for STDs, syphilis or HIV at DIC clinic or were accompanied for appropriate treatment at skin clinic or ART centre.

In a systematic review done by Richard Steen (2012), it was concluded that periodic presumptive treatment can reduce prevalence of gonorrhoea, chlamydia and ulcerative STIs among sex workers populations where prevalence is high. Sustained STI reductions can be achieved when periodic presumptive treatment is implemented together with peer interventions and condom promotion. Additional benefits may include impact on STI and HIV transmission at population level⁷.

Presumptive treatment was given to Female Sex Workers who were newly enrolled with the TI project for getting services. FSWs who have not visited the DIC clinic within 6 months duration due to any reason were also provided with presumptive treatment. In a study done by Richard Steen (2003) Targeted presumptive periodic treatments attempt to bypass the need for treatment seeking, since STIs are frequently asymptomatic, with the aim to reduce incidence by reducing the pool of infected individuals in populations with high STI prevalence or incidence⁷.

Assessment of rate of adherence to targeted screening program for prevention of STIs was done using parameters like —

(1) How many FSWs have received regular medical check-ups (RMCs)?

(2) Presumptive treatment given to how many sex workers?

(3) How many have completed course of syndromic management for STDs?

(4) How many underwent RPR testing for syphilis?

(5) How many underwent ICTC testing for HIV?

Looking to the importance of on-going TIs each and every component is very much essential for effective running of the TI project. As per TI guidelines, FSWs have to undergo regular medical check-up quarterly each year. In this study, quarter wise proportion of Regular Medical Check-up testing was calculated. What we have done in our study is, we have tried to identify the long term causality among different set of variables, and how different variables are associated with each other. Whether RMC can be helpful in improving attendance at counselling sessions or vice versa or both run parallel (bi-directional causality)? We have tried to answer these types of questions using time series data analysis as this project is following the FSWs since long time and record maintenance is also being done. Data was collected retrospectively from 2009 to 2012 while for 2013-2014 it was collected prospectively.

Data of variables like Regular Medical Check-ups,

presumptive treatment, RPR testing (for syphilis), ICTC testing (for HIV), attendance at counselling sessions, STDs (sexually transmitted diseases), RPR positivity for syphilis and ICTC positivity for HIV was collected quarter wise each year from 2009 onwards till 2014.

Upon analysis, it was found that there was a *long run unidirectional causal relationship* running from *attendance at counselling sessions to RPR testing*. It emphasizes that those who were going for attending counselling sessions were also undergoing RPR testing for syphilis. If we want to improve RPR testing, sex workers must be motivated for attending counselling sessions also. There was a long run unidirectional causal relationship running from attendance at counselling sessions to ICTC testing. Similarly if we want to improve ICTC testing for HIV, sex workers must be motivated for attending counselling sessions. If we want to improve the RPR testing for syphilis and ICTC testing for HIV attendance at counselling sessions is very much important (*Each FSW has to attend counselling sessions at the DIC Clinic. There is a separate post of counsellor at the clinic. They have to attend minimum four counselling sessions each year (quarterly)*). Our study is proving this relationship as one-to-one cause and effect relationship. There are very few studies in medical literature which can prove these associations between different set of variables on the basis of cause and effect relationship. Over the WHO tool kit (2005) gives the importance of attendance at counselling sessions, Effective STD control in commercial sex is feasible and has been achieved in diverse settings. When STD interventions are implemented with the active involvement of sex workers themselves, chances for success are greater and additional benefits accrue—increased sexual health knowledge and skills acquired by sex workers lead to greater diffusion of prevention information through often hard-to-reach transmission networks. Rather than remaining passive recipients of services, sex workers can become “part of the solution”⁸. Causal relationship is also in agreement with correlation findings of our study results; correlation between attendance at counselling sessions and RPR testing for syphilis among FSWs was positive and statistically significant ($p < 0.05$) each year from 2009-10 to 2013-14. Correlation between attendance at counselling sessions and ICTC testing for HIV among FSWs was also positive and statistically significant ($p < 0.05$) each year from 2009-10 to 2013-14.

According to WHO, greater than or equal to 5% sex workers were infected with Syphilis in 18 of 31 countries in 2017⁹. As per policy of targeted intervention programme, each FSW has to undergo at least two

times RPR testing for syphilis each year. RPR testing is very much important for detection of active syphilis and its timely treatment.

Lucy M in a study in rural Uganda (2002) establishes that HIV transmission has been shown to be strongly associated with repeated Sexually Transmitted Infections (STIs) and sexual behaviour¹⁰.

As per the NACO guidelines, all core HRGs should be tested for HIV once every six months. These include interventions to change behaviour, promote the use of condoms, improve condom availability, introduce voluntary HIV counselling and testing, educate about sexual health and the effective management of STDs¹¹.

There was a *long run unidirectional causal relationship* running from *RPR testing to ICTC testing*; Those who are going for RPR testing are also availing ICTC testing for HIV. In TI project, also as per guidelines, sex workers should undergo RPR testing and ICTC testing simultaneously twice a year. Somehow those who are undergoing ICTC testing each and every one is not availing RPR testing these reasons need to be explored, according to TI programme both should be done simultaneously.

There was strong *long run bi-directional relationship* running between *STD positivity and RPR positivity*; means STD positivity and RPR positivity are interrelated to each other as evident in literature also, those having STDs are at risk of getting syphilis and vice versa.

There was *long run unidirectional causal relationship* running from *HIV positivity to STD positivity*; those who were HIV positive were at risk of getting other STDs this is also in correspondence with available literature. In Mahapatra B, *et al* (2013), Karnataka study among FSWs, HIV prevalence was positively and significantly related to Syphilis prevalence. For example, 21% of clients with Syphilis were also HIV positive, compared to 5% of clients who were not infected with Syphilis ($p < .0001$)¹².

CONCLUSION

Importance of targeted interventions in any TI project cannot be ignored. Screening tests like Regular Medical Check-ups (RMCs), attendance at counselling sessions, RPR testing for syphilis, ICTC testing for HIV, positivity for sexually transmitted diseases (STDs), RPR positivity for syphilis and ICTC positivity for HIV are interrelated to each other.

Our study re-establishes the cause and effect relationship between regular medical check-ups and attendance at counselling sessions, RPR testing and ICTC testing, STD positivity, RPR positivity and HIV positivity using different steps of time series analysis. Unidirectional and bi-directional causal relationship

between pair of variables has been identified. Results of time series data analysis are also in match with positive correlation observed between regular medical check-ups and counselling sessions, RPR testing and counselling sessions and ICTC testing and counselling sessions.

ACKNOWLEDGEMENT

We would like to acknowledge SACS for data access and approval. We are thankful to Institutional Ethical Committee for providing permission to carry out this study. We are thankful to staff of DIC clinics for providing necessary support and co-operation at the time of data collection. We are thankful to study participants.

REFERENCES

- 1 National AIDS Control Organization, Ministry of Health and Family Welfare, Government of India. Targeted Interventions for High Risk Groups. [Internet]. [cited 2018 Oct 7]. Available from: <http://www.naco.gov.in/tis-high-risk-groups>
- 2 Granger CWJ — Investigating causal relations by econometric models and cross-spectral methods. *Econometrica* 1969; **37(3)**: 424-38.
- 3 David A D, Wayne A F — Distribution of the estimators for autoregressive time series with a unit root. *Journal of the American Statistical Association* 1979; **74(366)**: 427-31.
- 4 Johansen Søren. Statistical analysis of cointegration vectors. *Journal of Economic Dynamics and Control*. 1988; **12(2-3)**: 231-54.
- 5 Windy MVW, Erika O, Rintaro M, Ai K, Narumi H, Kenji S — Behavioral interventions to reduce the transmission of HIV infection among sex workers and their clients in low and middle income countries. *Cochrane Database of Systematic Reviews* 2012; (2).
- 6 Nicolas M, Ibra N, M'Boup Souleymane — Low and stable HIV infection rates in Senegal: Natural course of the epidemic or evidence for success of prevention? *AIDA* 1999; **13(11)**: 1397-405.
- 7 Richard S, Gina D — Sexually transmitted infection control with sex workers: regular screening and presumptive treatment augment efforts to reduce risk and vulnerability. *Reproductive Health Matters* 2003; **11(22)**: 74-90.
- 8 Overs C — Sex workers/ : part of the solution: an analysis of HIV prevention programming to prevent HIV transmission during commercial sex in developing countries. WHO tool kit. 2005; 6.
- 9 World Health Organization. Sexually transmitted infections global health observatory data. Geneva. 2018 [Internet]. [cited 2018 Oct 8]. Available from: <http://www.who.int/gho/sti/en/>
- 10 Lucy MC, Anatoli K, Mary P — Independent effects of reported sexually transmitted infections and sexual behavior on HIV-1 prevalence among adult women, men, and teenagers in rural Uganda 2002; **29**: 174-80. *Journal of Acquired Immune Deficiency Syndromes A*. 2002; **29(2)**: 174-80.
- 11 National AIDS Control Organization, Ministry of Health and Family Welfare, Government of India. Targeted Interventions for High Risk Groups. [Internet]. [cited 2018 Oct 7]. Available from: <http://www.naco.gov.in/tis-high-risk-groups>
- 12 Bidhubhusan M, Catherine ML, Sanjay Kumar M — Factors associated with risky sexual practices among female sex workers in Karnataka, India. *PLoS ONE* 2013; **8(4)**.

Original Article

A Clinical Study of Dyselectrolytemia in Patients with Cirrhosis of Liver and its Association with Severity of Disease and Development of Complications

Bikash Narayan Choudhury¹, Bhaskar Jyoti Baruah², Nikhil Gandhi³, Mallika Bhattacharyya⁴, Utpal Jyoti Deka², Jayanta Nanda⁵, Pallab Medhi⁶, Antara Sen⁶, Preeti Sarma⁷, Biswajit Kalita⁷, Suranjana Jonak Hazarika⁸, Juchidananda Bhuyan⁹

Background : Dyselectrolytemia is a commonly observed entity in patients with cirrhosis particularly at advanced stage. This occurs due to primary disease per se, side effects of the drugs as well as dietary restrictions.

Aims and Objects : To study the prevalence of dyselectrolytemia in cirrhotics and its correlation with disease severity and development of complications like HE and HRS.

Materials and Methods : A prospective observational study was conducted on 150 patients with liver cirrhosis. Routine investigations including electrolytes were obtained at admission and compared with Child Pugh and Model for End Stage Liver Disease (MELD) score. Values of these electrolytes were also compared with patients who had complications like HE and HRS with the ones who did not.

Results : Out of 150 cirrhotics, dyselectrolytemia was observed in 113 patients (75.30%). The mean sodium, potassium and magnesium level in the study was 128.40 ± 2.50 meq/l, 3.29 ± 0.48 meq/l and 1.55 ± 0.28 meq/l respectively. The most common abnormality was hyponatremia (69.3%) followed by hypokalemia (54.7%), hypomagnesaemia (53.3%), hyperkalemia (2%) and hypernatremia (1.3%). Compared to Child- Pugh class- A (20%), dyselectrolytemia was considerably greater in class B (76.1%) and C (90.2%). Similarly, the mean electrolyte levels were higher in those with MELD score ≤ 14 as compared to patients with MELD score ≥ 21 . This decrease in the electrolyte values with the increasing Child-Turcotte-Pugh (CTP) and MELD score was statistically significant ($p < 0.0001$). A strong association was observed between the low magnesium level and HE (95% CI: - 1.30 - 12.14; OR 4.0; $p < 0.05$). On the other hand, hyponatremia was observed to be strongly associated with HRS [95% CI: - 3.18 - 60.89; OR 13.935; $p < 0.05$].

Conclusion : Dyselectrolytemia is highly prevalent in cirrhotic patients. Their values may reflect the level of liver dysfunction as evidenced by their strong correlation with disease severity scores such as Child-Pugh and MELD score and association with complications like HE and HRS.

[J Indian Med Assoc 2023; 121(8): 22-6]

Key words : Cirrhosis, Dyselectrolytemia, MELD Score, CTP Score, Hepatic Encephalopathy, Hepatorenal Syndrome.

Cirrhosis is a chronic entity characterized by diffuse hepatic fibrosis with replacement of normal liver parenchyma by regenerative nodules. It is one of the leading causes of global disease burden with 1.6% and 2.1% of disability-adjusted life years and years of life lost respectively and kills more than a million people annually¹. High mortality and morbidity in

Department of Gastroenterology, Guwahati Medical College and Hospital, Guwahati, Assam 781032

¹DM, Professor & Head

²DM, Assistant Professor

³DM, Senior Resident (2nd year) and Corresponding Author

⁴PhD, MD, Associate Professor

⁵DM, Senior Resident (2nd year)

⁶DM, Senior Resident (1st year)

⁷MD, Registrar

⁸MDS, Senior Research Fellow

⁹MSc, Junior Research Fellow

Received on : 16/11/2022

Accepted on : 08/12/2022

Editor's Comment :

- Dyselectrolytemia is common in cirrhosis particularly in the advanced stage.
- Hyponatremia is the most common electrolyte abnormality observed in cirrhotics.
- The mean value of sodium, potassium and magnesium decreases proportionately with the increasing CTP and MELD score.
- Their values (sodium, potassium and magnesium) can help us determine the severity of disease and predict the development of complications like HRS and HE.

cirrhotic patients is likely due to progressive liver failure and development of various complications such as tense ascites, variceal bleed, hepatic encephalopathy, hepato-renal syndrome and hepatocellular carcinoma. This leads to frequent hospitalizations and imposes a heavy financial and administrative load on both the patient and the healthcare system².

Electrolyte disturbances are commonly documented in cirrhotic patients particularly at advanced stages. This occurs due to disease process per se, side effects of medications like diuretics as well as dietary restrictions imposed on them. Studies have suggested that altered electrolyte values acts as independent predictors of disease severity and poor prognosis in cirrhotic patients. Out of various electrolyte disturbances in hospitalized patients, hyponatremia has been found to be the most common electrolyte abnormality accounting for 57%³. Hyponatremia has been linked to more severe sequelae, as difficult-to-control ascites, post-transplant problems like neurological abnormalities, renal failure, infectious complications and even mortality⁴.

In unstable cirrhotic individuals, the serum potassium level varies greatly, with hypokalemia (20%) being more common than hyperkalemia (12%)⁵. Important causes of hypokalemia include decreased intake, usage of loop diuretics, laxative administration causing prolonged diarrhea and infections.

Likewise, prevalence of magnesium deficiency is about 10% in hospitalized cirrhotic patients⁶. Higher magnesium intake has been linked to lower risk of liver disease-related mortality, notably in alcoholics and people with hepatic steatosis⁷. Also, studies have shown that serum magnesium levels tend to decrease significantly with severity of liver cirrhosis⁸.

Limited research work has been done to highlight electrolyte imbalance in cirrhotic patients particularly, potassium and magnesium. Hence, this study was performed to determine the prevalence of dyselectrolytemia in cirrhotic patients and to stratify it according to disease severity scores like Model for End Stage Liver Disease (MELD) and Child Pugh score. Further, this study also tried to find any association between these electrolyte abnormalities and complications of liver cirrhosis like Hepatic Encephalopathy (HE) and Hepatorenal Syndrome (HRS).

MATERIALS AND METHODS

This study was carried out as a cross-sectional, observational study conducted on 150 patients with diagnosis of liver cirrhosis, admitted in the Department of Gastroenterology at Gauhati Medical College and Hospital, Guwahati. The data collection period spanned from August, 2021 to September, 2022. The study included patients of age 18 years and above who had liver cirrhosis of any etiology and expressed their willingness to participate in the study. The study excluded individuals who had heart failure, chronic

kidney disease, malignancies, were taking medications like Selective Serotonin Reuptake Inhibitors (SSRI) and Tricyclic Antidepressants (TCA), anti-hypertensive drugs such as Angiotensin-Converting Enzyme (ACE) and Angiotensin Receptor Blockers (ARB) and supplements of sodium, potassium and calcium, and those who refused to give written consent. The study participants underwent a comprehensive evaluation consisting of meticulous history, thorough clinical examination and various investigations. These tests included a complete blood count, liver function test, renal function test, serum electrolytes (sodium, potassium and magnesium), ascitic fluid analysis, ultrasonography, upper gastrointestinal endoscopy and disease severity assessment using the Child Pugh Score and MELD score. Approval of the study was granted by our Institutional Ethical Committee. Each patient provided informed written consent. Serum electrolytes (sodium, potassium and magnesium) obtained at the time of admission was compared with Child Pugh Score and MELD scores. Values of these electrolytes at admission were also compared between patients who had complications like hepatic encephalopathy and hepatorenal syndrome with the ones who did not.

Data analysis was carried out using Statistical Package for Social Sciences (SPSS) version 20.0. Categorical variables were calculated as frequency and percentages. Comparative analysis using chi square test was done to look for association between individual electrolyte abnormality and complications like HE and HRS. The level of statistical significance was set at 0.05.

RESULTS

Out of 150 patients, majority were males (80.6%) with the mean age of study population being 49.2±11.8 years. Alcohol (70.7%) was the most common etiology of liver cirrhosis followed by NASH (9.3%), hepatitis B (8%) and cryptogenic (6.7%). 90% of our patients presented with ascites, 65.30% with jaundice, and 45.3% with gastrointestinal bleed. Spontaneous Bacterial Peritonitis (SBP), Hepatic Encephalopathy (HE) and Hepatorenal Syndrome (HRS) was present in 22.60%, 24% and 37.30% respectively.

Most of our patients belonged to Child Pugh B (56%) followed by Child Pugh C (34%). 80% of our patients had MELD score greater than 14. The mean CTP and MELD scores of the participants were 9.36±2.38 and 19.72±7.02 respectively as depicted in Table 1. The mean serum sodium, potassium and magnesium values in meq/l were 128.40±2.50,

Characteristics		No of patients (N=150)
Mean age (years)		49.2±11.8
Gender		
	Male	121 (80.6%)
	Female	29 (19.3%)
Etiology of cirrhosis		
	Alcohol	106 (70.7%)
	NASH	14 (9.3%)
	Hepatitis B	12 (8.0%)
	Hepatitis C	05 (3.3%)
	Autoimmune	03 (2.0%)
	Cryptogenic	10 (6.7%)
Child-Pugh score		
	A (%)	15 (10.0%)
	B (%)	84 (56.0%)
	C (%)	51 (34.0%)
MELD score		
	≤14 (%)	30 (20.0%)
	15–21 (%)	68 (45.3%)
	>21 (%)	52 (34.7%)
Mean CTP score		09.36±2.38
Mean MELD score		19.72±7.02
Presenting features		
	Ascites	135 (90.0%)
	Jaundice	98 (65.3%)
	GI bleed	68 (45.3%)
	SBP	34 (22.6%)
	HE	36 (24.0%)
	HRS	56 (37.3%)

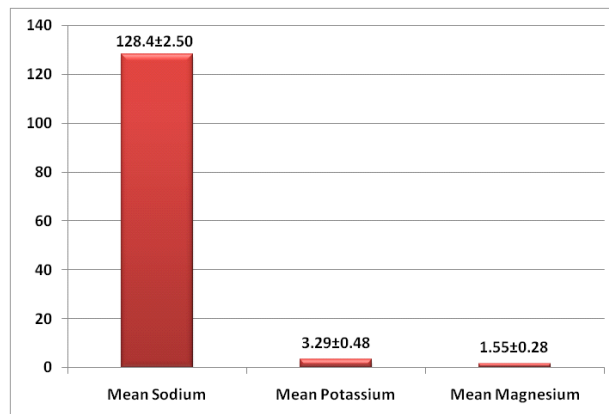


Fig 1 — Mean electrolyte levels in the study population

3.29±0.48 and 1.55±0.28 respectively (Fig 1).

Dyselectrolytemia was observed in 113 (75.3%)

patients of our study group. The most common electrolyte abnormality was hyponatremia (69.3%) followed by hypokalemia (54.67%), hypomagnesemia (53.3%), hyperkalemia (2%) and hypernatremia (1.3%) as shown in Fig 2.

When stratified according to CTP scores, 46 patients out of 51 (90.2%) in CTP- C class had dyselectrolytemia whereas 76.1% of patients in CTP-B class and 20% of patients (3 out of 15) in CTP-A class had electrolyte imbalance. Patients belonging to CTP-A group had the highest mean serum sodium level (133.8±1.70 meq/l) while those in CTP-C group had the lowest mean sodium levels (121.85±2.40 meq/l). The mean serum potassium level was 3.78±0.46 meq/l in CTP-A group and 2.82±0.51 meq/l in patients belonging to CTP-C group. Likewise, the mean serum magnesium level was highest in CTP-A (1.9±0.35 meq/l) and lowest in CTP-C (1.25 ±0.27 meq/l). This decrease in electrolyte values with the increasing CTP score was statistically significant for all the electrolytes (P< 0.0001) as shown in Table 2.

Similarly, electrolyte disturbance was

seen in 92.3%, 86.7% and 20% in patients belonging to MELD score group of >21, 15-21 and ≤14 respectively. The mean serum sodium, potassium and magnesium level was highest in those with MELD score ≤14 and the least in patients with MELD score ≥21. This decrease in electrolyte values with the increasing MELD score was statistically significant for all the electrolytes (P<0.0001) as shown in Table 3.

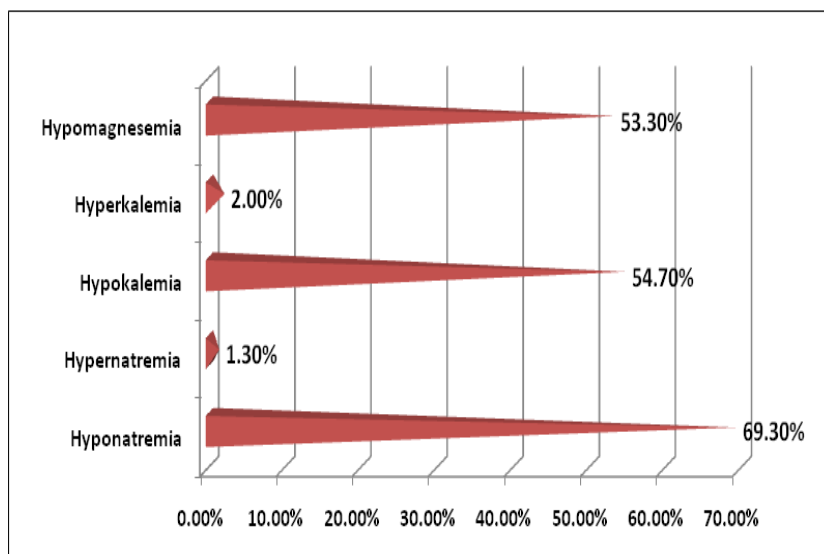


Fig 2 — Different electrolyte abnormalities in the study population

Electrolytes observed	CTP-A	CTP-B	CTP-C	p value
Mean sodium value	133.8±1.70	129.57±3.42	121.85±2.40	
Mean potassium value	3.78±0.46	3.28±0.47	2.82±0.51	<0.0001***
Mean magnesium value	1.90±0.35	1.51±0.24	1.25±0.27	

Electrolytes observed	MELD ≤14	MELD 15-21	MELD ≥21	p value
Mean sodium value	132.87±1.80	128.80±3.50	123.55±2.62	
Mean potassium value	3.86±0.50	3.14±0.41	2.88±0.53	<0.0001***
Mean magnesium value	1.88±0.31	1.58±0.27	1.20±0.28	

Out of 36 patients who had hepatic encephalopathy at admission, hypomagnesemia was observed in 32 patients (95% CI: - 1.30 - 12.14; OR 4.0; $p < 0.05$) indicating a strong association between the two (Table 4). However, for hyponatremia [95% CI: - 0.78 to 4.53] and hypokalemia [95% CI: - 0.48 to 2.54] no statistical significance was seen ($p > 0.05$). Hyperkalemia and hypernatremia was not seen in patients who had HE.

On the other hand, hyponatremia was observed in 54 out of 56 the patients who had HRS [95% CI: - 3.18 - 60.89; OR 13.935; $p < 0.05$] and statistical analysis indicated a strong association between the two (Table 5). For hypokalemia [95% CI: - 0.29 - 1.12] and hypomagnesemia [95% CI: - 0.33 - 1.28] no statistical significance was determined. Hyperkalemia and hypernatremia was not seen in patients who had HRS.

DISCUSSION

In our study group, the most common etiology of cirrhosis was alcohol (70.6%) with ascites being the most common clinical presentation (90%). This is similar to findings observed by Singh, *et al*⁸ and Almani, *et al*¹⁰.

In the present study, prevalence of dyselectrolytemia was 75.3% such that hyponatremia was observed in 69.3%, hypokalemia in 54.67%, hypomagnesemia in 53.3%, hyperkalemia in 2% and hypernatremia in 1.3%. The prevalence of hyponatremia in previous studies performed by Singh, *et al*⁸, Angeli, *et al*¹¹ and Borroni, *et al*¹² was observed to be 47%, 21.6% and 14.9% respectively whereas the prevalence of hypokalemia in the prior studies carried out by Devrajani, *et al*¹³ Kashyap, *et al*¹⁴ and

Murmtaz, *et al*¹⁵ was found to be 33%, 15%, and 6.4% respectively.

The mean serum sodium, potassium and magnesium values in meq/l were 128.40 ± 2.50 , 3.29 ± 0.48 and 1.55 ± 0.28 respectively which were lower than the normal accepted range. Most common reason for hyponatremia in Cirrhosis is mainly due to impairment of solute free water excretion which is due to the increased Anti Diuretic Hormone (ADH) secretion and decreased effective arterial volume¹⁶.

Magnesium deficiency in Cirrhosis is a burning research topic with few available literatures. It may result from low nutrient uptake, decreased absorption due to intestinal mucosal edema secondary to portal hypertension, greater urinary secretion due to diuretics, low serum albumin concentration, and/ or hormone inactivation¹⁷.

The mean serum sodium, potassium and magnesium levels were highest among the patients in CTP-A group (133.8 ± 1.70 , 3.78 ± 0.46 , 1.9 ± 0.35 meq/l) and lowest in CTP-C group (121.85 ± 2.40 , 2.82 ± 0.51 , 1.25 ± 0.27 meq/l) and this decrease in the electrolyte values with the increasing CTP score was statistically significant ($p < 0.0001$). The results were in accordance with the studies done by Quereshi, *et al*¹⁸ and Safarikish B, *et al*¹⁹.

The declining values of serum electrolytes with increasing MELD score was also observed in our study. The mean serum sodium, potassium and magnesium levels were higher (132.87 ± 1.80 , 3.86 ± 0.50 , 1.88 ± 0.31 meq/l) in those with MELD score ≤ 14 as compared to patients with MELD score ≥ 21 . This decrease in the electrolyte values with the increasing MELD score was statistically significant ($p < 0.0001$). Kim, *et al*²⁰ identified a significant interaction between the serum sodium concentration and the MELD score, demonstrating that the serum sodium concentration was greater in patients with a lower MELD score. In study by Safarikish, *et al*¹⁹, it was observed that patients with hypomagnesemia had higher MELD score (16.5 ± 5.8) than those with normal magnesium values (14.3 ± 5.4).

Our study found significant association between hypomagnesemia and HE (95% CI: - 1.30 - 12.14; OR 4.0; $p < 0.05$). This is in accordance to the work done by Lopes, *et al*²¹ who highlighted that lower levels of serum magnesium were associated with a greater risk of HE in both liver graft donors and recipients during the first few days after surgery. According to Nangliya, *et al*²², serum magnesium levels significantly decreased as liver cirrhosis progressed, which is consistent with our findings.

Table 4 — Correlation between different electrolyte abnormalities and hepatic encephalopathy (HE)

Electrolyte abnormality	HE+ (N=36)	Chi-square	OR (95% CI)	P value
Hyponatremia	28 (19%)	1.532	1.892 (0.78 to 4.53)	0.2158
Hypokalemia	26 (17%)	0.00063	1.105 (0.48 to 2.54)	0.9799
Hypomagnesemia	32 (21%)	5.645	4.0 (1.30 to 12.14)	0.0175

Table 5 — Correlation between different electrolyte abnormalities and hepatorenal syndrome (HRS)

Electrolyte abnormality	HRS+ (N=56)	Chi-square	OR (95% CI)	P value
Hyponatremia	54 (36%)	16.891	13.935 (3.18-60.89)	<0.0001
Hypokalemia	27 (18%)	2.080	0.5779 (0.29-1.12)	0.1493
Hypomagnesemia	32 (21%)	1.114	0.6600 (0.33-1.28)	0.2911

Hyponatremia was observed to be significantly associated with Hepatorenal Syndrome (HRS), [95% CI: - 3.18 - 60.89; OR 13.935; $p < 0.05$]. This is in accordance to the previous study conducted by; Shaikh, *et al*³ who found that the frequency of hepato renal syndrome was strongly associated with decreased serum sodium concentration, suggesting more severe circulatory dysfunction in cirrhotics with hyponatremia than those without it.

In our study, hypokalemia was not found to be significantly associated with both HE and HRS which is in contrast to the findings observed by Kaplan, *et al*⁴ where, hypokalemia was also stated to be an important prognostic factor in cirrhotic patients. Both hypernatremia and hyperkalemia was not seen in patients who had HE or HRS. Our study had few limitations such that potential causes of dyselectrolytemia (diuretics, infections or hypovolemia) were not assessed, sample size was small and follow up of the cases couldn't be done. Nevertheless, our study clearly highlights that electrolyte abnormalities are quite common in patients with cirrhosis of liver and warrants special attention during the treatment process. Their values can help us determine the severity of disease and predict the development of complications as evidenced by their significant association with complications like HE and HRS.

Credit authorship contribution statement : All authors contributed equally in carrying out the study, writing and drafting of the manuscript.

Conflicts of interest : None

Source of funding : None

REFERENCES

- Asrani S K — Burden of liver diseases in the world. *Journal of Hepatology* 2019; **70**: 151-71.
- Ge PS, Runyon BA — Treatment of patients with cirrhosis. *N Engl J Med* 2016; **375**: 767-77.
- Hassan ZBA, Kadum J — Electrolytes disturbance in liver cirrhosis Graduation thesis, Al-Nahrain College of Medicine, Iraq 2019 Available from: <https://www.colmed-alnahrain.edu.iq/upload/res/884.pdf>.
- Gaglio P — Hyponatremia in Cirrhosis and End-Stage Liver Disease: Treatment with the Vasopressin V2-Receptor Antagonist Tolvaptan. *Dig Dis Sci* 2012; **57(11)**: 2774-85.
- Artz SA, Paes IC, Faloon WW — Hypokalemia induced hepatic coma in cirrhosis: Occurrence despite neomycin therapy. *Gastroenterology* 1966; **51**: 1046-53.
- Swaminathan R — Magnesium metabolism and its disorders. *Clin Biochem Rev* 2003; **24**: 47-66. PMID 18568054.
- Wu L — Magnesium intake and mortality due to liver diseases: Results from the third national health and examination survey cohort. *Sci Rep* 2017; **7**:17913.
- Veena G, James R — Prevalence of hypomagnesemia in cirrhosis of liver and its association with severity of the disease. *Asian J Pharm Clin Res* ; **15(8)**: 92-5.
- Singh Y — Study of electrolyte disturbance in chronic liver disease patients attending a hospital in Kumaon region. *Journal of Family Medicine and Primary Care* 2022; **11(8)**: 4479-82.
- Almani SA — Cirrhosis of liver: Etiological factors, complications and prognosis. *JLUMHS* 2008; **2**: 61-6.
- Angeli P — Hyponatremia in cirrhosis: Results of a patient population survey *Hepatology* 2006; **44**: 1535-1542.
- Borroni G — Clinical relevance of hyponatremia for the hospital outcome of cirrhotic patients. *Dig Liver Dis* 2000; **32**: 605-10.
- Devrajani BR — Precipitating factors of hepatic encephalopathy at a tertiary care hospital Jamshoro, Hyderabad JPMA. *J Pak Med Assoc* 2009; **59**: 683.
- Kashyap C, Borkotoki S, Dutta RK — Study of serum sodium and potassium level in patients with alcoholic liver disease attending Jorhat Medical College Hospital—A hospital-based study. *Int J Health Sci Res* 2016; **6**: 113-6.
- Mumtaz K — Precipitating factors and the outcome of hepatic encephalopathy in liver cirrhosis. *J Coll Physicians Surg Pak* 2010; **20**: 514-8.
- Kim J H, Lee J S, Lee S H — The Association between the Serum Sodium Level and the Severity of Complications in Liver Cirrhosis. *Korean J Intern Med* 2009; **24(2)**: 106-112.
- Liu M, Yang H, Mao Y — Magnesium and liver disease. *Ann Transl Med* 2019; **7(20)**: 578.
- Qureshi Muhammad. Correlation of Hyponatremia with Hepatic Encephalopathy and Severity of Liver Disease. *Journal of the College of Physicians and Surgeons Pakistan*; **24**: 135-137.
- Safarikish B — The Relationship Between Plasma Magnesium Concentration and Hepatic Encephalopathy in Liver Cirrhosis Patients: A Preliminary Result of a Referral Center in Iran. *Middle East J Rehabil Health Stud* 2022; **9(2)**: e122978.
- Kim WR — Hyponatremia and mortality among patients on the liver-transplant waiting list. *N Engl J Med* 2008; **359**: 1018-26.
- Lopes PJ — Correlation between serum magnesium levels and hepatic encephalopathy in immediate post liver transplantation period. *Magnes Res* 2013; **45(3)**: 1122-5.
- Nangliya V — Study of trace elements in liver cirrhosis patients and their role in prognosis of disease. *Biol Trace Elem Res* 2015; **165(1)**: 35-40.
- Shaikh S — Frequency of hyponatraemia and its influence on liver cirrhosis-related complications. *J Pak Med Assoc* 2010; **60(2)**: 116-20.
- Kaplan M — Prognostic Utility of Hypokalemia in Cirrhotic Patients. *Acta Gastro-Enterologica Belgica* 2018: 398-403.

Original Article

A Study on the Evaluation of Swallowing in Post-CVA Patients

Anton Dev X¹, Gauranga Prosad Mondal², Somnath Saha³

Aims and Objectives : (1) To find the incidence of Swallowing difficulty in Cerebrovascular Accident (CVA) patients. (2) Evaluation of degree of dysphagia in post stroke patients by the use of Functional Endoscopic Evaluation of Swallowing (FEES). (3) Assess for any possible relationship between swallowing defects and region of brain involved.

Materials and Methods : The present study is an observational study done over a 1 year period in a Tertiary Care set-up. Mann Assessment of Swallowing Ability (MASA) test and Functional Endoscopic Evaluation of Swallowing (FEES) were used to assess swallowing function. The findings from FEES were graded using the Penetration – Aspiration Scale (PAS). We had used radiologic methods to determine the site of lesion and Arterial territory involved.

Results : In the present study, MASA scores were normal in 50% and Dysphagia was Mild in 16.0%, moderate in 6.0% and Severe in 28.0%. Based on the PAS interpretation, no entry was present in 20%. Aspiration was seen in 24% and penetration was seen in 56%. Patient age and MASA grade had a significant association. The MASA values and PAS scores were found to be inversely correlated. Swallowing abnormalities were detected in Stroke of the following regions : Basal Ganglia, Thalamus, Pons & Lateral Medulla. MCA territory infarcts were commonly found to cause Dysphagia.

Conclusion : In the present study, 50 %of the total stroke patients had dysphagia, as determined by the MASA test. FEES detected Dysphagia in 80 % of the patients. A strong inverse correlation was present between the MASA test score and the PAS score, with correlation coefficient as -0.935. Stroke of certain specific brain regions and arterial territories were more commonly found to cause Swallowing difficulties.

[J Indian Med Assoc 2023; 121(8): 27-31]

Key words : Post-CVA, Cerebrovascular Accident, Swallowing Dysfunction, Dysphagia, MASA test, FEES, Arterial Territory.

Global occurrence of stroke is high with numbers of upto 15 million¹ of which more than half will have swallowing problems, out of which half will be symptomatic². The cases of Stroke account for a significant volume of Disability and Morbidity, the world over³. A large number of stroke patients recover normal swallow spontaneously. Despite this, a significant number (upto half) of the patients may have dysphagia at 6 months^{4,5}. Persistent dysphagia has been found to independently predict overall poor outcome⁶.

Dysphagia leading to aspiration has also been seen to have significance for occurrence of pneumonia following stroke⁷. Confirmed aspiration confers a higher risk^{3,8}.

For Hospitalised Stroke patients, the relative risk of death due to pneumonia : 5.7⁷. Early studies had included referral patients with diagnosed Dysphagia. This inadvertently caused a false rise in the detected incidence of Aspiration^{9,10}. There have been no current studies based on an unselected population^{5,11}.

Department of Otorhinolaryngology, Calcutta National Medical College & Hospital, Kolkata 700014

¹MS, Senior Resident, At present : Senior Resident, Department of Otorhinolaryngology, M R Bangur Hospital, Kolkata 700033 and Corresponding Author

²MD (General Medicine), DM (Neurology), DCH, Professor and Head, Department of Neurology

³MS (ENT), Professor and Head

Received on : 02/04/2022

Accepted on : 25/06/2023

Editor's Comment :

- Swallowing difficulty is a common occurrence in Stroke patients and so a proper assessment tool to detect it, is of paramount importance.
- A greater proportion of stroke patients were found to have swallowing pathology when assessed with the Assessment tool Functional Endoscopic Evaluation of Swallowing (FEES) and scored using the Penetration-Aspiration Scale (PAS), as compared to Clinical methods (MASA test). The PAS scores and MASA test values were inversely correlated.
- Stroke of certain specific brain regions and arterial territories were seen to cause Swallowing disturbances more commonly.

In acute stroke, Dysphagia has been found to have a prevalence of about 28 to 65%^{5,11-13}. Dysphagia is found to improve significantly in the early days after the occurrence of Stroke^{2,5}. A certain small percentage of patients will have longer duration of Dysphagia⁴.

An observed finding is that, in patients whom the swallow does not recover in the first 10 days, recovery requires a longer period of upto 2-3 months¹⁴. Silent aspiration has been found to occur in about 40% of Dysphagic patients¹⁵. Patients with aspiration have associated Abnormal pharyngeal sensation with Silent aspiration seen to occur in 8%¹⁶.

The Presence of Swallowing difficulty following stroke depends on the following factors:

- (1) Site of Involvement (eg: Corticobasilarfibres,

Medulla → Lateral Medullary Syndrome, Brain Stem → Pons)

- (2) Size of lesion (Pressure effect)
- (3) Sensorium of Patient
- (4) Bilaterality (eg, Corticobulbar tract)

Specific Sites known to cause swallowing deficits in relation to their Arterial supply :

(1) Lacunar Infarcts - Mainly Bilateral MCA territory¹⁷

(2) Area surrounding Area 43 and 44 (Frontoparietal operculum) – Striate branches of MCA¹⁷

(3) Cerebellum and Lateral Medulla (Lateral Medullary Syndrome) – PICA^{18,19}

(4) Pyramids involvement²⁰

(5) Pons²¹ and Medulla¹⁹ – Perforating branches of Basilar Artery

(6) Corpus Striatum supplied by Recurrent Artery of Heubner²²

(7) Thalamus²³

Tests for Clinical Assessment of Dysphagia :

(1) 3-oz Water swallow test²⁴

(2) The Standardized Swallowing Assessment²⁵

(3) Acute Stroke Dysphagia Screen²⁶

(4) Yale Swallow Protocol²⁷

(5) Mann's Assessment of Swallowing Ability (MASA)²⁸

In the present study, we had used the MASA test for Clinical evaluation of Swallowing.

Mann's Assessment of Swallowing Ability (MASA) test²⁸ :

The MASA test employs a set of swallowing tasks, using which Trained healthcare professionals rate the patient's performance. The MASA defines risk of Dysphagia and Aspiration. It also provides a severity scale²⁸.

The newer technology in Swallowing assessment includes Videofluoroscopy (VFSS) and The Functional Endoscopic Evaluation of Swallowing (FEES). These modalities have surpassed the earlier tools.

In the present study, Dynamic assessment of Swallowing is done using FEES²⁹. Grading of the observed findings , was done using the Penetration - Aspiration Scale (PAS)³⁰.

Fiberoptic Endoscopic Evaluation of Swallowing (FEES)²⁹:

- Delayed swallow initiation and presence of pharyngeal residue are better evaluated using this modality.

- Swallowing of different food consistencies is evaluated.

In FEES, the following features are observed :

- Transition duration
- Evidence of penetration and aspiration

- Number of swallows to clear the bolus
- Extent of airway closure

MATERIALS AND METHODS

Study design :

Observational study at a Tertiary Centre in West Bengal.

Study population :

Patients admitted in the Neurology IPD.

Sample design :

Inclusion criteria —

All patients of Cerebrovascular Accidents (CVA) including :

- Patients with Ischemic stroke.
- Patients with Hemorrhagic stroke.
- Only Medically Stable patients

Exclusion criteria —

- (1) Recurrent stroke.
- (2) Hemodynamically unstable patients.
- (3) Unconscious patients.
- (4) Patient having Dysphagia from before the stroke due to any other cause.
- (5) Subarachnoid haemorrhage.
- (6) Patients with Severe agitation.
- (7) Severe movement disorders (Dyskinesia)
- (8) Severe bleeding disorders and/or Recent severe epistaxis (nosebleed).
- (9) History of recent trauma to the nasal cavity or surrounding tissue and structures secondary to surgery or injury.
- (10) Bilateral obstruction of the nasal passages.
- (11) Patients with any other progressive neurological condition such as parkinsonism, schizophrenia.
- (12) Mentally impaired patients who cannot provide a proper informed consent & who would be uncooperative for examination.
- (13) Patients of Childhood Stroke Syndromes with various underlying genetic defects are excluded as they may skew the inferences, as a result of the differences in their baseline Physiology.

Sample size : 50 cases

Study Tools :

- (1) History including any past history of Cerebrovascular Accidents.
- (2) Basic Haematology including Complete Blood Count, Platelets, BT/CT, Urea, Creatinine, Serology.
- (3) Mann Assessment of Swallowing Ability (MASA) test, used to assess swallow.
- (4) Fiberoptic Endoscopic Evaluation of Swallowing (FEES), was performed using the protocol defined by Susan Langmore³¹.
- (5) We have used Radiologic imaging methods coupled with expert radiologist opinion to ascertain the

region of brain involved and the arterial territories affected.

RESULTS

Comparison of Age and gender of the study population.

Mean ages:

- Males : 70.0±7.7 years
- Females : 58.1±11.3 years.
- No significant difference was detected , between the means (Tables 1&2).

Table 3 shows us that the MASA scores were normal in half of the patients. Dysphagia was Mild in 16.0%, moderate in 6.0% and Severe in 28.0% according to MASA test (Fig 2).

The Table 4 categorises the frequencies in the various grades of MASA score in our study.

The Table 5 categorises the PAS interpretations. Aspiration was seen in 24%, No entry was present in 20% and penetration was seen in 56%.

From Table 6, we infer the association that, as the age increased, the Dysphagia severity as determined by MASA grade was also increasing (Statistically significant).

Table 7, Correlates the MASA and PAS scores. The two variables were highly correlated. The correlation coefficient was -- 0.935. That means, when MASA score is increasing, the PAS value is decreasing. The decrease was 87.4%.

Table 8 states the relationship between the Dysphagia severity (determined from PAS score) and Lesion side. We find no significant relationship (P>0.05) (Table 9).

DISCUSSION

In the present study we have evaluated a total of 50 Post -CVA patients in the domain of swallowing. Evaluation was performed using both a clinical test (MASA) and an endoscopic study (FEES).

(1) In the study done by Chojin, *et al* an abnormal MASA score was seen in 71.9% patients. Out of them, maximum patients were in the severe category, followed by the mild and moderate categories³². In the present study, using MASA test, we have observed a lesser incidence of Dysphagia (50%). But upon categorization of MASA values, maximum patients were in the severe group, followed by the mild and then moderate groups, which is in accordance with the earlier study by Chojin, *et al*.

(2) Logeman JA, *et al* observed that the Clinical tests alone tend to underestimate the incidence of Dysphagia³³. In the present study, Fiberoptic endoscopy (FEES) revealed that 80% of the patients had swallowing dysfunction while in the MASA test, only 50% of the patients were found

Age group (years)	Males		Females		Total	
	No	%	No	%	No	%
30-39	0	0.0	2	4.0	2	4.0
40-49	1	2.0	4	8.0	5	10.0
50-59	7	14.0	8	16.0	15	30.0
60-69	9	18.0	10	20.0	19	38.0
70-79	6	12.0	3	6.0	9	18.0
Total	23	46.0	27	54.0	50	100.0
Mean ±SD	70.0±7.7		58.1±11.3		Mean=59.8±9.9	
Range=38-79 years						
Significance "t" = 1.393, df = 48, P = 0.170						

Insult classification	Frequency	%
Hemorrhage	16	32.0
Infarct	34	68.0
Total	50	100.0

Category	Score	Frequency	%
Normal	170-200	25	50.0
Mild	149-169	8	16.0
Moderate	141-148	3	6.0
Severe	≤140	14	28.0
Total		50	100.0

MASA grade	Frequency	%
Mild	9	27.3
Moderate	16	48.5
Severe	8	24.2
Total	33	100.0

PAS Score	PAS interpretation	Frequency	Percentage
1	No entry	10	20.0
2,3,4,5	Penetration	28	56.0
6,7,8	Aspiration	12	24
Total		50	100.0

Age group	Nil	Mild	Moderate	Severe	Total	Results
< 50	0	3	4	0	7	$\chi^2=25.156$ df=9 P=0.002
50-59	9	3	2	1	15	
60-69	7	3	7	2	19	
70-79	1	0	3	5	9	
Total	17	9	16	8	50	

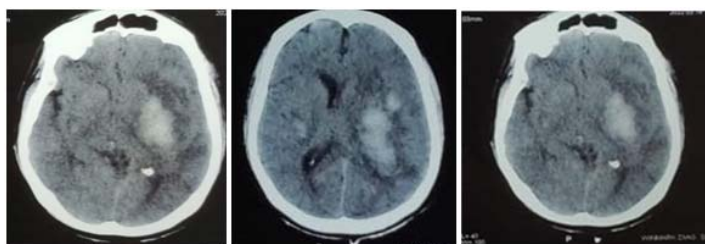


Fig 1 — CT Imaging from a patient of Basal Ganglia hemorrhage in the present study

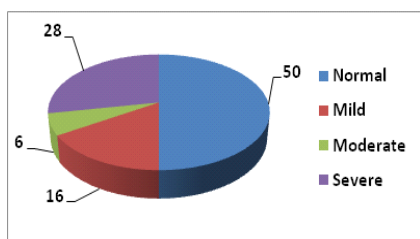


Fig 2 — Categorisation of MASA test scores

to have an abnormality. Therefore our findings are in concordance with the earlier study.

(3) EunKyu

Variables	r	significance	r ²	% of r ²	Determination
MASA X PAS	-0.935	P<0.001	0.874	87.4	87.4

PAS interpretation	B/L		Left		Right		Total		Results
	No	%	No	%	No	%	No	%	
Aspiration	0	0.0	8	16.0	4	8.0	12	24.0	χ ² =2.747 df=4 P=0.601
No Entry	0	0.0	5	10.0	5	10.0	10	20.0	
Penetration	1	2.0	20	40.0	7	14.0	28	56.0	
Total	1	2.0	33	66.0	16	32.0	50	100.0	

Ji, *et al* observed that the MASA score and the Penetration Aspiration Scale value obtained from FEES were found to be strongly negatively correlated³⁴. A similar finding was observed in the present study.

(4) Dehaghani, *et al* had observed that Stroke of certain specific Brain regions cause Swallowing dysfunction³⁵. Similar findings were observed in the present study.

(5) The individual regions we had observed to cause swallowing disturbance are as follows :

Infarcts :

- MCA territory infarcts & PCA territory infarcts (especially of P1 and P2 region) caused Swallowing Dysfunction. Similar findings were observed by Paciaroni M, *et al*¹⁷ and Javed K, *et al*⁶⁶ respectively.
- ACA territory infarcts caused Dysphagia when associated with MCA territory infarct.

	Number of Cases in the present study
Putamen Hemorrhage	3
Basal Ganglia Hemorrhage (with sensorium impairment)	3
Unilateral Cerebellar Hemorrhage	2
Hemorrhage of PCA territory	1
Thalamic Hemorrhage	1
Unilateral MCA territory infarct	12
Large Lacunar Infarct	2
Medullary Infarct (Lateral Medulla)	1
Unilateral PCA infarct	7
Pontine Infarct	2
Bilateral PCA infarct	1
Unilateral ACA and MCA infarct	5

- Pontine infarct & Lateral Medullary Infarct depending on the size and subsite involved caused Swallowing Dysfunction. Similar findings were observed by Chang MC, *et al*¹ and Ayodogdu, *et al*¹⁹ respectively.

Hemorrhage :

- Putamen hemorrhage & Basal Ganglia Hemorrhage were found to cause Swallowing dysfunction. Similar findings were reported by Maeshima S, *et al*³⁷ and Logeman JA, *et al* respectively³⁸
- Cerebellar Hemorrhage was found to cause Swallowing Dysfunction. Similar findings were observed by Pe'rie' S, *et al*⁸⁹
- Hemorrhage of PCA territory involving the Parieto-Occipital area also caused Swallow Dysfunction. Similar findings were observed by Dehaghani, *et al*⁸⁵

CONCLUSION

- We had observed Dysphagia in about half the patients in our study. Severity of Dysphagia as obtained from MASA questionnaire was graded and 16% had mild, 6% had moderate and 28% of the stroke patients had severe dysphagia.

- Using the FEES study we found varying degrees of Swallowing impairment in 80 % of the patients which is significantly higher than the frequency of impairment as determined using the clinical method (50%).
- On attempting to find correlation between the MASA score and PAS value, we found that the two variables were strongly negatively correlated. The correlation coefficient was — 0.935.
- Lesion side and the Presence of Dysphagia were not significantly associated with each other.
- Stroke of certain specific brain regions and arterial territories were found to cause Dysphagia.

Limitations :

- The various regions of brain we had observed to be related to Swallowing Dysfunction in the present study, were in concordance with that seen in earlier studies. But since the number of cases for each region of the brain were limited, we were unable to draw a Statistical significance.
- In the present study, we had considered the presence or absence of swallowing dysfunction but not the specific attributes of the Swallowing dysfunction associated with each arterial territory and brain region involved .
- We had not given consideration to the etiopathogenesis of the stroke and the impact they would have on the Resultant swallowing dysfunction.
- We did not have any cases of solely ACA

territory infarct, hence we could not determine the standalone significance of ACA territory stroke in causing Dysphagia.

REFERENCES

- Mackay J and Mensah G — Atlas of heart disease and stroke. Geneva, Switzerland: World Health Organization, 2004.
- Martino R, Foley N, Bhogal S, Diamant N, Speechley M, Teasell R — Dysphagia after stroke: incidence, diagnosis, and pulmonary complications. *Stroke* 2005; **36(12)**: 2756-63.
- Kumar S, Selim MH, Caplan LR — Medical complications after stroke. *Lancet Neurol* 2010; **9(1)**: 105-18. doi: 10.1016/S1474-4422(09)70266-2. PMID: 20083041.
- Smithard DG, O'Neill PA, Parks C, Morris J — Complications and outcome after acute stroke. Does dysphagia matter? *Stroke* 1996; **27(7)**: 1200-4.
- Mann G, Hankey GJ, Cameron D — Swallowing disorders following acute stroke: prevalence and diagnostic accuracy. *Cerebrovasc Dis* 2000; **10(5)**: 380-6.
- Smithard DG, Smeeton NC, Wolfe CD — Long-term outcome after stroke: does dysphagia matter? *Age Ageing* 2007; **36(1)**: 90-4 .
- Wilson RD — Mortality and cost of pneumonia after stroke for different risk groups. *J Stroke Cerebrovasc Dis* 2012; **21(1)**: 61-7.
- Rofes L, Arreola V, Almirall J, Cabré M, Campins L, García-Peris P, et al — Diagnosis and management of oropharyngeal Dysphagia and its nutritional and respiratory complications in the elderly. *Gastroenterology Research and Practice* 2011, 818979.
- Leder SB, Acton LM, Lisitano HL, Murray JT — Fiberoptic endoscopic evaluation of swallowing (FEES) with and without blue-dyed food. *Dysphagia* 2005; **20(2)**: 157-62.
- Schmidt J, Holas M, Halvorson K, Reding M — Videofluoroscopic evidence of aspiration predicts pneumonia and death but not dehydration following stroke. *Dysphagia* 1994; **9(1)**: 7-11.
- Smithard DG, O'Neill PA, England RE, Park CL, Wyatt R, Martin DF, et al — The natural history of dysphagia following a stroke. *Dysphagia* 1997; **12(4)**: 188-93.
- Ramsey D, Smithard D, Kalra L — Silent aspiration: what do we know? *Dysphagia* 2005; **20(3)**: 218-25. doi: 10.1007/s00455-005-0018-9.
- Falsetti P, Acciai C, Palilla R — Oropharyngeal dysphagia after stroke: incidence, diagnosis, and clinical predictors in patients admitted to a neurorehabilitation unit. *Cerebrovasc Dis* 2009; **18**: 329-35.
- Mann G, Hankey GJ, Cameron D — Swallowing function after stroke: prognosis and prognostic factors at 6 months. *Stroke* 1999; **30(4)**: 744-8.
- Leder SB, Cohn SM, Moller BA — Fiberoptic endoscopic documentation of the high incidence of aspiration following extubation in critically ill trauma patients. *Dysphagia* 1998; **13(4)**: 208-12.
- Kidd D, Lawson J, Nesbitt R, MacMahon J — The natural history and clinical consequences of aspiration in acute stroke. *QJM* 1995; **88(6)**: 409-13.
- Paciaroni M, Mazzotta G, Corea F — Dysphagia following Stroke. *European Neurology* 2003; **51**: 162-7.
- Teasell R, Foley N, Fisher J — The incidence, management, and complications of dysphagia in patients with medullary strokes admitted to a rehabilitation unit. *Dysphagia* 2002; **17**: 115-20.
- Aydogdu I, Ertekin C, Tarlaci S — Dysphagia in Lateral Medullary Infarction (Wallenberg's Syndrome). *Stroke* 2001; **32(9)**: 2081-7.
- Emilia G, Hooman K, Eric CB — Ischemic Stroke of the Pyramidal decussation causing Quadriplegia and Anarthria. *Journal of Stroke & Cerebrovascular Diseases* 2012; **21(7)**: 620.E1-620E2.
- Chang MC, Kwak SG, Chun MH — Dysphagia in patients with isolated pontine infarction. *Neural Regeneration Research* 2018; **13(12)**: 2156-9.
- Ghaemi H, Sobhani-Rad D, Arabi A — Role of Basal Ganglia in Swallowing Process: A Systematic Review. *Iranian Rehabilitation Journal* 2016; **14(4)**: 239-45.
- Maeshima S, Osawa A, Yamane F — Dysphagia following Acute Thalamic Haemorrhage : Clinical correlates and outcomes. *European Neurology* 2014; **71**: 165-72.
- DePippo — Validation of the 3-oz water swallow test for aspiration following stroke. *Arch Neurol* 1992; **49**: 1259-61.
- Jiang JL, Fu SY, Wang WH, Ma YC — Validity and reliability of swallowing screening tools used by nurses for dysphagia: A systematic review. *Ci Ji Yi XueZaZhi* 2016; **28(2)**: 41-8.
- Edmiaston J, Connor LT, Loehr L, Nassief A — Validation of a dysphagia screening tool in acute stroke patients. *American journal of critical care*. 2009.
- Validation of the Yale Swallow Protocol: a prospective double-blinded videofluoroscopic study. Suiter DMetal. *Dysphagia* 2014; **29(2)**: 199-203. doi: 10.1007/s00455-013-9488-3. Epub 2013 Sep 12.
- Mann G — MASA: The Mann Assessment of Swallowing Ability. Clifton Park, NY: Singular; 2002.
- Gonzalez-Fernandez M, Ottenstein L, Atanelov L, Christian AB — Dysphagia after Stroke: an Overview. *Curr Phys Med Rehabil Rep* 2013; **1(3)**: 187-96.
- John C. Rosenbek, Jo Anne Robbins, Ellen B — Roecker, Jame L. Coyle, Jennifer L. Wood. A penetration-aspiration scale. *Dysphagia* 1996; **11(2)**: 93. doi:10.1007/BF00417897
- Langmore SE — *Endoscopic evaluation and treatment of swallowing disorders*. New York, NY: Thieme, 2001
- Chojin Y, Kato T, Rikihisa M, Omori M, Noguchi S, Akata K, et al — Evaluation of the Mann Assessment of Swallowing Ability in Elderly Patients with Pneumonia. *Aging and Disease* 2017; **8(4)**: 420-33. doi:10.14336/AD.2017.0102
- Logemann JA, RoaPauloski B, Rademaker A, Cook B, Graner D, Milianti F, Beery Q, et al — Impact of the diagnostic procedure on outcome measures of swallowing rehabilitation in head and neck cancer patients. *Dysphagia* 1992; **7(4)**: 179-86. doi: 10.1007/BF02493468. PMID: 1424831.
- Ji EK, Wang HH, Jung SJ, Lee KB, Kim JS, Hong BY, et al — Is the modified Mann Assessment of Swallowing Ability useful for assessing dysphagia in patients with mild to moderate dementia? *J Clin Neurosci [Internet]* 2019; **70**: 169-72.
- Dehaghani SE, Yadegari F, Asgari A, Chitsaz A, Karami M — Brain regions involved in swallowing: Evidence from stroke patients in a cross-sectional study. *Journal of research in medical sciences : the official journal of Isfahan University of Medical Sciences* 2016; **21**: 45. https://doi.org/10.4103/1735-1995.183997
- Javed K, Reddy V, M Das J — Neuroanatomy, Posterior Cerebral Arteries. 2021 Jul 31. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. PMID: 30860709
- Maeshima S, Okazaki H, Okamoto S, Mizuno S, Asano N, Tsunoda T, et al — Dysphagia Following Putaminal Hemorrhage at a Rehabilitation Hospital. *J Stroke Cerebrovasc Dis* 2016; **25(2)**: 389-96.
- Logemann JA, Shanahan T, Rademaker AW, Kahrilas PJ, Lazar R, Halper A — Oropharyngeal swallowing after stroke in the left basal ganglion/internal capsule. *Dysphagia* 1993; **8(3)**: 230-4.
- Périé S, Wajeman S, Vivant R, St Guily JL — Swallowing difficulties for cerebellar stroke may recover beyond three years. *Am J Otolaryngol* 1999; **20(5)**: 314-7. doi: 10.1016/s0196-0709(99)90033-9.

Original Article

Implementation of an Interactive Teaching Session using 'Snowball Technique' for Introducing 1st Professional MBBS Students to Clinical Correlation in Biochemistry

Niket Verma¹, Kusum Singla², Bishambar Toora³, Richa Dixit⁴

Under the new Competency Based Medical Education curriculum in India, two-thirds of the teaching schedules must comprise of interactive teaching sessions. Snowball Discussion is an interactive and collaborative technique which starts with the introduction of a clinical challenge to individual learners and then proceeds by doubling. The current study was conducted with the aim of assessing the perception of learners from 1st professional MBBS towards a recently conducted teaching learning session using Snowball technique in Biochemistry. A Snowball teaching session was conducted on 'Diabetes Mellitus'. 73 learners attended the session. The facilitators sensitized the learners about the Snowball technique after which the session was conducted step-wise. This was followed by an integrated learning session in which guest speakers shared important points about diabetes mellitus relevant to their subjects. Feedback was obtained from the learners using an online feedback form 46 learners submitted the feedback form. There was a high level of satisfaction among the learners regarding the session. 45 respondents (97.8%) agreed that attending the Snowball session generated their interest in the topic and they were able to better correlate the topic clinically. 44 respondents (95.7%) agreed that after attending the Snowball session they were motivated to read further about the topic and that a Snowball session was better than a traditional lecture. The 'Snowball' technique is an interactive teaching learning method which can be utilized for introduction of clinical correlation to undergraduate medical students. Specific topics that are integrated with clinical subjects can be easily adapted to this teaching technique.

[J Indian Med Assoc 2023; 121(8): 32-6]

Key words : Curriculum, Learning, Clinical Reasoning.

"I hear and I forget. I see and I remember. I do and I understand."

— **Confucius**

In India, Biochemistry is taught in the first year of MBBS. The traditional pattern of teaching biochemistry includes didactic teacher-oriented lectures followed by small group tutorials and laboratory practical classes¹. The increase in the intake of MBBS learners in many medical colleges over the past few years has not been accompanied with a corresponding increase in faculty numbers. Didactic lectures have gained even more acceptability in such a scenario because they allow the sharing of knowledge with a large number of learners in a short period of time with minimum faculty requirements².

¹MBBS, MD, Assistant Professor, Department of General Medicine, AIIMS Bathinda, Punjab 151001

²MD, Associate Professor, Department of Biochemistry, Army College of Medical Sciences, Delhi Cantonment, New Delhi, Delhi 110010 and Corresponding Author

³MD, Professor, Department of Biochemistry, World College of Medical Sciences and Research, Haryana 124103

⁴PhD, Tutor, Department of Biochemistry, Army College of Medical Sciences, Delhi Cantonment, New Delhi, Delhi 110010

Received on : 25/07/2022

Accepted on : 21/01/2023

Editor's Comment :

- The 'Snowball' technique is an interactive teaching learning method which can be utilized for introduction of clinical correlation to undergraduate medical students.
- Specific topics that are integrated with clinical subjects can be easily adapted to this teaching technique.

However, with the introduction of the Competency Based Medical Education (CBME) curriculum in India from August 2019, a paradigm shift is already underway in medical education. Under the new guidelines two-thirds of the teaching schedules must comprise of interactive teaching sessions while didactic lectures must be limited to not more than one-third of the schedules³.

Snowball Discussion is one such interactive and collaborative teaching-learning technique; also referred to as a Pyramid discussion technique, the Snowball session starts with the introduction of certain information or a problem/clinical case/challenge to the individual learners and then proceeds by doubling. Therefore, students first work individually, then in pairs, then in groups of four, then eight and so on. Ideally, at each step the complexity of the problem should keep increasing, either by introducing more information or by setting new challenges. The end point may vary

from the stage of eight learners or sixteen learners to a large group involving the entire class. If working with multiple small groups, the final stage of the discussion usually involves inviting one or two representatives from each group to present their group's conclusions in front of the larger group. This may be followed by a large group discussion in which all students can share their knowledge and perceptions about the topic⁴⁻⁷.

The current study aims to assess the perception of student learners (from 1st professional MBBS) and faculty facilitators towards a recently conducted interactive teaching learning session using Snowball technique in the Department of Biochemistry.

MATERIALS AND METHODS

The Snowball teaching session was conducted in the Department of Biochemistry. All 100 1st Professional MBBS students consented to be a part of the study. However only 73 learners actually attended the session. The session was conducted during a three-hour Early Clinical Exposure (ECE) slot from 1030 hours to 1330 hours. A total of 5 facilitators were part of the session, 4 from the Department of Biochemistry and 1 from the Department of General Medicine. The topic selected for the session was 'Diabetes Mellitus'. 1 guest speaker was invited from each of the following Departments – General Medicine, Gynaecology & Obstetrics, and Microbiology. The coordinator of the Medical Education Unit was also invited as an observer.

The session was conducted in 2 adjacent rooms and seating arrangements were made accordingly. 48 learners (selected randomly from the class of 73 learners) were invited to Room 1. Facilitators sensitized the learners about the Snowball teaching methodology, explained the different steps of the technique and informed them that 2 clinical case cards (relating to the same case/patient) will be introduced at specific points in the session.

Step 1 - Card number 1 (containing brief history and chief complaints of a patient with diabetes mellitus) was then distributed to all the 48 learners and they were asked to read the case scenario given in the card individually (without any discussion) and write down the key points. The time allotted to this step was 10 minutes and at the end of time a bell was rung by the facilitators.

Step 2 - Learners were instructed to work in pairs (ie, a group of 2 participants) to discuss the case scenarios amongst themselves and compare the key points they had marked or written down. They were also asked to discuss the presenting signs and symptoms of the patient and the importance of each

sign and/or symptom in the given patient. 10 minutes were allotted to this step and a bell was rung at the end of time.

Step 3 - 2 consecutive pairs were asked to combine to form groups of 4 learners and discuss the preliminary approach to such a patient, including the diagnostic workup. Time allotted to this step was 10 minutes.

Step 4 - Adjacent teams of 4 were asked to combine and discuss in groups of 8 learners. Card Number 2 (containing a list of investigations conducted and sample test reports of the same patient) was distributed to each group (48 learners, 6 groups of 8 learners each, therefore 6 cards were used, 1 card per group). Groups were asked to discuss the sample investigation reports and the interpretation of the reports. They were also asked to suggest any further investigations they would want to get conducted. Time allotted for this step was 15 minutes. At this stage the groups were asked to follow principles of group dynamics (explained during the initial sensitization) and select a group leader, a summarizer and a time keeper. The group leader was asked to ensure that all 8 members in the team got a chance to put forth their views, the summarizer was tasked with noting down and summarizing the discussion.

Step 5 - All 16 learners seated at a table were now asked to form a single team and work together to discuss the approach to this patient. Once again, groups were asked to follow group dynamics and select a group leader, a summarizer and a timekeeper. Time allotted for this step was 15 minutes. The group leader was asked to ensure that all 16 members in the team got a chance to put forth their views, the summarizer was tasked with writing down the key points and summarizing the discussion for presentation in front of the large group.

The 2nd sub-session was being simultaneously conducted in the adjacent demonstration room and all the steps explained above were followed.

Thus, all the steps were completed at the end of approx. 75 minutes (60 minutes for conducting the steps and 15 minutes for sensitization, explaining the steps, clearing any doubts etc). After this the 2 groups from Room 2 were also invited to Room 1 and all the 5 groups were now seated in the Room 1. Each group was then asked to present a summary of their approach to the case in front of the large group and each group was allotted 6 minutes for the presentation. The summarizers were asked to first present the differential diagnosis and most probable diagnosis. (this was cross checked with the points written by the summarizer on the paper) All teams had reached the correct diagnosis

of Diabetes Mellitus; so the summarizers were asked to present the approach in 6 minutes. Then, 4 minutes were allotted for the discussion of one aspect of Diabetes Mellitus by the rest of the team members. This was extempore discussion based on the lectures and tutorials on Diabetes that had been conducted over the past week. Team 1 was asked to discuss the Metabolic and Biochemical changes associated with Diabetes Mellitus, Team 2 discussed Diagnostic Criteria, Team 3 discussed Investigations, Team 4 discussed Acute Complications and Team 5 discussed Chronic Complications of Diabetes Mellitus. All members of the presenting team therefore got a chance to speak and share their views and during this step questions were also asked to the other teams.

After all the 5 groups had finished their presentations, there was an integrated learning session in which guest speakers share some important points about diabetes mellitus relevant to their respective subjects. The guest speaker from Microbiology discussed about the common infections in diabetic patients with special focus on diabetic foot; the guest speaker from General Medicine discussed about acute and chronic complications of diabetes mellitus; the guest speaker from Gynaecology & Obstetrics discussed about Gestational Diabetes Mellitus and its complications. Finally, the facilitators answered any queries from the students regarding the topic after which the HOD of the department summarized the discussion.

At the end of the discussion, the students were administered an online feedback form to be completed by the end of the day (using Google Forms). For the purpose of obtaining feedback, the principal author also conducted individual interviews with the other facilitators.

RESULTS

A total of 46 learners submitted the feedback form. 45 respondents (97.8%) had attended a Snowball session for the first time.

Respondents were asked to rate the Snowball session on a 5-point Likert Scale (1=Highly UN-Satisfactory; 2=UN-Satisfactory; 3=Neutral; 4=Satisfactory; 5=Highly Satisfactory). 25 respondents (54.3%) rated the session 5 while 17 respondents (37%) rated the session 4 (Fig 1) thereby signifying a high level of satisfaction among the respondents.

45 respondents (97.8%) agreed that attending the Snowball session generated their interest in the topic being covered (Fig 2), that they were able to gain more knowledge about the topic being covered and were able to better correlate the topic clinically (Fig 3). 44 respondents (95.7%) agreed that after attending the Snowball session they were motivated to read further about the topic (Fig 4).

The respondents were then asked what in their opinion was the best part of the Snowball session. The thematic analysis of the responses is presented in Table 1.

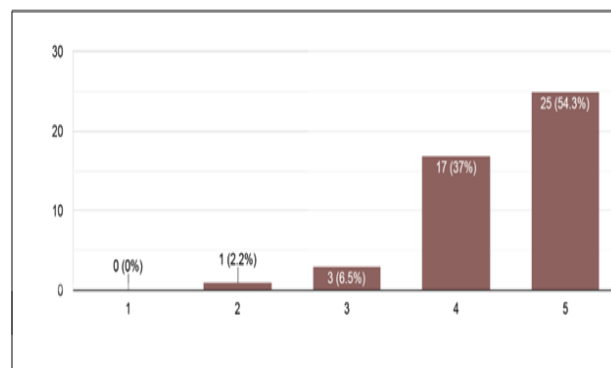


Fig 1 — Overall rating of the SNOWBALL session (on a scale of 1 to 5; 1=Highly UN-Satisfactory and 5=Highly Satisfactory) (n=46)

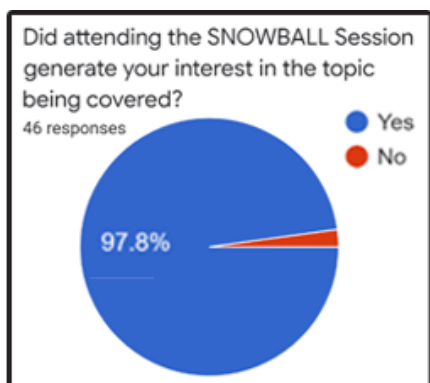


Fig 2 — Respondents' opinion when asked whether attending the Snowball session generated their interest in the topic (n=46)

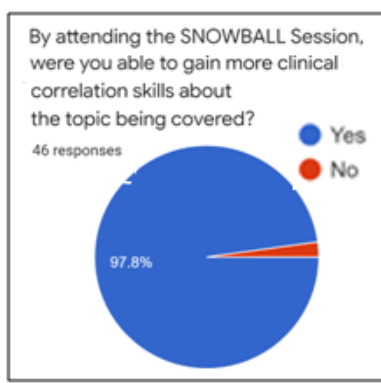


Fig 3 — Respondents' opinion when asked whether they were able to gain clinical correlation skills on the topic after attending the Snowball session

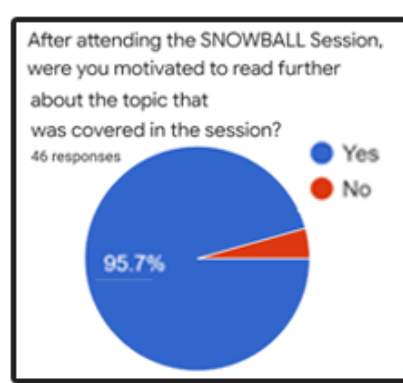


Fig 4 — Respondents' opinion when asked whether attending the Snowball session motivated them to read further on the topic

45 respondents (97.8%) agreed that they would like to attend more Snowball sessions in Biochemistry. The respondents were asked to suggest additional topics which could be taught in a Snowball session. Some of the suggestions received were Amino acid metabolism, Jaundice, Carbohydrate metabolism, Vitamin deficiencies, Nutritional disorders and Lipid metabolism.

39 respondents (84.8%) agreed that the session started and finished as per schedule. All 46 respondents (100%) agreed that the session was conducted in a safe non-threatening environment and that they were able to understand the steps of the Snowball session and the information given in the 'information cards' used during the session.

45 respondents (97.8%) agreed that the session was conducted without unnecessary interruptions. 44 respondents (95.7%) agreed that sufficient time was allocated for every step of the session

Regarding the faculty facilitators conducting the session, 45 respondents (97.8%) agreed that the facilitators explained the process and steps of Snowball at the beginning of the session. 44 respondents (95.7%) agreed that the facilitators answered all queries and doubts asked by the learners and guided the learners through the different stages of the Snowball session. 43 respondents (93.5%) agreed that the facilitators encouraged all students to participate actively in the snowball session while 41 respondents (89.1%) agreed that the facilitators helped facilitate discussion within the groups.

44 respondents (95.7%) agreed that a Snowball session was better than a traditional lecture. Learners were also asked the reason for their preference and a thematic analysis is presented in Table 2.

Finally, the respondents were asked for suggestions for further improvements in future Snowball sessions. Some of the responses obtained are presented verbatim below –

(a) "Time for each step should be increased by 1-2 minutes"

(b) "Should be conducted more frequently"

Theme	Selected Responses
Interactive learning	<ul style="list-style-type: none"> • Participation of all students and time for individual thinking and analysis • Every individual had a role in it • Ideas sharing by each group at the end • The progression of discussion was the best part
Improved learning outcomes	<ul style="list-style-type: none"> • More clinical knowledge • Building up concepts
Involvement of multiple departments	<ul style="list-style-type: none"> • Especially the last part when all the faculty gave there points on the applied part of concerned topic that were really helpful • Where different departments explained the clinical scenarios related to their respective departments"
Innovative / Interesting concept	<ul style="list-style-type: none"> • It was all very interesting • Innovative concept and best method ever

(c) "Provide opportunity for presentations by more number of students"

(d) "It should be done once in every month"

(e) "Good initiative. More topics should be covered"

The faculty/facilitators expressed satisfaction with the Snowball technique. All of them felt that it was a feasible interactive teaching learning method for introduction of clinical correlation. All facilitators felt that specific topics that are integrated with clinical subjects could be adapted to this teaching technique.

Theme	Selected Responses
More interactive	<ul style="list-style-type: none"> • Every student got the chance to speak and explore • We were able to gather views of different people on a particular topic
Sub-themes –	
a) equal chance to speak	<ul style="list-style-type: none"> • It helps in understanding other's point of view
b) understand different viewpoints	<ul style="list-style-type: none"> • Group discussion is quite helpful
c) group discussion	<ul style="list-style-type: none"> • It enabled is to analyse the situation individually and then discuss the possibilities and the solutions in the group
Active participation	<ul style="list-style-type: none"> • In traditional lecture we are more passive learner. But in snowball we participated actively • Student and teacher both are equally involved
Better understanding of the topic	<ul style="list-style-type: none"> • Snowball helped me understand the topic very well as it was not just one way teaching, in the first round I applied the knowledge that I had and in the progressing rounds discussed it.
Sub-themes –	
a) discussion promotes learning	<ul style="list-style-type: none"> • The discussion part helped me gain more knowledge about the topic
b) better clinical correlation	<ul style="list-style-type: none"> • We are introduced to clinical knowledge teaches us the different point of view to same case. And how to tackle it
More interesting	<ul style="list-style-type: none"> • Traditional lectures are generally boring and everything that is taught is not registered by the students
Self-satisfaction	<ul style="list-style-type: none"> • There is space for discussion, without the fear of getting judged • Everyone's involvement is appreciated

DISCUSSION

Interactive teaching learning goes one step ahead of active teaching learning. Whereas in the active approach, there is interaction between the teacher and the students, in the interactive approach the students interact not only with the teacher but also amongst themselves⁸. Interactive teaching ensures participation of all students in the learning process, makes learning fun and leads to better learning outcomes⁹.

While didactic lectures will always be useful in specific circumstances, student preference for interactive and collaborative teaching learning techniques means that supplementing didactic lectures with interactive teaching sessions can be extremely helpful in introducing topics such as clinical correlation¹⁰.

Edgar Dale theorized many decades ago that people remember only 10% of what they read and 20% of what they hear as opposed to 70% of what they say and write and 90% of what they say and do while performing a task¹¹. Malcolm Knowles propounded that adult learners prefer active learning techniques which are problem centred, have immediate relevance to their vocation or personal life and which respect the learners and their prior knowledge and past experiences.

The Snowball technique is almost always problem centred; learners are encouraged not only to speak, discuss but also to write down and summarize the important points at every step for easy collaboration with their peers; teaching clinical correlation of basic science topics has immediate relevance to the learners as it enables them to associate the knowledge of basic sciences with clinical concepts in later years¹² and interactivity and collaboration with their peers allows students to put forth their points of view in a respectful environment. Working in teams with their peers promotes teamwork and inculcates the importance of working as equal members of healthcare teams in the future¹³. Previous studies have shown that incorporation of clinical correlation in teaching learning sessions leads not only to better learning outcomes but also improves clinical reasoning ability and helps learners in making better diagnostic decisions¹⁴⁻¹⁶.

CONCLUSION

The 'Snowball' technique is a feasible interactive teaching learning method for introduction of clinical correlation to undergraduate medical students. In light of the inherent advantages of interactive teaching and the incorporation of clinical correlation in day-to-day learning, the authors recommend more widespread use of the Snowball technique for introducing clinical correlation in Biochemistry.

REFERENCES

- 1 Bobby Z, Nandeesh H, Sridhar MG, Soundravally R, Setiya S, Sathish Babu M, *et al* — Identification of mistakes and their correction by small group discussion as a revision exercise at the end of a teaching module in biochemistry. *Natl Med J India* 2014; **27**: 22-3.
- 2 Dipiro JT — Why do we still lecture? *Am J Pharm Educ* 2009; **73**: 137.
- 3 Nierenberg DW — The challenge of "teaching" large groups of learners: strategies to increase active participation and learning. *Int J Psychiat Med* 1998; **28**(1): 115-22. [Internet]. Mciindia.org. 2019 [cited 2 May 2020]. Available from: <https://mciindia.org/ActivitiWebClient/open/getDocument?path=/Documents/Public/Portal/Gazette/GME-06.11.2019.pdf>
- 4 Edmunds S, Brown G — Effective small group learning: AMEE Guide No. 48. *Medical Teacher* 2010; **32**(9): 715-26.
- 5 Duraman H, Shahrill M, Morsidi N — Investigating the Effectiveness of Collaborative Learning in Using the Snowballing Effect Technique. *Asian Journal of Social Sciences and Humanities* [Internet]. 2015 [cited 1 June 2020];4(1):148-155. Available from: [http://www.ajssh.leena-luna.co.jp/AJSSHPDFs/Vol.4\(1\)/AJSSH2015\(4.1-17\).pdf](http://www.ajssh.leena-luna.co.jp/AJSSHPDFs/Vol.4(1)/AJSSH2015(4.1-17).pdf)
- 6 Group Work in the Classroom: Types of Small Groups | Centre for Teaching Excellence [Internet]. Centre for Teaching Excellence. 2012 [cited 10 June 2020]. Available from: <https://uwaterloo.ca/centre-for-teaching-excellence/teaching-resources/teaching-tips/developing-assignments/group-work/group-work-classroom-types-small-groups>
- 7 Miller G — Snowball Technique — A Teaching Strategy [Internet]. bookunitteacher.com. 2018 [cited 10 June 2020]. Available from: <https://bookunitteacher.com/wp/?p=5826>
- 8 Giorgdze M, Dgebuadze M — Interactive Teaching Methods: Challenges And Perspectives. *IJAEDU- International E-Journal of Advances in Education* 2017; 544-8.
- 9 Surapaneni K, Tekian A — Concept mapping enhances learning of biochemistry. *Medical Education Online* [Internet]. 2013 [cited 1 June 2020]; **18**(1): 20157. Available from: <https://www.tandfonline.com/doi/full/10.3402/meo.v18i0.20157>
- 10 Lodhiya KK, Brahmabhatt KR — Effectiveness of collaborative versus traditional teaching methods in a teaching hospital in Gujarat. *Indian J Community Med* 2019; **44**: 243-6
- 11 Anderson H — Dale's Cone of Experience [Internet]. Queensu.ca. [cited 1 June 2020]. Available from: https://www.queensu.ca/teachingandlearning/modules/active/documents/Dales_Cone_of_Experience_summary.pdf
- 12 Klement B, Paulsen D, Wineski L — Clinical Correlations as a Tool in Basic Science Medical Education. *Journal of Medical Education and Curricular Development* [Internet]. 2016 [cited 1 June 2020];3:JMECD.S18919. Available from: <https://journals.sagepub.com/doi/full/10.4137/JMECD.S18919>
- 13 Lerner S, Magrane D, Friedman E — Teaching Teamwork in Medical Education. *Mount Sinai Journal of Medicine: A Journal of Translational and Personalized Medicine* 2009; **76**(4): 318-29.
- 14 Malau-Aduli B, Lee A, Cooling N, Catchpole M, Jose M, Turner R — Retention of knowledge and perceived relevance of basic sciences in an integrated case-based learning (CBL) curriculum. *BMC Medical Education* [Internet]. 2013 [cited 4 June 2020]; 13(1). Available from: <https://bmcmmededuc.biomedcentral.com/articles/10.1186/1472-6920-13-139>.
- 15 Jacobson K, Fisher D, Hoffman K, Tsoulas K — Integrated Cases Section: A Course Designed to Promote Clinical Reasoning in Year 2 Medical Students. *Teaching and Learning in Medicine* 2010; **22**(4): 312-6.
- 16 Woods N, Brooks L, Norman G — It all make sense: biomedical knowledge, causal connections and memory in the novice diagnostician. *Advances in Health Sciences Education* 2007; **12**(4): 405-15.

Original Article

Association between Reverse Osmosis Water and Heart Diseases, Back Pain and Joint Pain

Sangita Patel¹, Rahul Khokhariya², Greenam Tarani³, Jagruti Rathod⁴,
Deya Ghosh Chatterji⁵, Jesal Patel⁶

Background : Reverse Osmosis (RO) system causes demineralization of water which leads to various health problems. Therefore, this study was conducted to assess the association between RO water and heart diseases, back pain and joint pain.

Material and Methods : At urban Vadodara city a cross sectional study was carried out with 2609 participants among 720 households. 60 households from each selected water tank area were included. Interviews were conducted to know about usage of RO water and health problems such as coronary heart disease, joint pain and back pain. 38 water samples were tested for Total Dissolved Solutes, calcium hardness and total hardness.

Results : TDS, Calcium hardness and total hardness were within normal range. There was statistically significant association between RO water usage and joint pain (p value 0.0001) at 95% CI while no association was found between RO water usage and Coronary Heart Disease (CHD) (p value 0.3104) and back pain (p value 0.5230) at 95% CI.

Conclusion : Usage of RO water system is associated with joint pain while there is no association of coronary heart disease and back pain with RO water.

[J Indian Med Assoc 2023; 121(8): 37-40]

Key words : RO Water System, Joint Pain, Back Pain, Coronary Heart Disease, TDS, Calcium Hardness, Total Hardness.

One of the primary goals of the WHO and its member states is that "All people, whatever their stage of development and their social and economic condition, have the right to have access to an adequate supply of safe drinking water¹. Typical recommended dietary intake of calcium is 1000mg per day. Hard water is said to be responsible for kidney stone². Calcium and magnesium are essential minerals and beneficial to human health in several respects. Inadequate intake of calcium has been associated with increased risk of osteoporosis³, colorectal cancer, hypertension, stroke, coronary artery disease, insulin resistance and obesity⁴. Total body stores are in the order of 1200g with about 99% in bones and teeth. Magnesium is the 2nd most abundant cation in intracellular fluid. It is co-factor for some 350 cellular enzymes, many of which are involved in energy metabolism. It is also involved

Editor's Comment :

- Total hardness, calcium hardness and TDS was within normal range in all water tanks in Vadodara Municipal Corporation.
- Drinking RO Water was associated with joint pain and not associated with coronary heart disease and back pain.

in protein and nucleic acid synthesis and needed for normal vascular tone and insulin sensitivity. Magnesium deficiency has been implicated in the pathogenesis of hypertension⁵.

In 92-99% of beneficial calcium and magnesium is removed by Reverse Osmosis (RO) system. Consumption of RO water even for a few months leads to serious side effects⁶. Common complaints observed in Czech and Slovak populations were cardiovascular disorders, tiredness, weakness, and muscle cramps. This deficiency cannot be compensated by diet¹.

AIMS AND OBJECTIVES

To assess TDS, calcium hardness and total hardness of water and to know the association between RO water and heart diseases, back pain, and joint pain.

MATERIALS AND METHODS

A Cross sectional study was carried out at urban Vadodara city after taking permission from Institutional ethical committee. From north, south, east and west

Department of Community Medicine, Medical College Baroda, Gujarat 390001

¹MD, Associate Professor and Corresponding Author

²MD, Medical Officer

³MD, Senior Resident

⁴PhD, Associate Ecologist, Department of Ecology, Gujarat Ecology Society, Vadodara, Gujarat 390003

⁵MD, Senior Resident

⁶MBBS, Intern, Department of Community Medicine, GCS Medical College Hospital and Research Centre, Ahmadabad, Gujarat 380018

Received on : 09/12/2022

Accepted on : 02/04/2023

zones, average 3 water tanks were selected randomly. Therefore, water sample from 12 water tanks were tested. Two water samples were collected, one from near tank area and another from outer limit of water supply from household level to check TDS, Calcium hardness and total hardness. Thus, 12 water tanks, 24 household water samples, and 2 from main water bodies of Vadodara district (Ajwa and Mahi River) (38 samples) were tested. Standard operating procedure was followed for water sample collection and transport. The water samples were sent to Gujarat Ecological Society for TDS, Calcium hardness and total hardness testing.

Vadodara city has been assigned zones of north, south, east, and west. Randomly three water tanks were selected from each zone using a computerized generated random number. One hundred and eighty households were taken from each zone and a total of 720 households were included in the study. The expected total population to be covered was 3600, assuming the average family size of 5 persons. However, 2609 participants were available during data collection and consent was taken for participation. First house was randomly selected after which 60 sequential houses were included for the study. If any house was closed than sequential next house was selected. Those families who used bore well water, who lived in slum area and flat/apartment area were excluded from the study. The total study duration was 1 year, and the data was collected from November 2016 to August 2017.

A pre-validated and semi structured questionnaire was used to collect data regarding RO water usage and associated health hazards such as heart diseases, back pain, and joint pain after taking written informed consent. All those having coronary heart disease (Angina pectoris, Myocardial Infarction, and irregularities of heart), Joint pain and back pain due to any cause were included in the study.

The process of data collection did not pose any potential risk or harm to the participants. Data safety and confidentiality was given due consideration by keeping the file containing identity related details password protected. The filled Performa were kept in lock and key accessible only to researchers.

Statistical Analysis : The Data was entered in Microsoft excel using strict check files. Water quality parameters were measured in pre-defined measures. Chi square and Fishers exact test was used for categorical data using Epi info 7⁷.

RESULTS

Normal TDS value is <600 mg/l. TDS value in all

the water tanks were below 600 except for one area (Manjalpur water tank which was 786mg/l), Calcium Hardness in all the water tanks was within normal range. Normal Value total Hardness of water is 500mg/l. Total hardness of water was below 500mg/l in all water tanks.

Out of 2609 participants, 1340 (51.36%) were male and 1269 (48.63%) were female. Three fourth 1841 (70.56%) were between 20-64 years, 311 (11.92%) were between 10-19 years, 167 (6.40%) were above 65 years age, 165 (6.32%) participants were less than 5 years, 125 (4.79%) were between 6-9 years.

Most of the participants were graduates 1074 (41.16%), followed by education up to higher secondary 500 (19.16%), Secondary 404 (15.48%), Primary 371 (14.22%) and one tenth of the participants were illiterate.

259 (35.97%) participants were using RO. 147 (20.41%) participants were using UV (ultraviolet filter) filter for purification of water and small number of people used Jug water for drinking water.

141 (34.72%) household used RO/UV water for less than 5years, 160 (39.40%) household were using RO/UV water filter for 5 to 10 years and 105 (25.86%) were using RO/UV water filter for more than 10 years.

Table 1 shows that history of coronary heart disease was present in 3.64% RO users and 2.84% in non-RO users. There was no statistically significant association in heart problem between RO users and non-RO users. (p-value=0.3104)

Out of total 2609 participants, 644 (24.68%) had history of back pain out of which 14.85% males and 35.06% females had back pain. There was statistically significant association in back pain between male and female (p-value=0.0001) (Table 2).

According to Table 3, 25.44% of RO users and 24.24% of non-RO users had back pain. There was no statistically significant association in back pain

Table 1 — Comparison of Coronary Heart Disease between RO users and non-RO users (n=2609)

	H/O Coronary Heart disease	No H/O Coronary Heart disease	Total
RO users	35 (3.64%)	924 (96.35%)	959
Non-RO users	47 (2.84%)	1603 (97.15%)	1650
Total	82	2527	2609
Chi-square value = 1.029 p-value = 0.3104 DF = 1			

Table 2 — History of Back pain in study participants (n=2609)

	Male	Female	Total
Back pain present	199(14.85%)	445(35.06%)	644(24.68%)
Back pain absent	1141(85.14%)	824(64.93%)	1969(75.46%)
Total	1340	1269	2609
Chi-square value = 142.197 p-value = 0.0001 DF = 1			

between RO users and non-RO users (p-value = 0.5230).

Table 4 shows that out of total 2609 participants 11.79% males and 23.79% of females had history of joint pain. There was statistically significant association in joint pain between male and female (p-value = <0.0001).

Table 5. Shows age wise distribution amongst those with and without joint pain. In less than 9 years, no participant had joint pain. In 10-19 years, 10.32% had history of joint pain and 99.68% had no history. In 20-64 years, 19.66% had joint pain while 80.34% had no history and for participants above 65 years, 58.08% had joint pain and 41.92% had no history of joint pain.

According to Table 6, 20.33% RO users and 16.06% non-RO users had history of joint pain. There was statistically significant association in joint pain between RO and non-RO users (p-value=0.0068).

DISCUSSION

There was limited literature available on this topic. Usage of RO system leads to demineralization of water specifically calcium and magnesium which leads to

increase prevalence of coronary heart disease, joint pain and back pain and this deficiency cannot be compensated by diet. Therefore, our discussion is based on demineralized water and CHD, joint pain, and back pain.

TDS, calcium hardness and total hardness of water was similar in both RO and non-RO water so, demineralization in RO water was due to usage of RO system.

In all total 38 samples of water were checked, TDS of water was found to be normal except for one area (Manjalpur water tank which was 786mg/l), TSS ranged from 18-84 mg/l, Calcium Hardness of water ranged from 40-84 mg/l. Total Hardness of water ranged from 104 to 320 mg/l.

The association of drinking water hardness and Coronary Heart Diseases (CVDs) has been studied since more than five decades ago. A study in England and Wales showed that cardiovascular death rates had a favourable effect in towns with harder water and had an adverse effect in towns with softer water⁸. Other studies showed that high levels of drinking water hardness can be protective against CVD⁹.

However, a review of ecological studies showed that the results are inconsistent between studies. A meta-analysis revealed a negative association between concentration of magnesium in water and CVD mortality¹⁰.

Moreover, another review showed protective role of magnesium concentration in water against CVD in some case-control studies and one cohort study, but the analytical studies showed little evidence about the association of calcium and magnesium levels in drinking water and CVD risk¹¹.

Water hardness may be also associated with CVD risk factors, for instance positive correlations of water magnesium and calcium with blood pressure is documented.

In the Netherlands, another study found no overall association between calcium, magnesium or total hardness and ischemic heart disease or stroke mortality¹².

Our study showed that history of coronary heart disease was 3.14%. Calcium hardness in our study was found to be normal, which ranged from 40-84 mg/l. Total hardness ranged from 104-140mg/l. TDS value ranged from 137-786mg/l. All the water samples were found to be moderately hard so we have not studied the relationship between CVD and hardness of water, but we have studied the relationship of heart problem with RO users and Non-RO users but there was no statistically significant association in heart problem

Table 3 — Comparison of history of Back pain between RO users and non-RO users (n=2609)

	H/O Back Pain	No H/O Back Pain	Total
RO user	244 (25.44%)	715 (74.55%)	959
Non-RO users	400 (24.24%)	1250 (75.75%)	1650
Total	644	1965	2609
Chi-square value=0.408	p-value=0.5230	DF=1	

Table 4 — History of Joint pain in study participants (n=2609)

	Male	Female	Total
H/O Joint Pain	158(11.79%)	302(23.79%)	460(17.63%)
No H/O Joint Pain	1182(88.20%)	967(76.20%)	2149(82.36%)
Total	1340	1269	2609
Chi-square value = 63.880	p-value = <0.0001	DF = 1	

Table 5 — Age wise distribution of Joint pain in study participants (n=2609)

Age group in years	H/O joint pain	H/O no joint pain	Total
<9	0	290 (100%)	290
10-19	1 (0.32%)	310 (99.68%)	311
20-64	362 (19.66%)	1479 (80.34%)	1841
>65	97 (58.08%)	70 (41.92%)	167
	460	2149	2609

Table 6 — Comparison of history of joint pain between RO users and Non-RO users (n=2609)

	H/O Joint Pain	No H/O Joint Pain	Total
RO users	195 (20.33%)	764 (79.66%)	959
Non-RO users	265 (16.06%)	1385 (83.93%)	1650
Total	460	2149	2609
Chi-square value = 7.334	p-value = 0.0068	DF = 1	

between RO users and Non-RO users. The reason may be multifactorial reasons of CVD like cigarette smoking, obesity, behaviour problem, physical inactivity, diet pattern, family history etc.

The study done by Pallav Sengupta found that GI health is also being benefited from hard water since it provides potentially alleviating effects on the onset of constipation in the 85% cases. A rich union of calcium and magnesium in hard water, in a right combination, helps to combat constipation. The calcium in hard water results in teaming up with excess bile and its resident fats to lather up the soap like insoluble substance, which is emitted from the body during bowel movements. Indeed, many renowned scientists have considered hard water as a boon as it has some fantastic health benefits that seem to encourage longer life expectancy and improved health. Magnesium salt has laxative effect. This provides a rapid evacuation of intestine. The American Gastroenterology Association recommends milk of magnesia for the management of constipation as one of the therapeutic options⁴.

Statistically significant association was observed in joint pain between RO users and non-RO users. No statistically significant association was observed in back pain between RO users and non-RO users.

Age and sex distribution was similar in RO and non-RO users; therefore, it did not act as a confounder. The generalizability of above study data is applicable to whole Vadodara Municipal Corporation area.

CONCLUSION

RO water system usage is associated with joint pain and not associated with CHD and back pain. Further prospective studies are required to test whether RO water causes health problems like CHD, back pain, and joint pain.

REFERENCES

- 1 Water S — Nutrients in drinking water. Water, Sanitation, and Health Protection and the Human Environment, World Health Organization; 2005. 186.
- 2 Bellizzi V, DeNicola L, Minutolo R, Russo D, Cianciaruso B, Andreucci M, *et al* — Effects of Water Hardness on Urinary Risk Factors for Kidney Stones in Patients with Idiopathic Nephrolithiasis. *Nephron* 1999; **81(1)**: 66-70.
- 3 Power ML, Heaney RP, Kalkwarf HJ, Pitkin RM, Repke JT, Tsang RC, *et al* — The role of calcium in health and disease. *Am J Obstet Gynecol* 1999; **181(6)**: 1560-9.
- 4 Sengupta P — Potential health impacts of hard water. *Int J Prev Med* 2013; **4(8)**: 866-75.
- 5 Houston M — The Role of Magnesium in Hypertension and Cardiovascular Disease. *The Journal of Clinical Hypertension* 2011; **13(11)**: 843-7.
- 6 Verma KC, Kushwaha AS — Demineralization of drinking water: Is it prudent? Vol. 70, Medical Journal Armed Forces India. *Medical Journal Armed Forces India* 2014; 377-9.
- 7 Epi Info™ | CDC [Internet]. [cited 2022 Jul 15]. Available from: <https://www.cdc.gov/epiinfo/index.html>
- 8 Crawford MargaretD, Gardner MJ, Morris JN. Changes In Water Hardness and Local Death-rates. *The Lancet* 1971; **298(7720)**: 327-9.
- 9 Ferrandiz J, Abellan JJ, Gomez-Rubio V, Lopez-Quilez A, Sanmartin P, Abellan C, *et al* — Spatial analysis of the relationship between mortality from cardiovascular and cerebrovascular disease and drinking water hardness. *Environ Health Perspect* 2004; **112(9)**: 1037-44.
- 10 Monarca S, Donato F, Zerbini I, Calderon RL, Craun GF — Review of epidemiological studies on drinking water hardness and cardiovascular diseases. *European Journal of Cardiovascular Prevention & Rehabilitation* 2006; **13(4)**: 495-506.
- 11 Lake IR, Swift L, Catling LA, Abubakar I, Sabel CE, Hunter PR — Effect of water hardness on cardiovascular mortality: an ecological time series approach. *J Public Health (Bangkok)* 2010; **32(4)**: 479-87.
- 12 Leurs LJ, Schouten LJ, Mons MN, Goldbohm RA, van den Brandt PA — Relationship between tap water hardness, magnesium, and calcium concentration and mortality due to ischemic heart disease or stroke in The Netherlands. *Environ Health Perspect* 2010; **118(3)**: 414-20.

Disclaimer

The information and opinions presented in the Journal reflect the views of the authors and not of the Journal or its Editorial Board or the Publisher. Publication does not constitute endorsement by the journal.

JIMA assumes no responsibility for the authenticity or reliability of any product, equipment, gadget or any claim by medical establishments/institutions/manufacturers or any training programme in the form of advertisements appearing in JIMA and also does not endorse or give any guarantee to such products or training programme or promote any such thing or claims made so after.

— Hony Editor

Original Article

Clinical Profile of Drug Induced Parkinsonism in Eastern India

Praveen Kumar Yadav¹, Kumud Sahu²

Background : Drug Induced Parkinsonism (DIP) is a reversible condition in most of the cases therefore have to be identified and treat early. In our study we presented the dominant pattern of DIP and the medications causing it.

Materials and Methods : This is a retrospective study done on outpatient basis from 1st January, 2022 to 30th November, 2022 at a super speciality neuro clinic. In this study all patient, satisfying the criteria of DIP were included. *The Inclusion criteria were :* (1) All patients satisfying more than equal to two of the four criterias of Parkinsonism-bradykinesia, rigidity, tremor and postural instability. (2) Patients had no symptoms of parkinsonism before taking drug. 3. There is direct relation of drug intake and symptom onset, and the *Exclusion Criteria were :* (1) Other causes of secondary Parkinsonism- NPH, vascular parkinsonism, brain tumour, toxin induced etc by appropriate investigations. (2) All other drug induced motility disorder without the features of parkinsonism. The age, sex and other demographic criterias were studied. The dominant pattern of involvement- tremor, akinetic rigidity and mixed were noted. Results: Out of 32 patients 19(59.38%) were female and 13(40.63%) were male. The most common age group was ≥ 60 years (65.63%), followed by 51-60years (15.63%) and <30 years and between age 41-50 years with equal percentage of 3.13. The mean age was 62.37years with standard deviation of 13.09 years.

The most common clinical pattern observed in our study was tremor (50%) followed by akinetic rigidity (34.38%) and mixed pattern (15.63%). Orofacial dyskinesia along with bradykinesia, rabbit syndrome, head and jaw tremor along with parkinsonian features were all seen in our study with equal percentage of (6.66%). Atypical Parkinson with features of Parkinson plus syndrome is also seen in 6.66%. The most common drug associated with DIP in our study was pro-kinetic drug levosulpiride (46.88%) followed by flunarizine (25%), valproate and haloperidol (6.25%), sulpirid and itopride (3.13%). The combination drugs causing DIP was also seen in 9.36%.

Conclusion : DIP is a preventable and treatable condition in many cases, therefore safer drugs should be prescribed and have to be identified early, respectively.

[J Indian Med Assoc 2023; 121(8): 41-5]

Key words : Parkinsonism, Tremors Drug Induced Rigidity.

Parkinsonism is a motor syndrome, characterized by tremor, rigidity, bradykinesia and postural instability, which was first described by James Parkinson in his essay entitled "The Shaking Palsy"¹.

Idiopathic Parkinson Disease (IPD) is the most common cause of Parkinsonism with a prevalence of 3.3% and 4.5% followed by Drug Induced Parkinson (DIP) which is 2.7 and 1.7% in community based and population based survey respectively and also IPD is age related and overall the second most common cause of degenerative disease of central nervous system after Alzheimer Disease (AD)²⁻⁴.

IPD is pathologically characterized by decrease dopamine level in basal ganglia and alpha-synuclein deposition, causing direct neurotoxicity in cell bodies

Editor's Comment :

- Drug Induced Parkinsonism (DIP) is a very important cause of reversible secondary parkinsonism.
- Proper drug history should be taken in all patients with recent onset parkinsonism.
- Early diagnosis and stopping of offending drug can prevent permanent neurological issues.

and axons, known as Lewy bodies and Lewy neuritis, collectively known as Lewy pathology⁵.

It usually present as asymmetrical form in age more than 60 years and more common in males (1.5 times as compared to females) in contrast to DIP, which is less asymmetrical, common in elderly and in females⁶.

Among all the secondary causes of Parkinsonism like- NPH, vascular parkinsonism, toxin induced parkinsonism, chronic traumatic encephalopathy, brain tumour, DIP is the most common cause. Drug-induced movement disorders were described in 1954 in patients who were treated with chlorpromazine and reserpine⁷. It is frequently induced by anti-psychotics (Typical>Atypical). Others include anti-emetic and prokinetic - metoclopramide, levosulpiride, calcium channel blocker (Verapamil, Diltiazem, flunarizine,

¹MBBS, MD, DM, MRCP, FRCP, FEBN, FIAMS, FIACM, FIMSA, MNAMS, Senior Consultant Neurologist and Director, Department of Neurology, Aarogyam Neuro Clinic, Durgapur, West Bengal 713214 and Corresponding Author

²DNB, Resident, Department of General Medicine, DSP Main Hospital, Durgapur, West Bengal 713203

Received on : 06/02/2023

Accepted on : 24/03/2023

cinnarizine), anti arrhythmics- amiodarone, mood stabilizers- lithium, anti epileptic-valproate.

The mechanism behind DIP is interference of nigrostriatal pathway by various drugs. The pharmacological effect of anti psychotic is seen by blocking of post synaptic D2 receptor by 60-70% and the features of Parkinsonism is seen when blockade is $\geq 75\%$, identified by PET⁸. There are some relativity related to this, for example, aripiprazole (atypical anti psychotic), have D2 receptor occupancy of $>95\%$, rarely cause DIP as it is weak agonistic action on dopamine receptors and interacts with 5-HT1A and 5-HT2A receptors^{9,10}. Some drugs also act on pre-synaptic receptor like tetrabenazine.

The important risk factor are, age (causes destruction of nigral cells), female gender (estrogen act as a causative hormone), genetic predisposition, drug dosage, potency and route of its administration¹¹⁻¹³.

Many a times, DIP is missed and misdiagnosed as PD, as they have many similar clinical features. Table 1 summarize the difference between DIP and IPD¹⁴:

Since, treatment of PD and DIP is different, early diagnosis, polypharmacy, and stopping of offending drug is necessary. Although, in 20-25% it is persistent and progressive^{15,16}.

The most common drug induced motility disorder is DIP followed by tremors, tardive dyskinesia, tardive dystonia, akathisia and myoclonus.

Table 1 — Difference between DIP and IPD		
	DIP	IPD
Onset	More often in elderly	60s
Symmetry of clinical features	Often symmetric	Asymmetric
Lower/upper body involvement	More severe in upper part	Both
Tremor	Variable	Variable
Depression	Common	Common
Dementia	May be present before onset of parkinsonism	Rare at onset
Response to treatment with L DOPA or dopamine agonists	Poor	Good
Response to drug withdrawal	Good	Poor
HVA level in CSF	High	Low/normal
PET/SPECT imaging	Normal uptake of pre-synaptic markers, reduced uptake of dopamine receptor ligands	Reduced uptake of pre-synaptic markers, normal uptake of dopamine receptor ligands

The (DSM-IV), defines DIP as the presence of resting tremor, muscular rigidity, akinesia, or bradykinesia, developing within a few weeks of starting or raising the dosage of a medication (typically a neuroleptic) or after reducing the dosage of an anti-parkinsonian agent¹⁷.

Many scales have been developed one of which includes Simpson- Angus Scale, which emphasis more on rigidity than on bradykinesia¹⁸.

AIMS AND OBJECTIVES

The objective of this study is to find the medications leading to DIP and its clinical pattern of neurological involvement

MATERIALS AND METHODS

This is a cross-sectional study of PD patients at the out patient department of a super speciality neurology clinic in Durgapur, West Bengal. This study was done from 1st January 2022 to 30th November, 2022 considering, the inclusion criteria for DIP. The patients were examined thoroughly by a single neurologist in their initial visit and diagnosed to have DIP. All patients related to this study had signed their informed consent. Ethical Committee clearance was taken from the local Ethics Committee. The identity of the subjects was not revealed during the study period.

Inclusion Criteria :

- (1) All patients satisfying more than equal to two of the four criterias of parkinsonism- bradykinesia, rigidity, tremor and postural instability.
- (2) Patients had no symptoms of parkinsonism before taking drug.
- (3) There is direct relation of drug intake and symptom onset.

Exclusion Criteria :

- (1) Other causes of secondary parkinsonism- NPH, vascular parkinsonism, brain tumor, toxin induced etc by appropriate investigations.
- (2) All other drug induced motility disorder without the features of parkinsonism.

The evaluation of offending medications causing symptoms along with age, sex and other demographic features of population were studied. The parkinsonism pattern including tremor, akinetic rigidity and mixed type was noted and stopped the offending drug and prescribed another drug to prevent primary disease worsening after consulting with respective specialist.

RESULTS

In the study period, there were 32 patients, who satisfied the Inclusion criteria. Out of which,

19(59.38%) were female and 13(40.63%) were male. The most common age group was ≥ 60 years (65.63%), followed by 51-60 years (15.63%) and the least common group were < 30 years and between age 41-50 years with equal percentage of 3.13. The mean age was 62.37 years with standard deviation of 13.09 years (Fig 1).

The most common pattern observed in our study was tremor (50%) followed by akinetic rigidity (34.38%) and mixed pattern (15.63%)(Fig 2). Tremor was equally distributed in both males and females while akinetic rigidity and mixed pattern type of Parkinsonism is more common in females. Orofacial dyskinesia along with bradykinesia was seen in (6.66%), rabbit syndrome was seen in (6.66%), head and jaw tremor were seen along with parkinsonian features in (6.66%). Parkinson plus syndrome features was seen in 6.66%.

The most common drug associated with DIP in our study was pro-kinetic drug levosulpiride (46.88%) followed by flunarizine (25%), valproate and haloperidol (6.25%), sulpitac and itopride (3.13%). The combination drugs causing DIP was seen in 9.39%.

During the initial visit, patients were diagnosed and stopped the offending drug and trihexyphenidyl was added in to all the patients with a dose from 2mg to 10mg, according to the severity of symptoms.

DISCUSSION

In our study, DIP is more common among age group of > 60 yrs, correlating with the fact that, age being the most consistent risk factor, as dopamine level decreases with age due to nigral cells degeneration¹⁹. Therefore, it is better to avoid polypharmacy and especially the drugs causing motility disorders in elderly. There should be high suspicion and they should be kept under close observation to detect DIP.

We also found that DIP is more common among female gender (59.37%), as oestrogen suppresses the dopamine receptor expression, as per the studies done previously²⁰. Many studies done earlier too showed that the genes involved in GABA receptor signalling in Genome wide screening, leads to Tardive dyskinesia in Schizophrenic patients and DIP^{21,22}. In our study we had 6.25% patients who were schizophrenic, showed tremor predominance parkinsonian features.

It was studied that rigidity and bradykinesia is predominant as compared to tremor and postural instability in DIP²³, but we found tremor to be most dominant pattern with 50% in our study then akinetic rigidity (34.37%), and the remaining were mixed (15.62%). Therefore, DIP is easily misdiagnosed as PD. DAT scan by PET/SPECT has been done in past

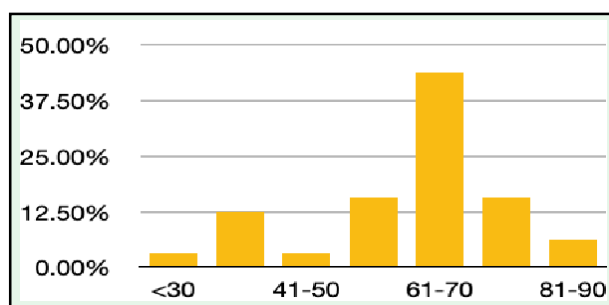


Fig 1 — Age distribution in our study

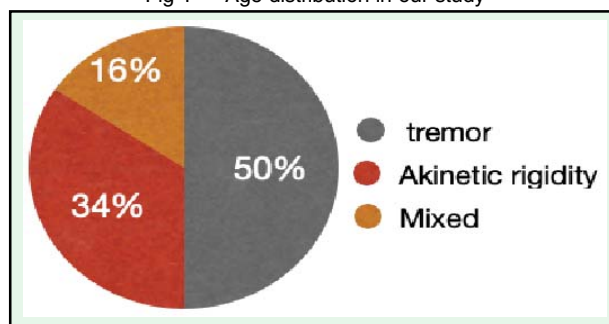


Fig 2 — Distribution of DIP pattern in our study

studies which differentiates between pre-synaptic parkinsonism and post synaptic parkinsonism. It showed decrease uptake in PD and normal uptake in DIP. But sometimes there is decrease uptake in DIP, due to the presence of unmasked PD. Thus, concluded that DIP is multifactorial origin²⁴.

Homovallenic Acid (HVA) level in CSF is another investigation done to differentiate DIP and IPD, which will be increased in DIP and decreased in IPD. The mechanism here is when a patient is treated with neuroleptics for long duration, there is compensatory increase in HVA for short duration, because of increase firing of dopaminergic neurons in response to blockade of dopamine receptor followed by development of tolerance and HVA level come to normal. But failure to come to normal or failure to develop tolerance leads to DIP and tardive dyskinesia^{25,26}.

In our study the most common medication leading to DIP was levosulpiride (46.87%). It is a newer emerging pro-kinetic, prescribed by many general physician, which acts on both CNS and gut by selective blocking of pre-synaptic D2 receptor²⁷. Out of the study population, rabbit syndrome was seen in 6.66% population, caused by levosulpiride. 13.33% having mixed predominant features, presented with orofacial dyskinesia along with bradykinesia and head and jaw tremor with equal percentage of 6.66%, more in female gender.

The second common drug in our study was

flunarizine (FNZ)(25%), for migraine prophylaxis, which is calcium channel antagonist.

Mitochondrial quality control is essential for normal function of a cell and its defect leads to parkinsonian features. As per the studies, chronic use of FNZ decrease mitochondrial numbers in neurone and astrocytes with or without affecting the nigrostriatal dopaminergic pathway. Also, FNZ inhibits complex 1 and 2 of electron transport chain system. Although the exact mechanism is still unclear²⁸⁻³¹.

Valproate (6.25%) as an anti-epileptic, act by blocking sodium, potassium and calcium channel in neuronal membrane. Therefore, its chronic use can cause physiological inactivation of neurons in basal ganglia and hence cause reversible parkinsonian features³².

There were also combination medicines caused Parkinsonian features in 9.36% population eg, Flunarizine and valproate in migraine prophylaxis caused DIP. Therefore, have to be used very cautiously. In a previous study haloperidol was associated with high risk of extra pyramidal system and clozapine was same as placebo³³. The following table summarizes the medicine leading to DIP in our study (Fig 3).

In our study, we did not find any correlation between the medications patients were taking for their comorbidities like anti-hypertensive, oral hypoglycaemic drugs, statins.

The treatment of DIP is to differentiate DIP and IPD, stopping the offending drugs, and change to other safer medication like atypical anti-psychotics in Psychiatric patients like Schizophrenia.

Anticholinergics like trihexyphenidyl, benztropine, amantadine, and levodopa have been tested for their ability to relieve symptoms but has not produced any clear evidence of their effects in DIP patients.^[34,35]

Limitations : Limitation of our study was that patient was only seen thoroughly in their first visit, they were not followed up.

CONCLUSION

DIP can present in varied manifestations, so high suspicion along with early diagnosis and treatment is must.

Financial Support : Nil

Conflict of Interest : There is no conflict of interest.

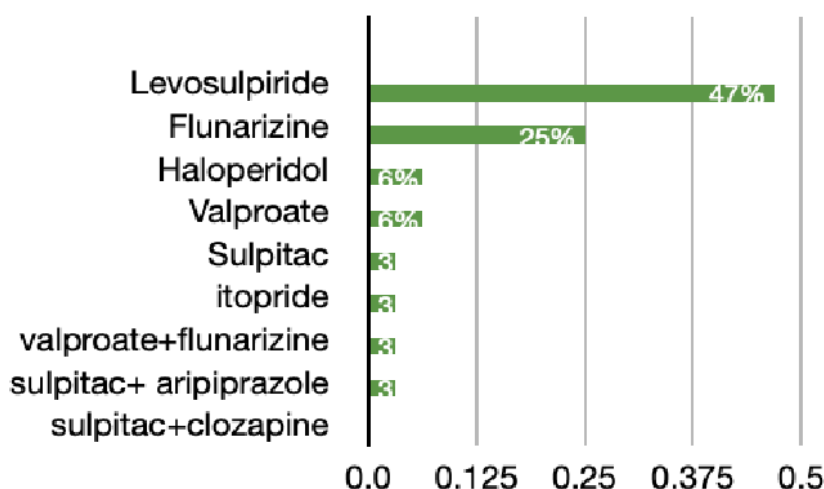


Fig 3 — Drugs causing DIP

REFERENCES

- Keener AM, Bordelon YM — Parkinsonism. *Semin Neurol* 2016; **36(4)**: 330-4.
- Barbosa MT, Caramelli P, Maia DP, Cunningham MC, Guerra HL, Lima-Costa MF, *et al* — Parkinsonism and Parkinson's disease in the elderly: a community-based survey in Brazil (the Bambuí study). *Mov Disord* 2006; **21**: 800-8.
- Benito-León J, Bermejo-Pareja F, Rodríguez J, Molina JA, Gabriel R, Morales JM — Neurological Disorders in Central Spain (NEDICES) Study Group. Prevalence of PD and other types of parkinsonism in three elderly populations of central Spain. *Mov Disord* 2003; **18**: 267-74
- Troiano AR, Germiniani FM, Werneck LC — Flunarizine, cinnarizine-induced parkinsonism: A historical and clinical analysis. *Parkinsonism Relat Disord* 2004; **10**: 243-5.
- Pacheco CR, Morales CN, Ramírez AE — Extracellular α -synuclein alters synaptic transmission in brain neurons by perforating the neuronal plasma membrane. *J Neurochem* 2015; **132**: 731-41.
- Benito-León J, Bermejo-Pareja F, Rodríguez J, Molina JA, Gabriel R, Morales JM — Neurological Disorders in Central Spain (NEDICES) Study Group. Prevalence of PD and other types of parkinsonism in three elderly populations of central Spain. *Mov Disord* 2003; **18**: 267-74.
- Steck H — [Extrapyramidal and diencephalic syndrome in the course of lergactil and serpasil treatments.] [article in French]. *Ann Med Psychol (Paris)* 1954; **112**: 737-44.
- Remington G, Mamo D, Labelle A *et al.*: A PET study evaluating dopamine D2 receptor occupancy for long-acting injectable risperidone. *Am J Psychiatry* 2006; **163(3)**: 396-401.
- Grunder G, Carlsson A, Wong DF — Mechanism of new antipsychotic medications: occupancy is not just antagonism. *Arch Gen Psychiatry* 2003; **60(10)**: 974-977.
- Sharma A, Sorrell JH — Aripiprazole-induced parkinsonism. *Int Clin Psychopharmacol* 2006; **21(2)**: 127-9.
- Rollema H, Skolnik M, D'Engelbronner J — MPP(+)-like neurotoxicity of a pyridinium metabolite derived from

- haloperidol: in vivomicrodialysis and in vitro mitochondrial studies. *Pharmacol Exp Ther* 1994; **268(1)**: 380-7.
- 12 Mena MA, Garcia de Yébenes MJ, Taberner C, et al. Effects of calcium antagonists on the dopamine system. *Clin Neuropharmacol* 1995; **18(5)**: 410-26.
- 13 Richardson MA, Haugland G, Craig TJ — Neuroleptic use, parkinsonian symptoms, tardive dyskinesia, and associated factors in child and adolescent psychiatric patients. *Am J Psychiatry* 1991; **148(10)**: 1322-8.
- 14 Maria A Mena, Justo G de Yébenes — Drug-induced parkinsonism, Expert Opinion on Drug Safety 2006; **56**: 759-71.
- 15 Llau ME, Nguyen L, Senard JM, Rascol O, Montastruc JL — Drug-induced parkinsonian syndromes: a 10-year experience at a regional center of pharmaco-vigilance. *Rev Neurol (Paris)* 1994; **150(11)**: 757-62.
- 16 MartiMasso JF, Poza JJ — Drug-induced or aggravated parkinsonism: clinical signs and the changing pattern of implicated drugs. *Neurologia* 1996; **11(1)**: 10-5.
- 17 American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. Fifth ed. Arlington, VA: American Psychiatric Association; 2013.
- 18 Simpson GM, Angus JW — A rating scale for extrapyramidal side effects. *Acta Psychiatr Scand Suppl* 1970; **212**: 11-9.
- 19 Jabs BE, Bartsch AJ, Pfuhlmann B — Susceptibility to neuroleptic-induced parkinsonism-age and increased substantia nigra echogenicity as putative risk factors. *Eur Psychiatry* 2003; **18(4)**: 177-81.
- 20 Bedard P, Langelier P, Villeneuve A — Oestrogens and extrapyramidal system. *Lancet* 1977; **2**: 1367-8. [PubMed] [Google Scholar]
- 21 Metzger WS, Newton JE, Steele RW, Claybrook M, Paige SR, McMillan DE, et al — HLA antigens in drug-induced parkinsonism. *Mov Disord* 1989; **4(2)**: 121-8. PMID: 2567491 DOI: 10.1002/mds.870040203
- 22 Liou YJ, Wang YC, Chen JY, Bai YM, Lin CC, Liao DL, et al — Association analysis of polymorphisms in the N-methyl-D-aspartate (NMDA) receptor subunit 2B (GRIN2B) gene and tardive dyskinesia in schizophrenia. *Psychiatry Res* 2007; **153**: 271-5.
- 23 Hardie RJ, Lees AJ — Neuroleptic-induced Parkinson's syndrome: clinical features and results of treatment with levodopa. *J NeurolNeurosurg Psychiatry* 1988; **51**: 850-4.
- 24 Lorberboym M, Treves TA, Melamed E — [123I]-FP/CIT SPECT imaging for distinguishing drug-induced parkinsonism from Parkinson's disease. *Mov Disord* 2006; **21(4)**: 510-4.
- 25 Saito T, Ishizawa H, Tsuchiya F, Ozawa H, Takahata N — Neurochemical findings in the cerebrospinal fluid of schizophrenic patients with tardive dyskinesia and neuroleptic-induced parkinsonism. *Jpn J Psychiatry Neurol* 1986; **40(2)**: 189-94.
- 26 Bowers MB Jr, Heninger GR — Cerebrospinal fluid homovanillic acid patterns during neuroleptic treatment. *Psychiatry Res* 1981; **4(3)**: 285-90.
- 27 Serra J — Levosulpiride in the management of functional dyspepsia and delayed gastric emptying. *Gastroenterol Hepatol* 2010; **33**: 586-90. [PubMed] [Google Scholar] [Ref list]
- 28 Goldman SJ, Taylor R, Zhang Y, Jin S — Autophagy and the degradation of mitochondria. *Mitochondrion* 2010; **10**: 309-15.
- 29 Lin MT, Beal MF — Mitochondrial dysfunction and oxidative stress in neurodegenerative diseases. *Nature* 2006; **443**: 787-95.
- 30 Brucke T, Wober C, Podreka I, Wober-Bingol C, Asenbaum S, Aull S, et al — Harasko-van der Meer, P. Wessely, L. Deecke, D2 Receptor blockade by flunarizine and cinnarizine explains extrapyramidal side Effects. ASPECT study. *Blood Flow Metab* 1995; **15**: 5138.
- 31 Veitch K, Hue L — Flunarizine and cinnarizine inhibit mitochondrial complexes I and II: Possible implication for parkinsonism. *Mol Pharmacol* 1994; **45**: 158-63.
- 32 Ogungbenro K, Aarons L — A physiologically based pharmacokinetic model for valproic acid in adults and children. *Eur J Pharm Sci* 2014.
- 33 José López-Sendón, Maria A Mena, Justo G de Yébenes — Drug-induced parkinsonism, Expert Opinion on Drug Safety 2013; **12**: 4, 487-496. 63: 45-52. 10.1016/j.ejps.2014.06.023
- 34 Hardie RJ, Lees AJ — Neuroleptic-induced Parkinson's syndrome: clinical features and results of treatment with levodopa. *J NeurolNeurosurg Psychiatry* 1988; **51**: 850-54.
- 35 Fann WE, Lake CR — Amantadine versus trihexyphenidyl in the treatment of neuroleptic-induced parkinsonism. *Am J Psychiatry* 1976; **133**: 940-3.

Submit Article in JIMA — Online

See website : [https:// onlinejima.com](https://onlinejima.com)

Any queries : (033) 2237-8092, +919477493027; +919477493033

Original Article

Feasibility of WHO Recommended 3 visit fractional dose Intra-dermal Rabies Vaccine Regimen (IPC) and only Wound Infiltration of RIG in Rabies Post Exposure Prophylaxis to 1,84,955 Patients — Evidence from India

Omesh Kumar Bharti¹

Background : In 2018, WHO recommended a 3 visit IPC regimen replacing 4 visit TRC regimen after due consultations and the field evidence but many countries are reluctant to follow this new IPC vaccine regimen thinking it to be risky and also practical difficulty of ID vaccine administration.

Method : We at our clinic in DDU Hospital, Shimla had started Pooling Strategy for sharing of Rabies Vaccine vials to optimize costs to patients since 2008. Later, only wound infiltration of eRIG was started since June 2014 owing to non-availability of RIG. Authors got brain samples of local freshly dead animals tested for FAT and found all of them to be positive including that of wildlife apart from getting serum samples of 30 patients for RFFIT after 3 ID injections. All patients were having titers ranging from 4.5 IU/ml- 30 IU/ml on day 14.

Results: Since May 29, 2018 we have followed new WHO guidelines and in four years time, we have vaccinated 184, 955 patients with IPC regimen in state of HP, India with only one confirmed failure of PEP reported due to injury to facial nerve of a girl child near Shimla.

Conclusion: IPC regimen is dose and cost sparing and equally effective to save lives of even those patients bitten by rabid dogs however additional local wound infiltration of RIG is must when indicated in lacerated wounds. Pooling Strategy is the most cost effective way to administer fractional doses of Rabies Vaccine and RIG free of cost to all and to achieve the objective of zero rabies by 2030.

[J Indian Med Assoc 2023; 121(8): 46-8]

Key words : IPC regimen, Pooling Strategy, Rabies Prophylaxis, Rabies, Free PEP.

Rabies is a viral zoonotic disease responsible for an estimated 59,000 human deaths and over 3.7 million Disability-Adjusted Life Years (DALYs) lost every year¹. Most cases occur in Africa and Asia, with approximately 40% of cases in children aged <15 years. Dogs are the most important reservoir for rabies viruses and dog bites account for >99% of human cases². Rabies can be prevented if timely prophylaxis is given to the bite victims in the form of rabies vaccine and Rabies Immunoglobulin (RIG) injection into the bite wounds³. One of the reasons for non-compliance to seek rabies Post Exposure Prophylaxis (PEP) after bite is its high cost. Recently two low cost solutions have been proposed by the new WHO guidelines 2018. Intradermal administration of rabies vaccine on days 0,3 and 7 (IPC Regimen) and only wound infiltration of RIG (Himachal Method). Both these strategies require sharing of vials and for that we at Anti Rabies Clinic & Research Centre (ARCRC) at DDU Hospital Shimla, started first pooling Centre in 2008 so that vials of vaccine and later that of RIG can be shared.

Editor's Comment :

- Pooling Strategy is the most cost effective way to administer fractional doses of rabies vaccine and RIG free of cost to all and to achieve the objective of zero rabies by 2030.

MATERIALS AND METHODS

We started this pooling strategy in 2008, when there was scarcity of Rabies vaccine in Himachal Pradesh in specific and in India in general. We thought of an idea of pooling the patients to optimize the vaccine use⁴. All nearby health centers in Shimla city were asked to send animal bite patients to a centralized place to DDU Hospital in Shimla, called "Pooling Centre" for vaccination after wound wash and first aid. Each patient was asked to purchase one vial of Rabies vaccine while coming for first dose of vaccine and rest we would give "FREE". Actually it was not free, we used to divide one vial among four patients by Intradermal (ID) vaccination and keep rest 3 vials of vaccine in the fridge, pull out next vial on subsequent visits and share among four and so on till the completion of 4 visit PEP. Later, author started to look for alternatives to make RIG also affordable to poor and developed a protocol of only wound infiltration of RIG for poor in 2013. While we were in the process of implementing this new protocol of only wound

¹MBBS, DHM, MAE (Epidemiology), State Epidemiologist and State Master Trainer IDRV, HP, India, State Institute of Health & Family Welfare, Kasumpti 171009 and Corresponding Author

Received on : 08/06/2022

Accepted on : 24/04/2023

infiltration among poor patients by sharing of RIG vials on the analogy of sharing of Rabies Vaccine in our pooling centers and took ethical clearance for the same, the RIG was out of stock not only in our state but throughout of Himachal Pradesh in 2014. We contacted CRI Kasauli, a Government owned manufacturer of eRIG to supply few vials of eRIG for at risk patients to save their lives. After due IEC approval, we now started to inject only wound/s of not only poor but everyone as RIG was not available in the market. These pooling centers came handy for sharing of RIG vials as now one vial of eRIG was being shared among 10-20 patients depending on the size and depth of the wound/s³ left out eRIG was used next day. With sharing of vaccine and RIG vials⁵ the total cost of PEP came down to just few dollars⁶ that lead our Government to give complete PEP including eRIG free to all since May 2018 in Himachal Pradesh.

RESULTS

Cost of USD 35 for 6 Intramuscular (IM) injections then came down to USD 6 for four visit ID vaccinations following TRC regimen. The patient load increased to 2.8 times and poor patient load increased to 3.2 times⁷. All these patients sought rabies vaccination for PEP after paying for only one vial of Rabies Vaccine rest of doses were shared by pooling. Patients from faraway places used to attend the clinic for cheaper prophylaxis as ours was the first clinic to start intradermal vaccination by adopting pooling strategy for the benefit of patients in the state of Himachal Pradesh and India. Later due to very small cost involved, the health authorities declared rabies vaccination free to all in the state of Himachal Pradesh. Now more than 90 "Pooling Centers" are operational in the state of Himachal Pradesh, some of them in land locked areas, where trained staff gives PEP by using intradermal strategy. Earlier four visit bilateral intradermal injections used to be given but now after WHO recommended three visit IPC schedule, only three visit bilateral intradermal Rabies Vaccination is administered as 2-2-2 schedule that have saved hundreds of vaccine vials for wider use saving costs of the Government and money of thousands of patients for visiting the clinic for the fourth dose. Further cost saving was done by omitting Rabies Vaccination to those who had consumed raw milk of a rabid cow or buffalo as per latest recommendation of WHO to not to give vaccination to those people having consumed raw milk of rabid cow or Buffalo. This saved large number of vaccine vials for PEP as vaccine remains in scarcity all over (Table 1).

Over a four years time, 184,955 PEP were given that have now exceeded 200,000 PEP mark by May

Table 1 — Dog Bite PEP using 3 visit IPC in Himachal Pradesh, India (Does not include PEP administered due to bites of other animals like Monkeys, Mongoose, Languor and Cats etc)

Year	Dog Bite PEP	Deaths due to suspected/Confirmed Rabies
2018	34279	1
2019	36227	4 (1 lab confirmed)
2020	48543	2
2021	65906	3 (1 lab confirmed)
Total	184,955	10

2022. Out of more than 184,955 PEP administered for dog bites in Himachal Pradesh with 3 visit 2 ID dose IPC regimen and only wound infiltration of eRIG there has been no confirmed PEP failure except in a girl child who was bitten on her face and her facial nerve was torn by the rabid dog⁸.

For 48,543 PEPs administered in 2020 in the state of Himachal Pradesh (HP) vaccine vials (0.5 ml) used were 50,114 and eRIG vials(5ml) used were 23,133 indicating cost saving potential of Pooling Strategy adopted at 90 pooling centers of HP.

DISCUSSION

While we were excited to have implemented this "Pooling Strategy" in the state leading to free distribution of the Rabies Vaccine to patients, mostly poor, we were worried about few reports of some of the patients dying despite Rabies Vaccination as rabies immunoglobulins were either scarce or not available at all. Human RIG (HRIG) was costing about USD 500 and equine RIG (eRIG) about USD⁹. Doctors would not prescribe eRIG for fear of anaphylaxis reaction and HRIG if prescribed, was not within the reach of majority of patients, so they would not purchase it and remain satisfied after taking Rabies Vaccine leading to some deaths due to rabies. This lead us to think of only wound infiltration of eRIG that proved to be successful in bringing cost down and save lives. We also provide/ advise Pre-Exposure Prophylaxis to people who come to our clinic to seek advice about it having a pet dog at home or having lots of stray dogs roaming around their locality and likely to be bitten by them. Equally high numbers of patients availing PEP at pooling centers are those bitten by monkeys as monkeys have been found to be rabid in Himachal along with other wildlife animals⁹ including Mongoose¹⁰ and squirrel¹¹. An Estimated 20 million people who receive PEP each year¹² and 60% of them require RIG as per data of our clinic having type-III wounds. Our method of only wound infiltration^{3,5,6} can help reduce costs¹³ by 60 % from 120 Million USD to 10 Million USD per year globally a saving of 110 Million USA annually considering Current eRIG costs @ \$5per 5 ml vial.

CONCLUSIONS

The evidence of successful PEP among thousands of patients proved without doubt that 3 visit IPC regimen recommended by WHO along with only wound infiltration of eRIG is life saving and giving rest of RIG into muscle as IM is not of any benefit. WHO recommended only wound infiltration of RIG except in rare circumstances where wound is not available for infiltration e.g. aerosol exposure etc. RIG is in limited supply world over and only wound infiltration would not only save costs^{14,15} but also spare up to 60% of RIG volume for India¹⁶ and other countries where RIG is not available¹⁷.

With such a low cost for eRIG due to only wound infiltration, the Himachal Government made total Rabies PEP free to all in 2018 that has enabled us to reach almost zero death due to Rabies in Himachal Pradesh. With free PEP to all the total PEP has gone up 4-5 times in the state of Himachal and yearly deaths due to Rabies have come down from about 35 in 2005¹⁸ to almost zero now (Table 1) mostly for not availing free PEP. The Himachal Model needs to be implemented in other states of India and other countries need to adapt to this new Pooling Strategy of Himachal to achieve the WHO goal of Human Rabies free world by 2030. Therefore, adopting pooling strategy globally to administer fractional doses of Rabies vaccine and RIG free of cost to all by sharing vials can help us achieve zero by 30 fast and with minimum cost, saving thousands of lives annually and sparing costly rabies biologicals for wider patient use.

Funding : Self-funded.

Conflict of Interest : None.

REFERENCES

- Hampson K, Coudeville L, Lembo T, Sambo M, Kieffer A, et al — Correction: Estimating the Global Burden of Endemic Canine Rabies. *PLOS Neglected Tropical Diseases* 2015; **9(5)**: e0003786; <https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0003709>
- Fooks A, Cliquet F, Finke S — Rabies. *Nat Rev Dis Primers* 3, 17091 (2017). <https://doi.org/10.1038/nrdp.2017.91>; <https://www.nature.com/articles/nrdp201791#rightslink>
- Bharti OK, Madhusudana SN, Gaunta PL, Belludi AY — Local infiltration of rabies immunoglobulins without systemic intramuscular administration: An alternative cost effective approach for passive immunization against rabies. *Hum Vaccin Immunother* 2016; **12(3)**: 837-42. doi:10.1080/21645515.2015.1085142
- Bharti O, Damme W, Decoster K, Isaakidis P — Breaking the Barriers to Access a Low Cost Intra-Dermal Rabies Vaccine Through Innovative "Pooling Strategy", *World Journal of Vaccines* 2012; **2(3)**: 121-4. doi: 10.4236/wjv.2012.23016. <https://www.scirp.org/journal/paperinformation.aspx?paperid=21524>
- Bharti OK, Madhusudana SN, Wilde H — Injecting Rabies Immunoglobulin (RIG) into wounds only: a significant saving of lives and costly RIG. *Hum Vaccin Immunother* 2017; **13(4)**: 762-5. <https://pubmed.ncbi.nlm.nih.gov/28277089/>
- Bharti OK, Thakur B, Rao R — Wound-only injection of rabies immunoglobulin (RIG) saves lives and costs less than a dollar per patient by "pooling strategy". *Vaccine* 2019; **37 Suppl 1**: A128-A131. <https://www.sciencedirect.com/science/article/pii/S0264410X19310084?via%3Dihub>
- Bharti O, Damme W, Decoster K, Isaakidis P — Breaking the Barriers to Access a Low Cost Intra-Dermal Rabies Vaccine Through Innovative "Pooling Strategy", *World Journal of Vaccines* 2012; **2(3)**: 121-4. doi: 10.4236/wjv.2012.23016.
- Bharti OK, Tekta D, Shandil A — Failure of postexposure prophylaxis in a girl child attacked by rabid dog severing her facial nerve causing possible direct entry of rabies virus into the facial nerve. *Human vaccines & Immunotherapeutics* 2019; **15(11)**: 2612-4. <https://doi.org/10.1080/21645515.2019.1608131>
- Bharti OK — Human rabies in monkey (*Macacamulatta*) bite patients a reality in India now!, *Journal of Travel Medicine* 2016; **23(4)**: taw028, <https://doi.org/10.1093/jtm/taw028>
- Bharti OK, Sharma UK, Kumar A, Phull A- Exploring the Feasibility of a New Low Cost Intra-Dermal Pre & Post Exposure Rabies Prophylaxis Protocol in Domestic Bovine in Jawali Veterinary Hospital, District Kangra, Himachal Pradesh, India. *World Journal of Vaccines* 2018; **8**: 8-20. <https://www.scirp.org/journal/paperinformation.aspx?paperid=82278>
- Bharti OK — Rabies in Squirrel and other wild animals, *APCRI Journal*; Volume XXII, Issue I, June 2020. https://www.researchgate.net/publication/344295752_RABIES_IN_SQUIRREL_AND_OTHER_WILD_ANIMALS
- WHO Technical Report Series No. 1012, 2018; <https://apps.who.int/iris/bitstream/handle/10665/272364/9789241210218-eng.pdf>
- Request for Reinstatement of Equine Rabies Immune Globulin to the EML and EMLc; available from; https://cdn.who.int/media/docs/default-source/essential-medicines/2021-eml-expert-committee/applications-for-addition-of-new-medicines/a.12_equine-rabies-ig.pdf?sfvrsn=772b7a5d_6; accessed on June 9, 2022
- Suijkerbuijk AW, Mangen MJ, Haverkate MR — Rabies vaccination strategies in the Netherlands in 2018: a cost evaluation. *Euro Surveill* 2020; **25(38)**: 1900716. doi:10.2807/1560-7917.ES.2020.25.38.1900716. <https://pubmed.ncbi.nlm.nih.gov/32975187/>
- Worathitanan B, Chockchalermwong S, Reongkhumkian S — Economic impact of revised rabies immunoglobulin administration protocol 2018 in the Emergency Department, NakhonPathom Hospital. *Dis Control J [Internet]* 2019; **45(3)**: 293-04. Available from: <https://he01.tci-thaijo.org/index.php/DCJ/article/view/174399>
- Sudarshan MK, AshwathNarayana DH, Jayakrishnappa MB — Market mapping and landscape analysis of human rabies biologicals in India. *Indian J Public Health* 2019; **63(Supplement)**: S37-S43. doi: 10.4103/ijph.IJPH_379_19. PMID: 31603090. <https://pubmed.ncbi.nlm.nih.gov/31603090/>
- Sreenivasan N, Li A, Shiferaw M, Tran CH, Wallace R — Working group on Rabies PEP logistics. Overview of rabies post-exposure prophylaxis access, procurement and distribution in selected countries in Asia and Africa, 2017-2018. *Vaccine* 2019; **37Suppl 1**: A6-A13. doi: 10.1016/j.vaccine.2019.04.024. Epub 2019 Aug 27. PMID: 31471150. <https://pubmed.ncbi.nlm.nih.gov/31471150/>
- Suraweera W, Morris SK, Kumar R — Deaths from symptomatically identifiable furious rabies in India: a nationally representative mortality survey. *PLoS Negl Trop Dis* 2012; **6(10)**: e1847. doi:10.1371/journal.pntd.0001847.

Original Article

Clinico-mycological Profile of Dermatophytoses in a Tertiary Care Hospital in Kolkata : A Cross Sectional Study

Subhendu Sikdar¹, Suranjan Pal², Reena Ray (Ghosh)³, Anindita Ballav⁴, Mitali Chatterjee⁵

Background : Dermatophytosis is a superficial fungal infection and a major public health problem in India. It is more prevalent due to favourable climatic conditions in India along with poverty, poor hygiene and overcrowding.

Aim and Objectives : The aim of this study is to evaluate clinical, epidemiological and mycological profile of Dermatophytosis from patients attending a tertiary care centre in Kolkata, India.

Materials and Methods : A cross sectional study was conducted in 1248 clinically diagnosed patients of Dermatophytosis attending the dermatology OPD of our hospital. Skin scrapings, nail clippings and plucked hair were taken as samples depending on the site of involvement. A thorough history was taken. Mycological examinations were done from all samples collected, with direct microscopy and culture on appropriate culture media as per standard laboratory protocol. Growths were macroscopically detected by colony characteristics and microscopically from LPCB mounting and slide culture method.

Results : Out of total 1248 clinically suspected cases of Dermatophytosis, male (53.93%) outnumbered than females (46.07%). The commonest age group affected was 21-40 years (48.96%). Regarding occupation, it was commonest among daily labour (28.85%) followed by housewives (22.04%). According to Modified B G Prasad Scale, maximum number of patients belongs to class IV socio-Economic class (53.69%). Sharing of footwear (69.95%) and towel (69.31%) was the commonest and significant risk factors. *T corporis* was the commonest (56.78%) clinical presentation. Growths of Dermatophytes were seen in 674 (69.62%) cases. Among these, *Trichophyton rubrum* was commonest (21.96%) followed by *Microsporum audouinii* (18.55%).

Conclusion : This study focused on the variations in Dermatophytosis presentation and the species involved and found that *Trichophyton rubrum* was the most common affecting the present population.

[J Indian Med Assoc 2023; 121(8): 49-53]

Key words : Dermatophytosis, Risk factors, *Tinea corporis*, *Trichophyton*, *Dermatophytes*.

Dermatophytosis, a type of superficial fungal infection comprises a group of disease involving skin, hair & nail. High heat and humidity along with other socio economic conditions make these tropical and subtropical countries including India more favourable¹. Keratinized tissues are affected most commonly by it and it is spread by direct contact from infected human beings (anthrophilic organisms),

Editor's Comment :

- Increasing trend of Dermatophytosis especially recalcitrant variety makes its treatment a headache for clinicians now a day imposing great economic challenge for the developing countries. So, it is the need of the hour to understand the epidemiological as well as microbiological profiles of Dermatophytes along with its antifungal resistance pattern, before initiation of the treatment.

¹MD (Microbiology), Assistant Professor, Department of Microbiology, RG Kar Medical College & Hospital, Kolkata 700004

²MD (Microbiology), Assistant Professor, Department of Microbiology, Raiganj Government Medical College & Hospital, Raiganj, West Bengal 733134

³MD, PhD (Microbiology), Professor and Head, Department of Microbiology, Diamond Harbour Government Medical College, Diamond Harbour, West Bengal 743331 and Corresponding Author

⁴MD (Microbiology), Senior Resident, Department of Microbiology, College of Medicine & Sagore Dutta Hospital, Kolkata 700058

⁵MD (Microbiology), Professor, Department of Microbiology, ICARE Institute of Medical Science and Research, Haldia, West Bengal 721645

Received on : 29/07/2022

Accepted on : 05/02/2023

animals (zoophilic organisms), and soil (geophilic organisms) and from fomites². Although the clinical signs of Dermatophytosis may vary depending on the affected region of the body, intense itching along with cosmetically poor appearance are common symptoms in humans³. The infection is not invasive usually and easy to cure, but its widespread nature and cost of the long term treatment is a major public health problem causing colossal damage to the economic status of the developing countries like India⁴. Our work was framed to study the clinical, epidemiological and mycological profile of Dermatophytosis from patients attending the Dermatology outpatient unit in a tertiary care centre in Kolkata, India.

MATERIALS AND METHODS

Collection of Specimens :

This is a cross-sectional and observational study over a period of two years from January 2018 to December 2019 conducted in the Department of Microbiology at RG Kar Medical College & Hospital, Kolkata in West Bengal. A total of 1248 clinically suspected patients of Dermatophytosis from Outpatient Department of Dermatology, were sent to Mycology Unit, Department of Microbiology.

Clinical History :

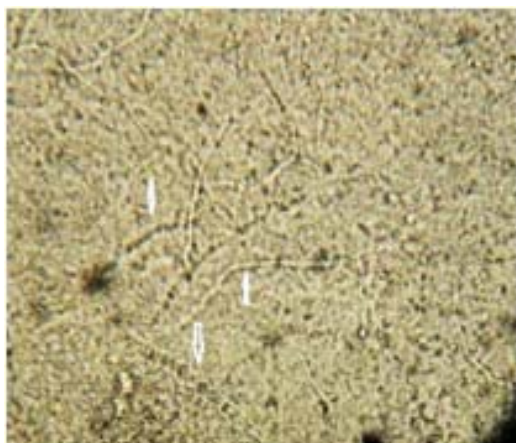
A detailed history of selected cases was taken in relation to name, age, sex, address, occupation, socio-economic status, risk factors associated and site of lesions.

Sample Collection :

Before collection of sample, 70% alcohol is used for cleaning the infected area. Then the samples were collected by scrapping the skin, clipping the nail or plucking the hair with the help of a sterile scalpel or forceps. Samples were collected in a sterile cellophane paper or container and transferred to the laboratory for further analysis³.

Direct Microscopy :

Skin scrapings and hair were mounted in freshly prepared 10% KOH and observed under 400x magnifications for fungal elements. 40% KOH was used for nail clippings⁵.



KOH mount of skin scraping showing fungal hyphae

Culture :

Specimens were inoculated simultaneously onto Sabouraud dextrose agar with chloramphenicol (0.05mg/ml) and cyclohexamide (0.5mg/ml). Specimens were inoculated on DTM slopes also. The tubes were incubated at room temperature and at 28°C in BOD incubator and checked for fungal growth at

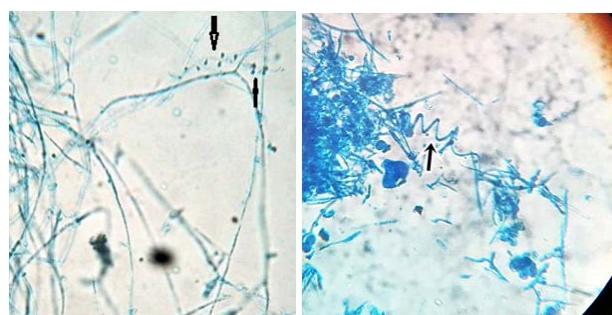
regular interval. Any visible growth on SDCA or SDCCA or DTM was examined for colony texture, morphology, pigmentation on obverse and reverse⁶.

Identification of Species :

Lacto-Phenol Cotton Blue (LPCB) mount was done for microscopic examination to examine the structure of hyphae, various vegetative and reproductive structures. Urea hydrolysis was also done⁶.

Growths of Non dermatophytic moulds were also identified by LPCB mounting morphologically.

Yeasts were identified by putting on germ tube tests, Dalmau on corn meal agar, sugar fermentation and assimilation tests.



LPCB mount showing tear drop micro conidia of *T. Rubrum* and spiral hyphae of *T. Mentagrophyte*

Slide Culture Technique :

All the isolates for which the morphology was not clear in LPCB were subjected to slide culture technique. The slide culture technique permits the microscopic observation of the undisturbed relationship of spores to hyphae⁶.

All culture media, reagents and chemicals were obtained from HI MEDIA Private Limited, Mumbai, India. All statistical analysis was done using Chi-square test. The software used for the statistical analysis was Graph Pad Prism 7.

RESULTS

A total of 1248 clinically suspected cases of Dermatophytosis were analysed in this study.

Age & Sex Distribution :

The study group comprised of 673 (53.93%) males and 575 (46.07%) females (Fig 1). Male outnumbered female with a ratio of 1.17:1. The commonest age group affected was 21-40 years (48.96%) followed by 41-60 years (32.05%) (Table 1).

Occupation and Socio-Economic Status :

Regarding occupation, it was commonest among daily labour (28.85%) followed by housewives (22.04%), farmers (18.59%) and students (10.98%). According to Modified BG Prasad Scale, maximum number of

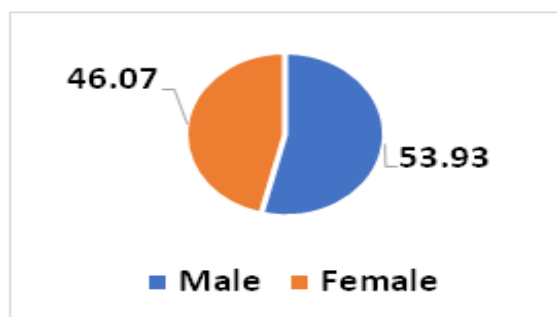


Fig 1 — Sex wise distribution

Age	Cases	%
0-20 years	181	14.50
21-40 years	611	48.96
41-60 years	400	32.05
>60 years	56	4.49
Total	1248	100

patients belongs to class IV Socio-economic class (53.69%) followed by class III (22.44%)(Table 2).

Risk Factors Analysis :

Various risk factors of Dermatophytosis were analysed thoroughly (Table 3). From this table, it was found that sharing of footwear (69.95%) and towel (69.31%) was the commonest and significant factors associated with this disease, followed by application of steroids (53.29%) and using tight clothes (51.28%).

Mycological Isolates :

Out of total 1248 cases of clinically suspected cases of Dermatophytosis, 968 (77.56%) cases were positive in culture. 280 (22.44%) cases were culture negative.

Out of 968 isolates, growth of dermatophytes was

Social Class	Cases	(%)
Class I	10	0.80
Class II	244	19.55
Class III	280	22.44
Class IV	670	53.69
Class V	44	3.53
Total	1248	100

Risk factors	Cases (%)	p value
Seasonal Exacerbation	432 (34.62)	0.4539
Family history +ve	192 (15.38)	0.8753
Skipping daily bath	356 (28.33)	0.2354
Not changing undergarments daily	459 (36.78)	0.1526
Using tight clothes	640 (51.28)	0.0001
Sharing of clothes	224 (17.95)	0.5913
Sharing of towels	865 (69.31)	0.0001
Sharing of footwear	873 (69.95)	0.0001
Application of Corticosteroid	665 (53.29)	0.0001

observed in 674 (69.62%) cases, whereas 178 (18.39%) were *Candida*, 76 (7.85%) were Non dermatophytic moulds and 40 (4.13%) were *Malassezia spp* (Tables 4 & 5).

Clinical Presentation :

Regarding clinical presentation of the lesions, *T corporis* was the commonest (44.39%) followed by *T cruris* (12.98%) and *T unguium* (9.70%) (Table 6).

Fungal Staining :

Out of total 1248 samples, 1103 (88.38%) were positive in KOH (Table 7).

Species of Dermatophytes :

Out of total 1248 samples, 280 (22.44%) cases were culture negative. Growths of Dermatophytes were seen in 674 (69.62%) cases. Among these, *Trichophyton rubrum* was commonest (21.96%) followed by *Microsporum audouinii* (18.55%)(Fig 2).

Isolates	Number	%
Dermatophytes	674	69.62
<i>Candida</i>	178	18.39
Non dermatophytic moulds	76	7.85
<i>Malasseziaspp</i>	40	4.13

<i>Candida</i>	No	%
<i>C. albicans</i>	68	38.20
<i>C. tropicalis</i>	41	23.03
<i>C. guilliermondii</i>	35	19.66
<i>C. parapsilosis</i>	34	19.10

Non Dermatophytic Moulds	No	%
<i>Aspergillus</i>	21	27.63
<i>Fusarium</i>	29	38.15
<i>Curvularia</i>	15	19.74
<i>Penicillium</i>	7	9.21
<i>Scopulariopsis</i>	4	5.26

Clinical presentation	No	%
<i>T. corporis</i>	554	44.39
<i>T. cruris</i>	162	12.98
<i>T. unguium</i>	121	9.70
<i>T. manuum</i>	26	2.08
<i>T. pedis</i>	22	1.76
<i>T. capitis</i>	65	5.21
<i>T. faciei</i>	18	1.44
<i>T. barbae</i>	11	0.88
Intertrigo	214	17.15
<i>Pityriasis versicolor</i>	55	4.40

Culture	KOH +ve	KOH -ve	Total
+ve	943	25	968
-ve	160	120	280
Total	1103	145	1248

DISCUSSION

The rapidly evolving Dermatophytosis since the last decade reflects the changes in behaviour, life style, Socio-economic conditions and migration. The higher incidence in tropical countries like India may be due to favourable environmental as well as Socio-economic conditions^{3,7}.

In the present study, 1248 clinically suspected case of Dermatophytosis were studied. Various earlier studies showed already that infection with dermatophytes was more frequent in males compared to females^{3,8-10}. In our study, the males were 53.93% which is marginally higher than the percentage of females (46.07%) with the male to female ratio 1.17 :1. It may be due to that increased outdoor exposure and more physical work that results in increased sweating which makes Male more susceptible! The study shows that the infection is predominant in the adult age group (21- 40 years). This may be due to increased level of physical activity in this particular age group leading to excessive sweating which favours the growth. Socialization with different people is also high compared to other age groups which eventually help in spreading of infection. This finding correlates with the other studies like Ahuja S, *et al*¹³, Satpathi P, *et al*¹², Sarkar M, *et al*¹¹ and Ghosh R, *et al*⁶.

Regarding occupation, it was commonest among daily labour (28.85%) followed by housewives (22.04%) in our study. Sarkar M, *et al*¹¹ and Ghosh R, *et al*⁶ showed in their study that housewives were the predominant population. This is probably due to more physical activity in outdoor and more sweating in case of daily labours. Maximum patients (53.69%) in our study belongs to Class IV Socio-economic status. This finding was similar with the study of Surekha A, *et al*⁴.

In the present study, sharing of footwear (69.95%) and towel (69.31%) were the commonest and significant factors associated with this disease, followed by application of steroids (53.29%) and using tight clothes (51.28%). Similar findings were also noted in Pathania S, *et al*¹⁵. Such objects like clothing, bedsheets, and towel may harbour fungal pathogens and facilitate fomite transmission among family members. Fungal spores remain viable for months in household dust, which may lead to recurrent episodes of clinical disease^{16,17}.

Among all the clinical types, tinea corporis was the predominant one (44.39%). The finding was comparable with the studies of Srinivasan, *et al*⁸, Kumar K, *et al* and Venkatesan G, *et al*¹⁰. Verma, *et al*¹⁸ and Sardari, *et al*¹⁹ found tinea cruris as the commonest clinical type, which contrasts with our study, where tinea cruris was the second common clinical types.

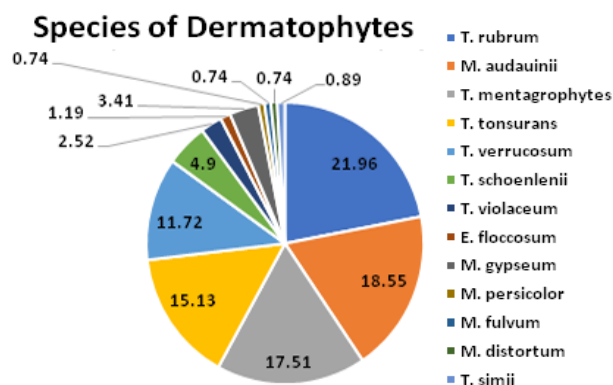


Fig 2 — Distribution of various species of Dermatophytes

Positivity rates of KOH mount in our study was found to be 88.38%. Out of which in 75.56% cases culture was positive and among KOH negative cases, 2.0% showed culture positivity. Higher positivity in KOH mount was also found in the study of Ghosh R, *et al*^{6,20}, Doddamani PV, *et al*²¹ and Singh S, *et al*²² who reported 65.0% KOH positive and 39.0% culture positive and 60.4% positive.

In the present study, dermatophytes were grown in 69.62% cases. This finding was comparable with the study of Sarkar M, *et al*¹¹, Surekha A, *et al*⁴ and Sanjiv Grover, *et al*³. *Candida albicans* was the commonest (38.20%) isolate in our study among *Candida*, whereas *Fusarium* was the most common isolate (38.15%) among NDM in our study. Similar findings were also noted in Sarkar M, *et al*¹¹.

Trichophyton species are the most frequent isolate as compared to *Microsporum* and *Epidermophyton* species. This finding has been noticed by many Indian studies as well as the Western countries²⁴. *T. rubrum* was the most common isolate (21.96%) in our study followed by *Microsporum audouinii* (18.55%). *T. rubrum* was the commonest isolate in various studies like Lakshmanan, *et al*⁵, S Das, *et al*⁶, Janardhan, *et al*²⁷, Aruna *et al*⁸, Manjunath, *et al*²⁹, Ramraj *et al*⁴, and Sarkar M, *et al*¹¹. *Microsporum audouinii* was the commonest isolate in the study of Ghosh R, *et al*²⁰, although it was found to be the second common isolate in our study. *T. mentagrophytes* has been the most frequently isolated organism in other reports from India^{16,17,30-37}. In a study by Grover, *et al*²³ the commonest isolate was *Trichophyton tonsurans* followed by *Trichophyton rubrum*. This difference could be attributed to changes in global climate and humidity favouring the of growth different pathogens over the years¹¹.

CONCLUSION

The present study gave clear picture regarding the causative agents of Dermatophytosis along with its

risk factors and Socio-economic status⁵. Diagnostic methodology and fungal susceptibility testing lag therapeutic advances. Our attention in future should be focused on molecular characterization of fungal pathogens along with antifungal susceptibility testing as it has been observed that patients are not responding to commonly used antifungals indicating emergence of drug resistance¹¹.

REFERENCES

- Kumar K, Kindo AJ, Kalyani J, Anandan S — Clinico–Mycological Profile of Dermatophytic Skin Infections in a Tertiary Care Center—A Cross Sectional Study. *Sri Ramachandra Journal of Medicine* 2007; **1(2)**: 12-5.
- Ranganathan S, Menon T, Sentamil GS — Effect of socioeconomic status on the prevalence of Dermatophytosis in Madras. *Indian J Dermatol Venereol Leprol* 1995; **61**: 16-8.
- Srinivasan B, Rajan S, Thiyagarajan T, Solomon J — Epidemiology of Dermatophytosis in and around Tiruchirapalli, Tamilnadu, India. *Asian Pacific Journal of Tropical Disease* 2012; **2(4)**: 286-9. DOI:10.1016/S2222-1808(12)60062-0.
- Emmons CW, Binford CH, Utz JP, Kwon-Chung KJ — Medical Mycology. 3rd ed. Philadelphia, Lea and Febiges. 1974. 117-67.
- Ramaraj V, Vijayarajaraman RS, Rangarajan S, Kindo AJ — Incidence and prevalence of Dermatophytosis in and around Chennai, Tamilnadu, India. *Int J Res Med Sci* 2016; **4**: 695-700.
- Ghosh R, Ray R, Ghosh TK, Ghosh AP — Clinico-mycological profile of Dermatophytosis in a Tertiary Care Hospital in West Bengal An Indian scenario. *Int J Curr Microbiol App Sci* 2014; **3(9)**: 655-66.
- Mycological study on Dermatophytosis in Seoul. *Korean Journal of Dermatology* 1994; **32**: 24-33.
- Bhaskaran CS, Rao PS, Krishnamoorthy T, Tarachand P — Dermatophytosis in Tirupathi. *Indian J Pathol Microbiol* 1977; **31**: 251-9.
- Maheshwariamma SM, Paniker CKJ, Gopinathan T — Studies on dermatomycosis in Calicut. *Indian J Pathol Microbiol* 1982; **25**: 11-7.
- Venkatesan G, Ranjit Singh AJA, Murugesan AG, Janaki C, Gokul Shankar S — Trichophyton rubrum—the predominant etiological agent in human dermatomycoses in Chennai, India. *Afr J Microbiol Res* 2007; **1(1)**: 9-12.
- Sarkar M, Ray (Ghosh) R, Halder P, Ghosh AP, Chatterjee M — Clinico- Mycological Profile of Onychomycosis –A Study in A Tertiary Care Hospital In Kolkata IOSR. *Journal of Dental and Medical Sciences* 2016; **15(9)**: 78-83.
- Satpathi P, Achar A, Banerjee D, Maiti A, Sengupta M, Mohata A — Onychomycosis in Eastern India - study in a peripheral tertiary care centre. *Journal of Pakistan Association of Dermatologists* 2013; **23(1)**: 14-9.
- Ahuja S, Malhotra S, Charoo H. Etiological agents of onychomycosis from a tertiary care Hospital in central Delhi, India. *Indian J Fundamental and Appl Life Sci* 2011; **1**: 11-4.
- Surekha A, Ramesh Kumar G, Sridevi K, Murty DS, Usha G, Bharathi G — Superficial Dermatophytosis: a prospective clinico-mycological study. *J Clin Sci Res* 2015; **4**: 7-15.
- Pathania S, Rudramurthy SM, Narang T, Saikia UN, Dogra S — A prospective study of the epidemiological and clinical patterns of recurrent Dermatophytosis at a tertiary care hospital in India. *Indian J Dermatol Venereol Leprol* 2018; **84**: 678-84.
- Bhatia VK, Sharma PC — Epidemiological studies on Dermatophytosis in human patients in Himachal Pradesh, India. *Springerplus* 2014; **3**: 134.
- Havlickova B, Czaika VA, Friedrich M — Epidemiological trends in skin mycoses worldwide. *Mycoses* 2008; **51(4)**: 2 15.
- Sen SS, Rasul ES — Dermatophytosis in Assam. *Indian Journal of Medical Microbiology* 2006; **24(1)**: 77-8.
- Sardari L, Sambhashiva RR, dandapani R — clinico mycological study of dermatophytes in a coastal area. *Ind J Dermatol Venereol Leprol* 1983; **49:2**: 71-5.
- Ghosh R — Changing trend in clinico-mycological profile of Dermatophytosis of skin in Eastern India: IP. *International Journal of Medical Microbiology and Tropical Diseases* 2018; **4(3)**: 159-65.
- Doddamani PV, Harshan KH, Kanta RC, Gangane Sunil R — Isolation, Identification and Prevalence of Dermatophytes in Tertiary care Hospital in Gulbarga District, *People's J Scientific Res* 2013; **6**: 2.
- Beena P M, Singh S — Profile of dermatophyte infections in Baroda, *Ind J Derm Venereol Leprol* 2003; **69**: 281-83.
- Wg Cdr Sanjiv Grover, Lt Col P Roy — Clinico-mycological Profile of Superficial Mycosis in a Hospital in North-East India; *MJAFI* 2003; **59(2)**:
- Kumar K, Kindo AJ, Kalyani J, Anandan S — Clinico – Mycological Profile of Dermatophytic Skin Infections In A Tertiary Care Center – A Cross Sectional Study. *Sri Ramachandra Journal of Medicine* 2007; **1(2)**: 12-5.
- Lakshmanan A, Ganeshkumar P, Mohan SR, Hemamalini M, Madhavan R — Epidemiological and clinical pattern of Dermatophytosis in rural India. *Indian J Med Microbiol* 2015; **33**: S134-6.
- Das S, De A, Saha R, Sharma N, Khemka M, Singh S, et al — The current Indian epidemic of Dermatophytosis: A study on causative agents and sensitivity patterns. *Indian J Dermatol* 2020; **65**: 118-22.
- Janardhan B, Vani G — Clinico mycological study of Dermatophytosis. *Int J Res Med Sci* 2017; **5**: 31-9.
- Aruna GL, Ramalingappa B — A clinico mycological study of human dermatophytosis in Chitradurga, Karnataka, India. *JMSCR* 2017; **5**: 25743-9
- Manjunath M, Mallikarjun K, Dadapeer, Sushma — Clinicomycological study of dermatomycosis in a tertiary care hospital. *Indian J Microbiol Res* 2016; **3**: 190-3.
- de Freitas RS, Neves PS, Charbel CE, Criado PR, Nunes RS, Santos Filho AM, et al — Investigation of superficial mycosis in cutaneous allergy patients using topical or systemic corticosteroids. *Int J Dermatol* 2017; **56**: e194-8.
- Morimoto K, Tanuma H, Kikuchi I, Kusunoki T, Kawana S — Pharmacokinetic investigation of oral itraconazole in stratum corneum level of tinea pedis. *Mycoses* 2004; **47**: 104-14.
- Hanumanthappa H, Sarojini K, Shilpashree P, Muddapur SB — Clinicomycological study of 150 cases of Dermatophytosis in a tertiary care hospital in South India. *Indian J Dermatol* 2012; **57**: 322 3.
- Bindu V, Pavithran K — Clinico mycological study of Dermatophytosis in Calicut. *Indian J Dermatol Venereol Leprol* 2002; **68**: 259-61.
- Vyas A, Pathan N, Sharma R, Vyas L — A clinicomycological study of cutaneous mycoses in Sawai man singh hospital of Jaipur, North India. *Ann Med Health Sci Res* 2013; **3**: 593-7.
- Bhatia VK, Sharma PC — Determination of minimum inhibitory concentrations of itraconazole, terbinafine and ketoconazole against dermatophyte species by broth microdilution method. *Indian J Med Microbiol* 2015; **33**: 533 7.
- Adimi P, Hashemi SJ, Mahmoudi M, Mirhendi H, Shidfar MR, Emmami M, et al — In vitro activity of 10 antifungal agents against 32 dermatophyte strains using microdilution method in Tehran. *Iran J Pharm Res* 2013; **12**: 537-45.
- Mahajan S, Tilak R, Kaushal SK, Mishra RN, Pandey SS — Clinico mycological study of dermatophytic infections and their sensitivity to antifungal drugs in a tertiary care center. *Indian J Dermatol Venereol Leprol* 2017; **83**: 436-40.

Original Article

Oral and Systemic Symptoms of COVID-19 among Patients Vaccinated and Unvaccinated against SARS-CoV-2

Pankaj Goel¹, Aman Kumar²

Background : Vaccination against SARS-CoV-2 has been developed and are being administered at rapid pace globally, however despite vaccination cases have been reported who got infected even after vaccination. It is important to find the effect of vaccination on symptoms experienced by COVID-19 positive patients.

Objective : The aim of the study was to assess the effect of vaccination on oral and systemic symptoms experienced by the patients.

Method : An observational study was carried out at a dedicated COVID care public hospital where the patients reporting to the Out Patient Department (OPD) for getting themselves tested for COVID-19 were interviewed regarding the symptoms experienced by them and data was recorded. Further investigation was carried out using Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) test.

Results : A total of 219 patients reported to the OPD between July 2021 to September 2021, out of which 119 were found to be COVID-19 positive and 100 were COVID-19 negative. Out of 119, COVID-19 positive patients, 45 were fully vaccinated (received both doses) against SARS-CoV-2, while 74 were unvaccinated or partially vaccinated (received single dose only). Statistically significant difference was found between fully vaccinated and unvaccinated / partially vaccinated patients in relation to ageusia, xerostomia, anosmia and fatigue in COVID-19 positive group.

Conclusion : Although there are chances of getting infected with SARS-CoV-2 even after receiving vaccination against it, the symptoms experienced by the patients are less.

[J Indian Med Assoc 2023; 121(8): 54-7]

Key words : COVID-19, Vaccination, Ageusia, Xerostomia, Anosmia.

SARS-CoV-2 is a single stranded RNA corona virus which has infected human beings^{1,2}. It has a high probability of zoonotic origin³. It can be transmitted directly by coughing, sneezing or indirectly by contact with mucous membrane like oral, ocular or nasal mucosa⁴. Dentists are at high risk of getting infected with the virus because of its air borne route of transmission and huge amount of aerosol generated during dental treatment make the situation even more precarious for the dentists. Various guidelines have been issued by different dental societies for the safe and effective management of acute dental infections which if not adhered to increases the risk of infection³.

Although devoid of any characteristic signs and symptoms, various systemic symptoms associated with COVID-19 are fever, dry cough, headache, tiredness, diarrhoea, sore throat or runny nose, however in certain cases it may cause pneumonia, kidney failure or even death⁴. There are certain infected patients who are asymptomatic but possess a risk of spreading infection, identification of such patients is important for the control of the disease⁵.

Department of Dentistry, AIIMS, Bhopal, Madhya Pradesh 462026

¹MDS, Professor and Head and Corresponding Author

²MDS, Junior Resident

Received on : 03/11/2022

Accepted on : 02/04/2023

Editor's Comment :

- Although it is possible to get infected with SARS-CoV-2 even after vaccination, the oral and systemic symptoms experienced by the individual are less as compared to unvaccinated individuals.
- As oral symptoms like xerostomia increases the chances of dental caries, decreased oral symptoms in vaccinated individuals will improve the oral health related quality of life in such patients.

Oral symptoms associated with the disease are dysgeusia, xerostomia, chemosensory alterations, bruxism and bleeding gums⁶. SARS-CoV-2 has affinity for Angiotensin-converting Enzyme 2 (ACE 2) receptors found in salivary gland, respiratory tract, gastro intestinal tract, leading to various signs and symptoms⁷. Decrease in salivary flow due to attachment of SARS-CoV-2 to ACE 2 receptors of salivary gland may cause the possible oral symptoms of the disease³. Cells with ACE 2 receptors may act as a host for the virus, which causes further inflammatory process in the organ concerned like tongue mucosa and salivary gland^{3,8}. Oral and systemic symptoms may be due to the infection by SARS-CoV-2 per se or may be the aftermath of treatment of the infection which may lead to immuno suppression causing various oral and systemic symptoms.

There can be many variables which influence the

oral and systemic symptoms of SARS-CoV-2 infection and one of the such variable is COVID-19 vaccination status. As the development of vaccination against SARS-CoV-2 has been fast and vaccination has been done at a rapid pace across the globe, it is imperative to assess the effect of vaccination on the oral symptoms.

The aim of this study was to assess the oral and systemic symptoms in COVID-19 vaccinated and unvaccinated patients of SARS-CoV-2 infection.

MATERIALS AND METHODS

An observational study was conducted in the Department of Dentistry and COVID Screening OPD of a dedicated COVID care public hospital during July 2021 to September, 2021. Convenience sample size was taken as all the patients who presented to the OPD were screened for enrolling into the study based on the eligibility and exclusion criteria.

Eligibility Criteria :

(a) Those patients who presented with classical symptoms of SARS-CoV-2 (b) Those having positive history of contact with COVID-19 positive patients.

Exclusion Criteria :

Those patients who are not willing to participate. Informed consent was taken from all the patients and only those willing to participate were included in the study. In the case of children assent form was used, which was filled by the parents of the children. A single investigator was trained to conduct the interview and perform oral examination of the participants to record symptoms associated with COVID-19 as reported by participants. Oral symptoms which were recorded were dysgeusia, xerostomia, halitosis, bruxism, ulcer in the oral cavity or at the corners of the mouth, bleeding gums and burning sensation in the oral cavity. Systemic symptoms which were recorded were altered smell, headache, diarrhoea, chills, dry cough, fatigue, nausea / vomiting, shortness of breath, fever, sore throat and body ache. All the symptoms were recorded in a survey sheet by the investigator after conducting the interview and oral examination.

Ethical clearance for the research was taken from the All India Institute of Medical Sciences Bhopal, Institutional Human Ethics Committee by letter number IHEC-LOP/2021/IM0378.

Socio-demographic variables such as age, gender, diet, smoking / alcohol habit, medical history of co morbidity and severity of COVID-infection was also recorded. Vaccination status of all the participants was recorded, however participants whose vaccination status was unknown were not included in the analysis of data. ChAdOx1 nCoV-19 Corona Virus Vaccine

(Recombinant) was used to vaccinate all those individuals who were in the vaccinated group. Those individuals who had received both the doses of vaccination and fifteen days had been passed post inoculation of second dose were considered to be vaccinated.

Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) test was done on all patients after the interview and examination of the patients was done. The participants got to know about the positive or negative diagnosis of COVID 24 hours after the RT-PCR test was done. Based on the confirmatory investigation, the patients were divided into two groups; COVID confirmed (cases) and COVID suspect (controls). Statistical Package for the Social Sciences (SPSS) software version 25 was used for data analysis. Chi-Square test were applied and p-value <0.05 was considered to be statistically significant.

RESULTS

A total of 219 patients were included in the study who visited the OPD having age range of 13 to 74 years with the mean age of 29.9 ± 11.9 years. Out of 219 participants, 119 participants tested COVID positive (52 males and 67 females). 100 participants tested negative (66 males and 34 females) (Table 1). There was a statistically significant difference between COVID-19 positive group and negative in relation to various oral and systemic symptoms (Table 2).

Among oral symptoms, ageusia, xerostomia, halitosis and bruxism were statistically significantly higher among COVID patients as compared to COVID negative patients ($P = <0.001, 0.021, 0.002, 0.001$ respectively). Among systemic symptoms, anosmia, headache, diarrhoea, chills and fatigue were statistically significantly higher among COVID positive patients as compared to COVID negative patients ($P = <0.001, <0.001, 0.010, 0.025, 0.001$ respectively).

Among those oral and systemic symptoms who were found to have statistically significant difference between COVID 19 positive and negative patients, further analysis was done according to vaccination status against SARS-CoV-2 in COVID-19 positive group (Tables 3, 4).

Among oral symptoms, there was statistically significant difference between vaccinated and unvaccinated participants in relation ageusia and xerostomia. Among systemic symptoms, there was statistically significant difference between vaccinated and unvaccinated participants in relation anosmia and fatigue.

DISCUSSION

This study reported the effect of vaccination status

Table 1 — Sample Characteristic

Variable	Total n (%)	Positive n (%)	Negative n(%)	P value ^a
Gender				0.001
Male	118 (53.9)	52 (43.7)	66 (66)	
Female	101 (46.1)	67 (56.3)	34 (34)	
Age (Years)		26.15 (10.86) ^b	34.3 (11.6) ^b	<0.001 ^c
Co morbidity				0.127
Co morbidity present	16 (7.3)	6 (5)	10 (10)	
Co morbidity absent	203 (92.7)	113 (95)	90 (90)	
COVID symptoms				0.019
COVID symptoms present	189 (86.3)	97 (81.5)	92 (92)	
COVID symptoms absent	30 (13.7)	22 (18.5)	8 (8)	
Vaccination status				0.004
One dose	39 (17.8)	17 (14.3)	22 (22)	
Both dose	57 (26)	45 (37.8)	12 (12)	
Unvaccinated	123 (56.2)	57 (47.9)	66 (66)	
Smoking status				0.056
Yes	20 (9.1)	7 (3.2)	13 (5.9)	
No	199 (90.9)	112 (51.1)	87 (39.7)	
Alcohol consumption				0.048
Yes	16 (7.3)	5 (2.3)	11 (5)	
No	203 (92.7)	114 (52.1)	89 (40.6)	
Diet				0.485
Vegetarian	130 (59.4)	70 (32)	60 (27.4)	
Non vegetarian	89 (40.6)	49 (22.4)	40 (18.3)	

a : Chi-square test was performed, b : Standard deviation, c : 't' test was performed

breakthrough cases among 1497 fully vaccinated participants⁹. Taste alterations have been reported in 59.5% (n=66 out of 111) of patients and xerostomia in 45.9% (n= 51 out of 111) of COVID-19 patients by Fantozi, *et al*, 2020¹⁰. Xerostomia found in SARS-CoV-2 infection may play an aggravating role in halitosis¹¹. Increase in bruxism and Temporomandibular Dysfunction (TMD) symptoms has been reported during corona virus pandemic¹². The increase in bruxism can be attributed to adverse effects on the psycho-emotional status and increase in psychological stress during COVID-19 pandemic.

Human strains of the corona virus have been demonstrated to invade the Central Nervous System through the olfactory neuroepithelium and propagate from within the olfactory bulb. Furthermore, nasal epithelial cells display the highest expression of the

SARS-CoV-2 receptor, angiotensin converting enzyme 2, in the respiratory tree¹³. As statistically significant

Table 2 — Difference in relation to various oral and systemic symptoms between COVID-19 positive and COVID-19 negative patients

Oral and Systemic symptoms	COVID Suspected (Negative), n (%)	COVID Confirmed (Positive), n (%)	P value ^a
Ageusia	19 (19)	49 (41.2)	< 0.001
Xerostomia	30 (30)	56 (47.1)	0.021
Halitosis	4 (4)	11 (9.2)	0.002
Bruxism	3 (3)	11 (9.2)	0.001
Ulcer at corner of mouth	1 (1)	7 (5.9)	0.102
Bleeding gums	1 (1)	4 (3.4)	0.244
Ulcer in oral cavity	12 (12)	15 (12.6)	0.647
Burning sensation in mouth	3 (3)	4 (3.4)	0.651
Anosmia	10 (10)	51 (42.9)	< 0.001
Headache	18 (18)	52 (43.7)	< 0.001
Diarrhoea	5 (5)	19 (16)	0.010
Chills	3 (3)	13 (10.9)	0.025
Dry cough	30 (30)	48 (40.3)	0.112
Fatigue	33 (33)	65 (54.6)	0.001
Nausea/ Vomiting	6 (6)	13 (10.9)	0.197
Shortness of breath	8 (8)	16 (13.4)	0.199
Fever	64 (64)	69 (58)	0.364
Sore throat	43 (43)	56 (47.1)	0.548
Body ache	46 (46)	57 (47.9)	0.779

a : Chi-square test was performed

against SARS-CoV-2 on oral and systemic symptoms experienced by the patients in COVID-19 positive group. Statistically significant difference was found in relation to ageusia and xerostomia between vaccinated and unvaccinated population. Our results are found to be consistent with Bergwerk, *et al*, 2021 who reported less symptoms or asymptomatic cases in

Table 3 — Oral symptoms in fully vaccinated and unvaccinated / partially vaccinated individuals among COVID-19 positive participants

Oral symptoms	Fully Vaccinated	Unvaccinated/ partially vaccinated	Chi square	p value ^a
Ageusia	12	37	6.29	0.012
No ageusia	33	37		
Xerostomia	15	41	5.472	0.019
No xerostomia	30	33		
Halitosis	3	8	0.5729	0.449
No halitosis	42	66		
Bruxism	3	8	0.5729	0.449
No bruxism	42	66		

a : Chi-square test was performed

Table 4 — Systemic symptoms in vaccinated and unvaccinated individuals among COVID-19 positive participants

Systemic symptoms	Fully Vaccinated	Unvaccinated/ partially vaccinated	Chi square	p value ^a
Anosmia	11	40	10.0179	0.001
No anosmia	34	34		
Headache	18	34	0.4021	0.526
No headache	27	40		
Diarrhoea	9	10	0.8775	0.349
No diarrhoea	36	64		
Chills	3	10	1.3481	0.246
No chills	42	64		
Fatigue	19	46	4.4888	0.034
No fatigue	26	28		

a : Chi-square test was performed

difference was found between vaccinated and unvaccinated participants in COVID-19 positive group in relation to anosmia, it can be said that vaccination do have a protective role in mitigating the symptoms associated with infection.

Statistically significant difference was found in relation to fatigue between COVID-19 positive and negative participants as well as between vaccinated and unvaccinated participants in COVID-19 positive group. It can be said that although fatigue is common finding in covid positive patients, vaccinated patients are less likely to experience it. Fatigue has been reported with a prevalence of 52.3% (n= 67 out of 128) in COVID-19 positive patients¹⁴. Chronic Fatigue Syndrome (CFS) has been associated with a large number of differing changes in the inflammatory markers and immune cell population. The lack of distinct immune signature, coupled with the association with depression, lends credence to the multifactorial aetiology of CFS¹⁴.

Headache has been reported in COVID-19 positive patient¹⁵. Headaches reported can be a mixture of tension-type headache and headaches attributed to systemic viral infection, heterophoria, cough or hypoxia¹⁵. A case has been reported of a 27 years old COVID-19 positive male with type 2 diabetes, who had presented with a complaint of watery diarrhoea five to six times per day¹⁶. The presence of gastrointestinal symptoms in corona virus infection (SARS-CoV-1 and SARS-CoV-2) can be linked to the distribution of ACE2 receptor, which is present in lung alveolar type 2 cells, as well as in enterocytes¹⁶.

Caponio, *et al* 2022 reported a case of fully vaccinated individual who developed ageusia after 55 days post vaccination¹⁷.

Although it is possible to develop symptomatic COVID-19 post vaccination, the findings of our study are in agreement with the studies which reported less symptoms in breakthrough cases of vaccinated individuals^{9,18}.

CONCLUSION

It can be concluded that patients who were fully vaccinated against SARS-CoV-2 experienced less oral and systemic symptoms of COVID-19 in relation to ageusia, xerostomia, anosmia and fatigue as compared to unvaccinated patients, which was found to be statistically significant. Although patient may get infected with SARS-CoV-2 even after receiving vaccination against it, less symptoms experienced by them.

Recommendation : Further studies on larger sample size are needed to corroborate these findings.

Conflict of Interest : Authors declare no conflict of interest.

REFERENCES

- Andersen KG, Rambaut A, Lipkin W, Holmes EC, Garry RF — The proximal origin of SARS-CoV-2. *Nat. Med* 2020; **26**: 450-2.
- Wu F, Zhao S, Yu B, Chen YM, Wang W, Song ZG, *et al* — A new coronavirus associated with human respiratory disease in China. *Nature* 2020; **579**: 265-9.
- Sinjari B, D'Ardes D, Santilli M, Rexhepi I, D'Addazio G, Di Carlo P, *et al* — SARS-CoV-2 and Oral Manifestation: An Observational, Human Study. *Journal of Clinical Medicine*. 2020; **9**(10): 3218.
- Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, *et al* — Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A descriptive study. *Lancet Lond Engl* 2020; **395**: 507-13.
- Epidemiology Working Group for NCIP Epidemic Response, Chinese Center for Disease Control and Prevention. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China. *Zhonghua Liu Xing Bing Xue Za Zhi Zhonghua Liuxingbingxue Zazhi* 2020; **41**: 145-51.
- Vinayachandran D, Balasubramanian S — Is gustatory impairment the first report of an oral manifestation in COVID-19? *Oral Dis* 2021; **27** Suppl 3(Suppl 3): 748-9.
- Freni F, Meduri A, Gazia F, Nicastrò V, Galletti C, Aragona P, *et al* — Symptomatology in head and neck district in coronavirus disease (COVID-19): A possible neuroinvasive action of SARS-CoV-2. *Am J Otolaryngol* 2020; **41**: 102612
- Xu H, Zhong L, Deng J, Peng J, Dan H, Zeng X, *et al* — High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. *Int J Oral Sci* 2020; **12**: 8.
- Bergwerk M, Gonen T, Lustig Y, Amit S, Lipsitch M, Cohen C, *et al* — COVID-19 Breakthrough Infections in Vaccinated Health Care Workers. *N Engl J Med* 2021; **385**: 1474-84.
- Fantozzi PJ, Pampena E, Vanna DD, Pellegrino E, Corbi D, Mammucari S, *et al* — Xerostomia, gustatory and olfactory dysfunctions in patients with COVID19. *Am J Otolaryngol* 2020; **41**(6): 102721
- Dziedzic A, Wojtyczka R — The impact of coronavirus infectious disease 19 (COVID19) on oral health. *Oral Dis* 2020; **27**(3): 703-6.
- Emodi-Perlman A, Eli I, Smardz J, Uziel N, Wieckiewicz G, Gilon E, *et al* — Temporomandibular Disorders and Bruxism Outbreak as a Possible Factor of Orofacial Pain Worsening during the COVID-19 Pandemic—Concomitant Research in Two Countries. *J Clin Med* 2020; **9**(10): 3250.
- Boscolo-Rizzo P, Borsetto D, Fabbris C, Spinato G, Frezza D, Menegaldo A, *et al* — Evolution of altered sense of smell or taste in patients with mildly symptomatic COVID-19. *JAMA Otolaryngol Head Neck Surg* 2020; **146**(8): 1-5.
- Townsend L, Dyer AH, Jones K, Dunne J, Mooney A, Gaffney F, *et al* — Persistent fatigue following SARS-CoV-2 infection is common and independent of severity of initial infection. *PLoS ONE*. 2020; **15**(11): e0240784
- Belvis R — Headaches during COVID-19: My clinical case and review of the literature. *Headache* 2020; **60**(7): 1422-6.
- Ata F, Almasri H, Sajid J — *BMJ Case Rep* 2020; **13**: e235456
- Caponio VCA, Lipsi MR, Fortunato F, Arena F, Lo Muzio L — Symptomatic SARS-CoV-2 Infection with Ageusia after Two mRNA Vaccine Doses. *Int J Environ Res Public Health* 2022; **19**: 886
- Hacisuleyman E, Hale C, Saito Y, Blachere NE, Bergh M, Conlon EG, *et al* — Vaccine Breakthrough Infections with SARS-CoV-2 Variants. *N Engl J Med* 2021; **384**: 2212-8.

Original Article

Effectiveness of Nursing Care Bundles in Hospitalized Patients with Chronic Obstructive Pulmonary Disease (COPD)

Smita Roba Tirkey¹, Rashmi P John², Anuj Kumar Pandey³, Ajay Kumar Verma⁴, Surya Kant⁵

In Chronic Obstructive Pulmonary Disease (COPD) exacerbation care bundle is essential to reduce not only clinical manifestations but also the severity of the disease condition. Here, we aimed to explore the effectiveness of care bundles by comparing the pre-test and post-test level of Quality of Life (QOL) and Activities of Daily Living (ADL) among hospitalized COPD patients. In this study sixty-six hospitalized COPD patients were included. The care bundle intervention was given thrice a day for consecutive seven days. Data were collected 24 hours after admission by St. George Respiratory Questionnaire-COPD (SGRQ-C) for pre-test and the same tool was used after intervention for post-test. The results were analyzed using descriptive statistics and making comparisons between the groups with respect to various parameters. There was a significant difference in the mean score of pre-test and post-test QOL & ADL. Aftercare bundle intervention patients felt better in their current situation, so, it is interpreted that patient's quality of life increased. The main conclusions drawn from this study was nursing care bundle can improve the care of COPD exacerbation. The use of a bundle of cares not only streamlines care but also has the potential to reduce the risk of adverse effects from unnecessary medications or treatments.

[J Indian Med Assoc 2023; 121(8): 58-63]

Key words : Chronic Obstructive Pulmonary Disease (COPD), Care bundles, Exacerbation, Quality of life, Activities of Daily Living.

Chronic Obstructive Pulmonary Disease (COPD) is the major cause of hospitalization and disability due to lung disease. Its chronic progressive and acute exacerbations will affect the quality of life and life expectancy of COPD patients. Respiratory tract infections commonly develop in COPD because of the changes in the normal defense mechanism and decreased immune resistance. Further, infection frequently leads to acute respiratory failure. COPD and emphysema may worsen at night with sleep onset dyspnea and frequent awakenings. Because of the decrease in the muscle tone and activity of respiratory muscles leads to hypoventilation, increases in the resistance of the airways and becomes hypoxemic.¹ Exercise program is a very essential step to control COPD. For people with lung disease, exercise restriction is very common because they are anxious of shortness of breath, however routine physical work

Editor's Comment :

- The implementation of nursing care services may result in shorter hospital stays, lower readmission rates, and reduces the risk of adverse effects caused by unnecessary medications or treatments in hospitalized COPD patients.

can improve the heart, lungs, muscles, and can help breathing easier and healthier. Generally, people with COPD and chronic bronchitis produce mucus. Techniques to remove mucus are often done after using inhaled bronchodilator medication.

Care bundle is used to promote the health of the patients with COPD. The nursing care bundle includes: effective huff coughing exercise, breathing retraining and relaxation techniques energy conservation techniques and upper and lower limb exercise. These interventions help the patient to decrease the symptoms, improving exercise ability and physical functioning. The quality of nursing care for the patient with respiratory disease is ensured based on the evidence based practice and holistic approach. This approach encompasses a comprehensive assessment, planning, intervention and evaluation process. Today nursing seems to be more creative and nurses incorporate critical thinking in rendering comprehensive care to patients in pulmonary care unit. This critical analysis helps them to identify the problems of the patient in its early stage and institute appropriate interventions².

King George's Medical University, Uttar Pradesh, Lucknow 226003

¹MSc Nursing, Department of Medical Surgical Nursing

²MSc Nursing, Acting Principal, Department of Medical Surgical Nursing

³PhD, Department of Respiratory Medicine

⁴MD, Professor (Junior Grade), Department of Respiratory Medicine

⁵MD, Professor & Head, Department of Respiratory Medicine and Corresponding author

Received on : 13/07/2022

Accepted on : 21/01/2023

The respiratory rate of COPD patients increases and the exhalation time is extended to compensate for airflow obstruction that causes breathing difficulties. Long-term use of accessory muscles can lead to increased patient fatigue. Pursed lip breathing prevents the bronchioles from collapsing and air retention. Patient is taught to breathe in slowly through the nose, and then breathe out slowly through the pursed lips, just like blowing a whistle. Use lips for positive pressure, because excessive resistance may increase the work of breathing. An effective cough will clear the airways from the sputum. The main purpose of coughing is to save energy, reduce fatigue and promote the removal of secretions. In 2011, CTS developed guidelines for the treatment of shortness of breath in patients with advanced COPD. Learning new breathing retraining techniques (such as lips breathing and coughing cough exercises) will help move air in and out of the lungs, which is very effective. Using effective breathing techniques and exercise helps to minimize shortness of breath and adequate oxygen to working muscles³.

The goal of the nursing care bundle is to reduce the clinical manifestations of COPD and reduce the severity of the disease conditions. It is very effective to use the selected nursing interventions in improving the quality of life as well as activities of daily living in COPD patients and it can reduce cost of care and easily available in all settings. Exercise, activities of daily living, and health related quality of life which can be severely affected by the disease. These are interrelated and that impact the lives of these patients. The nursing care bundle will improve the patients exercise tolerance and subsequently quality of life.¹ However, data are lacking in this area. In the present study we aimed to evaluate the effectiveness of selected nursing interventions to improve the quality of life and activities of daily living in COPD patients.

MATERIALS AND METHODS

Study Design and Setting :

Quantitative pre experimental research approach was applied in the current study. The work was conducted at ward of respiratory medicine department of a tertiary care hospital. Participants between 30-60 years age-group, clinically diagnosed with COPD and fulfilled the selection criteria were included. After obtaining ethical approval from committee and formal administrative permission from the department of respiratory medicine study was conducted. Self introduction and purpose of the study was explained to the subject, willingness to participate in the study

was ascertained and written informed consent was taken from each participants. The demographic, and clinical characteristics of subjects was collected in preformed questionnaire which was formed by experts from respiratory medicine, nursing, medicine, and pharmacology. The present study included two variables: first, dependent variable- quality of life and activities of daily living among COPD patients; second, independent variables- nursing care bundle.

Operational Definitions and Tools :

Effectiveness refers to the optimising physical health, reducing symptoms and functional impairment, and increasing emotional and social well being after giving nursing care bundle.

Bundle care refers to nursing interventions those are used to promote the health of the patients with COPD. Those interventions are purse lip breathing, diaphragmatic breathing, huff coughing, chest physiotherapy and upper and lower limb exercise. Quality of life refers to self determined evaluation of satisfaction with issues important to person. Activities of daily living refers to daily activities which patient do in their daily life like brushing, toileting, bathing, exercise etc.

St. George Respiratory Questionnaire - COPD (SGRQ-C) :

The SGRQ-C was developed by SGRQ which was structured to understand the health status of asthma and COPD patients. A study found that SGRQ-C contains the best original items, no longer specifies the recall period and produces the same scores as the original product⁴. SGRQ-C is divided into two categories- Part 1 (Questions 1-7) which explains the frequency of resolving respiratory symptoms. It was not intended to be an accurate epidemiological tool, but to assess patients' perceptions of their recent respiratory illness. Part 2 (Questions 8-14) discusses the patient's current status, the most recent condition. Activity scores were used to measure interference with daily physical activities. The impact score covers a series of psychosocial dysfunction. This component is partly related to respiratory symptoms, but also closely related to exercise performance, dyspnea in daily life and mood disturbances. Therefore, the impact score is the most extensive part of the questionnaire, covering all the disturbances experienced by respiratory patients during their lifetime. All of these depend on the quality of life and activities of daily living.

A total score was calculated in terms of symptoms, activity, and impacts. By dividing the total weight by the maximum possible weight of the component and

expressing the result as a percentage, the score for each component was calculated separately. Score was inversely proportional to the health condition means, higher the score worsen the condition.

Inclusion and Exclusion Criteria :

Inclusion criteria was as follows : (1) age group 30-60 years, (2) patients admitted in the ward more than seven days, (3) patient who are literate, (4) subjects clinically diagnosed with COPD. **Exclusion criteria was as :** (1) other concomitant pulmonary diseases viz, tuberculosis, asthma, pneumonia etc, (2) patient is on ventilator support or critically ill. (3) patient denied to participate in the study.

Interventional Procedure :

Intervention was given to COPD subjects at their bedside in the direct observation of specialist in the ward for two times in a day for a total duration of six days. And the duration of each interventional procedure was between 15-45 min⁵. These nursing care was provided to each subjects : pursed lip breathing -4 minute; diaphragmatic breathing -4 minute (to better control over breathing); huff coughing -2 min (which adequately clears sputum from airway); chest physiotherapy- 4 min (to prevent infections and helps easy breathing); upper and lower limb exercise for 3 min to improve the activities of daily living.

RESULTS

Demographic Profile of COPD Subjects :

Demographic characteristics of the studied population was shown in Table 1. Forty-three (65.2%) subjects were in the age group of ≥ 50 years. Majority of the subjects were males with 95.5% proportion, while 4.5% were females. All the subjects were married. Majority of the subjects were farmers with 62.1% proportion.

Pre & Post test comparison of Quality of Life (QOL), Activities of Daily Life (ADL), and Overall Impact Score (OIS) :

As shown in Table 2 the total score of QOL among the patients at pre test level had a mean of 76.94 ± 5.63 with minimum value 47.89 and maximum value 90.85. After post test level the impact score was changed to the mean value 53.63 ± 4.50 with minimum value 44.41 and maximum value 84.89. After post test, this change of

30.30%, among the subjects was found highly significant ($P < 0.001$).

Pre & Post Test Comparison of ADLs was represented in Table 2. The ADL score among the patients at pre test level had a mean 92.36 ± 0.00 with minimum and maximum value 92.36 (pre test activity score was constant). After post test level the activity score was changed to the mean value 68.56 ± 3.18 with minimum value 68.15 and maximum value 92.36. This percentage change of 25.77% after post test among the subjects was found to be highly significant ($P < 0.001$).

As shown in Table 2, the impact score among the patients at pre test level had a mean 74.04 ± 7.41 with minimum value 34.81 and maximum value 86.81. After post test level the impact score was changed to the mean value 43.03 ± 4.31 with minimum value 42.47 and maximum value 75.27. Percentage change of 41.88% after post test among the subjects was found to be highly significant ($P < 0.001$).

Pre & Post Test Comparison of Item Scores of Symptoms and Activity :

When we compared the item scores of symptoms (cough, sputum, shortness of breath, wheezing, chest trouble, good days, morning wheezing) the maximum % change was seen for the symptom cough with 0.46%

Table 1 — Demographic profile of studied participants

Characteristics	No of participants (n)	Participants's percentage (%)
Age group (years)	30-39	4
	40-49	19
	≥ 50	43
Gender	Male	3
	Female	63
Marital Status	Married	66
	Un-married	0
Occupation	Unemployed	2
	Unskilled	2
	Semi skilled	4
	Skilled	2
	Clerk/shop-owner/ farmer	56

Table 2 — Pre and post test comparison of Quality of Life (QOL), Activities of Daily Life (ADL), and Overall Impact Score (OIS)

Variables	Mean	SD	Median	Min	Max	Statistical analysis
QOL	Pre Test Level	76.94	5.63	77.49	47.89	90.85
	Post Test Level	53.63	4.50	53.32	44.41	84.89
% Change			30.30			
ADL	Pre Test Level	92.36	0	92.36	92.36	92.36
	Post Test Level	68.56	3.18	68.15	68.15	92.36
% Change			25.77			
OIS	Pre Test Level	74.04	7.41	74.89	34.81	86.81
	Post Test Level	43.03	4.31	4.31	42.47	75.27
% Change			41.88			

change. However, no significant difference was found in any symptom score (Fig 1).

On comparing the item scores of activity, the maximum % change was seen for the activities of 'washed/dressed', 'take long time to washed/dressed' and 'taking bath' with 98.28% change, each. Significant difference were found in activity scores of these with $P < 0.001$ for each (Fig 2).

Pre & Post Test Comparison of Item Scores of Impact

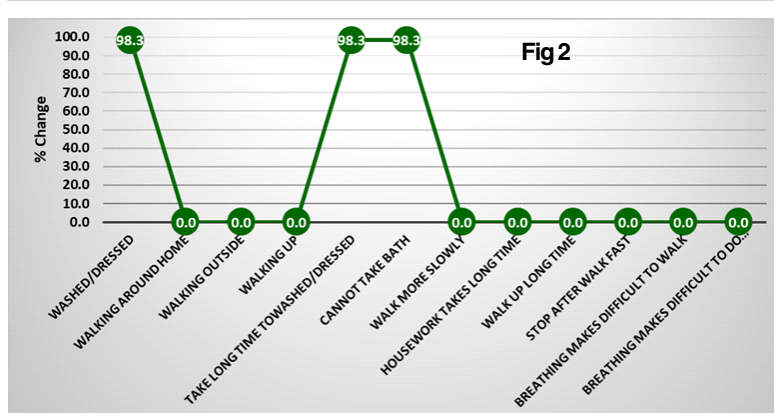
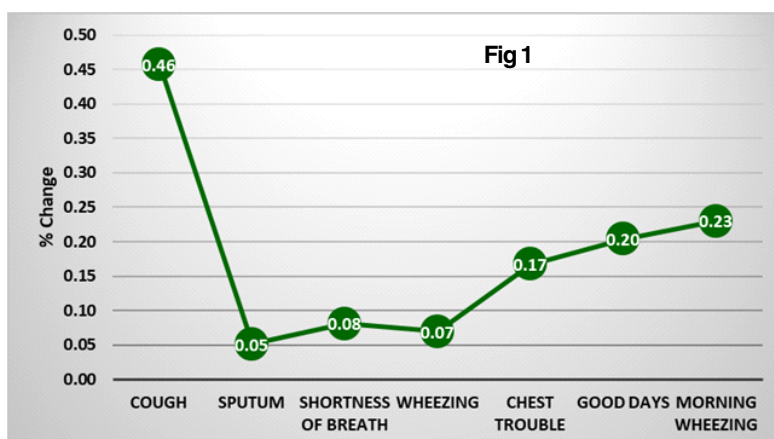
On comparing the item scores of impact, the maximum % change was seen for the impact on 'cannot move far' ($P < 0.001$) depicted in Table 3. Other remarkable changes were found for breathless with talk, breathless when bend over, and safe exercise with 98.28% change ($P < 0.001$). However, significant difference were found in impact scores of cough makes tired, breathless with talk, breathless when bend over, get afraid, control chest problem, safe exercise, can move far and describing chest effect ($P < 0.001$).

Association of Post Symptoms, Activity, Impact and Quality of Life (QOL) Scores :

Association of post symptoms, activity, impact, and Quality of Life (QOL) was stated in Table 4. No post QOL domain was found to be significantly associated with age group ($P = 0.753$). Activity and symptom domains were found significantly associated with gender ($P < 0.001$). Activity and symptom domains were found significantly associated with occupation ($P < 0.001$).

Association of age-group, gender and occupation with post Activities of Daily Living (ADL) scores:

As shown in Table 5, no ADL was found significantly associated with age-group ($P = 0.784$). ADL domains was found associated with gender ($P < 0.001$). Also, ADL domains was found to be significantly associated with occupation ($P < 0.001$).



DISCUSSION

The present study demonstrated the role of care bundle in the assessment and management of patients with acute exacerbations of COPD. The use of a nursing care bundle is simple and easy to follow. Out

Table 3 — Pre & post test comparison for impact scores

Impact	Pre test impact		Post test impact		% Change	Z	p-value
	Mean	SD	Mean	SD			
Chest condition	35.38	6.13	35.43	6.34	0.15	0.000	1.000
Cough hurts	78.48	14.45	81.10	0.00	3.33	-1.414	0.157
Cough makes tired	76.55	14.09	1.36	10.39	98.22	-7.416	<0.001
Breathless when talk	84.50	0.00	1.46	11.10	98.28	-7.550	<0.001
Breathless when bend over	76.80	0.00	1.32	10.08	98.28	-7.550	<0.001
Breathing disturbs sleep	85.06	15.66	87.90	0.00	3.33	-1.414	0.157
Exhausted daily	84.00	0.00	84.00	0.00	0.00	0.000	1.000
Breathing embarrassing in public	0.00	0.00	0.00	0.00	-	0.000	1.000
Chest trouble is nuisance	0.00	0.00	0.00	0.00	-	0.000	1.000
Get afraid or panic	87.70	0.00	1.51	11.52	98.28	-7.550	<0.001
Not in control of chest problem	90.10	0.00	1.55	11.83	98.28	-7.550	<0.001
Frail because of chest	87.00	16.01	89.90	0.00	3.33	-1.414	0.157
Exercise is not safe	75.70	0.00	1.31	9.94	98.28	-7.550	<0.001
Seems too much of an effort	81.77	15.05	84.50	0.00	3.33	-1.414	0.157
Cannot go out for recreation	77.23	14.21	79.80	0.00	3.33	-1.414	0.157
Cannot go out for shopping	79.67	10.37	81.00	0.00	1.67	-1.000	0.317
Cannot do housework	77.80	10.13	79.10	0.00	1.67	-1.000	0.317
Cannot move far	1.52	11.94	94.00	0.00	61.00	-7.550	<0.001
Best describe chest affects	46.97	14.11	93.37	17.80	98.79	-7.014	<0.001

Particulars	Post symptom score	Post activity score	Post impact score	Post QOL score
Age group (years) (mean±SD) :				
30-39	59.27	68.15	42.47	53.32
40-49	56.34±13.18	68.15	42.47	52.80±2.33
≥50	59.44±10.58	68.77±3.88	43.31±5.25	53.98±5.28
Chi-square	0.57	0.49	0.49	0.57
P value	0.753	0.784	0.784	0.753
Gender (mean±SD) :				
Female	79.64±28.80	80.25±17.12	58.87±23.20	69.11±22.32
Male	57.87±9.58	68.15	42.47	53.07±1.69
Mann-Whitney test	30.50	28.00	28.00	30.50
P value	0.10	<0.001	<0.001	0.10
Occupation (mean±SD) :				
Unemployed	79.64± 28.80	80.25±17.12	58.87±23.20	69.11±22.32
Unskilled	59.27	68.15	42.47	53.32
Semi-skilled	59.27	68.15	42.47	53.32
Skilled	60.34±1.86	68.15	42.47	53.51± 0.33
Clerk/shopowner/ Farmer	57.50±10.54	68.15	42.47	53.01± 1.86
Chi-square test	4.17	28.00	28.00	4.17
P value	0.383	<0.001	<0.001	0.383

Characteristics	Post activity score (Mean)	Statistical analysis
Age group (Years) :		
30-39	68.15	Chi-square test=0.49 P=0.784
40-49	68.15	
≥50	68.77	
Gender :		
Male	80.25±17.12	Mann-Whitney test, U=28P<0.001
Female	68.15	
Occupation :		
Unemployed	80.25±17.12	Chi-square test=0.28 P<0.001
Unskilled	68.15	
Semi skilled	68.15	
Skilled	68.15	
Clerk/shop-owner/farmer	68.15	

of the five elements in the nursing care bundle, all the elements that were correctly implemented, and after comparison of pre and post test the value was significant. The care package can improve the appropriateness of care and treatment, and allow for more effective long-term follow-up. In pre test assessment 15% patient perceives their health status very poor and 85% patient perceives poor, after intervention 3.1% patient perceive poor but 96.9% patient perceives fair in their health status. The results of the study showed that after receiving the care bundle, the quality of life and activities of daily living increased significantly after the test.

A quasi-experiment showed that after choosing nursing interventions, COPD patients had differences in their health-related quality of life and activities of

daily living. The selected nursing interventions have effectively improved the health status, which is related to the quality of life and activities of daily living of COPD patients⁶. An experimental study was carried out to study the effect of pursed lip breathing and diaphragm muscle breathing on the rehabilitation of COPD patients⁷. The author selected one group of pursed lip breathing and another group of diaphragm muscle breathing and concluded that diaphragm muscle breathing has both positive and positive effects but pursed lip breathing can improve people's breathing. The use of nursing bundle improved the care of COPD worsening after implementation, and the average bundle score increased out of 10 (7 from 4.6)⁸. There was a significant reduction in the unnecessary use of intravenous corticosteroids from

60% to 32% and also a marked improvement in the use of oxygen therapy, with appropriate treatment increasing from 76% to 96%. These results were in line with our findings.

A study reported that the activity increased with a subsequent reduction from baseline to muscle activity at different time points. Rico-Blázquez M, *et al* conducted a study which shows that standardized intervention can enhance the quality of life⁹. Bendstrup KE, *et al* showed that economical, comprehensive, and well-tolerated rehabilitation programs can improve the daily life, quality of life and functional capacity of patients with moderate to severe COPD¹⁰. All the above studies have shown that the health-related quality of life and activities of daily living of COPD patients have improved after care.

Current study has some drawbacks. First, elderly more than 60 years old and critically ill patients were not enrolled in the present study. Second, the intervention was applied for limited period of time; however early intervention gives positive result. Third, sample size was low and study was single centre. Similar study with larger sample size with different care bundles are required.

The results of this research can be implemented in the fields of nursing, education, administration and research. This research provides evidence-based practice. Nurses can provide this kind of care package for COPD patients. The results of this study can be used to teach nursing students the appropriate teaching methods for COPD patient care packages in

the classroom. A lot of work is needed in this area to educate the subjects of COPD on various aspects of nursing strategies. As a nurse researcher, nurses should encourage the improvement of medical care practices, so appropriate intervention measures need to be formulated, and the feasibility and effectiveness of their implementation should be required in in-depth research.

CONCLUSION

This study demonstrated that simple care bundle can improve care for COPD worsening. Using these nursing care bundle not only simplifies care, but also reduces the risk of adverse effects caused by unnecessary medications or treatments. The implementation of nursing care services may result in shorter hospital stays and lower readmission rates, but this requires further research. In addition care bundle can change the prescription of medicines, so it may have an impact on reducing unnecessary drug costs.

ACKNOWLEDGEMENTS

We thank to all the participants who had given their consent to participate in the study.

Ethics Approval : Study protocol was approved by Institutional Ethics Committee of the institution. Also, study was performed in the accordance of the approved protocol.

Consent to Participate : Informed written consent was taken from all the participants prior to enrolling in the study.

Conflicts of Interest: Authors declare no competing financial interest.

REFERENCES

- 1 Black MJ, Hawkins J, Kane MA — Medical Surgical Nursing.8th edition. Missouri. Saunders Elsevier; 2005.
- 2 Bunker C — Rosedale Text Book of Basic Nursing. 7th edition. Philadelphia. Lippincott Publishers. 1999.
- 3 Pulaski LA, Taro ES — Linkman's Core Principles and Practice of Medical Surgical Nursing.1st edition. India: WB Saunders Elsevier's Publisher. 2010.
- 4 Meguro M, Barley EA, Spencer S, Jones PW — Development and validation of an improved, COPD-specific version of the St. George Respiratory Questionnaire. *Chest* 2007; **132(2)**: 456-63.
- 5 Gupta D, Agarwal R, Aggarwal AN, Maturu VN, Dhooria S, Prasad KT, *et al* — Guidelines for diagnosis and management of chronic obstructive pulmonary disease: Joint ICS/NCCP (I) recommendations. *Lung India: official organ of Indian Chest Society* 2013; **30(3)**: 228.
- 6 Gopinath S, Malathi V, Quasi A — Experimental Study to Assess the Effectiveness of Selected Nursing Interventions on Health Related Quality Of Life and Activities Of Daily Living Among COPD Patients In Selected Tertiary Hospital. *IOSR Journal of Nursing and Health Science (IOSR-JNHS)* 2015; **4(1)**: 19-23.
- 7 Parikh R, Shah TG, Tandon R — COPD exacerbation care bundle improves standard of care, length of stay, and readmission rates. *International Journal of Chronic Obstructive Pulmonary Disease* 2016; **11**: 577.
- 8 McCarthy C, Brennan JR, Brown L, Donaghy D, Jones P, Whelan R, *et al* — Use of a care bundle in the emergency department for acute exacerbations of chronic obstructive pulmonary disease: a feasibility study. *International Journal of Chronic Obstructive Pulmonary Disease* 2013; **8**: 605.
- 9 Rico-Blázquez M, Escortell-Mayor E, del-Cura-González I, Sanz-Cuesta T, Gallego-Berciano P, de Las Casas-Cámara G, *et al* — CuidaCare: effectiveness of a nursing intervention on the quality of life's caregiver: cluster-randomized clinical trial. *BMC Nursing* 2014; **13(1)**: 1-0.
- 10 Bendstrup KE, Ingemann Jensen J, Holm S, Bengtsson B — Out-patient rehabilitation improves activities of daily living, quality of life and exercise tolerance in chronic obstructive pulmonary disease. *Eur Respir J* 1997; **10(12)**: 2801-6.

JIMA is now fully **ONLINE** and
Publishes only **ONLINE** submitted Articles
through
<https://onlinejima.com>

Original Article

Study of Cardiac Dysfunction in Non-alcoholic Cirrhotic Patients in a Tertiary Care Hospital

Antarleena Ray¹, Manjari Saha², Tanmay Roy³, Jayanti Ray⁴, Udas Chandra Ghosh⁵, Soumya Sarathi Mondal⁵

Background : Cirrhotic Cardiomyopathy is one of the most important but apparently overlooked complications that significantly increase morbidity and mortality among patients of Liver Cirrhosis. Most studies are based on Alcoholic Cirrhosis and very limited data is available on non-alcoholic causes.

Aims and Objectives : The purpose of this study is to evaluate Cardiac Dysfunction among non-alcoholic cirrhotic patients and to correlate the severity of Cardiac Dysfunction with severity of Liver Cirrhosis assessed by Child Pugh scoring.

Methodology : In this cross sectional study 50 diagnosed patients of Chronic Liver Disease (CLD) were included who underwent Electrocardiography (ECG) and Echocardiography. Mean values of Left Ventricular Ejection Fraction (LVEF), Left Ventricular Internal Diameter-Diastolic [LVID (D)], E/A ratio and QTc interval were calculated and compared to Child Turcotte Pugh Class A, B and C to demonstrate correlation between Cardiac Dysfunction and severity of CLD.

Results : Significant association between the reduction of LVEF and Child Turcotte Pugh class A *versus* C ($p < 0.001$) and B *versus* C ($p < 0.001$) was found. Difference of mean LVID (D) among A *versus* C ($p < 0.001$) and B *versus* C ($p < 0.001$) was statistically significant. Relation between Diastolic Dysfunction and Child Pugh score in three groups was statistically significant, A *versus* C ($p < 0.001$), B *versus* C ($p < 0.001$).

Conclusion : Recognition of Cirrhotic Cardiomyopathy is suboptimal as it is mostly a subclinical cardiac failure. Significant Cardiac Dysfunction was found in our study as expressed by grade I Diastolic Dysfunction in 60% and grade II Diastolic Dysfunction in 20% of patients. Correlation between severity of Cardiac Dysfunction and severity of Liver Cirrhosis was also established.

[J Indian Med Assoc 2023; 121(8): 64-7]

Key words : Cirrhosis, Non-alcoholic Cirrhosis, Cardiac Dysfunction, Diastolic Dysfunction.

Cirrhosis of Liver is defined histopathologically as development of fibrosis to the point that there is architectural distortion with the formation of regenerative nodules. It has a variety of clinical manifestations and complications. Cirrhotic Cardiomyopathy is one of the most important but apparently overlooked complications that significantly increase morbidity and mortality among such patients.

In 2005, The World Congress of Gastroenterology in Montreal Working Group defined Cirrhosis associated cardiomyopathy as a form of chronic cardiac dysfunction in patients of cirrhosis, characterized by blunted contractile response to stress and/or altered

Editor's Comment :

- Cirrhotic cardiomyopathy is mostly a subclinical heart failure that significantly increases morbidity in patients of liver cirrhosis.
- There is very limited data available on cardiac dysfunction in non alcoholic cirrhosis.
- ECG and echocardiography are the best screening methods, using which we found significant diastolic dysfunction correlating with the severity of liver cirrhosis.

diastolic relaxation with electrophysiological abnormalities in the absence of other known cardiac diseases.

Most studies are based on Alcoholic Cirrhosis and very limited data is available on non alcoholic causes. The purpose of this hospital based observational study is to evaluate prevalence of Cardiac Dysfunction among non-alcoholic cirrhotic patients and to correlate the severity of Cardiac Dysfunction with severity of Liver Cirrhosis assessed by Child Pugh scoring.

Pathophysiology :

- Systemic circulation in patients with decompensated Cirrhosis is hyper dynamic and

Department of General Medicine, Kolkata Medical College, Kolkata 700073

¹MD, Postgraduate Trainee and Corresponding Author

²MD, Associate Professor

³MD, RMO *cum* Clinical Tutor, Department of General Medicine, Raiganj Government Medical College and Hospital, Raiganj 733134

⁴MD, Associate Professor, Department of General Medicine, College of Medicine & Sagore Dutta Hospital, Kolkata 700058

⁵MD, Professor

Received on : 13/07/2022

Accepted on : 21/01/2023

characterized by increased heart rate and cardiac output and decreased systemic vascular resistance with low-normal or decreased arterial blood pressure. The factors that increase the cardiac output are increased sympathetic nervous activity, increased preload and blood volume and the presence of arteriovenous communications. However, the Cardiac Stroke Index and Left Ventricular Ejection Fraction (LVEF) fall during exercise which indicates an abnormal ventricular response to an increased ventricular filling pressure.

- After exercise the LVEF increases significantly less in Cirrhosis patients as compared to matched controls. The reduced cardiac performance is probably caused by a combination of blunted heart rate response to exercise, reduced myocardial contractility and profound wasting of skeletal muscles with impaired extraction of peripheral oxygen. Reduced left ventricular end diastolic volume and LVEF after standing has also been noted which indicates an impaired myocardial response to erect posture.

- The fluidity of the Plasma membrane and the function of K and Ca ion channels have been shown to be impaired in Cirrhosis. Delayed repolarisation of cardiomyocytes secondary to defects in K⁺ channel function could lead to electrophysiological abnormalities in cardiac excitation. A prolonged QT interval (>440ms) has been previously described in Liver Disease leading to ventricular arrhythmias and sudden cardiac death.

- Response to Noradrenaline and other potent pressor substances such as Angiotensin II and Vasopressin is blunted in Cirrhosis patients.

Studies in animal models have shown down regulation with reduced beta adrenergic receptor density in cardiomyocytes and receptor desensitization. In non-alcoholic Cirrhosis cardio depressant substances are produced such as endotoxins, endothelins, bile acid and cardiac cytokines such as TNF Alfa and IL1b.

In its most benign form, Cirrhotic Cardiomyopathy manifests as subtle ECG and Echo abnormalities, most commonly as prolonged QT interval and Diastolic Dysfunction, but typically with preserved systolic function in the resting and pre transplant vasodilated state. At the extreme, Cirrhotic Cardiomyopathy progresses to fulminant Myocardial Failure under the hemodynamic stress of Liver Transplant Surgery, unmasked by the demands of bleeding, high doses of vasopressors, reversal of low to high afterload, withdrawal of cardio protective medications such as beta blockers and mineralocorticoid antagonists used

in End-stage Liver Disease (ESLD), and worsened by concomitant sepsis or Systemic Inflammatory Response Syndrome (SIRS).

MATERIALS AND METHODS

Study setting : Department of General Medicine at Kolkata Medical College, West Bengal, India

Study design : hospital based observational study

Time line: February 2016-January 2017

Definition of population : patients with Liver Cirrhosis attending Medicine OPD or admitted under the Department of Medicine

Sample size : 50

Sample design : all cirrhotic patients without having previous Cardiac Dysfunction attending Medicine OPD/admitted and given written informed consent will be made part of the study

Inclusion Criteria :

- (1) Age 12-60
- (2) Patient of CLD/Cirrhosis(documented by clinical/biochemical/radiological/histological criteria) who has no history of previous alcohol intake

Exclusion Criteria :

- (1) Cirrhosis/CLD associated with alcohol intake
- (2) Preexisting cardiac disease or obvious cardiac abnormality
- (3) Preexisting Lung Disease or other systemic co morbidities affecting cardiac function

Parameters to be studied :

(1) Parameters to find out evidence of CLD : Clinical, Biochemical (Liver Function Tests), Radiological (USG) or Histopathological (Liver Biopsy).

(2) Parameters to find out Cardiac Dysfunction: Clinical, ECG, Echo.

Using basic 2D indices of Diastolic Dysfunction, pulsed wave Doppler at the mitral valve leaflet tips provides information about early and late diastolic filling in normal sinus rhythm with rapid passive filling (E-wave) followed by atrial contraction (A wave). Pulse wave Doppler estimates of Diastolic parameters can guide in categorizing patients on the spectrum of diastolic abnormalities using a validated grading system.

Study tools :

- (1) Predesigned and pretested proforma.
- (2) Tests to diagnose CLD (clinical, biochemical, Radiological and Histological).
- (3) Tests to find out etiology of CLD[Hepatitis B Surface Antigen(HBsAg), Hepatitis C Antibody(anti HCV), Anti Nuclear Antibody (ANA), serum ceruloplasmin, serum ferritin, anti-liver kidney

microsomal antibody (anti LKM1), anti Smooth Muscle Antibody (anti SMA), anti soluble liver antigen (anti SLA antibodies)] according to clinical suggestion.

(4) Echo, ECG, Digital Chest X-ray.

(5) Tests to assess systemic disease status and co-morbidities (complete hemogram, lipid profile, Fasting Blood Sugar (FBS), Post Prandial Blood Sugar (PPBS), serum urea, serum creatinine, serum Na, serum K and other investigations as per clinical suggestion).

(6) Other relevant investigations to be done to rule out systemic conditions affecting cardiac function.

Diagnostic Criteria (Fig 1) :

Cirrhotic patient with	
1.	Abnormal contractile response to stress
2.	Diastolic dysfunction
3.	Absence of another clinically significant cardiopulmonary Disease
Systolic function (at least 1)	
>	Blunted increase in cardiac output with exercise, volume challenge or pharmacologic stimuli.
>	Resting left ventricular ejection fraction (LVEF) < 55%
Diastolic function (at least 1)	
>	E/A ratio < 1 (age corrected)
>	Prolonged mitral deceleration time (DT > 200 ms)
>	Prolonged isovolumetric relaxation time (>80 ms)
Supportive criteria	
>	Abnormal chronotropic response to stress
>	Electromechanical uncoupling
>	Dysynchrony
>	Prolonged QTc interval
>	Enlarged left atrium
>	Increased left ventricular mass
>	Increased BNP or proBNP

Fig 1 — Diagnostic criteria for Cirrhotic Cardiomyopathy according to the World Gastroenterology Organization (Montreal 2005)

Study Technique and Data Analysis :

Informed written consent was obtained from the patients and their relatives and the study protocol was approved by the Ethics Committee.

All data was tabulated in a master chart and analyzed by standard statistical procedures. Descriptive states expressed in terms of ratio, proportion, percentage for categorical data and in terms of mean, median, range for quantitative data.

Continuous variables are expressed as Mean and Standard Deviation (SD) and compared across the groups using Mann-Whitney U test/Kruskal Wallis Test as appropriate.

Categorical data was analyzed by Chi square test and Cochran tests.

P value of <0.05 will be considered significant.

ANALYSIS AND RESULTS

In this cross sectional, observational, hospital based study- a total of 50 diagnosed patients of CLD were included. Patients having co morbid conditions that maybe associated with Cardiomyopathy such as Hypertension, Dyslipidemia and CKD- were excluded. Known cases of heart disease and pulmonary disease were excluded. Included patients underwent ECG and Echocardiography.

Child Turcotte Pugh class was calculated for each of the cases and was subdivided into 3 classes- A (5-6), B (7-9) and C (10-15). Mean values of Left Ventricular Ejection Fraction (LVEF), Left Ventricular Internal Diameter-Diastolic [LVID(D)], Left atrial diameter, E value, A value, E/A ratio and QTc interval were calculated. Mean values of these parameters were compared to Child Pugh class A, B and C to demonstrate whether there is any correlation between levels of these parameters and severity of CLD.

Out of 50 patients, 38 were Male and 12 were Females.

Median age of study was 44.50 ranging from 17-60 years.

42 patients had cryptogenic CLD, 5 had autoimmune Hepatitis and 3 had Chronic Hepatitis B contributing 84%, 10% and 6% to the etiology respectively (Tables 1-4).

Thus,

- Significant association between reduction of LVEF and Child Turcotte Pugh class A *versus* C (p<0.001) and B *versus* C (p<0.001) was found.
- Difference of mean LVID (D) among A *versus* C

	Child Pugh Class A	Child Pugh Class B	Child Pugh Class C	Total
No Diastolic Dysfunction	6(60)	4(16.7)	0	10(20)
Diastolic Dysfunction Grade 1	4(40)	19(79.17)	7(43.75)	30(60)
Diastolic Dysfunction Grade 2	0	1(4.17)	9(56.25)	10(20)
Total	10(100)	24(100)	16(100)	50(100)
A <i>versus</i> B 0.034 Not Significant		A <i>versus</i> C <0.001 Significant		
B <i>versus</i> C <0.001 Significant				

	Child Pugh Class A	Child Pugh Class B	Child Pugh Class C	Total
No QTc Prolongation	9(90)	22(91.6)	11(68.75)	43(86)
QTc Prolongation	1(10)	2(8.3)	5(31.25)	7(14)
Total	10(100)	24(100)	16(100)	50(100)
A <i>versus</i> B 0.875 Not Significant		A <i>versus</i> C 0.210 Not Significant		
B <i>versus</i> C 0.061 Not Significant				

Table 3 — Distribution of LVEF with Child Pugh Score

	LVEF (%)
Child Pugh Class A Mean	55
Child Pugh Class A Standard Deviation	3.13
Child Pugh Class B Mean	53.33
Child Pugh Class B Standard Deviation	2.50
Child Pugh Class C Mean	46.19
Child Pugh Class C Standard Deviation	3.25
A versus B	0.136 Not Significant
A versus C	<0.001 Significant
B versus C	<0.001 Significant

Table 4 — Distribution of LVID (D) with Child Pugh Score

	LVID (D)
Child Pugh Class A Mean	44.90
Child Pugh Class A Standard Deviation	1.52
Child Pugh Class B Mean	45.50
Child Pugh Class B Standard Deviation	1.77
Child Pugh Class C Mean	54.44
Child Pugh Class C Standard Deviation	3.72
A versus B	0.363 Not Significant
A versus C	<0.001 Significant
B versus C	<0.001 Significant

($p < 0.001$) and B versus C ($p < 0.001$) was statistically significant.

- Relation between Diastolic Dysfunction and Child Pugh score in three groups was statistically significant, A versus C ($p < 0.001$), B versus C ($p < 0.001$).
- Association between QTc prolongation and Child Pugh score was not significant.
- No significant correlation between etiology of Cirrhosis and Cardiac Dysfunction was found.

SUMMARY AND CONCLUSION

Recognition of Cirrhotic Cardiomyopathy is suboptimal because of a lack of sensitive, noninvasive diagnostic tests. Similarly, management of Cirrhotic Cardiomyopathy is largely empirical because of a paucity of existing literature. It is a subclinical Cardiac Failure. The prevalence remains unknown mostly due to the disease being generally latent, overt Heart Failure is very rare. It is manifested only when the patient is subjected to stress such as exercise, drugs, hemorrhage, infections and surgery. Echocardiography allows the detection of LVDD with the E/A ratio being the best screening test to detect the condition. The severity of Cardiac Dysfunction may be a sensitive

marker for mortality. Treatment is non-specific but Orthotopic liver transplantation may normalize the Cardiac Function.

LIMITATIONS

Biggest limitation of this study is the small sample size. A large prospective and multicentric trial is necessary in this field.

Control population of healthy adults should have been incorporated to have a more reliable set of data.

This study does not have a therapeutic arm. Whether available therapeutic options can modify Cirrhotic Cardiomyopathy or not should be properly studied.

REFERENCES

- 1 Shorr E, Zweifach BW, Furchgott RF, Beaz S — Hepatorenal factors in circulatory homeostasis IV. Tissue origins of the vasotropic principles, VEM and VDM, which appear during evolution of hemorrhagic and tourniquet shock. 1951; **3**: 42-79.
- 2 Lunseth JH, Olmstead EG, Abbound F — A study of heart disease in one hundred eight hospitalized patients dying with portal cirrhosis. *Arch Intern Med* 1958; **102**: 405-13.
- 3 Gould L, Schariff M, Zahir M, Lieto M, Di Lieto M — Cardiac haemodynamics in alcoholic patients with chronic liver disease and presystolic gallop. *J Clin Invest* 1969; **48**: 860-8.
- 4 Llach J, Gines P, Arroyo V — Prognostic value of arterial pressure, endogenous vasoactive system, and renal function in cirrhotic patients admitted to the hospital for the treatment of ascites. *Gastroenterology* 1988; **22**: 88-95.
- 5 Fernandez-Rodriguez CM, Prieto J, Zoyaya JM — Arteriovenous shunting, hemodynamic changes and renal sodium retention in liver cirrhosis. *Gastroenterology* 1993; **104**: 1139-45
- 6 Moller S, Wiinberg N, Henriksen JH — Noninvasive 24 hour ambulatory arterial blood pressure monitoring in cirrhosis. *Hepatology* 1995; **22**: 88-95.
- 7 Donovan CL, Marcovitz PA, Punch JD, Bach DS, Brown KA, Lucey MR — Two dimensional and dobutamine stress echocardiography in the preoperative assessment of patients with end stage liver disease prior to orthotopic liver transplantation. *Transplantation* 1996; **61**: 1180-8.
- 8 Pozzi M, Carugo S, Boardi G — Evidence of functional and structural cardiac abnormalities in cirrhotic patients with and without ascites. *Hepatology* 1997; **26**: 1131-7
- 9 Henriksen JH, Moller S, Ring Laesen H — The sympathetic nervous system in liver disease. *J Hepatol* 1998; **29**: 328-41.
- 10 Wong F, Liu P, Lilly L, Bomzon A, Blendis L — Role of cardiac structural and functional abnormalities in the pathogenesis of hyperdynamic circulation and renal sodium retention in cirrhosis. *Clin Sci (Lond)* 1999; **97**: 259-67.

Original Article

Summer Surge of Acute Appendicitis in Adults

Abdul Razack G S¹, Harindranath H R², Uday C³, Nashwath Kumar K H⁴

Background : The most common acute surgical condition of the abdomen is Appendicitis. There is growing evidence base to suggest the seasonal variation in causation of acute Appendicitis. Some studies have concluded that acute Appendicitis is a more common summer with reason still not clear. The rationale for our study is to determine whether there is seasonal association with the incidence of acute Appendicitis. The strong association if found will help in preplanning the management and preventing the incidence of severe complication of the disease.

Materials and Methods : This retrospective model was conducted from 01/05/2016 to 30/04/2021 in a patient who was diagnosed with acute Appendicitis. The total admission for acute Appendicitis were collated with calendar month to compare with seasonal variation. Then the number of cases of acute Appendicitis were segregated with respect to age and gender. Results were analysed in terms of number of cases and complications of acute Appendicitis in adults with respect to corresponding months in a year.

Results : During the observation period, 620 cases had been admitted with the diagnosis of acute appendicitis. The highest incidence of acute Appendicitis was seen in the 18-29 years age group (54%). In all age groups the incidence declined with age increment. A significant seasonal effect was also observed, the rate of acute Appendicitis was high in summer and was highest in the month of May (11.8%) and the lowest number of cases were in January (6%). The complication of acute Appendicitis was highest in the month of May (4.9%).

Conclusion : Acute Appendicitis and its complications is more common in the summer month and is maximum in the month of May. The clear association will help in preplanning the management and preventing the incidence of severe complication of the disease.

[J Indian Med Assoc 2023; 121(8): 68-70]

Key words : Acute Appendicitis, Seasonal variation.

The most common acute surgical condition of the abdomen is appendicitis¹. The most common operation worldwide is Appendectomy². The clinical syndrome which results in inflammation of vermiform appendix is called Appendicitis³. Among males and females there is equal distribution⁴.

The causes of appendicitis are unclear and multifactorial. There are a variety of attributable causes like mechanical obstruction⁵, inadequate dietary fibre, smoking⁶, air pollution and familial susceptibility⁷. There is growing evidence base to suggest the seasonal variation in causation of acute Appendicitis⁸.

Acute Appendicitis begins with the classical features of poorly localized colicky abdominal pain. The pain is first noticed in the periumbilical region with anorexia and nausea. Later due to involvement of somatic nerves because of irritation of parietal peritoneum pain gets shifted to the right iliac fossa. The cardinal features of acute Appendicitis is low grade pyrexia, localized abdominal tenderness, muscle guarding and rebound tenderness³.

Department of General Surgery, Bangalore Medical College and Research Institute, Karnataka 560004

¹MBBS, MS, Assistant Professor

²MBBS, MS, Professor

³MBBS, Postgraduate Student and Corresponding Author

⁴MBBS, Postgraduate Student

Received on : 03/12/2021

Accepted on : 14/04/2023

Editor's Comment :

- In summer months, younger patients coming with pain abdomen and tenderness in right iliac fossa is more likely to be acute Appendicitis.
- Early preparedness and early intervention is necessary to avoid complications.

Variable results are obtained from various studies done to determine the seasonal variation of acute Appendicitis⁹. Some studies have concluded that acute Appendicitis is more common summer with reason still not clear. Most epidemiological studies of acute Appendicitis have been conducted and focused on western population¹⁰. The rationale for our study is to determine whether there is seasonal association with the incidence of acute Appendicitis. The strong association if found will help in preplanning the management and preventing the incidence of severe complication of the disease (Tables 1&2, Figs 1&2).

MATERIALS AND METHODS

This retrospective observational study was conducted at the Department of General Surgery, (Victoria Hospital and Bowring and Lady Curzon Hospital), Bangalore Medical College and Research Institute, Bengaluru, from 01/05/2016 to 30/04/2021. Ethical Committee and Medical records department permission was taken. Data was collected from the registers in the medical records department of both

Age (Years)	Frequency	Percentage
18-29	335	54
30-39	166	26.8
40-49	64	10.3
50 And Above	55	8.9
Total	620	100

Month	Abscess	Mass	Perforation	Total (Percentage)
January	0.3	0.2	0.3	0.8
February	0.2	0.3	0.5	1.0
March	0.5	0.3	1.0	1.8
April	0.3	0.8	1.1	2.2
May	0.8	1.8	2.3	4.9
June	0.5	1.3	1.5	3.3
July	0.6	0.6	0.6	1.8
August	0.2	0.5	0.8	1.5
September	0.5	0.0	0.5	1.0
October	0.0	0.2	1.0	1.2
November	0.2	0.3	0.0	0.5
December	0.0	0.3	0.6	0.9
Total	4.1	6.6	10.2	20.9

hospitals. Registers include Surgery case completion register updated by General surgery residents, Anaesthesia case register updated by Anaesthesia residents, and Nurses case register updated by Floor nursing staff of the respective operation theatre complex. Inclusion criteria were set to identify the number of patients over the age of 18 years with an associated diagnosis of acute Appendicitis. There were total number of cases were further analysed to create anonymous database having admission number, age, sex, date of admission and final diagnosis. After entries were made of the patient's data, date-resolved analysis was made. The total admission for acute Appendicitis were collated with calendar month to compare with seasonal variation. Then the number of cases of acute Appendicitis were segregated with respect to age and gender.

An expected number of cumulative admissions per month was established on the basis of a null hypothesis. This was taken to be that the incidence of acute Appendicitis is normally distributed across the year; that there is no seasonal variation over the 12 months and an equal number of episodes should be recorded in each month regardless of the analysed independent variables. An expected number of incident cases for each month was therefore one twelfth of the total figure, $620/12 =$ approximately 52 cases per calendar month.

Based on the data collected from these registers, the total numbers of cases of acute Appendicitis were tabulated. The data collected was analysed. Results were analysed in terms of number of cases and complications of acute Appendicitis in adults with respect to corresponding months in a year. The study also analysed age wise distribution of acute Appendicitis in adults.

Statistical Analysis :

The summer surge in the incidence of acute Appendicitis in adults is presented as the number and percentage of total acute Appendicitis cases during the study period. Using the SPSS software package (SPSS 27.0 grad pack) the data were analysed. Count and frequency of patients in each gender, age groups and months were analysed. Comparisons between the frequencies were performed using Chi-square test.

RESULTS

During the observation period, 620 cases had been admitted with the diagnosis of acute Appendicitis. Of these, 77.4% were males and 22.6% were females (Male: Female=3.424). The highest incidence of acute Appendicitis was seen in the 18-29 years age group (54%). The incidence was highest in males aged 18-29 years. In all age groups the incidence declined with age increment. A significant seasonal effect was also observed, the rate of acute Appendicitis was high in summer and was highest in the month of May (11.8%) and the lowest number of cases were in January (6%). Age group of 18-29 years had the highest number of cases in the month of April (6.1%) and May (6.1%). There was significant association between complication of acute Appendicitis and age groups ($p=0.040$). The complication of acute Appendicitis was highest in the month of May (4.9%). The complication was lowest in the month of January (0.8%).

There was no significant association found between the seasonal changes and the sex of the patient of acute Appendicitis ($p=0.783$).

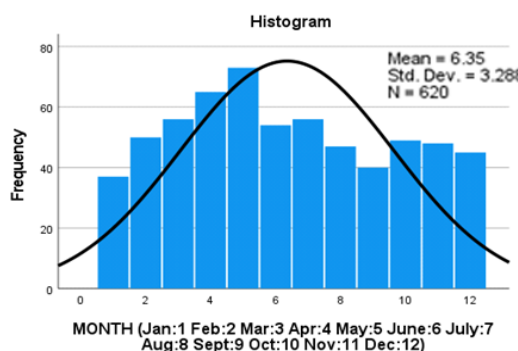


Fig 1 — Seasonal distribution of acute Appendicitis in adults

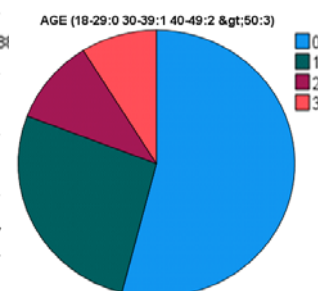


Fig 2 — Age wise distribution of acute Appendicitis in adults

DISCUSSION

The demographic information from the contributing 620 admission episodes of acute Appendicitis appears consistent with that observed in prior work. In our study a significant seasonal effect was also observed, the rate of acute Appendicitis was high in summer and was highest in the month of May (11.8%) and the lowest number of cases were in January (6%). Age group of 18-29 years had the highest number of cases in the month of April (6.1%) and May (6.1%). The complication of acute Appendicitis was highest in the month of May (4.9%). The complication was lowest in the month of January (0.8%).

Many studies have shown seasonal variation in acute Appendicitis¹¹⁻¹⁵ and a recent metanalysis, representing some of the strongest evidence for this, showed a peak incidence in the summer months for 9 of the 11 included studies¹⁶.

A study was conducted by Babita, *et al*¹⁷ in India over from January 2003-July 2012. A total of 395 cases were included. The cases were maximum in the month of August and minimum was noticed in January¹⁷ while in our study maximum incidence was seen in May and minimum in January.

In a study conducted in by Rai, *et al*¹⁸ a clear seasonal variation was observed in the incidences of acute Appendicitis and Appendectomy for both genders. The peak incidence was seen in the summer season and decreased in the winter season. In addition, the present study observed a slight but consistent increase in the incidence of perforated appendicitis in the summer season¹⁸.

A study was conducted in Taiwan by Lin, *et al*¹⁹ all in 2015. The highest incidence of Appendicitis was found in persons aged 15 to 29 years and males had higher rates of appendicitis than females at all ages except for 70 years and older. Appendicitis rates were 11.76 % higher in the summer than in the winter months¹⁹.

In a study conducted at Finland by Imre, *et al*²⁰ in various centres of Finland showed clear correlation of seasonality with acute Appendicitis with increased incidence in summer season.

CONCLUSION

Acute Appendicitis and its complications is more common in the summer month and is maximum in the month of May. The age group most commonly affected in adults is 18-29 years. The clear association will help in preplanning the management and preventing the incidence of severe complication of the disease. The seasonal variations of acute Appendicitis are consistent with other studies.

Conflicts of interest : There are no conflicts of interest.

REFERENCES

- Liu CD, McFadden DW — Acute abdomen and appendix. In: Greenfield LJ, Mulholland MW, Zelenock GB, Oldham KT, Lillemoie KD, editors. *Surgery: scientific principles and practice*. 3rd ed. Philadelphia: Lippincott-Raven; 1997. p. 1246e61
- Blomqvist P, Ljung H, Nyren O, Ekbohm A — Appendectomy in Sweden 1989-1993 assessed by the inpatient registry. *J Clin Epidemiol* 1998; **51(10)**: 859e65.
- Williams N, O'Connell PR, McCaskie AW — Bailey & Love's Short Practice of Surgery, 27th Edition; Chapter 72 - The vermiform appendix. In: Bailey & Love's Short Practice of Surgery 2018; p. 1329, 1302-03.
- Khattak S, Aslam S, Kamal A — Acute Appendicitis: An audit of 663 cases. *Gomal J Med Sci* 2010; **8**: 209-11.
- Oldmeadow C, Wood I, Mengersen K, Visscher PM, Martin NG, Duffy DL — Investigation of the relationship between smoking and appendicitis in Australian twins. *Ann Epidemiol* 2008; **18**: 631-6. doi:10.1016/j.annepidem.2008.04.004.
- Kaplan GG, Dixon E, Panaccione R, Fong A, Chen L, Szyszkowicz M, *et al* — Effect of ambient air pollution on the incidence of appendicitis. *CMAJ* 2009; **181**: 591-7. doi:10.1503/cmaj.082068.
- Ergul E — Heredity and familial tendency of acute appendicitis. *Scand J Surg* 2007; **96**: 290-2. doi:10.1177/145749690709600405.
- York TJ — Seasonal and climatic variation in the incidence of adult acute appendicitis: a seven year longitudinal analysis. *BMC Emerg Med* 2020; **20(1)**: 24.
- Noudeh YJ, Sadigh N, Ahmadian AY — Epidemiologic features, seasonal variations and false positive rate of acute appendicitis in Shahr-e-Rey, Tehran. *Int J Surg* 2007; **5**: 95-8. doi:10.1016/j.ijisu.2006.03.009.
- Rai R, D'Souza RC VV, Sudarshan SH, PSA, Pai JR, *et al* — An Evaluation of the Seasonal Variation in Acute Appendicitis. *J Evol Med Dental Sci* 2014; **3**: 257-60. doi:10.14260/jemds/2014/1818.
- Luckmann R, Davis P — The epidemiology of acute appendicitis in California. *Epidemiology* 1991; **2(5)**: 323-30.
- Körner H, Söndena K, Söreide J, Andersen E, Nysted A, Lende T, *et al* — Incidence of acute nonperforated and perforated appendicitis: age-specific and sex-specific analysis. *World J Surg* 1997; **21(3)**: 313-7.
- Ahmed W, Akhtar M, Khan S — Seasonal variation of acute appendicitis. *Pakistan J Med Sci* 2018; **34(3)**: 564-7.
- Ilves I, Paaianen H, Herzig K, Fagerström A, Miettinen P — Changing incidence of acute appendicitis and nonspecific abdominal pain between 1987 and 2007 in Finland. *World J Surg* 2011; **35(4)**: 731-8.
- Stein G, Rath-Wolfson L, Zeidman A, Atar E, Marcus O, Joubran S, *et al* — Sex differences in the epidemiology, seasonal variation, and trends in the management of patients with acute appendicitis. *Langenbeck's Arch Surg* 2012; **397(7)**: 1087-92.
- Fares A — Summer appendicitis. *Ann Med Health Sci Res* 2014; **4(1)**: 18.
- Jangra B, Jangra M, Rattan KN, Kadian Y — Seasonal and day of week variations in acute appendicitis in north Indian children. *J Indian Assoc Pediatr Surg* 2013; **18(1)**: 42.
- Rai R, D'Souza RC, Vijn, Sudarshan SH, Aithala, Pai. J R, *et al* — An evaluation of the seasonal variation in acute appendicitis. *J Evol Med Dent Sci* 2014; **3(2)**: 257-60.
- Lin KB, Lai KR, Yang NP, Chan CL, Liu YH, Pan RH, *et al* — Epidemiology and socioeconomic features of appendicitis in Taiwan: a 12-year population-based study. *World J Emerg Surg* 2015; **10**: 42. doi: 42.1186/s13017-015-0036-3.
- Ilves I, Fagerström A, Herzig KH, Juvonen P, Miettinen P, Paaianen H — Seasonal variations of acute appendicitis and nonspecific abdominal pain in Finland. *World J Gastroenterol* 2014; **20**: 4037-42. doi: 10.3748/wjg.v20. i14.4037.

Original Article

Post Mortem Renal Pathological Changes in Snake bite Patients and Association with Clinical Features

Pinaki Mukhopadhyay¹, Joydeep Khan², Piyali Banerjee³, Palas Bhattacharya⁴, Manik Kataruka⁵, Suparna Datta⁶

Snake bite is very common in rural India and incidence of renal failure and death following snake bite is high. We have studied the different histopathological changes in renal tissue in deceased patient following snake bite. Acute interstitial nephritis was the most common histological feature followed by acute tubular necrosis. Presence of DIC was most commonly associated with acute tubular necrosis.

[J Indian Med Assoc 2023; 121(8): 71-4]

Key words : Snake bite, Post-mortem, Renal histology.

Snakes have always managed to grab human attention and being an object of fear and veneration since historic civilizations. Snake bite is a common medical emergency and an occupational hazard, more so in tropical India, where farming is a major source of employment¹. India has the highest mortality in the world, nearly 35000-50000 per year². The World Health Organization (WHO) has estimated that nearly 1,25,000 deaths occur among 2,50,000 poisonous Snake bites worldwide every year, of which India accounts for 10,000 deaths¹. Snake bite is a real problem in rural and urban India as mainly involve healthy, young, working population in their working area. There are nearly 3000 species of snake are known worldwide, of which nearly 600 are conserved poisonous. Snake bite results in multisystem involvement including kidneys. Renal manifestation ranges from AKI, Thrombotic Microangiopathy to Chronic kidney disease. Renal failure is mostly associated with Russell's Viper and E Carinatus bites (13-32%)³. Several mechanisms including

Editor's Comment :

■ Post mortem Renal histopathology following Snake bite AKI varies. Though different series showed ATN as commonest, our series AIN predominant and DIC and shock was the surrogate clinical Predictor.

haemorrhage, hypertension, haemolysis, haemoglobinuria, rhabdomyolysis and DIC as well as the direct effect of the venom have been incriminated in the pathogenesis of Snake bite related nephropathy. Renal replacement therapy, bite to needle time, hospital stay, bleeding manifestations, shock and DIC, number of vials AVS are known factors affecting the outcome in Snake bite patients. This study has been done to evaluate the different renal histopathological changes on Post mortem and associated clinical findings in Snake bites patients who had renal failure at presentation.

AIMS AND OBJECTIVE

The present study has been done to evaluate the surrogate predictors of mortality and the spectrum of histopathological changes of Kidney in death due to venomous snake bite.

MATERIALS AND METHODS

The study was conducted on death due to venomous Snake bite at Hospital ward of NRS Medical College & Hospital and cases sent for medicolegal autopsy at the hospital mortuary of I during the period September, 2017 to August, 2018. It was a Descriptive, Observational, Cross-sectional, Hospital based study. Any patient with previous history of renal dysfunction were excluded from the study. Informed consent had been taken from the legal representative of the deceased. Kidneys were preserved in 10% formalin and histopathological studies has been done by with

Department of Nephrology, Sir Nil Ratan Sircar Medical College & Hospital, Kolkata 700014

¹MBBS, DCH, MD, DM (Nephrology), Professor & Head

²MBBS, MD (FSM), Assistant Professor, Department of Forensic Medicine and State Medicine, Santiniketan Medical College, Bolpur, West Bengal 731204

³DA, MD (Anaesthesia), Medical Officer, Lady Dufferin Victoria Hospital, Kolkata 700009

⁴MBBS, MD (Pathology), Associate Professor, Department of Pathology, Sir Nil Ratan Sircar Medical College & Hospital, Kolkata 700014

⁵MBBS, MD (Paediatric Medicine), DM (Nephrology), Assistant Professor and Corresponding Author

⁶MBBS, MD (FSM), Professor and Director, State Institute of Health and Family Welfare, West Bengal

Received on : 02/08/2022

Accepted on : 18/09/2022

Hematoxylin and Eosin (H&E) and Periodic Acid Schiff (PAS) stains. All the clinical and laboratory findings were noted in a pre-specified proforma and Post mortem findings were also studied. Gross examination and histopathological findings of kidneys in Post mortem period were recorded and all data were analysed in SPSS software version 16 (SPSS, Chicago, IL, United States).

Inclusion Criteria :

All dead bodies with history of death following a venomous Snake bite.

Exclusion Criteria :

- Decomposed bodies.
- History of renal disease prior to Snake bite.
- Doubtful cases of Snake bite.

OBSERVATIONS

Total 49 patients were analysed. Out of 49 cases, 29 patients were admitted in NRS Medical College, while 20 were brought from outside. Among these patients, 34 (69.4%) were male. Most of the patients are in age group of 20 to 30 years (26.5%) followed by 10 to 20 years (24.5%). There were no patients below 10 years and above 70 years. Most of the snake bite cases occurred between June to October (n=37,75.5%). Highest number (36.7%) of Snake bite occurred between 6am to 12pm, most being between 6am to 6:30am, followed by those between 6pm to 12midnight (28.6%). Highest number of bite were in the lower limb (91.8%), followed by upper limb (6.1%) and (2.0%) in the abdomen. Out of 49 Snake bite, 47 involved vasculotoxic snake, while 2 were involved neurotoxic snake. 24.5% of victims received Anti Snake Venom (AVS) between 2 to 3 hours. The maximum time to receive AVS was between 10 to 11 hours Post Snake bite. Most of the patients who succumb to death, were within 1 to 3 day of hospitalization. Longest stay to hospital before death was 29 days.

Among clinical manifestation, shock needing vassopressor was present in 57% of patients, bleeding manifestation in 73.5% cases and DIC was present in 47%.

Most of the patients (73.5%) does not required Haemodialysis (HD) before death and rest received haemodialysis varying from 1 to 5 sessions.

Gross examination and histopathology of kidney performed in all cases in Post mortem. On gross examination, congestion with diffuse haemorrhage over kidney surface was the most common Post mortem finding (51%) followed by congestion with focal medullary haemorrhage (36.7%), congestion with patchy cortico- medullary haemorrhage (8.2%) and only

external congestion in 4.1%. Two patients with neurotoxic bite had shown only external renal congestion (Table 1).

On histopathology, interstitial inflammation was found in all the renal biopsy followed by acute tubular necrosis (57.1%), thrombotic microangiopathy in 14.3% and acute cortical necrosis in 8.2% cases (Tables 2&3).

On multivariate analysis, presence of shock and DIC was significantly associated with acute tubular necrosis. Acute cortical necrosis was positively associated with DIC and thrombotic microangiopathy was found to be significantly associated with presence of shock.

Table 1 — Histopathological Findings In Kidney

Histopathology	Number	Percentage
Interstitial Inflammation	49	100.0
Tubular Necrosis	28	57.1
Cortical Necrosis	4	8.2
Thrombi In Blood Vessels	7	14.3

Table 2 — Correlation Between Risk Factors And Renal Histopathological Findings (Chi Square Test)

Renal Histopathological Findings	Surrogate Predictors	P Value (2-sided)
Tubular Necrosis	Bite to Needle Time	0.020
	Number of HD	0.010
	Shock	0.000
	DIC	0.001
Cortical Necrosis	Bite to Needle Time	0.004
	Number of HD	NS
	Shock	NS
	DIC	0.026
Thrombi In Blood Vessels	Bite To Needle Time	0.030
	Number of HD	0.038
	Shock	0.013

HD- Haemodialysis, DIC- Disseminated Intravascular coagulation, NS-Non Significant

Table 3 — Multivariate Analysis of Risk Factors and Renal Histopathological Findings

Renal Histopathological Findings	Surrogate Predictors	P Value (2-sided)
Tubular Necrosis	Bite to Needle Time	0.206
	Number of HD	0.822
	Shock	0.000
	DIC	0.000
Cortical Necrosis	Bite to Needle Time	0.906
	Number of HD	0.311
	Shock	0.073
	DIC	0.026
Thrombi In Blood Vessels	Bite To Needle Time	0.153
	Number of HD	0.219
	Shock	0.013
	DIC	0.820

HD- Haemodialysis, DIC- Disseminated Intravascular coagulation

DISCUSSION

The present study was descriptive, cross sectional, hospital and mortuary based study, conducted at NRS Medical College & Hospital (NRS MC&H) during September 2017 to August 2018 and included cases which fulfilled the selection criteria. During this period of 1 year, there were 49 cases of death due to Snake bite, comprising 2.02% of all the autopsies done at NRS MC&H morgue.

Snake bite poisoning is a known problem in rural India. Most of the Snake bite cases are found during monsoon season⁴. In our study, 75.5% cases occurred in monsoon season. Most of the victims in our study were male. In the present study, the population comprises of 34(69.4%) males and 15(30.6%) females with a sex ratio of 2.26:1 in the study group. The probable reason for male predominance is males are more involved in outdoor activities compared to females. Similar results were seen from other studies⁵⁻⁷ in India except studies from hilly areas where the main workforce is female^{8,9}. Mean age of subjects was 44.62 years with a range between 14 to 68 years consistent with other studies from India^{5,7,9}.

Snake venom causes damage to multiple organs in the body. Kidney being one of the most vascular tissue in the body, it receives a significant burden of venom, resulting in damage of kidney tissue, leading to Acute Kidney Injury (AKI). The exact pathogenesis of AKI following Snake bite is not well established, due to the lack of a reproducible animal model. The factors that may contribute are direct cytotoxicity, bleeding, hypotension, circulatory collapse, Intravascular haemolysis, disseminated intravascular coagulation and Micro-angiopathic Haemolytic Anaemia (MAHA). Doing renal biopsy is the most definite method to know the exact pathogenesis of renal failure. But doing renal biopsy may not always be possible due to bleeding manifestations and co-morbidity in Snake bite patients. So Post mortem renal biopsy gives us an insight in the renal pathology and possible pathogenesis. Incidence of AKI post Snake bite, has been reported to be 8-45% in different studies¹⁰⁻¹³. This study being primarily a Post mortem study, all of the deceased had some degree of renal failure. During hospital stay, 26.5% patients received haemodialysis. Earlier studies had shown much higher requirement of dialysis in snake bite AKI patients ranging from 45% to 90.9%⁸. This low number of patients requiring dialysis may be explained by the fact that most of the patients in our study were too sick to initiate haemodialysis or died before dialysis could be initiated. Probably the patients who received

haemodialysis has better outcome and survivability, and so does not qualify for our study. Similarly, the patients in our study had much higher incidence of shock (57%) and DIC (73.5%) compared to older studies. In the study by Chugh, *et al*¹⁰ incidence of shock was 16% and DIC 43%. In the study by Athappan, *et al*¹⁴ incidence of shock and DIC were 17.7% and 27.8% respectively. Study by Dharod, *et al*¹³ had shown incidence of shock and DIC were 19.5% and 55.2% respectively.

On Post mortem examination, congestion with diffuse haemorrhage of the kidney parenchyma was the most common (50.2%) feature in our patients followed by focal medullary haemorrhage and patchy cortical medullary haemorrhage. As most of the studies are Pre-mortality in nature, gross description of kidney was absent. Only one study by Pal, *et al*¹⁵ described diffuse haemorrhage to be the most common finding. Among the histo-pathological findings, all patient's biopsies showed acute interstitial inflammation (AIN) followed by Acute Tubular Necrosis (ATN) in 57% cases. Thrombotic microangiopathy was present in 14.3% and diffuse cortical necrosis in 8.2% cases. Neurotoxic cases showed only congestion & inflammation with no haemorrhagic features. Chugh, *et al*¹⁰ had reported ATN in 73% cases and cortical necrosis in 18% cases. In the study by Vikrant, *et al*⁸, 91% has ATN followed by AIN in 41% patients. In a study from Pakistan by Naqvi, *et al*¹⁶, ATN and cortical necrosis were most common finding. Pal, *et al*¹⁵ had reported ATN in 100% biopsies, cortical necrosis in 25% cases and proliferative glomerular changes in 1 case. Sathish, *et al*¹⁷ had reported interstitial congestion as most common finding (65.8%) followed by ATN in 55.3% cases and glomerular changes in 4.3% cases. Mittal BV¹⁸ in his study has shown cortical necrosis as predominant finding in 60.9% cases and ATN in 12.1% cases.

In our study, on multivariate analysis, presence of shock and DIC was significantly associated with acute tubular necrosis. Acute cortical necrosis was positively associated with DIC and thrombotic microangiopathy and cortical necrosis was found to be significantly associated with presence of shock. Number of haemodialysis and bite to needle time had not been found to be associated with renal histo-pathological outcome.

Hypotension is the most common cause resulting in ATN and ACN. Acute tubular necrosis is reversible in most of the cases, while acute cortical necrosis results in residual renal damage and patient may need lifelong renal replacement therapy. Acute interstitial inflammation is usually secondary to direct venom

toxicity and cytokine activation¹⁹. Thrombotic microangiopathy is now a more and more getting recognised in Snake bite patients, characterised by thrombocytopenia and renal failure. Pathogenesis of thrombotic microangiopathy is supposed to be secondary to direct endovascular damage by venom or secondary to cytokine reaction Post envenomation.

CONCLUSION

Our study is one of the largest study including 49 post Snake bite victims with detailed pathological analysis of renal tissue. Contrast to previous studies, acute interstitial inflammation was the most common finding followed by acute tubular necrosis. Presence of shock and DIC was associated with poorer histological description.

Limitation : Being a Post mortem study, detailed clinical evaluation was not possible in all cases. We have to rely on documentation in in-patients records and history given by the patient relatives. Victim bodies, which were referred from other centre had poor clinical data. So detail renal parameter study and their association with pathological finding was not possible.

Conflicts of Interest : The authors declare no conflict of interest.

REFERENCES

- 1 Kasturiratne A, Wickremasinghe AR, de Silva N, Gunawardena NK, Pathmeswaran A, Premaratna R, *et al* — The global burden of snakebite: a literature analysis and modelling based on regional estimates of envenoming and deaths. *PLoS Med* 2008; **5**: e218 [PMID: 18986210 DOI: 10.1371/journal.pmed.0050218]
- 2 Mohapatra B, Warrell DA, Suraweera W, Bhatia P, Dhingra N, Jotkar RM, *et al* — Snakebite mortality in India: a nationally representative mortality survey. *PLoS Negl Trop Dis* 2011; **5**: e1018 [PMID: 21532748 DOI: 10.1371/journal.pntd.0001018]
- 3 Mulay DV, Kulkarni VA, Kulkarni SG, Kulkarni ND, Jaju RB — Clinical profile of snakebite at SRTR Medical College Hospital, Ambajogai (Maharashtra). *Indian Medical Gazette* 1986; **131**: 363-6.
- 4 Ahuja ML, Singh G — Snake bite in India. *Indian J Med Res* 1954; **42**: 661-686 [PMID: 13232717]
- 5 Hati AK, Mandal M, Mukherjee H. Epidemiology of Snakebite in the district of Burdwan. *J Indian Med Assoc* 1992; **90**: 145-7.
- 6 Suchitra N — Snakebite Envenoming in Kerala, South India: Clinical profile and factors involved in adverse outcomes. *EMJ* 2008; **25**: 200-4.
- 7 Kulkarni M Ances S — Snake venom Poisons, experience with 633. *Indian Paed* 1994; **31**: 1239-43.
- 8 Vikrant S, Jaryal A, Parashar A — Clinicopathological spectrum of snake bite-induced acute kidney injury from India. *World J Nephrol* 2017; **6(3)**: 150-61.
- 9 Monterio NP, Kanchan T, Bhagavath P, Pradeep Kumar G — Epidemiology of Cobra bite in Manipal, Southern India. *J Indian Acad Forensic Med* 2010; **32(3)**: 224-27.
- 10 Chugh KS — Snake-bite-induced acute renal failure in India. *Kidney Int* 1989; **35**: 891-907.
- 11 Pinho FM, Zanetta DM, Burdmann EA — Acute renal failure after *Crotalus durissus* snakebite: a prospective survey on 100 patients. *Kidney Int* 2005; **67**: 659-667.
- 12 Harshavardhan L, Lokesh AJ, Tejeshwari HL, Halesha BR, Siddharama SM — A study on the acute kidney injury in snake bite victims in a tertiary care centre. *J Clin Diagn Res* 2013; **7**: 853-856.
- 13 Dharod MV, Patil TB, Deshpande AS, Gulhane RV, Patil MB, Bansod YV — Clinical predictors of acute kidney injury following snake bite envenomation. *N Am J Med Sci* 2013; **5**: 594-9.
- 14 Athappan G, Balaji MV, Navaneethan U, Thirumalikulundusubramanian P — Acute renal failure in snake envenomation: a large prospective study. *Saudi J Kidney Dis Transpl* 2008; **19**: 404-10.
- 15 Pal M, Maiti AK, Roychowdhury UB, Basak S, Sukul B — Renal Pathological Changes in Poisonous Snake Bite: *J Indian Acad Forensic Med* 2010; **32(1)**: 19-21.
- 16 Naqvi R — Snake-bite-induced Acute Kidney Injury. *J Coll Physicians Surg Pak* 2016; **26**: 517-20.
- 17 Sathish K, Shaha KK, Patra AP — Histopathological profile of fatal snake bite autopsy cases in a tertiary care center in South India. *Egypt J Forensic Sci* 2021; **11**: 3.
- 18 Mittal BV — Acute renal failure following poisonous snake bite. *J Postgrad Med* 1994; **40**: 123.
- 19 Priyamvada PS, Shankar V, Srinivas BH, Rajesh NG, Parameswaran S — Acute Interstitial Nephritis Following Snake Envenomation: A Single-Center Experience. *Wilderness Environ Med* 2016; **27**: 302-6.

Original Article

Evaluation of Organoleptic Properties and Compliance with Marketed Cough Syrups : A Cross Sectional Consumer Survey in Indian Patients

Ketan K Mehta¹, Akil Contractor², Sanjiv Maniar³, Atul Mashru⁴, Manoj Kumar Singh⁵, Atul Gogia⁶, Rohan Mahajan⁷, Harsh Mittal⁸, Monil Yogesh Neena Gala⁹, Mayank R Dhore¹⁰, Snehal Muchhala¹¹, Gauri Dhanaki¹², Arti Sanghavi¹³, Rahul Rathod¹⁰, Bhavesh Kotak¹⁴

Background : With growing burden of respiratory symptoms, it is crucial to develop cough syrups with appealing organoleptic properties. This study investigated the consumer feedback on various organoleptic properties and patient compliance to eight leading marketed cough syrups prescribed in routine clinical practice in India.

Materials and Methods : In this cross-sectional 3-months survey, adult patients prescribed with leading cough syrups were enrolled from 8 sites. A survey questionnaire was administered to collect data on the color, taste, viscosity, mouth feel, flavor, aroma, and aftertaste of the syrups using Likert scale ranging from 1-5. The compliance with prescribed regimens were also assessed. $P < 0.05$ was considered statistically significant.

Results : In total, 240 participants were enrolled in this survey. The syrups were generally prescribed for dry cough, fever, headache, productive cough, shortness of breath, and sneezing. Brand C (Bromhexine+ Guaiphenesin+Terbutaline) was the most commonly prescribed cough syrups (n=47). A significant association was found between the dose frequency and duration of cough syrups across all groups ($P=0.005$ for both). Brand D (Ambroxol+Levosulbutamol+Guaiphenesin), Brand A (Chlorpheniramine Maleate+Dextromethorphan), Brand C (Bromhexine+Guaiphenesin+Terbutaline) received the highest responses for "I liked it somewhat" and "I liked it extremely" for different organoleptic features. 97.1% of patients had consumed the cough syrup were compliant.

Conclusions : We found that Brands A, B, C, D (marketed by Dr. Reddy's laboratory Ltd.) were the most accepted and liked cough syrups compared to other 4 leading marketed cough syrup brands. A high percentage of patients (ie, 97.1%) adhered to the recommended dosage and duration.

[J Indian Med Assoc 2023; 121(8): 75-80]

Key words : Cough syrups, Dr Reddy's laboratories, India, Organoleptic, Sensory properties.

The acceptability of cough syrups to the Indian patients not only depends on its efficacy, but also on organoleptic properties such as taste, smell, color, and texture. Pharmaceutical companies often focus

Editor's Comment :

- Organoleptic properties significantly affect patient compliance and overall effectiveness of cough syrups
- Pharmaceuticals prioritize developing cough syrups with attractive organoleptic properties.
- Dr. Reddy's Laboratory Ltd.s cough syrups (Brand A, Brand B, Brand C, and Brand D) were highly accepted and preferred, surpassing four other leading cough syrup brands in the market

¹MD, Health Harmony, Dattani Chambers, West Mumbai 400064
²MBBS, Sai Clinic, Railway colony, Santacruz, West Mumbai 400054

³MBBS, Dr. Sanjiv Maniar Clinic, Somwari bazar Malad, West Mumbai 400064

⁴MBBS, Mumbai Citi Clinic, Khetwali Girgaon, Mumbai 400004

⁵MD, Flores Hospital, Pratap Vihar, Ghaziabad, Uttar Pradesh 201009

⁶MBBS, DNB, Good Health Clinic, Rajouri Garden, New Delhi 110027

⁷MD, Mahajan Hospital, Uttam Nagar, New Delhi 110059

⁸MBBS, DNB, Panchsheel Hospital, Yamuna Vihar, Shahdara, Delhi 110053

⁹MD, Dr Reddy's Laboratory Ltd, Hyderabad and Corresponding Author

¹⁰MD, Dr Reddy's Laboratory Ltd, Hyderabad

¹¹MBBS, MBA, Dr Reddy's Laboratory Ltd, Hyderabad

¹²MSc, PGDCR, Dr Reddy's Laboratory Ltd, Hyderabad

¹³BHMS, PGD, Dr Reddy's Laboratory Ltd, Hyderabad

¹⁴MS, FRCS, Dr Reddy's Laboratory Ltd, Hyderabad

Received on : 10/06/2023

Accepted on : 06/07/2023

on developing cough syrups with appealing organoleptic properties to improve patient compliance and ultimately, treatment outcomes. Several excipients such as colors, flavors and pleasant aroma are used to enhance the palatability of cough syrups as these can significantly affect a patient's willingness to take it, hence, play a crucial role in producing overall effectiveness. Cough syrups have varying textures from thicker and more viscous to thinner and more liquid-like, which make them easier to pour and swallow¹. Organoleptic properties are vital as they can affect a patient's adherence to prescribed medication and improve patient compliance²⁻⁶. There have been clinical studies that suggest that organoleptic properties can

have a significant impact on patient compliance⁶.

We undertook a survey to understand consumer feedback upon organoleptic properties and compliance of various leading marketed cough syrups prescribed in routine clinical practice in India. Also, we compared consumer survey response to the various cough syrups based on their organoleptic properties.

MATERIALS AND METHODS

Eight leading marketed cough syrup Brands were evaluated in this cross-sectional, observational, multi-center consumer survey to provide an initial assessment of their organoleptic properties. Adult patients aged 18 years or older, who were prescribed leading cough syrups, willing to complete the survey and provide data disclosure consent, were enrolled from 8 study centers located across 2 cities in India (New Delhi and Mumbai). Patients with unsuitable medical histories were excluded from the survey.

The study was approved by an independent ethics committee via a letter dated 17 May 2022 and 22 June 2022 (CTRI/2022/06/043040). All activities related to the collection, access, processing, and transfer of protected health information or sensitive personal data were conducted in compliance with applicable regulations. Each patient was assigned a unique patient identifier.

Survey duration and data collection :

The survey had a duration of ~3 months, during which patients attended 2 visits to the site/clinic. A follow-up visit was conducted either on-site or by phone after 5 days of enrollment. Patients were contacted by phone to complete the organoleptic questionnaire, but if they visited the site/clinic for follow-up, they completed the questionnaire during their visit. At baseline, demographic data such as age, gender, city/state, height, weight, BMI, presenting symptoms, clinical signs, and diagnosis

were collected by investigators or study personnel, along with comorbid diseases and vitals such as pulse rate, oral body temperature, and respiratory rate. Patients were also asked about the Brand, dosage, and duration of the prescribed cough syrup, and any concomitant medication.

Survey questionnaire :

The survey questionnaire contained a Likert scale ranging from 1-5 for participants to respond to various organoleptic properties of the syrup. These included the color, taste, viscosity, mouth feel, flavor, aroma, and aftertaste of the syrup. The scoring was mapped against the following responses: "I dislike it extremely," "I dislike it somewhat," "Neutral," "I like it somewhat," and "I like it extremely."

Statistical analysis

Statistical analyses were performed using R software Version 4.1.2. Descriptive statistics, such as mean and Standard Deviation (SD) are used to present continuous data. Categorical data are summarized using counts. The survey questionnaire data were presented descriptively. Comparisons were made using the Chi square/ Fisher's exact test and t-test for categorical and continuous variables respectively. The p-value less than 0.05 was considered statistically significant.

RESULTS

In total, 240 participants prescribed with 8 cough syrups were enrolled. The details of ingredients for each cough syrup are listed in Fig 1. Of total participants, 122 (50.8%) were male and 118 (49.2%) were female. The mean \pm SD age of patients was 45.52 ± 16.54 years and mean \pm SD BMI was 26.60 ± 4.76 kg/m². Table 1 summarizes the demography and clinical characteristics of patients as per cough syrups. The age, gender and BMI were comparable across all eight groups ($P > 0.05$).

Table 1 — Summary of demographic characteristics and clinical characteristics as per cough syrups

	Brand A (n=28)	Brand B (n=26)	Brand C (n=47)	Brand D (n=27)	Brand E (n=28)	Brand F (n=28)	Brand G (n=29)	Brand H (n=27)	P-value
Age (years)	46.75 \pm 16.81	42.35 \pm 17.67	48.74 \pm 18.31	45.63 \pm 17.44	46.57 \pm 16.27	47.11 \pm 15.08	41.76 \pm 15.84	42.89 \pm 14.01	0.6128
Gender, n (%)									
Female	9 (32.1)	18 (69.2)	22 (46.8)	14 (51.9)	14 (50.0)	14 (50.0)	15 (51.7)	12 (44.4)	0.3371
Male	19 (67.9)	8 (30.8)	25 (53.2)	13 (48.1)	14 (50.0)	14 (50.0)	14 (48.3)	15 (55.6)	
BMI	26.52 \pm 4.22	25.28 \pm 4.87	26.63 \pm 5.05	28.37 \pm 5.58	27.12 \pm 4.48	25.42 \pm 3.37	26.23 \pm 3.79	27.26 \pm 5.98	0.2955
Presenting Symptoms, n (%)									
Dry Cough	26 (92.9)	19 (73.1)	21 (44.7)	13 (48.1)	25 (89.3)	23 (82.1)	14 (48.3)	8 (29.6)	<0.0001
Fever	10 (35.7)	8 (30.8)	17 (36.2)	9 (33.3)	13 (46.4)	9 (32.1)	14 (48.3)	15 (55.6)	
Headache	2 (7.1)	6 (23.1)	13 (27.7)	5 (18.5)	8 (28.6)	7 (25.0)	8 (27.6)	5 (18.5)	
Productive Cough	2 (7.1)	5 (19.2)	23 (48.9)	15 (55.6)	1 (3.6)	5 (17.9)	15 (51.7)	19 (70.4)	
Shortness of breath	0	4 (15.4)	6 (12.8)	4 (14.8)	2 (7.1)	4 (14.3)	2 (6.9)	1 (3.7)	
Sneezing	9 (32.1)	8 (30.8)	16 (34.0)	8 (29.6)	8 (28.6)	13 (46.4)	7 (24.1)	4 (14.8)	

The symptoms for which cough syrups were generally prescribed were fever, headache, dry and productive cough, shortness of breath, and sneezing. Brand C was mostly prescribed for productive cough (n=23; 48.9%), followed by dry cough (n=21; 44.7%). The other Brands were prescribed for both dry and productive cough (Fig 1).

Brand C was the most prescribed cough syrup (n=47; 19.6%, males: 25 [53.2%] and females: 22 [46.8%]) followed by Brand G (n=29; 12.1%, males: 14 [48.3%] & females: 15 [51.7%]) and Brand A (n=28; 11.7%, males: 19 [67.9%] & females: 9 [32.1%]).

No significant association was observed for medical history of patients across all cough syrup groups (P=0.988). Hypertension was the most frequently reported medical history across all the cough syrup groups. None of the participants taking Brand G had any reported medical history (Table 2).

A significant association was found between the dose frequency and duration of cough syrups across all groups (P=0.005 for both). The most frequently prescribed dose and frequency across all cough syrups was 1 TSF (Table Spoon Full) twice daily, with 17 patients (60.7%) receiving this dose for Brand E, followed by 16 patients (57.1%) for Brand A and 15 patients (55.6%) for Brand H. Brand C was most commonly prescribed as 1 TSF thrice daily. The majority of cough syrups were prescribed for 5 days in over 50% of patients (Table 3).

The study evaluated patient preferences for different aspects of cough syrups, including aftertaste, aroma, color, flavor, mouthfeel, taste, and viscosity (Table 4). Brand D received the highest number of responses for “I liked it somewhat” and “I liked it extremely” regarding the aftertaste of the syrup (n=16; 59.3%), followed by Brand B (n=14; 53.8%), Brand A (n=12; 42.9%), and Brand C (n=20; 42.6%).

For aroma, Brand A (n=19; 67.9%) had the highest responses for “I liked it somewhat” and “I liked it extremely”, followed by Brand C (n=28; 59.5%), Brand D (n=16; 59.2%), and Brand B (n=14; 53.8%).

Brand C (n=19; 40.4%) received the highest number of responses for “I liked it somewhat” and “I liked it extremely” regarding the color of the syrup, followed by Brand A (n=10; 35.7%), and Brand B (n=7; 26.9%).

Brand A (n=15; 53.6%) and Brand C (n=24; 51.0%)



Fig 1 — Compositions of cough syrups used in the study

Table 2 — Medical history of patients by cough syrup			
Cough syrups	Medical History	n (%)	P value
Brand A (N=28) :			
	Hypertension	3 (10.7)	0.9880
	Hypothyroidism	1 (3.6)	
	Diabetes Mellitus	1 (3.6)	
Brand B (N=26) :			
	Hypertension	1 (3.8)	
Brand C (N=47) :			
	Bronchitis	1 (2.1)	
	Chronic kidney disease	1 (2.1)	
	Cold and Fever	1 (2.1)	
	Coronary artery disease	1 (2.1)	
	Hypothyroidism	1 (2.1)	
	Dyslipidemia	1 (2.1)	
	Hypertension	5 (10.6)	
	Type 2 diabetes mellitus	3 (6.4)	
	Thyroid	1 (2.1)	
	Osteopetrosis	1 (2.1)	
	Vertigo	1 (2.1)	
Brand D (N=27) :			
	Arthritis	1 (3.7)	
	Hypertension	6 (22.2)	
Brand E (N=28) :			
	Hypertension	1 (3.6)	
	Diabetes	1 (3.6)	
Brand F (N=28) :			
	Hypertension	4 (14.3)	
Brand H (N=27) :			
	Hypertension	3 (11.1)	
	Type 2 diabetes mellitus	1 (3.7)	

were the cough syrups which received the highest number of responses for “I liked it somewhat” and “I liked it extremely” regarding the flavor of the syrup, followed by Brand D (n=12; 44.4%) and Brand B (n=11;

	Brand A (n=28)	Brand B (n=26)	Brand C (n=47)	Brand D (n=27)	Brand E (n=28)	Brand F (n=28)	Brand G (n=29)	Brand H (n=27)	P-value
Dose & Frequency, n (%)									
1 TSF twice daily	16 (57.1)	11 (42.3)	11 (23.4)	11 (40.7)	17 (60.7)	9 (32.1)	12 (41.4)	15 (55.6)	0.0052
1 TSF thrice daily	5 (17.9)	7 (26.9)	22 (46.8)	4 (14.8)	0	4 (14.3)	3 (10.3)	5 (18.5)	
2 TSF twice daily	3 (10.7)	5 (19.2)	10 (21.3)	9 (33.3)	6 (21.4)	9 (32.1)	8 (27.6)	3 (11.1)	
2 TSF thrice daily	4 (14.3)	3 (11.5)	4 (8.5)	3 (11.1)	5 (17.9)	6 (21.4)	6 (20.7)	4 (14.8)	
Duration, n (%)									
5 days	14 (50.0)	15 (57.7)	34 (72.3)	23 (85.2)	15 (53.6)	20 (71.4)	18 (62.1)	18 (66.7)	0.0057
< 5 days	7 (25.0)	7 (26.9)	6 (12.8)	3 (11.1)	8 (28.6)	4 (14.3)	9 (31.0)	7 (25.9)	
> 5 days to < 10 days	7 (25.0)	4 (15.4)	7 (14.9)	1 (3.7)	2 (7.1)	4 (14.3)	2 (6.9)	2 (7.4)	
> 10 days	-	-	-	-	3 (10.7)	-	-	-	

TSF, Table spoon full.

42.3%). For remaining cough syrups, patients ranging from 32–39% had such responses.

For mouthfeel, Brand A (n=14; 50%) had the highest responses for “I liked it somewhat” and “I liked it extremely”, followed by Brand C (n=22; 46.8%), and Brand D (n=12; 44.4%). Brand E (n=5; 17.8%) and Brand G (n=5; 17.2%) had least number of responses for “I liked it somewhat” and “I liked it extremely” regarding the mouthfeel of the syrup. Brand C (n=26; 55.3%), Brand A (n=13; 46.4%) and Brand D (n=11; 40.7%) cough syrups received the highest number of responses for “I liked it somewhat” and “I liked it extremely” regarding the taste of the syrup. Brand G (n=5; 17.2%) received the least number of such responses for the taste. Brand C (n=23; 48.9%), and Brand D (n=13; 48.1%) cough syrups received the highest number of responses for “I liked it somewhat” and “I liked it extremely” regarding the viscosity of the syrup.

Overall, 233 (97.1%) patients had consumed the cough syrup in the same dosage and duration as prescribed and were compliant. Patients consuming Brands C, E, F, and H reported 100% compliance to the dosage and duration as prescribed (Fig 2).

DISCUSSION

The study is the first of its kind to assess the organoleptic features of 8 leading marketed cough syrups and compared them to understand the patients’ preference. A cough syrup with good organoleptic properties can improve patient compliance, satisfaction, and overall health outcomes.

If a medication has an unpleasant taste or odor, the patient may be less likely to comply with the prescribed regimen, leading to suboptimal

treatment outcomes. The aftertaste of cough syrups can be impacted by several factors, including the active ingredients, excipients, sweeteners, flavorings, and preservatives used in the formulation. Our results indicate that Brand D received the highest number of positive responses for aftertaste, followed by Brands B, A, and C. Most of these cough syrups have used mentholated flavored sugar base and menthol can improve the aftertaste of cough syrups by providing a refreshing sensation and masking unpleasant flavors, making the syrup more palatable and easier to swallow⁶. Flavored syrupy bases are often added to cough syrups to improve the aftertaste of the active ingredients. These bases typically contain sweeteners to make the syrup taste better. The addition of a syrupy base also helps to make the cough syrup thicker and more viscous, which can provide a more soothing effect on the throat⁵.

Our study demonstrated the highest positive responses for aroma for Brands A and C which could be attributed to the presence of menthol as one of the excipients. Brand C received the highest positive responses for color. Brand A and C had the highest

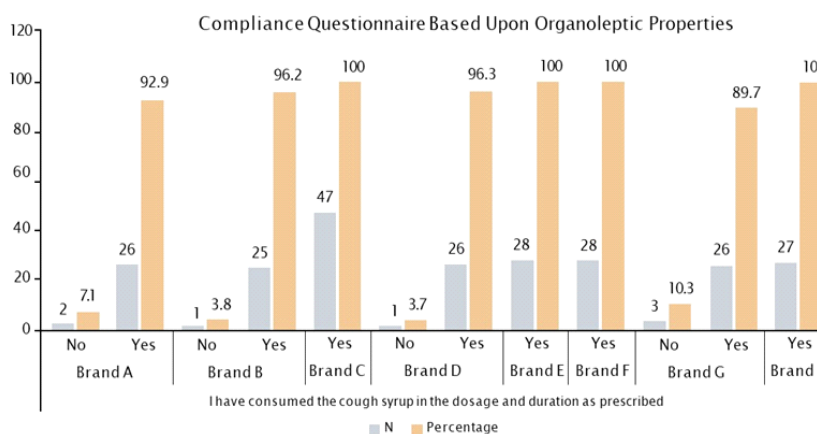


Fig 2 — Compliance Questionnaire Based on Organoleptic Properties – Overall

Table 4 — *Organoleptic properties of cough syrups*

Cough Syrup	Question	I dislike it extremely n (%)	I dislike it somewhat n (%)	Neutral n (%)	I like it somewhat n (%)	I like it extremely n (%)
Brand A(N=28)	After Taste of the syrup	0	4 (14.3)	12 (42.9)	8 (28.6)	4 (14.3)
	Aroma of the syrup	0	4 (14.3)	5 (17.9)	12 (42.9)	7 (25.0)
	Color of the syrup	2 (7.1)	2 (7.1)	14 (50.0)	9 (32.1)	1 (3.6)
	Flavour of the syrup	2 (7.1)	2 (7.1)	9 (32.1)	12 (42.9)	3 (10.7)
	Mouth feel of the syrup	0	3 (10.7)	11 (39.3)	13 (46.4)	1 (3.6)
	Taste of the syrup	0	3 (10.7)	12 (42.9)	11 (39.3)	2 (7.1)
	Viscosity of the syrup	0	4 (14.3)	17 (60.7)	7 (25.0)	0
Brand B (N=26)	After Taste of the syrup	1 (3.8)	2 (7.7)	9 (34.6)	9 (34.6)	5 (19.2)
	Aroma of the syrup	1 (3.8)	2 (7.7)	9 (34.6)	7 (26.9)	7 (26.9)
	Color of the syrup	4 (15.4)	2 (7.7)	13 (50.0)	5 (19.2)	2 (7.7)
	Flavour of the syrup	0	7 (26.9)	8 (30.8)	9 (34.6)	2 (7.7)
	Mouth feel of the syrup	0	7 (26.9)	9 (34.6)	8 (30.8)	2 (7.7)
	Taste of the syrup	2 (7.7)	4 (15.4)	10 (38.5)	8 (30.8)	2 (7.7)
	Viscosity of the syrup	0	5 (19.2)	11 (42.3)	9 (34.6)	1 (3.8)
Brand C(N=47)	After Taste of the syrup	0	8 (17.0)	19 (40.4)	13 (27.7)	7 (14.9)
	Aroma of the syrup	0	6 (12.8)	13 (27.7)	16 (34.0)	12 (25.5)
	Color of the syrup	2 (4.3)	3 (6.4)	23 (48.9)	11 (23.4)	8 (17.0)
	Flavour of the syrup	1 (2.1)	6 (12.8)	16 (34.0)	16 (34.0)	8 (17.0)
	Mouth feel of the syrup	1 (2.1)	5 (10.6)	19 (40.4)	16 (34.0)	6 (12.8)
	Taste of the syrup	1 (2.1)	5 (10.6)	15 (31.9)	22 (46.8)	4 (8.5)
	Viscosity of the syrup	1 (2.1)	4 (8.5)	19 (40.4)	19 (40.4)	4 (8.5)
Brand D (N=27)	After Taste of the syrup	0	6 (22.2)	5 (18.5)	14 (51.9)	2 (7.4)
	Aroma of the syrup	0	4 (14.8)	7 (25.9)	13 (48.1)	3 (11.1)
	Color of the syrup	4 (14.8)	3 (11.1)	16 (59.3)	2 (7.4)	2 (7.4)
	Flavour of the syrup	0	3 (11.1)	12 (44.4)	8 (29.6)	4 (14.8)
	Mouth feel of the syrup	0	6 (22.2)	9 (33.3)	9 (33.3)	3 (11.1)
	Taste of the syrup	1 (3.7)	3 (11.1)	12 (44.4)	8 (29.6)	3 (11.1)
	Viscosity of the syrup	0	2 (7.4)	12 (44.4)	11 (40.7)	2 (7.4)
Brand E(N=28)	After Taste of the syrup	6 (21.4)	7 (25.0)	7 (25.0)	5 (17.9)	3 (10.7)
	Aroma of the syrup	2 (7.1)	7 (25.0)	9 (32.1)	9 (32.1)	1 (3.6)
	Color of the syrup	4 (14.3)	3 (10.7)	14 (50.0)	6 (21.4)	1 (3.6)
	Flavour of the syrup	1 (3.6)	4 (14.3)	12 (42.9)	10 (35.7)	1 (3.6)
	Mouth feel of the syrup	2 (7.1)	8 (28.6)	13 (46.4)	3 (10.7)	2 (7.1)
	Taste of the syrup	1 (3.6)	8 (28.6)	10 (35.7)	9 (32.1)	0
	Viscosity of the syrup	0	9 (32.1)	13 (46.4)	4 (14.3)	2 (7.1)
BrandF (N=28)	After Taste of the syrup	0	9 (32.1)	6 (21.4)	9 (32.1)	4 (14.3)
	Aroma of the syrup	1 (3.6)	1 (3.6)	13 (46.4)	11 (39.3)	2 (7.1)
	Color of the syrup	5 (17.9)	3 (10.7)	13 (46.4)	2 (7.1)	4 (14.3)
	Flavour of the syrup	2 (7.1)	5 (17.9)	12 (42.9)	6 (21.4)	3 (10.7)
	Mouth feel of the syrup	0	5 (17.9)	12 (42.9)	10 (35.7)	1 (3.6)
	Taste of the syrup	3 (10.7)	3 (10.7)	13 (46.4)	8 (28.6)	0
	Viscosity of the syrup	0	11 (39.3)	9 (32.1)	8 (28.6)	0
Brand G(N=29)	After Taste of the syrup	4 (13.8)	8 (27.6)	8 (27.6)	6 (20.7)	3 (10.3)
	Aroma of the syrup	1 (3.4)	2 (6.9)	16 (55.2)	5 (17.2)	5 (17.2)
	Color of the syrup	6 (20.7)	2 (6.9)	14 (48.3)	5 (17.2)	2 (6.9)
	Flavour of the syrup	3 (10.3)	1 (3.4)	14 (48.3)	11 (37.9)	0
	Mouth feel of the syrup	2 (6.9)	8 (27.6)	14 (48.3)	4 (13.8)	1 (3.4)
	Taste of the syrup	2 (6.9)	10 (34.5)	12 (41.4)	5 (17.2)	0
	Viscosity of the syrup	1 (3.4)	9 (31.0)	14 (48.3)	5 (17.2)	0
Brand H(N=27)	After Taste of the syrup	4 (14.8)	6 (22.2)	9 (33.3)	7 (25.9)	1 (3.7)
	Aroma of the syrup	2 (7.4)	8 (29.6)	8 (29.6)	6 (22.2)	3 (11.1)
	Color of the syrup	5 (18.5)	2 (7.4)	14 (51.9)	4 (14.8)	2 (7.4)
	Flavour of the syrup	0	6 (22.2)	10 (37.0)	7 (25.9)	3 (11.1)
	Mouth feel of the syrup	1 (3.7)	4 (14.8)	12 (44.4)	9 (33.3)	1 (3.7)
	Taste of the syrup	1 (3.7)	7 (25.9)	11 (40.7)	7 (25.9)	1 (3.7)
	Viscosity of the syrup	2 (7.4)	6 (22.2)	11 (40.7)	7 (25.9)	1 (3.7)

positive responses for flavor, and Brand A had the highest positive responses for mouthfeel. Brand C and D had the highest positive responses for taste and viscosity.

Menthol is a commonly used ingredient in cough syrups because it provides a cooling and soothing sensation in the throat and nasal passages. When combined with a flavored syrup base, it can improve the taste and odor of the cough syrup, making it more palatable for patients. In addition to menthol, some cough syrups, such as Brand C, contain Carmoisine. Carmoisine is a food coloring that is added to improve the color and appearance of the cough syrup. This can have a positive impact on patients, as colors are known to evoke emotions and feelings. For example, warm colors such as red and orange can evoke feelings of warmth and comfort, which may help patients feel more at ease when taking the cough syrup.⁷

The study found that a high percentage of patients, 97.1%, were adhering to the recommended dosage and duration of the cough syrup. This is a positive finding because it suggests that these patients are following the instructions provided by their healthcare provider, and are taking the cough syrup as intended. It's worth noting that the study also found that the cough syrup had unsatisfactory organoleptic properties and despite this, the patients still adhered to the prescribed regimen. This indicates that the patients may be placing more importance on the effectiveness outcomes of the cough syrup rather than its sensory properties. Overall, the study suggests that patients are willing to follow the prescribed regimen for cough syrup, even if they find it unpleasant to take. This is an important finding for healthcare providers, as it highlights the importance of providing effective treatments that patients are willing to adhere to, even if they are not always palatable.

Our study had several limitations. Firstly, the study was observational in nature, which means that we did not control for other confounding factors that could have influenced the subject's response. This limits the ability to establish a cause-and-effect relationship between the variables. It is important to acknowledge that subjective responses are subject to individual interpretation and may be influenced by various factors, such as personal beliefs and expectations. Lastly, the study sample was limited to patients from only two cities, which may affect the generalizability of the findings to other populations. Differences in demographics, cultural background, and healthcare practices between different regions can influence patient behavior. While the study provides valuable insights into patient adherence to cough syrup

regimens, further research is necessary to validate these findings.

CONCLUSION

In our study, we observed that Dr Reddy's laboratories marketed syrups (Brands A, B, C and D) were the most accepted and liked cough syrups among the studied population as compared to other 4 leading marketed cough syrup brands. Overall, a high percentage of patients (ie, 97.1%) adhered to the recommended dosage and duration of the cough syrup, indicating that patients may prioritize the effectiveness outcomes of the cough syrup over its sensory properties.

Disclosures : Dr Monil, Dr Mayank, Dr Snehal, Gauri, Dr Arti, Dr Rahul, and Dr Bhavesh are employees of Dr Reddy's laboratory Ltd. The other authors declare no conflict of interest

ACKNOWLEDGEMENTS

We would like to thank Dr Archana Karadkhele, Colette Pinto and Dr Amey Mane for being a part of the initial conceptualization of the study protocol. We thank NeoCrest Life Sciences Consulting (P) Ltd. for providing the medical writing support and IR Innovate Research Pvt Ltd for overall co-ordination and conduct of the study. The study and publication were financially supported by Dr Reddy's Laboratories.

REFERENCES

- 1 Eccles R — What is the Role of Over 100 Excipients in Over the Counter (OTC) Cough Medicines? *Lung* 2020; **198(5)**: 727-34.
- 2 Kashyap B — Evaluation of Organoleptic Properties Preferred for Oral Dosage form by Students and Faculty Members of ADIT Campus (Gujarat Technological University/Sardar Patel University), New VV Nagar. *Inventi Rapid: Pharmacy Practice*, 2012(4): 1-3.
- 3 Soares N, Mitchell R, McGoff T, Bailey T, Wellman GS — Taste Perceptions of Common Pediatric Antibiotic Suspensions and Associated Prescribing Patterns in Medical Residents. *J Pediatr Pharmacol Ther* 2022; **27(4)**: 316-23.
- 4 Raji MIO, Ibikunle MT — Organoleptic Property and Bacteriological Analysis of Cough Syrups Sold in Sokoto Metropolis, North-Western Nigeria. *Journal of Medical Sciences* 2022; **22**: 113-8.
- 5 Sohi H, Sultana Y, Khar RK — Taste masking technologies in oral pharmaceuticals: recent developments and approaches. *Drug Dev Ind Pharm* 2004; **30(5)**: 429-48. doi: 10.1081/ddc-120037477. PMID: 15244079.
- 6 Sana S, Rajani A, Sumedha N, Mahesh B — Formulation and evaluation of taste masked oral suspension of dextromethorphan hydrobromide. *Int J Drug Dev & Res* 2012; **4(2)**: 159-72.
- 7 Biswal PK, Mishar MK, Bhadouriya AS, Yadav VK — An Updated Review On Colorants As The Pharmaceutical Excipients. *International Journal of Pharmaceutical, Chemical & Biological Sciences* 2015; **5(4)**.

Case Series

Gossypiboma : Word of Caution for an Unexpected Guest in the Abdomen — A Case Series and a Review of the Literature

Afzal Anees¹, Yaqoob Hassan², Shereen Fatima³, Surbhi Gupta³

Gossypiboma, an infrequent surgical complication, is defined as retained surgical sponge in the abdominal cavity following any operation. Aside from being medico-legal trouble for an operating surgeon, the implications for both the patient and the surgeon are grave. We present three cases of Gossypiboma admitted and managed over a period of 8 years. A 55 year- old female was referred for a mass in her right upper quadrant of abdomen that had been present for four months. She had surgical history of open cholecystectomy five months back in peripheral health care centre. On Laparotomy removal of sponge with primary repair of transected gastroduodenal junction was made (Billroth 1 procedure). A 42-year-old lady was referred for colicky pain in the abdomen and bleeding per rectum of 3 weeks duration. She had an open abdomen hysterectomy six months prior in a private hospital. Exploration revealed a walled off necrotic collection with spong in the pelvis and blow out of the rectosigmoid junction. Rectosigmoidectomy with primary anastomosis and spong removal was performed. A 43-year-old woman presented with a history of open cholecystectomy in private centre, presented with right upper abdominal pain and decreased appetite. Computed Tomography (CT) confirmed the presence of gossypiboma. The patient underwent exploration with Billroth 11 procedure. All the three patients are doing well and on regular follow up. Though rare, Gossypiboma should be included in the differential diagnosis of postoperative cases presenting as vague pain or chronic lump even years after the operation .The risk that every surgical procedure carries is inherent but Gossypiboma remains largely an easily preventable hazard. Strict adherence to the standard protocols of gauze count and better display of team work by everyone present in the operating room is important in decreasing the incidence.

[J Indian Med Assoc 2023; 121(8): 81-5]

Key words : Gossypiboma, Foreign body, Retained surgical mops.

Gossypiboma is the presence of cotton based foreign body that is in place of concealment following surgery. It is an uncommon but a grave surgical complication that has repercussions for both the patient as well the surgeon. The true incidence of Gossypiboma is almost certainly underestimated due to medicolegal implications, however it is reported that one in every 3000 to 5000 abdominal procedures will result in a retained surgical sponge¹. Retained foreign bodies (mops or gauzes) can be found in any body cavity (thorax, pelvis, pericardium), but they are most frequently discovered in the intra-peritoneal cavity². Because of the wide range of non-specific symptoms associated with Gossypibomas, an attending surgeon may struggle to make a diagnosis. The clinical presentation can range from a subacute exudative reaction resulting in an abscess or a fistula formation to chronic aseptic fibrinous adhesions or granuloma formation. Gossypiboma can have

Editor's Comment :

- Gossypibomas are rare, largely asymptomatic, and difficult to diagnose. Therefore, a high index of suspicion is needed to make a diagnosis and prompt commencement of intervention. Although it is unlikely to be completely eradicated, the risk can essentially be avoided by following established gauze count practises in operating rooms.

disappointing, unfavorable and serious medicolegal repercussions for a surgeon, hence it should be avoided by performing adequate routine theatre swab counts before closing the abdomen. This article discusses the clinical presentation, diagnosis, treatment and complications of Gossypibomas, in addition to adding three cases to the existing literature. A brief review in the context is also present.

CASE 1

A 55-year-old female was referred to our tertiary care centre after experiencing a right upper quadrant mass, early satiety, and dull aching pain for four months. There was no history of constipation, loose stools, fever, rigors, or rectal bleeding; however, had an open cholecystectomy five months previously. The detailed surgical, medical, personal and family history was not clinically relevant. nothing significant. The patient was thoroughly examined, resuscitated and subjected to standard baseline investigations. On physical examination, the patient was

Department of Surgery, Jawaharlal Nehru Medical College Aligarh, Uttar Pradesh 202001

¹MBBS, MS, FACS, FRCS, FICS, Professor and Chairman

²MBBS, MS, "Fellow of National Board (FNB), Minimal Access Surgery", Department of General and Minimal Invasive Surgery, Sher-i-Kashmir Institute of Medical Sciences (SKIMS), Srinagar, Jammu and Kashmir 190011 and Corresponding Author

³MBBS, MS, Resident

Received on : 12/01/2022

Accepted on : 29/06/2023

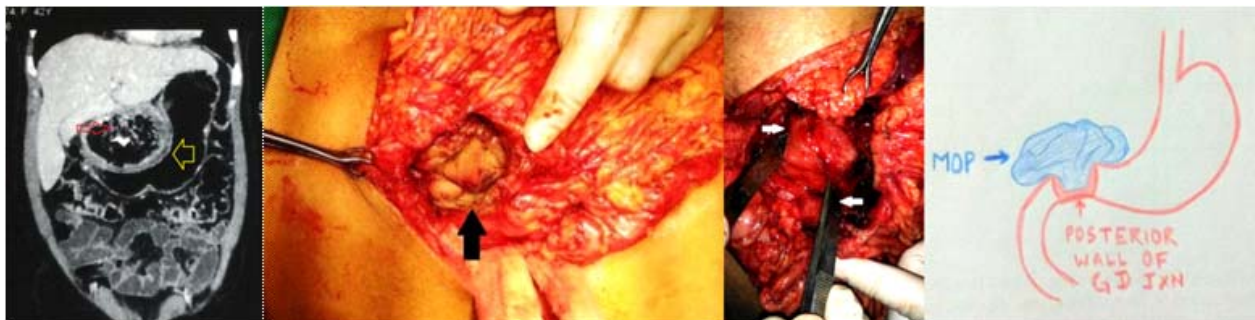


Fig 1 — Contrast Enhanced Tomography Scan showing well defined walled off lesion (yellow arrow) with admixed air and soft tissue particle. Intra-operative photograph showing surgical mop (black arrow) and disrupted gastroduodenal junction. Diagrammatic representation showing surgical mop.

found to be haemodynamically stable, a pulse rate of 82 beats per minute, a blood pressure of 120/86 mm Hg, respiratory rate of 16 breaths per minute, temperature recorded was 98.80°F and saturation of 96 percent on room air. There was no pallor, icterus, cyanosis or pedal edema. The Respiratory and Cardiovascular examinations were unremarkable. The biochemical investigations and abdominal radiograph were normal. A surgical scar mark in the right subcostal region was discovered during an abdominal examination. A mobile 5x7cm lump was present in the right hypochondrium and epigastric region, adjacent to the scar mark. Ultrasonography revealed heterogeneity in the anterior abdominal wall. Computed Tomography with oral contrast revealed a walled-off lesion with admixed air and soft tissue particles abutting pancreas and compressing the second part of the duodenum, causing luminal narrowing,

however distal passage of contrast was present. During an exploratory laparotomy, walled-off infected collection with surgical sponge was discovered embedded in the anterior wall of 1st part of the Duodenum (Fig 1). The sponge that was embedded in the anterior wall of the first part of the duodenum was removed and the transected gastroduodenal junction was repaired (Billroth 1 procedure). A feeding jejunostomy was performed to expedite enteral nutrition. The abdomen was closed back in layers and the patient was extubated and shifted to the postoperative care ward. The postoperative period was uneventful; liquid orals were introduced after 48 hours, followed by semisolids and solids. On the fourth postoperative day, the patient was discharged and was assigned to our Out Patient Department (OPD) for weekly follow-up. The patient is doing well and is being monitored on a regular basis.

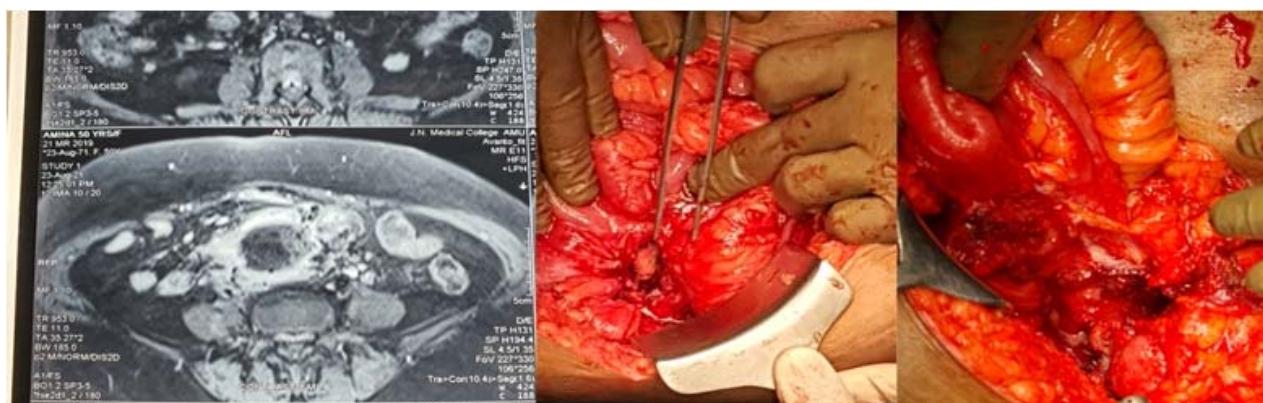


Fig 2 — Contrast Enhanced Tomography Scan showing a round well-defined soft-tissue mass containing an internal high-density area in the lower abdomen. Intra-operative picture showing retained sponge and disrupted recto-sigmoid junction.

CASE 2

A 42-year-old lady, P2L2 (Para 2 Live 2) was referred to our surgical clinic in view of recurrent colicky pain abdomen, constipation, mucous discharge and bleeding per rectum of 3 weeks duration. She had history of open abdomen hysterectomy done six months before at a

private hospital. The patient had history of lower abdominal discomfort in the postoperative period which was attributed to wound site pain by the attending doctor. Following discharge after hysterectomy patient had always experienced colicky pain abdomen relieved by simple over the counter medications. However since the

3 weeks, patient had been concerned about the episodes of bleeding per rectum and difficulty in defecation. She was stable with pulse 86bpm, blood pressure 136/78 mmHg, respiratory rate 16 breaths/minute and Oxygen saturation 96% on room air. The physical examination was unremarkable except infra-umbilical surgical scar and tenderness was present. Digital rectal examination was unremarkable. Radiograph of abdomen revealed gaseous dilatation of large gut loops and an abdomino-pelvic ultrasound suggested thickened sigmoid wall and mild free fluid in the pelvis. Contrast enhanced Computed

Tomography scan revealed a cystic lesion of 3*4 cm with internal spongiform appearance abutting the sigmoid colon and surrounded by omentum. The patient was optimized and taken up for elective exploratory laparotomy as we did not have availability of Laparoscopy at that time. On exploration the sponge was present in the pelvis with blow out of rectosigmoid junction (Fig 2). Localised faecal contamination was also present. Recto-sigmoidectomy was done; continuity of remaining hollow viscera was restored with stapling device. Postoperatively, the patient recovered uneventfully and is on regular outpatient follow-up.



Fig 3 — Abdominal CT scan showing a heterogeneous cystic soft tissue mass in the right upper quadrant of abdomen. Intra-operative picture showing surgical sponge and disrupted gastro-duodenal junction.

CASE 3

A 43 year old woman presented with a history of open cholecystectomy 3 months before in a private hospital and was admitted to our tertiary care institute in view of eight days history of pain in right upper abdomen, vomiting, nausea, decreased appetite and early satiety. Abdominal pain was continuous, non-radiating and relieved by medication. On general examination, she was stable, obese with a Body Mass Index (BMI) of 32. As regards to her vital signs, her Blood Pressure (BP) was 130/88 mmHg, respiratory rate of 18 breaths per minute and Oxygen saturation 98% on room air. Local per abdominal examination showed right sub-costal incision scar, and tender right upper abdomen. A plain abdominal radiograph was normal and abdomen-pelvic ultrasound suggested an echoic mass surrounded by irregular hyperechoic areas in right hypochondrium. In the abdominal Computed Tomography (CT) scan, a heterogeneous cystic soft tissue mass of 24*12 cm size was found in the right upper quadrant of abdomen and diagnosis of Gossypiboma was made. The patient was taken for exploratory laparotomy under General Anesthesia. Abdomen was opened with upper midline incision. A sponge was discovered between the duodenum and the stomach and the anterior wall of the Stomach and Duodenum was disrupted (Fig 3). The damaged and gangrenous portions were excised followed by Billroth - II Gastrojejunostomy and abdominal washes were given (Fig 3). A tube drain was kept in situ and abdomen was closed back in layers. Postoperative

period was uneventful, drain was removed on 3rd day, and patient was discharged on 5th day. Patient is doing well, and on regular follow-up.

DISCUSSION

Following surgery, leaving surgical sponge in the abdominal cavity is a serious but generally avoidable complication. Despite the fact that it is preventable, it still happens, causing mental anguish, embarrassment, humiliation, job loss, legal action and undesirable consequences for the operating surgeon, as well as exacerbating the patient's morbidity and death. These retained surgical sponge were named as Gossypiboma in 1978, a Latin term 'Gossipium' meaning cotton^{3,4} and the first case was reported by Wilson in 1884⁵. Because of the concern of medico-legal implications, the exact incidence of retained foreign bodies is difficult to verify⁶. The current reported rate is 0.01 percent to 0.001 percent following surgery with Gossypiboma accounting for 80 percent of cases⁷.

Pathologically, retained surgical mops cause two types of foreign body reactions; exudative inflammatory reactions with abscess formation and aseptic fibrinous responses with granuloma formation^{5,8-10}. The patients with Gossypiboma often remain asymptomatic or have non-specific symptoms and they may present immediately in postoperatively period or decades later¹¹. A 66-year-old man with Gossypiboma was discovered after 24 years of Gastrectomy¹². However, the signs and

symptoms depend upon the location, duration and body response to the retained foreign body. All postoperative patients who present with non-specific symptoms such as abdominal pain, infection or a palpable mass should be evaluated for the possibility of a retained foreign body. In the literature, patients with Gossypiboma have been reported with Gastrointestinal bleeding, bowel perforation, peritonitis, obstruction, sepsis and even mortality¹¹. Two cases of intraperitoneal Gossypiboma have been described by Biswas RS, *et al* one of which had an intraluminal surgical sponge 15 cm proximal to the ileocaecal junction and required resection anastomosis; the other had eroded the duodenum and died as a result of a postoperative duodenal fistula and septicemia¹³. There have also been reports of intraperitoneal Gossypibomas that spontaneously passed through the rectum after eroding in the bowel¹⁴.

Due to silent nature and non-specific symptoms, gossypiboma is often difficult to diagnose pre-operatively. Radiological imaging including Radiograph of abdomen, Ultrasonography and Computed Tomography contribute significantly to the detection of Gossypiboma. Detection by abdominal radiograph is impossible in cases where sponge with no radio-opaque marker is retained or fragmented with time. Ultrasonography shows echogenic area with distinct posterior shadow or a complex mass with internal hyperechoic wavy striped pattern¹⁵. Computed Tomography shows well capsulated mass with presence of air and internal heterogeneous density⁵.

The prevention of retained surgical sponges by following proper standard guidelines during operation can significantly decline the occurrence of such regrettable complications^{16,17}. The operating surgeons and team should be aware of the risk factors that lead to retained sponges and make concerted efforts to avoid them. Emergency surgeries, prolonged procedures, unplanned changes in procedure or operating team, patients with higher BMI, female gender, inexperienced staff, improper counting of surgical towels/sponges and poor communication among the surgical team all increase the risk of foreign body retention after surgery^{18,19}. The retention of a foreign body is reported to be nine times more common in emergency operation and four times more likely when an operation involves an unexpected change in procedure¹⁹.

Keeping a meticulous pack and instrument count by hand before and after surgeries, tagging the packs with radio-opaque markers, avoidance of small sponges during Laparotomy and avoidance of staff changes during procedures, open communication and teamwork all are some of the key steps to avoid occurrence of retained foreign body. Four separate counts are recommended: one when the instruments and sponges are first unpacked and set up, a second before the surgical procedure begins, a third while closure begins, and a fourth as the final skin closure occurs²⁰. The American College of Surgeons and the Joint Commission have

both advocated for additional guidelines²¹. Some of the new technologies that can be used to reduce the incidence of retained foreign bodies include radiofrequency identification systems, electronic article surveillance and the application of bar codes to surgical sponges²².

Once diagnosed, the only treatment option for reducing morbidity and mortality in such patients is prompt implementation of appropriate surgical intervention, either open or Laparoscopy. Laparoscopic removal of Gossypibomas is more difficult, but it has advantages such as less post-operative pain, a faster return of bowel function, smaller incisions, and a better cosmetic result²³.

CONCLUSION

Gossypiboma, a rare but a grave postoperative complication, is associated with a significant morbidity and medico-legal litigations against the operating surgeon. The risk that every surgical procedure carries is inherent but Gossypiboma remains largely an easily preventable hazard. Therefore, it can be avoided with strict adherence to the standard protocols of gauze count and better display of team work by everyone present in the operating room, after all an ounce of prevention is worth a pound of cure.

Disclosures Human subjects : Consent was obtained from all the participants in this study.

Ethical Issue : None

Financial and competitive interest : None

The authors declare that no financial support was received from any organization for the submitted work.

Other Relationships : The authors declare that there are no other relationships or activities that could appear to have influenced the submitted work.

Conflict of Interest : On behalf of all authors, the Corresponding author states that there is no conflict of interest.

The authors have no other disclosure.

REFERENCES

- 1 Kiernan F, Joyce M, Byrnes CK, O'Grady H, Keane FB, Neary P — Gossypiboma: a case report and review of the literature. *Irish Journal of Medical Science* 2008; **177(4)**: 389-91.
- 2 Manzella A, Filho PB, Albuquerque E, Farias F, Kaercher J — Imaging of gossypibomas: pictorial review. *AJR. American Journal of Roentgenology* 2009; **193(6 Suppl)**: S94-S101.
- 3 Williams RG, Bragg DG, Nelson JA — Gossypiboma—the problem of the retained surgical sponge. *Radiology* 1978; **129**: 323-6.
- 4 O'Connor AR, Coakley FV, Meng MV — Imaging of retained surgical sponges in the abdomen and pelvis. *Am J Roentgenol* 2003; **2013**: 481-9.
- 5 Lauwers PR, Van Hee RH — Intraperitoneal gossypibomas: the need to count sponges. *World J Surg* 2000; **2013**: 521-7.
- 6 Uluçay T, Dizdar MG, SunayYavuz M, Asirdizer M — The importance of medico-legal evaluation in a case with intraabdominal gossypiboma. *Forensic Sci Int* 2010; **198**: e15-8.

- 7 Kim HS, Chung TS, Suh SH, Kim SY — MR imaging findings of paravertebral gossypiboma. *AJNR. American Journal of Neuroradiology* 2007; **28(4)**: 709-13.
- 8 Gibbs VC, Coakley FD, Reines HD— Preventable errors in the operating room: retained foreign bodies after surgery. *Curr Probl Surg* 2007; **44**: 281-337.
- 9 Lauwers PR, Van Hee RH — Intraperitoneal gossypibomas: the need to count sponges. *World J Surg* 2000; **2013**: 521-7.
- 10 Yamamura N, Nakajima K, Takahashi T — Intra-abdominal textiloma. A retained surgical sponge mimicking a gastric gastrointestinal stromal tumor: report of a case. *Surg Today* 2008; **2013**: 552-4.
- 11 Dux M, Ganten M, Lubienski A, Grenacher L — Retained surgical sponge with migration into the duodenum and persistent duodenal fistula. *Eur Radiol* 2002; **12**: 874-7.
- 12 Kubota A, Haniuda N — A case of retained surgical sponge (gossypiboma) and MRI features. *Jpn J Gastroenterol Surg* 2000; **33**: 1719-23
- 13 Biswas RS, Ganguly S, Saha ML, Saha S, Mukherjee S, Ayaz A — Gossypiboma and surgeon- current medicolegal aspect - a review. *Indian J Surg* 2012; **74(4)**: 318-22.
- 14 Crossen HA, Crossen DF — Foreign bodies left in the abdomen. CV Mosby Co, St Louis, 1940; p 49.
- 15 Karasaki T, Nomura Y, Nakagawa T, Tanaka N — Beware of gossypibomas. *BMJ Case Rep* 2013; **2013**: bcr2013010059. Published 2013 Jun 21.
- 16 Yamato M, Ido K, Izutsu M, Narimatsu Y, Hiramatsu K — CT and ultrasound findings of surgically retained sponges and towels. *J Comput Assist Tomogr* 1987; **11**: 1003-6.
- 17 Operating Room Nurses Association of Canada (2007) Surgical counts. In: Recommended standards, guidelines, and position statements for perioperative nursing practice. Canadian Standards Association, Mississauga
- 18 South African Theatre Nurse (2007) Swab, instrument and needle counts. In: Guidelines for basic theatre procedures. Panorama, South Africa
- 19 Patial T, Thakur V, Vijhay Ganesun N, Sharma M— Gossypibomas in India - A systematic literature review. *J Postgrad Med* 2017; **63(1)**: 36-41. doi:10.4103/0022-3859.198153
- 20 Gawande AA, Studdert DM, Orav EJ, Brennan TA, Zinner MJ — Risk Factors for Retained Instruments and Sponges after Surgery. *N Engl J Med* 2003; **348**: 229-35.
- 21 Gibbs VC, Auerbach AD — The retained surgical mops (chapter 22) In retained surgical surgical foreign body. Prevention and severity of target safety problem .Agency for Healthcare Research and Quality (2008). From the AHRQ publication.
- 22 Aminian A — Gossypiboma: a case report. *Cases Journal* 2008; **1(1)**: 220.
- 23 Soori M, Shadidi-Asil R, Kialashaki M, Zamani A, Ebrahimian M — Successful laparoscopic removal of gossypiboma: A case report. *International Journal of Surgery* 2022; Case Reports; Volume 91.

If you want to send your queries and receive the response on any subject from JIMA, please use the E-mail or Mobile facility.

Know Your JIMA

Website : <https://onlinejima.com>
For Reception : **Mobile** : +919477493033
For Editorial : jima1930@rediffmail.com
Mobile : +919477493027
For Circulation : jimacir@gmail.com
Mobile : +919477493037
For Marketing : jimamkt@gmail.com
Mobile : +919477493036
For Accounts : journalaccts@gmail.com
Mobile : +919432211112
For Guideline : <https://onlinejima.com>

Case Report

Angina Ludovici — A Rare Case Report

Ishwariya¹, Madhan Raja², Jude Vinoth³

Here we elaborate a case report on Ludwig's angina, a diffuse cellulitis of the neck that has an acute onset that spreads rapidly affecting the sublingual, submandibular and submental spaces resulting in a state of emergency¹. It is an uncommon cause of upper airway obstruction whose instantaneous diagnosis and treatment in the emergency department could be life-saving.

[J Indian Med Assoc 2023; 121(8): 86-7]

Key words : Ludwig's angina, Cellulitis, Odontogenic, Upper airway obstruction, Life-saving ED treatment.

CASE REPORT

A 66-year-old gentleman presented to the emergency department with breathing difficulty. He was on antibiotics for sore throat that developed after dental extraction 2 days ago. His breathing worsened rapidly with increase in swelling of the neck past 12 hours with decrease in level of consciousness. He is a known diabetic.

On arrival, his airway was not patent. His vitals were, heart rate 106/mt, Blood pressure of 110/70 mmHg, temperature 101.8°F and oxygen saturation was 94% in room air. His GCS was low 6/15. On examination he was dyspneic, anterior swelling of upper neck and back fall of tongue, trismus and stridor were noted. With effective hydration, his sensorium improved. He was immediately started on antibiotics after the collection of blood samples for cultures. His initial blood reports disclosed elevated leucocytes, liver and renal parameters. He was then electively intubated with preparedness for difficult intubation. He was started with Inj. Teicoplanin and Inj. Metronidazole, intravenous steroids (inj. Hydrocort 50 mg 6th hourly) were given to bring down airway edema, nebulizers, gastroprotectives, analgesics and insulin. CT chest and CT neck showed extensive subcutaneous fat stranding and soft tissue emphysema involving all free spaces of neck extending up to the superior mediastinum. Diffuse circumferential wall thickening and edema of the walls of the pharynx is seen. ENT opinion was obtained

Editor's Comment :

- Early recognition is required for prompt treatment and management.

and patient underwent Ludwig's abscess drainage with cervical decompression and debridement. He improved clinically after the surgery. In spite of vigorous management, he showed only partial improvement due to underlying sepsis. He was then started on inotropes to maintain Mean Arterial Pressure above 65mm/Hg. He then gradually showed improvement and discharged after 1 week.

DISCUSSION

Ludwig's angina is an infection of the submandibular space. This space lies between the floor of mouth and tongue on one side and cervical fascia ranging between the hyoid bone and mandible on the other. Mylohyoid muscle splits it into two as:

Above - Sublingual compartment

Below - Submental and submaxillary compartment

These two compartments are unremitting in the vicinity of the posterior border of mylohyoid muscle

Dental infections credit for about 80% of the etiology. Roots of premolars lie above the mylohyoid cause sublingual space infection while roots of the molar teeth extending below the mylohyoid primarily cause submaxillary space infection. Other causes include submandibular sialadenitis, injuries to oral mucosa and fractures of the mandible. In children, it can occur de novo, without any noticeable cause. Streptococci viridans (40.9%), staphylococcus aureus(27.3%), staphylococcus epidermis (22.7%) and pigmented bacteroids were isolated from the infections of deep neck². Most patients report neck swelling frequently with either dental pain or

Department of Emergency Medicine, Apollo hospitals, Madurai, Tamilnadu 625020

¹MBBS, MEM, Resident and Corresponding Author

²MD, FAECS, Consultant,

³MD, MRCEM, Senior Consultant and Head

Received on : 21/07/2022

Accepted on : 25/08/2022

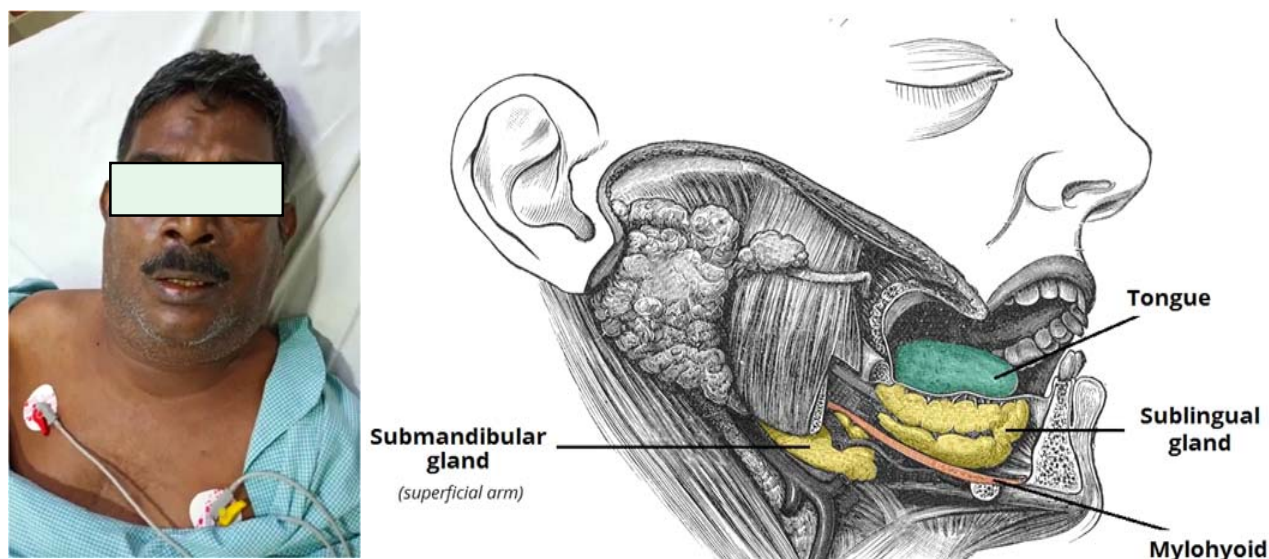


Fig 1 — Images of the Patient and Saces of Neck

following a recent dental procedure followed by sore throat, dysphagia (35%) pharyngodynia (25%), fever (25%), trismus (15%) and dysphonia (15%). Involvement of sublingual space bring about swelling of the structures in the floor of the mouth and tongue appears to be pushed upwards and backwards menacing the airway. The involvement in other spaces causes the swelling of soft tissues, woody hard in consistency, cellulitis instead of frank pus, occasionally with palpable crepitus. In ER perspective, airway compromise is synonymous with the name Ludwig's angina, which should be managed immediately and appropriately. The stage of the disease at the time of presentation, available resources, physician experience, are all key factors in the decision for airway management either by elective intubation or tracheostomy. Tracheostomy remains the gold standard when stridor is present but sometimes it may be impossible in cases of anatomical distortion and in advanced cases of the disease. Blind nasotracheal intubation should not be endeavored in patients with Ludwig's angina given the possibility for bleeding and abscess rupture. Early antibiotic therapy is of critical

importance for successful treatment. Penicillin G, metronidazole or clindamycin are suitable as initial coverage. Additionally, intravenous steroids and nebulized adrenaline use helps to allow easier intubation avoiding tracheostomy or cricothyroidotomy and letting antibiotic penetration into the facial spaces by reducing airway edema. Complications of Ludwig's angina consist of thrombophlebitis of the internal jugular vein, carotid artery rupture or sheath abscess, empyema, subphrenic abscess, pericardial effusion, pleural effusion, mediastinitis, osteomyelitis of the mandible and aspiration pneumonia^{1,3}.

REFERENCES

- 1 Candamourty R, Venkatachalam S, Babu M, Kumar G — Ludwig's angina—an emergency: a case report with literature review. *J Nat Sci Biol Med* 2012; **3**: 206-8. [PMC free article] [PubMed] [Google Scholar]
- 2 jnsbm.com/jnsbmsite/wpcontent/uploads/2021/07/JNatScBiolMed-3-2-206.pdf
- 3 Saifeldeen K, Evans R — Ludwig's angina. *BMJ*; **21(2)**: emj.bmj.com/content/21/2/242. <http://dx.doi.org/10.1136/emj.2003.012336>

Commentary

Health Care Systems during Pandemic : Role of Government and Regulatory Authorities

Ankur Gupta¹, Alok Pandey², Puja Bansal³, Anureet Kaur⁴, Pranava Prakash⁵

This paper presents a review of literature on resilience of health care systems during pandemic. Resilience of health care systems through the review of literature has been defined as capacity of a system to bounce back from an adverse event such as a pandemic. We have reviewed 35 articles published on the issue during last five years (ie, 2018-2022) from different countries, both developed and developing. Most researchers have undertaken studies in this area and have conceptualized resilience of health systems with respect to infrastructure development, safety, awareness, connectivity, self-regulation, adaptability, integrity, disaster management, inventory and stock management of essential supplies, quality of services, community involvement, reactive capabilities and risk management. The aim of this paper is to describe how health care system resilience is defined and prepare an introductory conceptual review as a preliminary step for further studies. This paper helps us in identifying the key research themes that characterize the inquiry around resilience in context of a health care system during and post COVID-19 and also the structural improvements and characteristics to improve the competence of a health care system to deem it resilient during pandemic.

[J Indian Med Assoc 2023; 121(8): 88-90]

Key words : Health Care Systems, Post COVID-19.

During December 2019, novel “coronavirus” (COVID-19) which is a highly transmittable and pathogenic viral infection emerged first in China and rapidly spread around the world. On March 11, 2020 WHO declared the COVID-19 as a global outbreak of a pandemic (Padhan R, Prabheesh KP, 2021). The COVID-19 pandemic presented an unprecedented challenge to the global health care system. The pandemic exposed inherent weaknesses in our preparedness and response. Also, the health systems were grossly overwhelmed by the pandemic.

The novel coronavirus, or COVID-19, has resulted in several human deaths and socio-economic issues that have heavily damaged community health systems. India's health care system now faces structural issues due to the pandemic. A number of immediate and long-term repercussions, primarily on the healthcare sector, have been affected by this global pandemic (Ayati, *et al* 2020).

The pandemic COVID-19 has brought the spot light on India as well. While there were some successes in the response to the pandemic, there were also several ways in which the health care system fell short. Overall, the COVID-19 pandemic exposed several weaknesses and flaws in the global health care system. There is much work to be done to address these issues and prepare for

future pandemics. Financial and logistical resources should be accessible and well exploited so that health care systems can bring about immense benefit for the general public. Health care systems would also benefit from good governance and control systems along with sufficient funding for emergency medical care programme. Both public and private sectors should be involved in Infrastructure development so as to expand access to life-saving medical care through upgraded facilities (Shukla, *et al* 2021).

In India, the COVID-19 pandemic has also exposed several weaknesses and flaws in the health care system. The first wave presented a livelihood disaster due to an ill-planned lockdown. The second wave presented a health disaster that was due to government inaction (Pellissery S, *et al* 2021).

Some of the areas in which healthcare failed during the COVID-19 pandemic in India are:

Lack of preparedness : The health care system in India was not adequately prepared for the scale and severity of the pandemic. There was a shortage of critical resources such as Personal Protective Equipment (PPE), ventilators and hospital beds.

Testing and contact tracing failures : Initially, there were significant delays in testing and contact tracing in India, which contributed to the rapid spread of the virus. The testing capacity was inadequate, and there were issues with the quality of tests and delays in receiving results.

Overwhelmed health care systems : The rapid surge in COVID-19 cases in India overwhelmed the health care system, with hospitals and health care workers stretched thin. There were shortages of critical resources, such as oxygen cylinders and medication, which led to many deaths. During April 2021 the number of reported positive cases crossed 200,000 per day, hospitals had no capacity

¹Research Scholar, Department of Management, GD Goenka University, Gurugram, Haryana 122103

²Professor and Vice Dean, Department Jindal School of Banking and Finance, OP Jindal Global University, Sonapat 131001

³Research Scholar, Guru Jambheshwar University of Science and Technology, Hisar, 125001 and Corresponding author

⁴Assistant Professor, G D Goenka Institute of Management, Gurugram, Haryana 122103

⁵MBBS, Associate Professor & Head, Public Health, GD Goenka University, Gurugram Haryana 122103

Received on : 06/04/2023

Accepted on : 07/05/2023

to admit patients and also where beds were available, oxygen and life-supporting machines, were absent (Pellissery S, *et al* 2021). In such conditions individuals kept sick loved ones at home and started procuring medical essentials from the black market. The rule of law also becomes ineffective when citizens are left to their own devices to manage their health during a pandemic.

Inadequate communication and coordination : There were issues with communication and coordination between different health care organizations and the Government in India. This led to confusion and delays in implementing effective measures to control the spread of the virus. While during the first wave of the COVID-19 crisis, the government was visible through the lockdown measures but the second wave made it invisible. There was huge gap between public information on bed availability and the reality on the ground during COVID-19, an important debate occurred in India among doctors as to whether CT scans could be used for COVID-19 diagnosis (Pellissery S, *et al* 2021)

Health disparities : The pandemic highlighted existing health disparities in India, with certain communities and populations being disproportionately affected by COVID-19. This was due to a variety of factors, including socio-economic status, lack of access to healthcare and underlying health conditions. India with its deep economic and social inequality was in shambles as the pandemic left vulnerable citizens to look on while well-off citizens grabbed the available resources (be it a hospital bed or a respectable funeral) and also hoarding and black marketing of medicines like Remdesivir (Pellissery S, *et al* 2021).

India's Burial Infrastructure : The way in which the pandemic brought pressure on India's burial infrastructure created graded dignity. Those who could afford the expenses of burial were able to respect their emotions toward the dead body of a relative. Impoverished villagers without resources to buy wood for cremation, had floated the dead bodies down rivers. Bribes were demanded both in public crematoriums as well as by middle-men to execute the task (Pellissery S, *et al* 2021).

These are some examples of how the system as a whole did actual harm, while most individual doctors were caring. Overall, the COVID-19 pandemic has exposed several weaknesses in the health care system in India. There is a need for significant investment in healthcare infrastructure and resources, as well as better coordination between different healthcare organizations and the Government to prepare for future pandemics and provide better healthcare to the population.

A regulatory framework is essential for ensuring the quality and safety of healthcare services. The health care system must have appropriate regulations and standards for healthcare providers, facilities, and medical products. It should also be sustainable, adaptable, and able to respond to the changing healthcare needs of the population. Appropriate response and responsibility by the Government towards health-related shock creates a resilient response by a nation (Augustynowicz A, *et al*,

2022; Khan Y, *et al* 2018; Rogers HL, *et al* 2021; Thomas S, *et al* 2020). Issue of policy guidelines and development of various health related clinical protocols for hospitals should be created (Burke DS, *et al*, 2021; Øyri SF, Wiig S, 2022; Barbash IJ, Kahn JM, 2021). The involvement of top policy makers in expanding of Government budget on health and provision for health facilities before and during a pandemic and creation of long-term plans and policies and tertiary level interventions at hospital level can improve healthcare capabilities of a nation (Burke DS, *et al* 2021; Khetrpal SR, Bhatia, 2020; Rogers HL, *et al* 2021; Thomas S, *et al* 2020).

The role of Government during a pandemic is multifaceted and can involve a range of activities and interventions. Some ways in which the Government can play a role in managing a pandemic is by providing accurate and timely information the pandemic, how it spreads, how to protect oneself and what measures are being taken to control the spread of the virus. This information should be communicated clearly and effectively, and in a manner that is accessible to everyone, regardless of their level of education or literacy.

There is a need to implement public health measures like travel restrictions, mandatory quarantine for those who have been exposed to the virus, mandatory mask-wearing, social distancing measures, and restrictions on public gatherings. These measures can help slow the spread of the virus and prevent the health care system from becoming overwhelmed.

Mobilization of the healthcare resources is another important area where the Government can play a critical role to respond to the pandemic. This may involve procuring critical resources such as Personal Protective Equipment (PPE), ventilators and medication, as well as recruiting and training health care workers. The Government can also set up temporary healthcare facilities to accommodate the surge in patients during a pandemic.

As Pandemics are global in nature and coordination with other countries and International Organizations is essential to manage the spread of the virus. The Government can play a key role in coordinating with other countries to share information and resources, as well as collaborate on research and development of treatments and vaccines. International cooperation can also help to prevent the spread of the virus across borders.

The vulnerable populations of a country require Government support which may involve providing financial assistance to those who have lost their jobs or are unable to work due to the pandemic, as well as ensuring access to healthcare services for marginalized communities. The Government can also set up support systems for elderly people, disabled individuals, and those with pre-existing medical conditions who may be particularly vulnerable to the virus.

Roll out vaccines: As vaccines become available, the Government can play a critical role in rolling them out to the population. This may involve setting up vaccination centers, coordinating with healthcare providers, and communicating the importance of vaccination to the

public. The government can also work to ensure equitable distribution of vaccines across different regions and populations.

A society's ability to respond collectively, to pool resources and risk while safeguarding its population, especially the most vulnerable, will determine how much of an impact a pandemic or similar threat will have on society and the economy. These factors include public confidence in the Government's actions, a balance between values and policies that promote health, wealth, and prosperity and a society's willingness to take collective action. These characteristics define a strong and harmonious community (Etienne, 2020). Governments and other institutions cannot exclusively achieve resilience through top-down, unilateral strategies. Community involvement is as important to resilience as rules and hospital capacity. Managing challenges to health as well as other threats, such as climate and environmental change, requires a strong focus on community participation and how it relates to community resilience (Haldane, 2021). The national Governments must create and put into action plans to strengthen and bolster the resilience of their health systems with the aid of outside partners.

It is vital to implement new frameworks and policy instruments affecting health care organisations to adequately plan for anticipated crises and other difficulties that may impact health care delivery (Rogers, 2021). While according to Biddle, *et al*, 2020, resilience is no longer seen as a quality of the health care system but as a strength that depends on actors' ability to adapt and adjust. So, the country's National Health plans must prioritize the resilience of the health-care system (Arsenault, *et al* 2022). This is because all system levels and sectors' stakeholders must see volatility as an opportunity to improve the health system rather than as a danger to its viability and integrity. Resilience must be understood as a multi-tiered notion in which resilience requirements at one level may be influenced by activities at other levels (Turner, 2022). Therefore, efforts to improve the resilience of health systems should place a major emphasis on state, Non-governmental Organisations (NGOs), as well as private health personnel.

The considerable research on flexibility of hospitals in terms of safety precautions, reorganizing spaces, managing resources, using technology and training and development of workforce is required. Also, disaster management systems, disaster resources, and disaster medical care capabilities should be prioritized by Government and regulatory authorities of a nation.

Overall, the Government plays a crucial role in managing a pandemic like COVID-19. By providing accurate information, implementing public health measures, mobilizing healthcare resources, coordinating with other countries and organizations, supporting vulnerable populations and rolling out vaccines, the Government can help to slow the spread of the virus and protect public health

REFERENCES

- 1 Arsenault C — COVID-19 and resilience of healthcare systems in ten countries. *Nat Med* 1922; **28**: 1314-24 <https://doi.org/10.1038/s41591-022-01750-1>
- 2 Augustynowicz A — Resilient Health and the Healthcare System. A Few Introductory Remarks in Times of the COVID-19 Pandemic. *Int. J. Environ. Res. Public Health* 2022; **19**: 3603. <https://doi.org/10.3390/ijerph19063603>
- 3 Ayati N, Saiyarsarai P, Nikfar S — Short and long term impacts of COVID-19 on the pharmaceutical sector. *DARU Journal of Pharmaceutical Sciences* 2020; **28(2)**: 799-805.
- 4 Barasa E, Mbau R, Gilson L — What Is Resilience and How Can It Be Nurtured? A Systematic Review of Empirical Literature on Organizational Resilience. *International journal of health policy and management* 2018; **7(6)**: 491-503. <https://doi.org/10.15171/ijhpm.2018.06>
- 5 Biddle L — Health system resilience: a literature review of empirical research. *Health policy and planning* 2020; **35(8)**: 1084-109. <https://doi.org/10.1093/heapol/czaa032>
- 6 Burke DS — Building health system resilience through policy development in response to COVID-19 in Ireland: From shock to reform / *The Lancet Regional Health* 2021; - Europe 9 (2021) 100223.
- 7 Etienne CF — COVID-19: transformative actions for more equitable, resilient, sustainable societies and health systems in the Americas. *BMJ Global Health* 2020; **5(8)**: e003509.
- 8 Haldane V — Health systems resilience in managing the COVID-19 pandemic: lessons from 28 countries. *Nature Medicine* 2021; **27(6)**: 964-80.
- 9 Khan Y, O'Sullivan T, Brown A, Tracey S, Gibson J, Génèreux M, et al — Public health emergency preparedness: a framework to promote resilience. *BMC public health* 2018; **18(1)**: 1-16.
- 10 Khetrpal S, Bhatia R — Impact of COVID-19 pandemic on health system & Sustainable Development Goal 3. *Indian Journal of Medical Research* 2020; **151(5)**: 395-9. | DOI: 10.4103/ijmr.IJMR_1920_20
- 11 Øyri SF, Wiig S — Linking resilience and regulation across system levels in healthcare – a multilevel study. *BMC Health Services Research* 2022; **22**: 510 <https://doi.org/10.1186/s12913-022-07848-z>
- 12 Padhan R, Prabheesh KP — The economics of COVID-19 pandemic: A survey. *Econ Anal Policy* 2021; **70**: 220-37. doi: 10.1016/j.eap.2021.02.012. Epub 2021 Feb 25. PMID: 33658744; PMCID: PMC7906538.
- 13 Pellissery S — The Case of India A Moral Foundation for the Impact of COVID-19 on Health and Society in the World's Largest Democracy. *International Journal of Social Quality* 2021; Volume 11, Issues 1 & 2, Summer & Winter 2021: 63-84.
- 14 Rogers HL — Resilience testing of health systems: How can it be done? *International Journal of Environmental Research and Public Health* 2021; **18(9)**: 4742.
- 15 Shukla D, Pradhan A, Malik P — Economic impact of COVID-19 on the Indian healthcare sector: an overview. *Int J Comm Med Public Health* 2021; **8(1)**: 489-94.
- 16 Thomas S — Strengthening health systems resilience: Key concepts and strategies [Internet]. Copenhagen (Denmark): European Observatory on Health Systems and Policies 2020; PMID: 32716618
- 17 Turner S — We are all vulnerable, we are all fragile: COVID-19 as opportunity for, or constraint on, health service resilience in Colombia? *Public Management Review* 2022; 1-22.

Image in Medicine

Bhoomi Angirish¹, Bhavin Jankharia²

Quiz 1

A 23-year-old male present with Recurrent Headache which Worsened since 15 days.

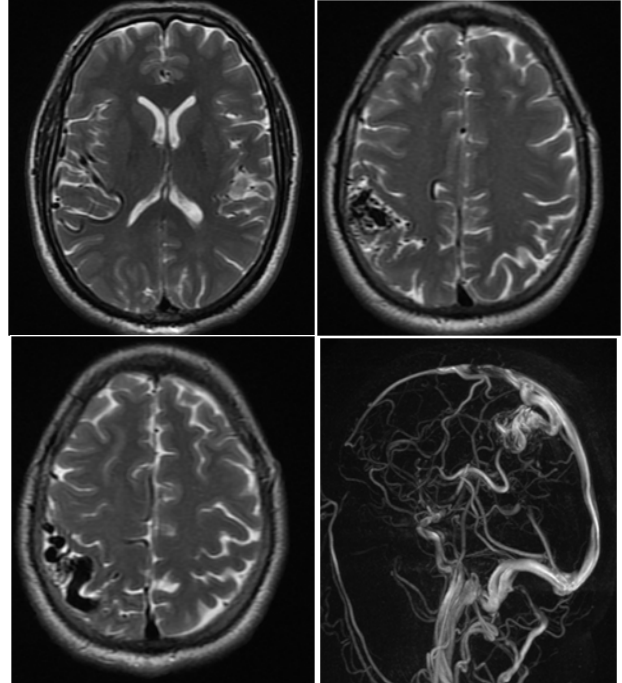
Questions :

- (1) What is the diagnosis ?
- (2) If such lesions are multiple in number, what syndrome are usually associated ?

Answers :

(1) An intracranial Arteriovenous Malformation (AVM) is seen composed of enlarged feeding arteries, a nidus of vessels and draining veins. In this case, the feeding arteries are seen arising from cortical branches of middle cerebral artery and draining veins are seen draining into superior sagittal sinus through cortical veins.

(2) Usually arteriovenous malformations are solitary, however multiple AVM are seen associated with Hereditary Hemorrhagic Telangiectasia and Craniofacial arteriovenous metamerism syndrome.



Quiz 2

A 19-year-old male present with Subcutaneous Fatty Tissue with Abnormal Hair Tuft in Lower Back.

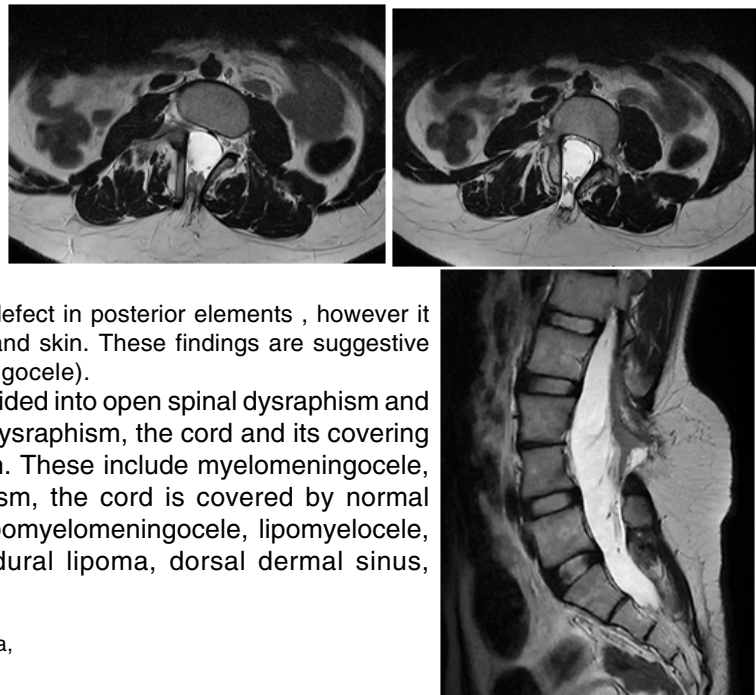
Questions :

- (1) What is the diagnosis ?
- (2) What are the different types of spinal dysraphism ?

Answers :

(1) Spina bifida is seen at L3 and L4 vertebral levels. Low lying cord is seen with herniation of cord and meninges through the defect in posterior elements, however it is covered by overlying subcutaneous tissue and skin. These findings are suggestive of closed spinal dysraphism (lipomyelomeningocele).

(2) Spinal dysraphism can be broadly divided into open spinal dysraphism and closed spinal dysraphism. In open spinal dysraphism, the cord and its covering are exposed and there is no overlying skin. These include myelomeningocele, myelocele etc. In closed spinal dysraphism, the cord is covered by normal mesenchymal elements. These include lipomyelomeningocele, lipomyelocele, meningocele, isolated spina bifida, intradural lipoma, dorsal dermal sinus, diastematomyelia etc.



Department of Radiology, Picture This by Jankharia,

Mumbai, Maharashtra 400004

¹MD, DNB (Radiology)

²MD, DMRD (Radiology)

Letter to the Editor

[The Editor is not responsible for the views expressed by the correspondents]

Dengue — The Remedial Steps

SIR, — The dengue recently have become more rampant and awareness regarding remedial steps both by public and health workers will be helpful in long way in curbing the dreadful disease.

(1) People need to be aware that dengue is of four serotypes. Infection from one serotype gives life long immunity to that but only cross protection to other 3 serotypes for 2 years, due to sharing of seventy percent aminoacid sequences identity. Secondary infection is more severe due to present antibodies. Primary prevention is best solution.

(2) Destroying breeding of dengue vector and emphasis on proper sanitation, avoiding exposure of body and use of mosquito nets and repellants specially when dengue is rampant.

(3) Notification of disease to government authorities for better policy making.

(4) Educating people about prevention and primary care of the disease as delay in treating patients increases mortality from 1-5 percent to 20 percent.

(5) Patients having comorbidities like diabetes, kidney disease, hypertension, elderly, obese, pregnant women, etc should be taken care at the earliest by the physicians and not home treated.

(6) People should be made aware that late presentation of dengue fever to the hospital leads to increased development of dengue haemorrhagic fever, dengue shock syndrome, multi-organ involvement like acute kidney injury, and increased mortality.

(7) The guide lines for hospital admission — if the platelet count is <100,000, or platelet count between 100,000-150,000 with a rapid drop in platelets, fever for three days with any warning signs such as abdominal pain, persistent vomiting, mucosal bleeding, lethargy and restlessness.

(8) Elisa based NS1 tests best and can not be false positive. NS1 antigen is tested positive in first few days and has a sensitivity of 60-90%. IgM antibody become positive after the 5th day of illness. Timing of testing should be made aware. In primary dengue IgG becomes + at the end of 7 days while IgM+ is after day 4.

Value of IgG and IgM with thrombocytopenia and looking sick on day 3 or 4 of illness, a very high titre of IgG with borderline rise in IgM signifies secondary dengue infection and are more prone to complications.

If Immature platelet fraction IPF is >10% despite a platelet count of less than 20,000, one is out of danger

and platelet will rise in 24 hours. However if less than 5% then bone marrow not responding for at least 3-4 days and is the candidate for platelet transfusion. Better to do IPF even in borderline low platelet count. Low mean platelet volume MPV are functionally not good and need more attention.

(9) Public awareness through social media is fruitful.

(10) Treatment of choice is paracetamol, plenty of liquid diet to prevent hypotension.

(11) Fluid of choice in is normal saline.

(12) Platelet transfusion when platelet count is less than 10,000 or when active bleeding or purpuric spots occur.

(13) Drugs to be avoided like aspirin, ibuprofen, nimuselide, acenofenac and steroid.

(14) Storage of platelets at 24 to 26 degrees Celsius. Half life of platelets is 6 to 9 days.

(15) Goat milk, papaya leaf, kiwi fruits have no role and any benefit is due to antioxidants but can affect liver which is often deranged.

(16) While treating dengue patients, formula of 20 is very handy. That is rise in pulse by more than 20, fall of BP by more than 20, difference between upper and lower BP of less than 20, and presence of more than 20 haemorrhagic spots on the arm after a tourniquet test suggest a high risk situation and the person requires care.

(17) The primary cause of mortality is due to capillary leakage causing hypotension due to decrease in intravascular compartment volume leading to multiple organ failiure. Fluid replacement amounting to 20 ml per kg body weight per hour must be administered. This must be continued till difference between the upper and lower blood pressure is over 40 mm of mercury or the patient passes adequate urine. This is sufficient and giving unnecessary platelet transfusion can make patient more deteriorated.

Eye sees what the mind knows. So education and awareness of dengue control and management is key to curbing effectively this dreaded disease.

¹MBBS, MS, MCh (Plastic Surgery),
Hony IMA Professor,
Department of Plastic Surgery,
Getwell Hospital, Varanasi

Sudhir Singh¹
Manoj Kumar Srivastava²

²MBBS, MD, Professor,
Department of Medicine,
Narayan Medical College, Bihar



98th All India Medical Conference

National Conference of Indian Medical Association

Organised by : IMA Thiruvananthapuram, Kerala State



DATE

27th & 28th December 2023

Venue

**Kovalam,
Thiruvananthapuram
(Kerala)**

CORRESPONDENCE ADDRESS

Indian Medical Association,
IMA Building, Redcross Road,
GH Jn, Vanchiyoor, Thiruvananthapuram
Phone: +91 0471 2463514, 9400406881
Email: imanatcontvm@gmail.com
imatrivandrum@gmail.com
Website: www.imatrivandrum.org

IMA KERALA STATE OFFICE ADDRESS

IMA Kerala State Branch
Headquarters, Anayara P.O
Thiruvananthapuram
Phone 91 0471 2741144
Email. imaksbhq@gmail.com
Website : www.imakerala.com

Conference Registration tariff (GST included)

Delegate Registration Fees Category	Till 31st July	August to November	December & Spot
IMA Members	6000	7000	8500
Non Members	7500	8500	10000
Medical Student / PG / Junior Resident	3500	4500	5500
Accompanying Person	5000	6000	7500

Registration help line, Mob no : +91 94004 06881

• *NEFT DETAILS* •

A/C NO: 50100623505980
NAME : ALL INDIA MEDICAL CONF 2023-IMA TVM BR
IFSC: HDFC0005125

(For Online Transfer it is mandatory to send Transaction details to 94004 06881)

Scan QR to pay
ALL INDIA MEDICAL CONF 2023
IMA TVM BR



CORRESPONDENCE ADDRESS

Indian Medical Association
 IMA Building, Redcross Road
 GH Jn, Vanchiyoor, Thiruvananthapuram
 Phone: +91 0471 2463514, 9400406881
 Email: imanatcontvm@gmail.com
 imatrivandrum@gmail.com
 Website: www.imatrivandrum.org

Dr Sreejith N Kumar
 Organising committee Chairman
 Mob: 8921440079

Dr G S Vijaykrishnan
 Co Chairman
 Mob: 7012580479

Dr Sulphi N
 Organising committee Secretary
 Mob : 94473 87739

Dr Sreejith R
 Finance Secretary
 Mob: 9947157775



In Hypertension

^{Rx} Nebicard

Nebivolol 2.5 / 5 / 10 mg Tablets

Also available

Nebicard T

Nebivolol 5 mg + Telmisartan 40 mg Tablets

Nebicard SM

Nebivolol 5 mg + Sitagliptin 2.5 mg Tablets

Nebicard LN

Nebivolol 2.5 / 5 mg + Cln dlpine 10 mg Tablets

In T2DM patients with HbA1c >8.5%*

^{Rx} GLUCRETA-SM

Dapagliflozin 10mg + Metformin SR 500/1000mg + Sitagliptin 100mg Tablet

Protect Fast...Protect Early

Also available

GLUCRETA

Dapagliflozin 5 mg/10 mg Tablets

GLUCRETA-M

Dapagliflozin 5 mg/10 mg Tablets + Metformin Extended Release 500 mg/1000 mg Tablets

GLUCRETA-S

Dapagliflozin 5/10 mg + Sitagliptin 50/100 mg



Torrent House, Off. Ashram Road, Ahmedabad - 380009, Gujarat, India
E-mail : medicalquery@torrentpharma.com

* Diabetes Ther (2022) 13:1097-1114

Date of Publication : 20th August, 2023

UNS
 Universal NutriScience

In NAFLD recommend,

NEW
E-COD[®] Plus
 Tocotrienols, Cod Liver Oil, Wheat Germ Oil, Vitamins **Softgels**

With the power of 5

Vit. B₆¹
 Crucial role in glucose and lipid metabolism

Folic acid²

Tocotrienol - Vitamin E of 21st century

- 40-60X higher potency than conventional vitamin E
- Unsaturated side chain facilitates smooth and efficient penetration into the liver
- Posses anti-oxidant, anti-inflammatory & anti-fibrotic action

Wheat germ oil³
 Improves lipid profile and reduces hepatic steatosis

Cod liver oil⁴
 Rich in vitamin A & D, reduces hepatic steatosis

Dosage:
 1-2 Softgels/day for 3 to 6 months

UNS
 Universal NutriScience Private Limited
 2nd Floor, Fleet House, Marol, Andheri - Kurla Road, Andheri East - Mumbai 400059.
 Website: <https://universalnutriscience.com> | E-mail: corporatecommunications@unsc.co.in

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

NAFLD, Non-alcoholic fatty liver disease; NASH, Non-alcoholic steatohepatitis
References:
 1. Kobayashi T, Kessoku T, Ozaki A, Iwaki M, Honda Y, Ogawa Y, Imajo K, Yoneda M, Saito S, Nakajima A. Vitamin B6 efficacy in the treatment of nonalcoholic fatty liver disease: an open-label, single-arm, single-center trial. *J Clin Biochem Nutr.* 2021 Mar;58(2):181-186. 2. Sid, V., Slow, Y. L. & O. K. Role of folate in nonalcoholic fatty liver disease. *Canadian Journal of Physiology and Pharmacology.* 2017;95(10):1141-1148. 3. Salehi-Sab abadi A, Kord-Varkaneh H, Kocadam-Bozkurt B, Seraj SS, Alavian SM, Hekmatdoost A. Wheat germ improves hepatic steatosis, hepatic enzymes, and metabolic and inflammatory parameters in patients with nonalcoholic fatty liver disease: A randomized, placebo-controlled, double-blind clinical trial. *Phytother Res.* 2022 Nov;36(11):4201-4209. doi: 10.1002/ptr.7553. Epub 2022 Jul 17. PMID: 35843540. 4. Zhu FS, Liu S, Chen XM, Huang ZG, Zhang DW. Effects of n-3 polyunsaturated fatty acids from seal oils on nonalcoholic fatty liver disease associated with hyperlipidemia. *World J Gastroenterol.* 2008;14(41):6395-6400.

If not delivered please return to
 Journal of the IMA (JIMA)
 53, Sir Nilratan Sarkar Sarani,
 (Creek Row), Kolkata - 700014

Printed and Published by **Dr Jyotirmoy Pal** on behalf of Indian Medical Association and printed at Prabaha, 45, Raja Rammohan Sarani, Kolkata - 700009 and Published from Sir Nilratan Sircar IMA House, 53, Sir Nilratan Sarkar Sarani (Creek Row), Kolkata 700014, Editor : **Dr Tamonas Chaudhuri**