Indexed with IndMED
Indexed with MedIND
Indian Citation Index (ICI)

ISSN 0971-0876
RNI 50798/1990
University Grants Commission 20737/15554

IJCP
A Medical Communications Group
www.ijcpgroup.com

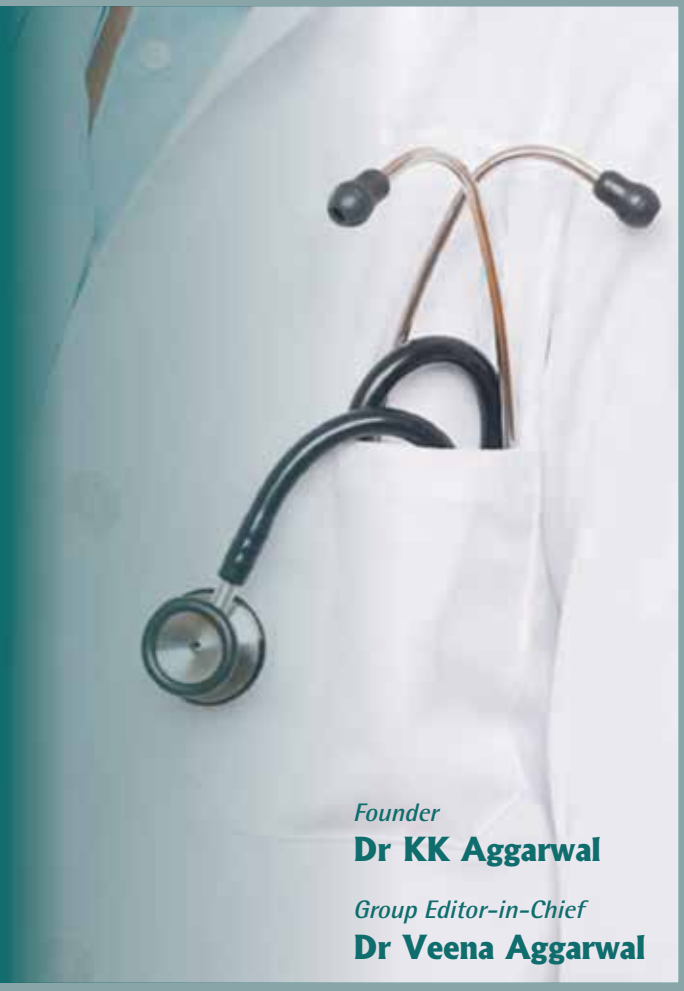
Indian JOURNAL of CLINICAL PRACTICE

A Multispecialty Journal

Volume 33, Number 3 August 2022, Pages 1–60 **Single Copy Rs. 300/-**

Peer Reviewed Journal

In this issue



Full text online: https://ijcp.in/
IJCP Publications | https://goo.gl/j2nXQQ

www.emedinexus.com

HealthPlus
Diagnostic & Imaging Centre

One Stop for All Diagnostics

MRI

- Latest MRI by Siemens
- Ultra Short Magnet = No Claustrophobia
- 1st MRI in India on VC 15 Platform

CT Scan

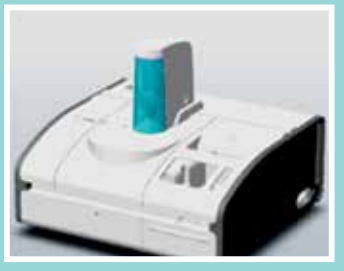
- 16- Multislice Spiral CT
- Safest Scanner
- Least Radiation Dose

Health Packages

- Executive Health Check Up
- Risk Categories
- Age Based Health Packages

Fully Automated Digital Pathology Laboratory - NABL Accredited

Immunology



Biochemistry

Haematology

Special Tests

Contact Us

S-63 Greater Kailash Part 1
Opposite M Block Market, New Delhi 110048
Tel.: 011- 41234567

This journal is indexed in IndMED (http://indmed.nic.in) and full-text of articles are included in medIND databases (http://mednic.in) hosted by National Informatics Centre, New Delhi.

Indian JOURNAL of CLINICAL PRACTICE
A Multispecialty Journal

Volume 33, Number 3, August 2022

Published, Printed and Edited by
Dr Veena Aggarwal, on behalf of
IJCP Publications Ltd. and
Published at
3rd Floor, 39 Daryacha, Hauz Khas Village,
New Delhi - 110 016
E-mail: editorial@ijcp.com

Printed at
New Edge Communications Pvt. Ltd., New Delhi
E-mail: edgecommunication@gmail.com

Editorial Policies

The purpose of IJCP Academy of CME is to serve the medical profession and provide print continuing medical education as a part of their social commitment. The information and opinions presented in IJCP group publications reflect the views of the authors, not those of the journal, unless so stated. Advertising is accepted only if judged to be in harmony with the purpose of the journal; however, IJCP group reserves the right to reject any advertising at its sole discretion. Neither acceptance nor rejection constitutes an endorsement by IJCP group of a particular policy, product or procedure. We believe that readers need to be aware of any affiliation or financial relationship (employment, consultancies, stock ownership, honoraria, etc.) between an author and any organization or entity that has a direct financial interest in the subject matter or materials the author is writing about. We inform the reader of any pertinent relationships disclosed. A disclosure statement, where appropriate, is published at the end of the relevant article.

Note: Indian Journal of Clinical Practice does not guarantee, directly or indirectly, the quality or efficacy of any product or service described in the advertisements or other material which is commercial in nature in this issue.

IJCP's EDITORIAL & BUSINESS OFFICES

Delhi	Mumbai	Bangalore	Chennai	Hyderabad
Dr Veena Aggarwal 9811036687 3rd Floor, 39 Daryacha, Hauz Khas Village, New Delhi - 110 016 Cont.: 011-40587513 editorial@ijcp.com **Subscription** Dinesh: 9891272006 subscribe@ijcp.com	Mr Nilesh Aggarwal 9818421222 Unit No: 210, 2nd Floor, Shreepal Complex Suren Road, Near Cine Magic Cinema Andheri (East) Mumbai - 400 093 nilesh.ijcp@gmail.com	H Chandrashekar **GM Sales & Marketing** 9845232974 11, 2nd Cross, Nanjappa Garden Doddaiah Layout Babusapalya Kalyananagar Post Bangalore - 560 043 chandra@ijcp.com	Chitra Mohan **GM Sales & Marketing** 9841213823 40A, Ganapathypuram Main Road Radhanagar, Chromepet Chennai - 600 044 Cont.: 22650144 chitra@ijcp.com	Venugopal **GM Sales & Marketing** 9849083558 H. No. 16-2-751/A/70 First Floor Karan Bagh Gaddiannaram Dil Sukh Nagar Hyderabad - 500 059 venu@ijcp.com

GM: General Manager

Dr KK Aggarwal
5th September 1958 - 17th May 2021

HCFI DR KK AGGARWAL RESEARCH FUND

Recent United Nations Resolution Declaring Access to Clean and Healthy Environment a Universal Human Right

- On 28th July, the United Nations General Assembly declared access to clean and healthy environment, a universal human right. One hundred sixty-one member countries voted in favor, while 8 countries abstained.
- The resolution calls upon states, international organizations and business enterprises to scale up efforts to ensure a healthy environment for all.
- Environment health and human health are interrelated.
- "A safe, clean, healthy and sustainable environment is integral to the full enjoyment of a wide range of human rights, including the rights to life, health, food, water and sanitation" (ohchr.org).
- This landmark decision will help in the collective fight against the triple planetary crisis of climate change, biodiversity loss and pollution, which together account for the death of around 9 million people every year.
- It will help reduce environmental injustices, close protection gaps and empower people. "This resolution sends a message that nobody can take nature, clean air and water, or a stable climate away from us – at least, not without a fight," said Inger Andersen, Executive Director of the UN Environment Programme (UNEP).
- This resolution has been passed after 50 years. It is not binding; it is only suggestive. But it will encourage countries to incorporate the right to a healthy environment in national constitutions and regional treaties.
- Other human rights are interlinked to this right.
- Climate change and environmental degradation are the most critical threats awaiting humanity in the future.
- The declaration sheds light on almost all the rights connected to the health of our environment.
- A healthy environment allows an individual to lead a life of dignity and well-being.
- "Every person, everywhere, has the right to eat, breathe and drink without poisoning their bodies", said UN High Commissioner for Human Rights, Michelle Bachelet.
- The subject of environment came to the forefront for the first time at the United Nations Conference on the Environment in Stockholm in 1972.
- In 2010, the UN General Assembly recognized the right to water and sanitation and said that clean drinking water and sanitation "are essential to the realization of all human rights". This led to change in the laws and regulations related to water and sanitation in many countries.
- However, we have still not been able to define what is "clean", "healthy" and "sustainable".
- However, this is not a landmark decision for India as the Indian Constitution has already defined the right to environment.

- India was the first country to safeguard environment through an amendment in the constitution.
- Article 21 in The Constitution of India on "Protection of life and personal liberty" says that "No person shall be deprived of his life or personal liberty except according to procedure established by law".
- While interpreting the right to life, the Supreme Court of India has already said that right to clean and healthy environment is a fundamental right.
- Under Article 39, Directive Principles of State Policy, it is the duty of the government to maintain a clean and healthy environment.
- As per Article 48A, states have a duty "to protect and improve the environment and to safeguard the forests and wild life of the country".
- Article 51-A (g) says that "It shall be duty of every citizen of India to protect and improve the natural environment including forests, lakes, rivers and wildlife and to have compassion for living creatures".
- There are many laws but the problem lies in their implementation. It is a challenging task.
- To save the environment, we have to also talk about accountability and responsibility and not just right.
- In MC Mehta vs. Union of India, the Supreme Court considered the right to good environment as a part of the right to life under Article 21 of the Constitution. This is a very clear and explicit enunciation of the law.
- Institutional set up is very fragmented and duplicated. There is a need to reform the institutional set up. Only then enforcement and implementation will come up.
- There is also lack of awareness about the subject and the related laws.
- Environment is being neglected in favor of development whereas the purpose of development is to improve the living environment. Any development should take into consideration the living environment.
- Under the Environment Protection Act, environmental impact assessment (EIA) has been made compulsory for all development projects. This statement describes the impact of the project on the environment. The Ministry of Environment and Forests has to very carefully review the EIA to see if the project is improving the environment of the people. The new UN resolution may strengthen this and improve the quality of EIA. The number of conditions to be implemented needs to be reduced so that they can be properly monitored. There has to be a penalty. Until this happens, EIA is of little value.

Participants: Dr Anil Kumar, Mr Paritosh Tyagi, Dr SK Gupta, Dr Sanjeev Agrawal, Mr Neeraj Tyagi, Mr Ankit Sethi, Ms Ira Gupta, Dr S Sharma

HCFI Dr KK Aggarwal Research Fund Round Table Environment Expert Zoom Meeting – July 31, 2022 (Sunday, 12 noon - 1 pm)

■■■■

Study Reveals BA.5 Subvariant 4 Times More Resistant to COVID-19 Vaccines

According to a recent study published in *Nature*, the newest Omicron subvariant, BA.5, has been found to be four times more resistant to COVID-19 vaccinations. The two BA.4 and BA.5 Omicron subvariants are currently the most prevalent strains in newly diagnosed COVID-19 infections in the US.

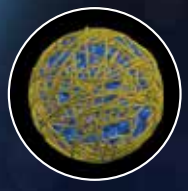
The Mayo Clinic stated in a recent analysis that the strain is "hypercontagious" and is responsible for increased hospitalization and ICU admission rates. The risk of getting infected by the virus was roughly five times higher in the unvaccinated group compared to those who are vaccinated including the booster dose. Rate of hospitalization was 7.5 times higher, and death rate was 14 to 15 times higher.

The US CDC reported that the BA.5 strain accounted for 65% of COVID-19 infections in the US for the week ending July 9. The WHO Director has warned people about new COVID-19 waves and advised the countries to be ready to address any such emergency in light of the emergence of new variations that are more transmissible, immune evasive and causing significant concerns about more hospitalizations. (*Source: Livemint, July 16, 2022)*

MD CE 0344

SelutionSLR™
SUSTAINED LIMUS RELEASE

Breakthrough DEB Technology Sustained Limus Release for upto 90 days[1]



Proprietary MicroReservoir Technology
Sirolimus combined with Biodegradable Polymer

MicroReservoirs
Precision Engineered Miniature Drug-Delivery Systems

Cell Adherent Technology (CAT™)
Patented Balloon Coating

MedAlliance

1. Effective drug concentration in tissue present up to 90 days - Data on file at M.A. Med Alliance SA

+ 41 22 363 78 90 info@medalliance.com www.medalliance.com

Dr Hanjabam Barun Sharma
Dept. of Physiology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India

Dr Sanjay Kalra
Dept. of Endocrinology, Bharti Hospital, Karnal, Haryana, India; University Center for Research & Development, Chandigarh University, Mohali, Punjab, India

Winning Gold for India: The Role of Health and Health Care Providers

AZADI KA AMRIT MAHOTSAV

The last 75 years have seen the evolution of independent India as a global power house. Thanks to contributions from our health care ecosystem, we have improved our life expectancy and other health parameters.[1,2] A welcome spin-off is that Indian athletes and sports persons are now climbing the winner's podium with ever-increasing regularity, and making their presence felt in the global arena. The government is trying its best, working both at grassroots and elite levels with various initiatives and programs, like Khelo India,[3] Target Olympic Podium Scheme (TOPS),[4] formation of task force for 2020 to 2028 Olympic Games[5] and Scheme of Human Resource Development in Sports, etc.[6]

Critics, of course, may find a lot to criticize, and pessimists, a lot to be upset about. In this editorial, however, we focus on optimism, on action and on celebration. We celebrate our Azadi ka Amrit Mahotsav, we suggest actions that all of us should undertake, and we conclude with optimism that India will claim its rightful place among the nations of the world. Specifically, we focus on how we, as health care professionals, can ensure that India becomes a global sports power.

HEALTH AND FITNESS

Physical fitness has always been considered an integral part of health. Physical activity, games, exercise and sports are encouraged as a preventive as well as therapeutic intervention in medicine. India has a long history of physical activity and exercise or vyayama. Both Charaka, the "Indian Father of Medicine" and Sushruta, the "founding Father of Surgery", advocated regular daily exercise or vyayama.[7] Infact, Charaka Samhita contains one of the oldest definitions of exercise. The concept of use of exercise as medicine can also be traced back to ancient Indian Indus valley civilization.[7] While yoga is an ancient Indian philosophy,[8] the upcoming fields of sports and exercise medicine or sports medicine,[7] reinforce the importance of these activities. This specialty of medicine deals with health promotion and fitness, and therapeutic use of exercise and physical activity, in addition to the comprehensive medical care of exercising and active individuals to elite sports players.[7]

However, somewhere in our development, perhaps, physical fitness has lost the attention and respect that it deserves. The changes in our macro-environment, coupled with the stresses and demands of fast-paced life, have reduced the amount of physical activity performed by the average individual.[9] Lack of incentivization for manual labor, and a misplaced sense of prestige associated with use of labor-saving mechanical gadgets, have contributed to this as well. Physical inactivity is increasing at such a high rate that it can now be considered as a pandemic[10] and one of the leading cause of noncommunicable diseases (NCDs).[11] Lack of physical fitness like low cardiorespiratory fitness has been associated with all-cause mortality and morbidity.[12] With very high prevalence of diabetes, metabolic syndrome, hypertension and other NCDs in India,[13-15] it is high time for immediate and effective pro-active action to be taken.

The sporting performance of India relative to her population size also needs much improvement. This is especially true as India is also one of the youngest nations, with 64% to 66% of the population under the age of 35 years.[3] What can we do, as doctors and

health care providers to change this? What can we do to ensure that India achieves its full potential in the sporting stadia?

PRIMORDIAL AND PRIMARY ACTION

The first action is to begin with ourselves. Follow a physically active lifestyle, and lead by example. Do spare at least half an hour for games, sports or the gymnasium every day. Avoid sitting for prolonged periods in your clinic: stand or walk whenever and wherever possible.

The second step is to promote physical activity in all patients, and the public at large. Discuss and demonstrate the benefits of exercise on metabolic health, and encourage patients to take professional support from qualified exercise medicine specialists, if needed. Along with this, it is equally important to address the misconceptions and misinformation related to exercise. Following the wrong type, duration, intensity or timing of exercise can be as harmful as not exercising. The use of exercise as medicine, and exercise in medicine is the need of the present time.[7]

As clinicians, we should also use various physiological interventions including exercise, sleep, nutrition and psychology, etc. in addition to the usual pharmacological and surgical treatments. Besides the usual pathology- or sickness-based models, we should, thus focus on the physiology- or wellness-based approach.[7] A proper prescription of exercise for health promotion and fitness, as well for treatment of various NCDs including diabesity, and rehabilitation of various injuries[7] should be incorporated as a part of routine clinical practice. We should encourage more movement and less sedentary activity. A clear and loud message of movement as medicine and exercise as medicine should be given. A minimum of 150-300 min/week of moderate-intensity, or 75-150 min/week of vigorous-intensity, or an appropriate combination of moderate- and vigorous-intensity of aerobic activity should be targeted, for 18 to 64 years old adults.[16] Higher intensity may be needed for additional health benefits. Similarly, moderate- to vigorous-intensity resistance exercise targeting all major muscle groups of the body, should be done for at least 2 days/week.[16] This is particularly important for body composition and muscle strength optimization, and to fight against sarcopenia or sarcopenic obesity.

Apart from the recommendation of minimum physical activity for health, one should also aim to reduce sedentary activity time as much as possible, to less than 8 hours/day, with less than 3 hours of recreational screen time, for an 18 to 64 years old adult. We should encourage at least 7 to 9 hours of good quality night sleep for adults, which may be more for sports players as per requirements.[16]

Good nutrition goes hand in hand with physical activity and sleep for health and fitness. Healthy nutrition is a must for optimal exercise and sports performance. We must follow, and propagate, a balanced diet and not fall prey to the allures of fads or restricted diets.[17] Healthy nutrition should be promoted at every phase of life, including pregnancy, infancy, childhood, adolescence, adulthood and later. India being a protein-deficient consuming community, emphasis should be laid on adequate and high quality protein intake. Micronutrient sufficiency, including calcium, iron and vitamin D, must also be ensured. Attention to these, in conjunction with physical activity will lead to an increase in sports prowess.

SECONDARY AND TERTIARY ACTION

As the pool of physically active Indians grows, a pyramid will automatically start to form. At the peak of this pyramid will be our elite sportspersons, who will compete for the country, and bring us glory. The role of qualified sports medicine specialists and sports nutrition professionals in developing this team cannot be overemphasized. Along with other specialists such as sports psychologists and endocrinologists, they are an important part of the team that wins gold.

Each athlete is unique, and has specific nutritional, medical, coaching and mentoring needs. A team of specialists is required to provide this, under the leadership of a sports medicine specialist. Sports and exercise medicine is developing as a distinct specialty in India.[7] However, there is minimal emphasis on this, in medical curricula and in public discourse. This needs to be addressed. Although sports medicine is a distinct and separate medical specialty, this specialty is highly multidisciplinary and interdisciplinary in nature, with sports medicine physicians trained in sports-exercise and performance sciences, in addition to the medical-clinical and allied health sciences.[7]

The need for dedicated, individualized interventions for different sportspersons must be explained to policymakers and administrators. This will facilitate earmarking of funds and resources for specialized sports medicine consultations. As physicians, we should also support sports and exercise medicine as a distinct specialty. We can contribute to its growth by informing all stakeholders about its relevance, and putting them in touch with qualified sports medicine specialists.

Attention should also be paid to sports endocrinology, to encourage management of subclinical hormone deficiency in a rational manner, and to prevent misuse of anabolic steroids.[18]

SUMMARY

As we celebrate our Azadi ka Amrit Mahotsav, we should not lose sight of the need for action. Focusing on sports and exercise medicine will improve our health, not only as individuals, but as a society as well. Concerted action at various levels, beginning with healthy health care providers, can assist the country in achieving greater heights of success. Each clinician should incorporate the principle and practice of "exercise is medicine", as well as other physiological interventions, adopting the physiology- or wellness-based approach, in addition to the sickness or pathology based model, and use of pharmacological and surgical treatments. This is especially important for combating NCDs and diseases of lifestyle.

Engaging oneself in some form of sports activity and becoming physically active, as well as prescribing the minimum recommendation physical activity, limiting sedentary time and advising good nutrition to general public is a must for every clinician. By supporting and promoting the growth and development of the recently introduced medical specialty of sports and exercise medicine, as well as becoming part of its multidisciplinary and interdisciplinary team, we, as clinicians and health care providers, can have an important role in keeping our nation not only fit and healthy, but also optimization of dope- and injury-illness free sports performance.

REFERENCES

1. GBD 2019 Demographics Collaborators. Global age-sex-specific fertility, mortality, healthy life expectancy (HALE), and population estimates in 204 countries and territories, 1950-2019: a comprehensive demographic analysis for the Global Burden of Disease Study 2019. Lancet. 2020;396(10258):1160-203.
2. Akansha S, Laishram L. Increasing life expectancy and convergence of age at death in India. Genus. 2013;69(1):83-99.
3. Department of Sports. Khelo India-National Programme for Development of Sports New Delhi, India: Ministry of Youth Affairs and Sports, Government of India; 2018 [cited 2019 3rd December]. Available from: https://yas.nic.in/sports/khelo-india-national-programme-development-sports-0.
4. Sports Authority of India. Target Olympics Podium Scheme. New Delhi, India: Ministry of Youth Affairs and Sports, Government of India; 2019 [cited 2019 16th December]. Available from: https://sportsauthorityofindia.nic.in/index1.asp?ls_id=3812.
5. Press Information Bureau. Ministry of Youth Affairs and Sports: National Centre of Sports Sciences and Research for High Performance of Elite Athletes. New Delhi, India: Press Information Bureau, Ministry of Youth Affairs and Sports, Government of India; 2017. Available from: https://pib.gov.in/newsite/PrintRelease.aspx?relid=157775.
6. Department of Sports. Scheme of Human Resources Development in Sports. New Delhi, India: Ministry of Youth Affairs and Sports, Government of India; 2019 [cited 2019 6th December]. Available from: https://yas.nic.in/sports/scheme-human-resources-development-sports-0.
7. Sharma HB. Sports and exercise medicine in India: the past and the challenges. J Clin Diagn Res. 2022;16(2):CE01-6.
8. Saraswati SS, Hiti JK. Asana pranayama mudra bandha: Yoga Publications Trust Bihar, India; 1996.
9. Hallal PC, Andersen LB, Bull FC, Guthold R, Haskell W, Ekelund U; Lancet Physical Activity Series Working Group. Global physical activity levels: surveillance progress, pitfalls, and prospects. Lancet. 2012;380(9838):247-57.
10. Haseler T, Haseler C. Lack of physical activity is a global problem. BMJ. 2022;376:o348.
11. Forberger S, Wichmann F, Comito CN. Nudges used to promote physical activity and to reduce sedentary behaviour in the workplace: results of a scoping review. Prev Med. 2022;155:106922.
12. Steell L, Ho FK, Sillars A, Petermann-Rocha F, Li H, Lyall DM, et al. Dose-response associations of cardiorespiratory fitness with all-cause mortality and incidence and mortality of cancer and cardiovascular and respiratory diseases: the UK Biobank cohort study. Br J Sports Med. 2019;53(21):1371-8.
13. Federation ID. IDF Diabetes Atlas. 9th Edition. Brussels, Belgium: International Diabetes Federation; 2019.
14. Sinha N, Bhattacharya A, Deshmukh PR, Panja TK, Yasmin S, Arlappa N. Metabolic syndrome among elderly care-home residents in southern India: a cross-sectional study. WHO South East Asia J Public Health. 2016;5(1):62-9.
15. Ramakrishnan S, Zachariah G, Gupta K, Rao JS, Mohanan P, Venugopal K, et al. Prevalence of hypertension among Indian adults: results from the great India blood pressure survey. Indian Heart J. 2019;71(4):309-13.
16. Singh TD, Sharma HB. How much time to spend in physical activity, sleep and be sedentary in 24 h to achieve good health? Sleep Vigilance. 2022. Available from: https://doi.org/10.1007/s41782-022-00213-4.
17. Tahreem A, Rakha A, Rabail R, Nazir A, Socol CT, Maerescu CM, et al. Fad diets: facts and fiction. Front Nutr. 2022;9:960922.
18. Kalra S, Sahoo A, Das S, Kumar KVSH, Baliarsinha AK, Mohanty B, et al. The Bhubaneswar declaration on sports endocrinology, 2018. Indian J Endocrinol Metabol. 2018;22(Suppl 1):S14-6.

REVIEW ARTICLE

Noncommunicable and Communicable Diseases: Finding Common Ground

FERDINANT M SONYUY*, MADHUR VERMA†, LABRAM MUSAH MASSAWUDU‡, KAUSHIK RAMAIYA#, SANJAY KALRA¥

ABSTRACT

As the world grapples with unprecedented health challenges, such as coronavirus disease 2019 (COVID-19) and now monkeypox, the focus on traditional concerns, like maternal and child health, and relatively newer pandemics, e.g., diabetes and obesity tend to get diluted. This is especially concerning in countries which face a dual challenge of both communicable and noncommunicable diseases (NCDs). In this article, we list the factors that are common to both communicable disease and NCDs, and suggest measures to integrate procedures for their screening, management and prevention.

Keywords: COPD, cancer, diabetes, hypertension, CAD, infections

CONNECTIONS: CAUSATION, CLINICAL PRESENTATION, CARE

The term communicable diseases and noncommunicable diseases (NCDs) are based on a binary classification, which may not always be accurate. Some NCDs can be triggered by infectious agents.[1] Examples include diabetes and obesity secondary to viral infections,[2] Burkitt's lymphoma due to Epstein-Barr virus, cervical cancer because of human papillomavirus (HPV) and repeated viral and bacterial lower respiratory infections leading to chronic obstructive pulmonary disease (COPD). The long-term effects of coronavirus disease 2019 (COVID-19) on cardiovascular and metabolic health are being unraveled as well.[3] Tuberculosis (TB) and human immunodeficiency virus (HIV) are two "chronic" communicable diseases, which are associated with a relatively high NCD burden as well.[4,5]

Quite often, people living with NCDs present to the health care system with a communicable disease. People living with diabetes, COPD and cancer are more prone to infections, due to their immunocompromised state.[1] At other times, management of acute disease may lead to iatrogenic metabolic derangements, e.g., dysglycemia and fluctuations in blood pressure. The situation in African region is that most of the patients with NCDs come to the health system with complications due to poor control/management or lack of diagnosis.[6]

At times environmental factors facilitate the spread of both communicable disease and NCDs.[7] Air pollution, smoking and urbanization play a role in the pathogenesis of not only upper and lower respiratory infections, but COPD, hypertension, coronary artery disease (CAD) and cancer as well.

SIMULTANEOUS, NOT SEQUENTIAL

Prevention of both communicable disease and NCD is equally important to ensuring optimal health.[1] People with NCDs; however, utilize a disproportionately higher share of health care facilities than their peers without NCDs.[8] Because of their immunocompromised status they fall prey more often to acute infections. In turn these precipitate inflammatory and metabolic complication, which may require hospitalization for management. Various drugs used to treat communicable diseases such as corticosteroids in COVID-19, may lead to iatrogenic NCD complications such as diabetes.[9] Hence, prevention and control of NCDs contribute to communicable disease prevention as well.

*African NCDs Network, Bamenda, Cameroon
†Dept. of Community Medicine, All India Institute of Medical Sciences, Bathinda, Punjab, India
‡African NCDs Network, Ghana
#Hindu Mandal Hospital, Dar es Salaam, Tanzania and President-Elect, African NCDs Network
¥Dept. of Endocrinology, Bharti Hospital, Karnal, Haryana, India; University Centre for Research and Development, Chandigarh University, Mohali, Punjab, India
Address for correspondence
Dr Sanjay Kalra
Dept. of Endocrinology, Bharti Hospital, Karnal, Haryana, India; University Centre for Research and Development, Chandigarh University, Mohali, Punjab, India
E-mail:brideknl@gmail.com

LIMITED RESOURCES, UNLIMITED RESILIENCE

Resources for health care are always finite, and need to be utilized parsimoniously. NCD prevention and care can be integrated in existing health care programs to improve the quality of care, while minimizing extra cost. Examples include screening for diabetes in people with TB and HIV, for hypertension and CAD in people presenting at menopause and for COPD in adults with repeated visits for respiratory tract infection.

Personnel involved in NCD management can contribute to comprehensive health care coverage, too. Blood glucose measurement can be clubbed with hemoglobin estimation, and public health awareness messages against smoking may be linked to those focused on dengue and malaria prevention. An umbrella campaign on environmental stewardship can incorporate preventive measures for both communicable disease and NCDs. Due to lower rates, some efforts against HIV have moved from mass/universal to targeted screening meanwhile for NCDs, mass screening is still preferred. HIV screening can be made optional (offered) in NCD screening campaigns while highlighting target groups for screening at same campaigns.[10] This will facilitate timely diagnosis for HIV. Such linkages make the health care system more resilient and prepare it to handle future challenges effectively.

ADVOCACY: THE NEED TO BE HEARD, THE NEED TO HEAR

NCD care still does not receive the attention it deserves in many countries. Advocacy for NCDs is important, so as to draw the required resources to prevent and manage NCDs.[11] The public's need to be heard has to be fulfilled, by those who need to hear-the policymakers and planners. This conversation should be bidirectional: NCD management should take place within available resources, should not disregard acute health care needs and should promote resource-building and resilience in the community.

The Africa NCDs Network (ANN) is an example of an organization, which seeks to hear and be heard, to encourage simultaneous (not sequential) NCD care, and promote resilient resourcefulness in communities across the continent. The ANN was conceived in 2015 and it took off in 2020 with a 4-person secretariat spread across the east, west, center and southern African sub-regions. In coordination among its members, the ANN has researched on the needs, challenges and concerns of African people living with NCDs and collaborated with the Global NCD Alliance to develop the global charter on meaningful involvement of people living with NCDs, currently working on the Advocacy Agenda of African People living with NCDs[12] to further build a continent that is responsive to NCDs as it has been to infectious diseases over the years.

FROM ADVOCACY TO ACTION

Advocacy for NCDs is meaningful only if it is accompanied by action. Kickstarting programs on NCD care, and integrating screening/diagnostic/management activities with existing health care services should be done in a cautious and sustainable manner. The opportunity provided by COVID-19 and long COVID-19,[13] in terms of attention to public health, should be utilized to enhance NCD prevention and management. Our focus should be on prevention, advocacy and action, and our target should be the control of NCDs, so that we can achieve our goal of health for all.

REFERENCES

1. Coates MM, Kintu A, Gupta N, Wroe EB, Adler AJ, Kwan GF, et al. Burden of non-communicable diseases from infectious causes in 2017: a modelling study. Lancet Glob Health. 2020;8(12):e1489-98.
2. Kapoor N, Kota S, Kalra S. Obesity a communicable disease – A new age paradigm. J Pak Med Assoc. 2021;71(8):2100-2.
3. Nikoloski Z, Alqunaibet AM, Alfawaz RA, Almudarra SS, Herbst CH, El-Saharty S, et al. Covid-19 and non-communicable diseases: evidence from a systematic literature review. BMC Public Health. 2021;21(1):1-9.
4. Kalra S, Agrawal N. Diabetes and HIV: current understanding and future perspectives. Curr Diab Rep. 2013;13(3):419-27.
5. Kalra S, Atreja A. Diabetic tuberculosis. J Pak Med Assoc. 2016;66(9):1194-5.
6. Atun R, Davies JI, Gale EAM, Bärnighausen T, Beran D, Kengne AP, et al. Diabetes in sub-Saharan Africa: from clinical care to health policy. Lancet Diabetes Endocrinol. 2017;5(8):622-67.
7. Kalra S, Kapoor N. Environmental endocrinology: an expanding horizon. [Updated 2021 Mar 14]. In: Feingold KR, Anawalt B, Boyce A, et al (Eds.). Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. Available at: https://www.ncbi.nlm.nih.gov/sites/books/NBK568568/. Last accessed June 28, 2022.
8. Brown JB, Ramaiya K, Besancon S, Rheeder P, Tassou CM, Mbanya JC, et al. Use of medical services and medicines attributable to diabetes in Sub-Saharan Africa. PloS One. 2014;9(9):e106716.

9. Shah P, Kalra S, Yadav Y, Deka N, Lathia T, Jacob JJ, et al. Management of glucocorticoid-induced hyperglycemia. Diabetes Metab Syndr Obes. 2022;15:1577-88.
10. Gillet C, Darling KEA, Senn N, Cavassini M, Hugli O. Targeted versus non-targeted HIV testing offered via electronic questionnaire in a Swiss emergency department: a randomized controlled study. PLoS One. 2018;13(3):e0190767.
11. Herrick C. The 'noncommunicable disease space': ethnographies of conferences, advocacy and outrage. Critical Public Health. 2021;31(5):521-32.
12. Africa NCDs Network. Available at: https://ncdsafrica.org/. Last accessed June 28, 2022.
13. Maani N, Abdalla SM, Galea S. Avoiding a legacy of unequal non-communicable disease burden after the COVID-19 pandemic. Lancet Diab Endocrinol. 2021;9(3):133-5.

■■■■

Mosaic Loss of Y Chromosome Enhances Heart Failure and Cardiac Fibrosis Risk in Aging Men

According to a study, published in the *American Association for the Advancement of Science (AAAS)* mosaic loss of Y chromosome, or mLOY increases the risk of developing heart failure and cardiac fibrosis in men as they age. Additionally, it was observed that neutralizing antibodies could change some of these cardiac impacts caused by mLOY. Increased mortality, cardiovascular disease and other age-related illnesses have been connected to mLOY in blood cells, which is the most commonly acquired mutation in the male's genome. But, the relationship between mLOY and pathogenesis has not yet been proved. Hence to study the link, the scientists designed a mouse model of hematopoietic mLOY in their bone marrow with cells lacking the Y chromosome. The mLOY macrophages from the bone marrow that penetrate the heart cause high levels of transforming growth factor-1 (TGF-1) activation, which accelerates the fibrosis of the cardiac tissue. It has been demonstrated that treatment with a TGF-1 neutralizing antibody can lessen these negative effects.

Additionally, a prospective study in human patients revealed that people with mLOY in blood were also at an increased risk for cardiovascular dysfunction and associated mortality which supports the results from the mouse model which states the importance of the Y chromosome in preserving a healthy innate immune system, but more studies are needed to clarify the mechanisms. (*Source: News-medical.net; July 16, 2022)*

Maharashtra Health Department Prioritizes the Use of Vaccine Doses Nearing Expiry

The Maharashtra state health department has instructed the district administrations to administer the Covishield and Covaxin doses nearing the expiry date on priority.

According to state statistics, over 27 lakh Covishield doses and 5,890 Covaxin doses are expected to expire by September. The state presently has access to 27 lakh doses of Covishield and 34 lakh doses of Covaxin.

In a letter to the district offices, Dr Nitin Ambadekar, the Additional Director of Health Services, suggested ensuring the use of all doses of the COVID-19 vaccine nearing expiry by the end of September on priority during the 75-day "COVID Vaccine Amrut Mahotsav", which began on 15th July and was providing free precautionary doses to adults at government vaccination facilities. A total of 9,037 precautionary doses were provided in the Pune district up to 5 pm on the first day of the COVID Vaccine Amrut Mahotsav, while 1,02,692 doses were given throughout the state. (*Source: ETHealthWorld, July 16, 2022*)

Pimavanserin Linked to Lower Mortality among Elderly with Parkinson's Psychosis

The American Journal of Psychiatry published a study revealing pimavanserin use was linked to lower mortality than atypical antipsychotics over other therapies for older persons with Parkinson's disease (PD) psychosis. The study included patients with PD who were treated with pimavanserin (n = 3,227) or an atypical antipsychotic (n = 18,442) between April 2016 and March 2019. Pimavanserin's relative protective effect was seen in 85% of the trial population among PD patients living in the community—but not in the 15% of patients who were hospitalized.

Mortality was almost 35% lower in the first 180 days of treatment for pimavanserin users compared to atypical antipsychotic users (HR, 0.65; 95% CI, 0.53-0.79). In nursing home patients, pimavanserin did not exhibit a mortality advantage. (*Source: Medscape - Jul 15, 2022*)

No.1 PRESCRIBED DOXYCYCLINE BRAND*

℞ In **Acute Undifferentiated Fever**

DOXT-SL™

Doxycycline hyclate 100 mg (as immediate release pellets),Lactic acid bacillus 5 billion spores (as enteric coated pellets) capsule

The one to trust

- **Broad-spectrum antibiotic**
- **Antiviral Activity**[1]
- **Anti-parasitic action**[2]

ALSO AVAILABLE

DOXT® Injection

Doxycycline 100mg

The one to trust

Scan here for ABPI

*SMSRC 2022

1. Gendrot M et al In Vitro Antiviral Activity of Doxycycline against SARS-CoV-2. Molecules. 2020 Oct 31;25(21):5064. doi: 10.3390/molecules25215064
2. Okada M, Guo P, Nalder SA, Sigala PA. Doxycycline has distinct apicoplast-specific mechanisms of antimalarial activity. Elife. 2020 Nov 2;9:e60246.

DCGI approved indication for doxycycline is Broad spectrum antibiotic& Doxycycline +Lactobacillus is for adult patient prone to Intra-abdominal bacterial infection & antibiotic associated diarrhoea

Marketed by Dr.Reddy's

Dr. Reddy's Laboratories Ltd, Global Generics India, 7-1-27, Ameerpet, Hyderabad-500016, Telangana. www.drreddys.com

For the use of a Registered Medical Practitioner or Hospital or Laboratory only. GGI-CO-A1-PR-D2-300024289-MB-E20-575

CLINICAL STUDY

Evaluation of Effectiveness of Doxycycline as Empirical Therapy for Treatment in Acute Undifferentiated Febrile Illnesses in Routine Clinical Practice: A Retrospective, EMR-based, Real-world Study

SUNDARAM ARULRHAJ*, GIFTY IMMANUEL†, RAJIV SAIKIA‡, ANUP UTTAM PETARE#, KRISHNA CHAITANYA VELIGANDLA#, RAHUL RATHOD#, SEEMA BHAGAT#, AMEY MANE#

ABSTRACT

Background: Tetracyclines, in particular doxycycline, are recommended for the treatment of patients with acute undifferentiated febrile illness (AUFI); however, real-world studies are scarce. **Methods:** This retrospective, multicenter, observational study reviewed electronic medical records (April 2018 to March 2021) of adult patients (outpatient and inpatient departments [OPD and IPD]) with AUFI, treated with doxycycline monotherapy (doxycycline group) or doxycycline in combination with other antimicrobials (combination therapy group), from 7 tertiary hospitals and clinics in India. **Results:** Overall, 473 patients were included; 73.8% and 26.2% patients were prescribed doxycycline alone or in combination with other antimicrobials, respectively. Defervescence was achieved in 65.6% and 57.3% patients, respectively at the second (8-14 days) follow-up visit. Clinical cure rate for symptomatic resolution varied between 89.6% and 100% in OPD settings. Time taken from treatment initiation to defervescence was 3.51 ± 3.16 days for the doxycycline group and 3.46 ± 3.07 days for the combination therapy group. Both groups showed improvements in body temperature in OPD settings (84.2% and 84.5%) as well as IPD settings (97.4% and 94.1%). Adverse events in OPD patients in both groups were nausea (7.8% and 8.7%), anorexia (1.6% and 33.0%) and dyspepsia (1.6% and 67.9%). **Conclusion:** Doxycycline appears to be a promising candidate for treating patients with AUFI due to its demonstrated real-world effectiveness and safety profile.

Keywords: Acute undifferentiated febrile illness, doxycycline, real-world, antimicrobials

Infectious diseases are the leading causes of morbidity and mortality in the tropical Indian subcontinent.[1] Acute undifferentiated febrile illness (AUFI) is common in developing countries, like India.[2] It is one of the most frequently encountered presentations in clinical practice, mostly in outpatient departments (OPDs) and emergency care.[3] AUFI generally lasts less than 21 days without any evidence of organ or system-specific etiology and is usually characterized by nonspecific pyrexia.[4] Initially, the clinical features include fever, headache, chills, myalgia and fatigue, but later, specific organs might be involved. AUFI can vary from a mild and self-limiting illness to progressive and life-threatening for a confirmed diagnosis, investigations are utmost essential.[5]

The etiology of AUFI remains largely unknown; although the most common causes include malaria, dengue, Chikungunya, Zika, Yellow fever, Japanese encephalitis, enteric fever, leptospirosis and scrub typhus.[6] The non-specific and overlapping clinical features pose a challenge to the treating clinicians. Diagnosis is ascertained based on the clinical presentation and specific diagnostic tests. But owing to the limited diagnostic facilities and lack of comprehensive local guideline recommendations,

*Dept. of Cardiology, Sundaram Arulrhaj Hospital, Thoothukudi, Tamil Nadu
†Dept. of Infectious Diseases, CSI Hospital, Bangalore/Center for AIDS and Anti-Viral Research, Tuticorin, Tamil Nadu
‡St. Augustine Hospital, Bongaigaon, Assam
#Dr. Reddy's Laboratories Ltd., Hyderabad, Telangana
Address for correspondence
Dr Anup Uttam Petare
Medical Advisor-Medical Affairs, Dr. Reddy's Laboratories Ltd., Hyderabad, Telangana
E-mail: anuputtampetare@drreddys.com

delay in drug therapy initiation can increase the severity, complications and mortality. Therefore, empirical treatment with antibiotics is initiated along with antipyretics and other supportive treatment.[7] An empirical approach is justified in AUFI owing to the similarity in clinical presentations and the unavailability of accurate diagnostic testing, particularly during the early phase of the illness.[7]

Doxycycline is a cost-effective antimicrobial agent with a wide spectrum of activity, and its re-emergence can prove to be an asset for a developing country like India, notably with the current trends of resistance to several antimicrobials.[8] Doxycycline presents a lower risk of *Clostridium difficile*-associated diarrhea than other antibiotics as doxycycline preparations are mostly fortified with lactobacillus.[9] Doxycycline also reduces the incidence of multiple organ dysfunction syndrome in patients with scrub typhus.[10] Doxycycline is a bacteriostatic agent with activity against both Gram-positive and Gram-negative bacteria.[11] The effect of doxycycline is primarily mediated by its immunomodulatory action exerted by reducing proinflammatory cytokines and inhibiting virus replication.[12,13] As per the Department of Health Research (DHR) and Indian Council of Medical Research (ICMR), doxycycline is recommended for the empirical treatment of acute undifferentiated fever presented with leptospirosis, rickettsia infections, pneumonia, cholera and scrub typhus.[14,15] Thus, doxycycline appears to be a potential treatment choice for managing patients with AUFI.

Investigations pertaining to empirical therapy is needed due to lack of comprehensive surveillance and delay in confirmatory laboratory diagnosis in resource-constraint countries like India.[4,16] Therefore, a real-world evidence-based study was conducted based on the review of electronic medical records (EMRs) to evaluate the effectiveness of doxycycline as empirical therapy for treating patients with AUFI in routine clinical practice in India.

METHODS

The study was designed as a multicenter, retrospective and observational study. Routine clinical data was sourced from the EMRs of OPD and IPD patients with AUFI from 7 tertiary hospitals and clinics across 2 states (Assam and Maharashtra) of India at baseline and at the first (1-7 days) and second follow-up visits (8-14 days) from April 2018 to March 2021. The primary outcome measure was the real-world effectiveness of empirical treatment with either doxycycline monotherapy or combination therapy in patients with AUFI based on the clinical cure rate determined by the proportion of patients achieving defervescence, resolution of symptoms and improved hemodynamic parameters from baseline to follow-up visits. Improvement was considered as normalized body temperature (≤98.6°F), stabilized heart rate (≤100 bpm), systolic (≤120 mmHg) and diastolic (≤80 mmHg) blood pressure. The secondary outcomes were any change from baseline in the laboratory investigations (peripheral blood smear, complete blood count, rapid diagnostic tests, dengue, scrub typhus, enteric fever, liver function tests and renal profile). Safety was evaluated based on the adverse events (AEs) reported by the patients and captured by the clinicians.

Data was analyzed using R studio 3.5.3 and Microsoft Excel version 2110. Descriptive statistics were used to summarize the patients' baseline characteristics. Continuous variables such as age, height, weight, body mass index (BMI), use of antipyretics, time taken for defervescence and laboratory investigations were presented as mean ± standard deviation. Inpatient department (IPD) vs. OPD and baseline vs. first and second follow-up visits comparison was conducted using the *t*-test or Chi-square test, wherever applicable. Statistical significance was considered at $p < 0.05$. The study was conducted as per protocol and principles of Declaration of Helsinki and was approved by the Royal Pune Independent Ethics Committee located at Pune, India (Ethics Approval Number: RPIEC0100521).

RESULTS

Overall, records of 473 patients with AUFI were analyzed in this study, out of which 349 (73.8%) patients were prescribed doxycycline monotherapy (doxycycline group) and 124 (26.2%) patients were prescribed doxycycline in combination with other antimicrobials (combination therapy group) (Fig. 1).

Treatment

Antimicrobial drugs

In doxycycline group, all the patients in OPD settings, were prescribed oral doxycycline 100 mg (1 patient received 200 mg) for 5 to 14 days (average). IPD patients were prescribed doxycycline 100 mg (oral; n = 28) and 200 mg intravenous (IV; n = 15) for 7 to 10 days. In the combination therapy group, doxycycline was co-prescribed with other antimicrobials, including cephalosporins (cefixime, cefuroxime, cefpodoxime, ceftriaxone), fluoroquinolones (ciprofloxacin and ofloxacin), nitrofurantoin, macrolides (azithromycin and

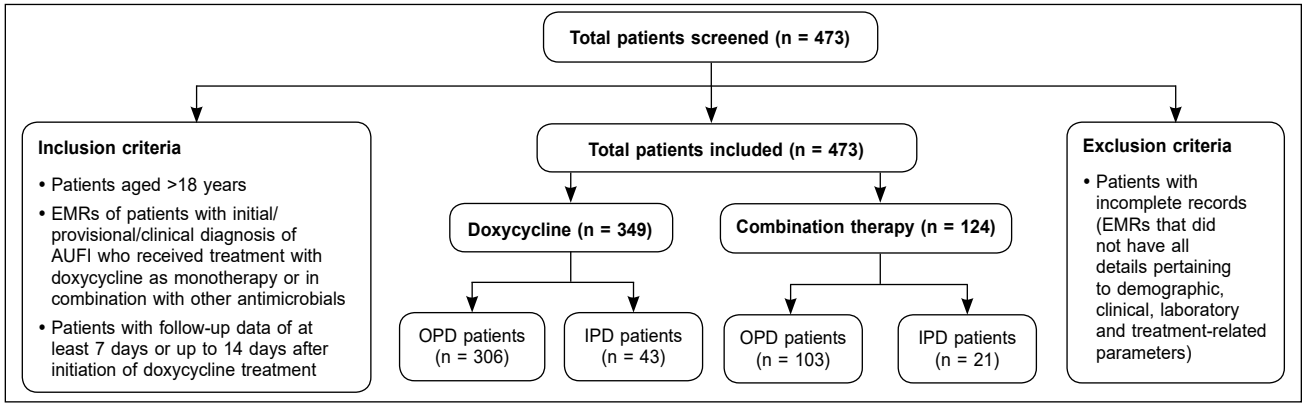


Figure 1. Flowchart of the study population.
IPD: Inpatient department; OPD: Outpatient department.

erythromycin), penicillin-like antibiotics (amoxicillin-clavulanic acid), carbapenems (faropenem) and oxazolidinones (linezolid). The oral formulations were administered for 5 to 14 days in OPD settings, while in IPD settings, both oral (12) and IV (9) formulations were prescribed for 7 to 14 days. None of the patients in OPD or IPD settings were switched to another antimicrobial at first and second follow-up visits. No other antimicrobials were added to the treatment regimen, except in one outpatient at the first follow-up visit who was prescribed an additional injection of artesunate 60 mg.

Antipyretics usage

Among patients treated with doxycycline monotherapy, paracetamol was the most common antipyretic prescribed to 300 (86.0%) patients in both settings. Nimesulide was prescribed to only 49 (14.0%) OPD patients. In the combination therapy group, paracetamol was prescribed to 112 (90.3%) patients, followed by nimesulide to 12 (9.7%) patients in OPD.

Concomitant medication

The most commonly prescribed concomitant medications in the doxycycline group were antipyretics, corticosteroid and proton pump inhibitor (PPI) + antiemetic in both OPD and IPD settings. In the combination therapy group, antipyretics, corticosteroid and PPI + prokinetic were more commonly prescribed in OPD settings, while antipyretics, corticosteroid and PPI + antiemetic were prescribed in IPD settings.

Effectiveness Outcomes

Occurrence of defervescence and symptomatic relief

In both doxycycline and combination therapy groups, 65.6% (229/349) and 57.3% (71/124) patients, respectively, achieved defervescence at the second follow-up visits. For OPD patients (n = 409), the proportion of patients showing defervescence in doxycycline group increased from the first follow-up (32.3%) to the second follow-up visits (56.0%), while in the combination therapy group, defervescence occurred in only 13.2% at the first follow-up and 17.4% at the second follow-up visits. In OPD settings, the clinical cure rate in the doxycycline group varied from 89.6% to 100% and 90.3% to 100.0% in the combination therapy group. In both groups, most patients achieved resolution of symptoms at the second follow-up visit.

Time taken for defervescence after treatment initiation

Reduction in body temperature was observed in both doxycycline (100.53 ± 1.44°F to 98.28 ± 0.19°F) and combination therapy groups (100.77 ± 1.59°F to 98.28 ± 0.20°F) from first to the second follow-up visits. Time taken from fever onset to defervescence was 6.69 ± 3.50 days for the doxycycline group and 6.57 ± 3.40 days for the combination therapy group. Time taken from the start of doxycycline treatment to defervescence was 3.51 ± 3.16 days for the doxycycline group and 3.46 ± 3.07 days for the combination therapy group.

Clinical cure rate

In OPD settings, the improvement was 84.2% for the doxycycline group and 84.5% for the combination therapy group. In IPD settings, improvement in the doxycycline and combination therapy groups were 97.4% and 94.1%, respectively (Fig. 2). Both doxycycline and combination therapy groups stabilized the heart rate (≤100 bpm) in OPD (48.2% and 39.5%) and IPD (16.2% and 0.0%) settings. For systolic BP (≤120 mmHg), minor improvements (0.8%) in OPD patients in the doxycycline group and 23.5% improvement in IPD patients in the combination therapy groups were observed. Diastolic BP (≤80 mmHg) was normal in all the patients in both OPD and IPD settings.

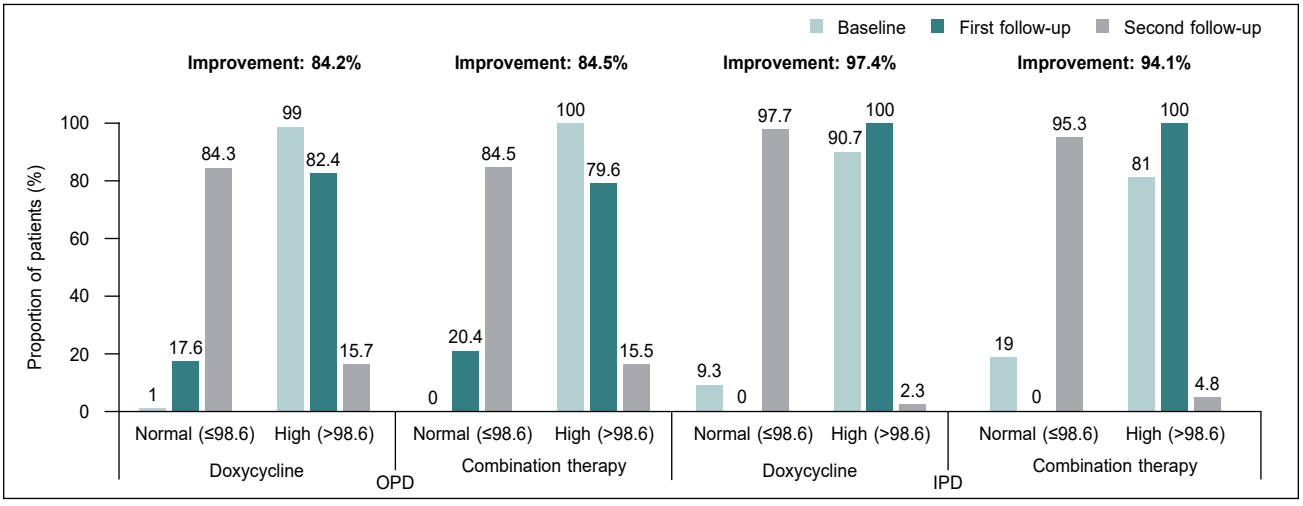


Figure 2. Clinical cure rate of body temperature (n = 473).

Laboratory Investigations of Patients with AUFI

Both doxycycline and combination therapy groups showed significant improvements (p = 0.000) in all the laboratory parameters except aspartate transaminase, direct bilirubin, gamma-glutamyl transferase, serum uric acid, serum albumin and serum protein at the second follow-up visits. In the doxycycline group, 1 (0.2%), 9 (2.6%), 31 (8.9%) and 2 (0.6%) patients tested positive for malaria, dengue, scrub typhus and typhoid, respectively. In the combination therapy group, 4 (3.2%), 7 (5.6%) and 29 (23.4%) patients tested positive for dengue, scrub typhus and typhoid.

Safety Outcomes

Patients in OPD setting, in both groups, reported nausea (7.8% vs. 8.7%), anorexia (1.6% vs. 33.0%) and dyspepsia (1.6% vs. 67.9%). In IPD settings, data regarding adverse events was not available.

DISCUSSION

In a prospective study conducted in Mumbai, most patients were male and below the age of 35 years.[17] Our study also had a male predominance and mean age ~45 years. The five major comorbidities in both groups included endocrinological (diabetes mellitus), cardiovascular (hypertension and ischemic heart disease [IHD]), urogenital (benign prostatic hyperplasia [BPH]) and thyroid disorders, similar to a study conducted in South India, which reported diabetes mellitus, essential hypertension, IHD and chronic liver disease as the most common comorbidities in AUFI patients.[7]

In the present study, the major complaints were fever, malaise, fatigue, headache, cough and myalgia. This was in accordance with a study conducted in the rural areas and suburbs of Maharashtra, wherein all the patients with AUFI complained of fever, in addition to nonspecific (such as headache, myalgia, generalized weakness), respiratory (cough with breathlessness, sore throat), neurological (altered sensorium, seizures, meningitis) and gastrointestinal (vomiting, diarrhea) symptoms.[18] Another study in Eastern India reported fever, headache, nausea, vomiting, abdominal pain, cough, myalgia and rash in scrub typhus patients presenting with AUFI.[19] With the emergence and re-emergence of pathogens, doxycycline seems to be a potential candidate for the empirical antibiotic of choice in AUFI patients.[3,20]

Oral doxycycline 100 mg BD was primarily prescribed in patients with AUFI in both OPD and IPD settings, which is in accordance with the 2019 ICMR "Treatment Guidelines for Antimicrobial Use in Common Syndromes", which recommends empirical treatment with a standard dose of doxycycline 100 mg BD (oral or IV) for patients with acute undifferentiated fever.[14] A study of hospitalized patients with febrile illness in South India also used doxycycline 100 mg twice daily for their management.[21] Aspirin, paracetamol, nimesulide, ibuprofen, mefenamic acid, etc., are also reportedly used for managing fever in patients with AUFI.[22,23]

In a retrospective observational study conducted at a tertiary care hospital in Hyderabad, defervescence was achieved in all the scrub typhus patients within 2 days of treatment initiation with doxycycline.[24] Overall, the clinical cure rate of defervescence, fatigue, malaise, diarrhea, abdominal pain, vomiting and rashes was found to be higher in both treatment groups in OPD and IPD settings in the present study.

In a multicenter trial of 296 adult patients with AUFI in Thailand, the median time to defervescence with doxycycline was 45 hours and 48 hours for patients with laboratory-confirmed leptospirosis and scrub typhus, respectively.[25] A study conducted at a tertiary care hospital in Southern India (n = 645) reported defervescence in all the scrub typhus patients with fever of 1 to 2 weeks (58.6%) within 2 days of initiating doxycycline treatment.[24] AUFI may have a similar clinical presentation, but their etiology can vary, due to which it often remains undiagnosed. A cross-sectional, prospective study conducted in Central India reported 18 (6.6%) undiagnosed patients.[26] In Asia, the frequencies of undiagnosed cases ranged from 8% to 80%.[27] In a study of 1,564 patients conducted in six states of India, the diagnoses were malaria (17%), dengue (16%), scrub typhus (10%), bacteremia (8%), leptospirosis (7%) and chikungunya (6%).[28] Other Indian studies too have reported scrub typhus, dengue, malaria, enteric fever, leptospirosis, typhoid as the different etiologies of AUFI.[1,2,7]

Doxycycline is the treatment of choice in clinically stable patients in co-endemic regions for AUFI, especially in South-East Asia, including India.[5] But for severely ill patients, a combination of third-generation cephalosporins and doxycycline is preferred.[29] Comorbidities, pregnancy, geriatrics and immunocompromised patients are other groups that benefit from combination therapy.[6] Combination therapy is effective in patients with AUFI with complications such as pneumonia or acute respiratory distress syndrome, encephalopathy, malaria and liver involvement.[29] In the current study, patients with multiple comorbidities were effectively treated by a combination of doxycycline with other antimicrobials. However, combination therapy facilitates development of multidrug resistance (MDR);[30] this can be curtailed if pathogen-specific diagnostics tests are conducted. A study conducted in Pune (India) showed that due to diagnostic uncertainty, all the hospitalized patients received antibiotics, which the physicians readily discontinued once they received the results of positive malaria or dengue tests.[31] Thus, doxycycline monotherapy can be considered over the combination therapy to ensure the judicious use of antibiotics, consequently avoiding thedevelopment of MDR.

Fewer patients on doxycycline monotherapy in our study reported anorexia and dyspepsia. A study evaluating the effectiveness of doxycycline for the treatment of scrub typhus and leptospirosis also reported nausea and vomiting.[25] Increased antibiotic use may cause gut microbiota dysbiosis.[32] Therefore, doxycycline monotherapy may avert unwanted gastrointestinal effects in patients with AUFI.

Hitherto, to the best of our knowledge, no studies have examined the effectiveness of combination of doxycycline with other antimicrobials. Our study included adult patients with a broad age range receiving various levels of care and visiting different settings providing greater external validity. However, our study has certain limitations, such as bias associated with a retrospective study design and missing information of some patients at the second follow-up visit. Information regarding many potential pathogens (spotted fever, hantavirus and chikungunya virus) and serological evidence (using indirect immunofluorescence and polymerase chain reaction) was also unavailable.

CONCLUSION

The management of AUFI warrants accurate diagnosis, for which it is imperative to identify the etiology. In addition to the indispensable need for a broader diagnostic approach, re-purposing of existing drugs is the need of the hour. Based on the findings of the current study, it can be concluded that doxycycline could be an effective approach for the treatment of patients with AUFI having different etiologies owing to its demonstrated real-world effectiveness safety profile, with both oral and injectable dosage forms. Further large-scale prospective studies are warranted to confirm these results.

Acknowledgments: The authors thank Saleha Rehman (Medical Writer), Rupali Jangid (Senior Medical Writer) and Dr Venugopal Madhusudhana (Vice President-Research) from Medical affairs, THB c/o Sekhmet Technologies Pvt Ltd. (Gurugram, Haryana, India) for their support in the manuscript preparation.

Conflicts of Interest: The authors Anup Uttam Petare, Krishna Chaitanya Veligandla, Rahul Rathod, Seema Bhagat and Amey Mane declare that they are an employee at Dr. Reddy's Laboratories Ltd., Hyderabad, Telangana, India. Sundaram Arulrhaj and Gifty Immanuel declare no conflict of interest for this publication, however, they have received speaker honorarium from Dr. Reddy's laboratories in the past. Rajiv Saikia declares no conflict of interest.

REFERENCES

1. Mittal G, Ahmad S, Agarwal RK, Dhar M, Mittal M, Sharma S. Aetiologies of acute undifferentiated febrile illness in adult patients - an experience from a tertiary care hospital in Northern India. J Clin Diagn Res. 2015;9(12):DC22-4.
2. Prasad D, Kumar S, Deepak RK, Kumar M. Evaluating the etiology and disease specific clinical profiles of acute undifferentiated febrile illness. Int J Sci Res. 2020; 9(11):73-5.

3. Aggarwal KK. Management of acute febrile illness: doxycycline, the empirical antibiotic of choice. Ind J Clin Pract. 2018;29(6):505-6.
4. Bhaskaran D, Chadha SS, Sarin S, Sen R, Arafah S, Dittrich S. Diagnostic tools used in the evaluation of acute febrile illness in South India: a scoping review. BMC Infect Dis. 2019;19(1):970.
5. Bhargava A, Ralph R, Chatterjee B, Bottieau E. Assessment and initial management of acute undifferentiated fever in tropical and subtropical regions. BMJ. 2018;363:k4766.
6. Joshi S, Immanuel G, Arulrhaj S, Tiwaskar M, Vora A, Samavedam S. Roadmap for the management of acute undifferentiated febrile illness: an expert discussion and review of available guidelines. J Assoc Physicians India. 2021;69(9):11-2.
7. Abhilash KPP, Jeevan JA, Mitra S, Paul N, Murugan TP, Rangaraj A, et al. Acute undifferentiated febrile illness in patients presenting to a tertiary care hospital in south india: clinical spectrum and outcome. J Glob Infect Dis. 2016;8(4):147-54.
8. Grossman TH. Tetracycline antibiotics and resistance. Cold Spring Harb Perspect Med. 2016;6(4):a025387.
9. Doernberg SB, Winston LG, Deck DH, Chambers HF. Does doxycycline protect against development of *Clostridium difficile* infection? Clin Infect Dis. 2012;55(5):615-20.
10. Venkategowda PM, Rao SM, Mutkule DP, Rao MV, Taggu AN. Scrub typhus: clinical spectrum and outcome. Indian J Crit Care Med. 2015;19(4):208-13.
11. Ziegler T, Winkler C, Wege K, Schmechel H. Doxycycline–the forgotten antibiotic. Med Klin (Munich). 2000;95(11):629-31.
12. Garg P. Role of doxycycline in the management of dengue fever. Ind J Clin Pract. 2018;29(2):132-5.
13. Fredeking RM, Zavala-Castro JE, González-Martínez P, Moguel-Rodríguez W, Sanchez EC, Foster MJ, et al. Dengue patients treated with doxycycline showed lower mortality associated to a reduction in IL-6 and TNF levels. Recent Pat Antiinfect Drug Discov. 2015;10(1):51-8.
14. Aggarwal S, Walia K, Madhumati J, Gopalkrishnan R, Ohri VC, Gangakhedkar R. Treatment Guidelines for Antimicrobial Use in Common Syndromes. 2nd Edition, ICMR: New Delhi, India; 2019.
15. Rahi M, Gupte MD, Bhargava A, Varghese GM, Arora R. DHR-ICMR Guidelines for diagnosis & management of Rickettsial diseases in India. Indian J Med Res. 2015;141(4):417-22.
16. Fernandes JP, Hazra D, David SN, Paul K, Abhilash P. Acute undifferentiated febrile illness in the elderly: a clinical profile. Curr Med Issues. 2019;17(4):103-7.
17. Salagre KD, Sahay RN, Pazare AR, Dubey A, Marathe KK. A study of clinical profile of patients presenting with complications of acute febrile illnesses during monsoon. J Assoc Physicians India. 2017;65(9):37-42.
18. Bhise SM, Taiwade PD, Zodpey SS, Agarwal VA. Scrub typhus in rural areas & suburbs of Vidarbha region of Maharashtra. Indian J Med Res. 2020;151(1):104-6.
19. Behera B, Biswal M, Das RR, Dey A, Jena J, Dhal S, et al. Clinico-epidemiological analysis of scrub typhus in hospitalised patients presenting with acute undifferentiated febrile illness: a hospital-based study from Eastern India. Indian J Med Microbiol. 2019;37(2):278-80.
20. Wangdi K, Kasturiaratchi K, Nery SV, Lau CL, Gray DJ, Clements ACA. Diversity of infectious aetiologies of acute undifferentiated febrile illnesses in south and Southeast Asia: a systematic review. BMC Infect Dis. 2019;19(1):577.
21. Varghese GM, Abraham OC, Mathai D, Thomas K, Aaron R, Kavitha ML, et al. Scrub typhus among hospitalised patients with febrile illness in South India: magnitude and clinical predictors. J Infect. 2006;52(1):56-60.
22. Tsaganos T, Tseti IK, Tziolos N, Soumelas GS, Koupetori M, Pyrpasopoulou A, et al. Randomized, controlled, multicentre clinical trial of the antipyretic effect of intravenous paracetamol in patients admitted to hospital with infection. Br J Clin Pharmacol. 2017;83(4):742-50.
23. Arulrhaj S, Tiwaskar M, Sabharwal M, Saikia R, Majid S, Rathod R, et al. Effectiveness of nimesulide in acute fever management in adults: retrospective electronic medical records database study outcome in outpatient department. J Assoc Physicians India. 2021;69(7):11-2.
24. Lakshmi RMMVN, Dharma TV, Sudhaharan S, Surya SMV, Emmadi R, Yadati SR, et al. Prevalence of scrub typhus in a tertiary care centre in Telangana, South India. Iran J Microbiol. 2020;12(3):204-8.
25. Phimda K, Hoontrakul S, Suttinont C, Chareonwat S, Losuwanaluk K, Chueasuwanchai S, et al. Doxycycline versus azithromycin for treatment of leptospirosis and scrub typhus. Antimicrob Agents Chemother. 2007;51(9):3259-63.
26. Shelke YP, Deotale YS, Maraskolhe DL. Spectrum of infections in acute febrile illness in central India. Indian J Med Microbiol. 2017;35(4):480-4.
27. Susilawati TN, McBride WJ. Acute undifferentiated fever in Asia: a review of the literature. Southeast Asian J Trop Med Public Health. 2014;45(3):719-26.
28. Mørch K, Manoharan A, Chandy S, Chacko N, Alvarez-Uria G, Patil S, et al. Acute undifferentiated fever in India: a multicentre study of aetiology and diagnostic accuracy. BMC Infect Dis. 2017;17(1):665.
29. Singhi S, Chaudhary D, Varghese GM, Bhalla A, Karthi N, Kalantri S, et al; Indian Society of Critical Care Medicine Tropical fever Group. Tropical fevers: management guidelines. Indian J Crit Care Med. 2014;18(2):62-9.
30. Mave V, Chandanwale A, Kagal A, Khadse S, Kadam D, Bharadwaj R, et al. High burden of antimicrobial resistance and mortality among adults and children with community-onset bacterial infections in India. J Infect Dis. 2017;215(8):1312-20.
31. Robinson ML, Kadam D, Kagal A, Khadse S, Kinikar A, Valvi C, et al. Antibiotic utilization and the role of suspected and diagnosed mosquito-borne illness among adults and children with acute febrile illness in Pune, India. Clin Infect Dis. 2018;66(10):1602-9.
32. Francino MP. Antibiotics and the human gut microbiome: dysbioses and accumulation of resistances. Front Microbiol. 2016;6:1543.

The Expanding Role of Dapagliflozin Beyond the Glucose-lowering Effect

SANJAY KALRA*, AG UNNIKRISHNAN†, ARUNDHATI DASGUPTA‡, ATUL DHINGRA#, GANAPATHI BANTAVAL¥, MANASH P BARUAH£, MATHEW JOHN§, RAKESH SAHAY^, SAPTARSHI BHATTACHARYA¶, BHARATH HS||

ABSTRACT

Sodium-glucose cotransporter 2 (SGLT2) inhibitors have varied metabolic effects beyond increasing glycosuria. This consensus review examines the role of dapagliflozin in health promotion, particularly its benefits in patients with and without type 2 diabetes mellitus (T2DM) and in cardiorenal rehabilitation post-coronavirus disease 2019 (COVID-19). Consensus recommendations were developed by subject experts in Endocrinology and Diabetology based on the online meeting held on 27 June 2020 to review the available evidence related to the role of SGLT2 inhibitors, with a focus on cardiovascular and renal metabolic therapy. Evidence suggests that dapagliflozin has a direct role in improving clinical outcomes in patients with chronic kidney disease (CKD) or heart failure (HF). These benefits of dapagliflozin were independent of reduction in blood pressure, glycemic control and weight, and also extend to patients without diabetes. The use of dapagliflozin in metabolic syndrome was endorsed by the majority of the experts; however, this would be off-label. It was opined that the role of dapagliflozin would currently be limited to treating T2DM with a focus on preventing HF or kidney disease progression. The need for conducting multidisciplinary academic meetings to have a balanced approach regarding the use of dapagliflozin among nondiabetic patients and the need for detailed evaluation of the role of SGLT2 inhibitors in vasculometabolic and cardiorenal rehabilitation post-COVID was also suggested.

Keywords: Dapagliflozin, heart failure, kidney disease, type 2 diabetes mellitus

Type 2 diabetes mellitus (T2DM) is the most prevalent progressive, complex and metabolic disorder that is characterized by inconsistent insulin production and utilization. Estimates indicate that approximately 573 million people aged 20 to 79 years are living with diabetes globally, which may increase to 783 million by 2045. Currently, India has around 74.2 million individuals diagnosed with diabetes, which may increase to 124.9 million by 2045.[1] Current international guidelines consider sodium-glucose cotransporter 2 (SGLT2) inhibitors as an alternative to metformin plus either sulfonylurea or dipeptidyl peptidase-4 (DPP-4) inhibitors.[2,3] SGLT2 inhibitors can be used in patients with T2DM and atherosclerotic cardiovascular disease (ASCVD) or kidney disorder or indicators of high risk, or heart failure (HF).[3]

According to the 2016 management protocols of stable coronary artery disease (SCAD) in India, oral antidiabetic agents, including SGLT2 inhibitors should be considered for diabetes management.[4] The 2020 Research Society for the Study of Diabetes in India (RSSDI) guidelines recommend SGLT2 inhibitors for patients with HF, ASCVD, diabetic kidney disease (DKD) or those who require weight reduction.[5] The South Asian Federation of Endocrine Societies (SAFES) also endorsed the use of SGLT2 inhibitors for managing various comorbid conditions associated with T2DM.[6] Dapagliflozin, a selective SGLT2 inhibitor, is suggested to improve glycemic control along with diet and exercise in T2DM. It may be preferred in patients with chronic kidney disease (CKD) or HF with reduced

*Dept. of Endocrinology, Bharti Hospital, Karnal, Haryana, India; University Centre for Research and Development, Chandigarh University, Mohali, Punjab, India
†CEO and Chief of Endocrinology, Chellaram Diabetes Institute, Pune, Maharashtra, India
‡Endocrinologist, Rudraksh Superspeciality Care, Siliguri, West Bengal, India
#Consultant Endocrinologist, Gangaram Bansal Hospital, Sri Ganganagar, Rajasthan, India
¥Professor and Head, Dept. of Endocrinology, St. John's Medical College Hospital, Bengaluru, Karnataka, India
£Director and Consultant Endocrinologist, Excel Hospital, Guwahati, Assam, India
§Consultant Endocrinologist, Providence Endocrine and Diabetes Specialty Centre, Thiruvananthapuram, Kerala, India
^Senior Consultant Endocrinologist, Aster Prime Hospital, Hyderabad, Telangana, India
¶Consultant Endocrinologist, Max Hospital, Patparganj, Delhi
||Therapy Area Lead - CVRM, AstraZeneca Pharma India Limited, Bengaluru, Karnataka, India
Address for correspondence
Dr Sanjay Kalra
Dept. of Endocrinology, Bharti Hospital, Karnal, Haryana, India; University Centre for Research and Development, Chandigarh University, Mohali, Punjab, India
E-mail:brideknl@gmail.com

ejection fraction (HFrEF), as it has favorable renal and cardiovascular (CV) effects.[7-9]

Prior studies have proven that most adults with diabetes in India have at least one comorbid condition.[10-12] In clinic-based studies, the prevalence of coronary artery disease among patients with diabetes was ~11% to 30%, while the prevalence in community-based studies was ~9% to 15%. CKD is also an inadequately addressed complication of T2DM affecting approximately 2 in every 5 patients. According to the Chennai Urban Rural Epidemiology Study (CURES), an urban population-based study of patients with diabetes in India, overall prevalence of nephropathy and microalbuminuria was 2.2% and 26.9%, respectively.[13]

Antidiabetic medications like metformin, originally indicated for the management of T2DM, have been prescribed for the management of polycystic ovarian syndrome. Liraglutide has the potential for being used as an antiobesity drug, while gliptins are being explored for their benefits beyond endocrinology.[14] Similarly, SGLT2 inhibitors, including dapagliflozin, have a role in several metabolic activities beyond glycosuria.[15] The chronic landscape of diabetes along with a high prevalence of concurrent chronic medical conditions necessitates multifaceted approach from both patients and health care providers. Considering the aforementioned literature views, this study aims to present expert opinions on the role of dapagliflozin beyond diabetes care.

METHODS

An advisory board comprising 9 regional endocrinologists/diabetes specialists from different parts of India was formed to review the role of SGLT2 inhibitors with a focus on CV and renal metabolic therapy. An online meeting of the advisory board was held on 27 June 2020 to arrive at conclusions regarding the benefits and drawbacks of SGLT2 inhibitors based on the existing knowledge and clinical experience. Recommendations were formulated based on the opinions and agreement of the majority post-discussion on the following:

- Role of dapagliflozin in health promotion
- Role of dapagliflozin in patients with and without T2DM
- Cardiorenal rehabilitation post-COVID.

Based on the agreed statements, supporting data was extracted from multiple databases including PubMed/Medline, Embase, Cochrane and Google Scholar. The criteria for consensus were set to statements with ≥80% agreement among experts. The experts' statements on each of these topics were recorded and are presented in this article.

ROLE OF DAPAGLIFLOZIN IN HEALTH PROMOTION

Dapagliflozin, when added to conventional antidiabetic agents, is associated with improvement in glycated hemoglobin (HbA1c) by 0.50%, weight loss of 2 kg, systolic/diastolic blood pressure (SBP/DBP) by 4/2 mmHg, fasting plasma glucose (FPG) by 18 mg/dL and body mass index by 1.1%, over 6 to 13 months.[16,17] Growing evidence suggests that SGLT2 inhibitors have several benefits beyond glycemic control.[18] They have a myriad of metabolic and hemodynamic effects, such as increasing glucagon levels and hematocrit production, while promoting lipolysis, hepatic fatty acid oxidation and ketone production.[19-21] Further, SGLT2 inhibition can trigger a fasting-like physiological environment.[21] Inhibition of SGLT2 directly activates AMP-activated protein kinase (AMPK) and also causes inhibition of mammalian target of rapamycin (mTOR) in the kidneys with beneficial effects on autophagy, mitofusion, mitofission and endoplasmic reticulum stress.[20] Inhibition of SGLT2 also decreases the progression of diabetic nephropathy by activating AMPK in mesangial cells, which causes a decrease in inflammatory mediators.[22] Notably, SGLT2 inhibitors may also influence several physiological functions that can improve HF outcomes. The decreased glucose absorption by tubular cells improves the interstitial hypoxia and promotes erythropoiesis in patients with diabetes.

This leads to an increase in both hemoglobin and hematocrit and a decrease in the afferent renal neural activity. Subsequently, SGLT2 inhibition has effects on the downregulation of sympathetic activity and reduces the effect on preload and afterload of the heart.[23] By improving cardiac energy metabolism through an indirect increase in ketone oxidation, SGLT2 inhibition may provide an additional source of energy for the failing heart. Moreover, SGLT2 inhibition may increase glucose oxidation in the heart. These factors may improve the overall heart functioning.[24]

PLEIOTROPIC EFFECTS OF SGLT2 INHIBITORS

Weight Loss

Weight loss associated with dapagliflozin has been mainly attributed to reduction in visceral fat. A recent meta-analysis of randomized controlled trials (RCTs) reported that SGLT2 inhibitors, including dapagliflozin

(2.5-10 mg/d), as an add-on to metformin were associated with significant reduction in body weight vs. non-SGLT2 inhibitors at 52 weeks. Significant reduction was also noted in both visceral and subcutaneous adipose tissue, along with lean mass.[25] Similarly, reduction in weight by approximately 1.5 to 3 kg with dapagliflozin alone and up to 5 kg reduction in weight with dapagliflozin and sulfonylurea combination therapy was also reported.[26]

Blood Pressure Reduction

With the combined effects of osmotic diuresis, natriuresis and reduction in arterial stiffness, SGLT2 inhibitors may reduce blood pressure (BP) in patients with T2DM and diabetic nephropathy.[27-30] In a recent meta-analysis, the pooled estimate (22 RCTs on treatment with dapagliflozin) of the weighted mean difference of dapagliflozin on SBP and DBP was −2.59 mmHg (95% confidence interval [CI] −2.70 to −2.49) and −1.09 mmHg (95% CI −1.18 to −1.01), respectively.[28] Another study reported that dapagliflozin decreased SBP by 3.6 mmHg and DBP by 2.0 mmHg in patients with T2DM. Post-dapagliflozin treatment, treatment-naive patients with T2DM with inadequate glycemic control with diet and exercise had the highest reductions in SBP.[29]

Lipid Management

Dapagliflozin has been associated with an increase in total cholesterol by 2.5%, high-density lipoprotein cholesterol (HDL-C) by 3.3%, low-density lipoprotein cholesterol (LDL-C) by 3.9% and a reduction in triglyceride levels by 2.0%.[26] Dapagliflozin as an add-on to metformin and/or sulfonylurea significantly increased HDL-C and LDL-C vs. DPP-4 inhibitors (linagliptin, gemigliptin) add-on therapy.[31]

Outcomes in Cardiovascular and Renal Disease

In a pooled analysis of five trials (up to 52 weeks duration) including patients with T2DM and HF, dapagliflozin 10 mg monotherapy or add-on therapy produced a clinically meaningful reduction from baseline in HbA1c (placebo-adjusted mean change: 0.55%), weight (−2.7 kg) and SBP (−2.1 mmHg) over 52 weeks.[32] In a post hoc analysis of phase 2/3 clinical trials, dapagliflozin was found to reduce weight and BP with improvement in glycemic control among patients with T2DM and renal impairment.[33] Similarly, findings from RCTs support the benefits of dapagliflozin 10 mg in improving glycemic control and weight loss and lowering BP among patients with T2DM with mild or moderate renal insufficiency.[34,35]

ROLE OF DAPAGLIFLOZIN IN PATIENTS WITH AND WITHOUT T2DM

Several RCTs have determined the effects of dapagliflozin on CV and renal outcomes, which are discussed below.

The Dapagliflozin Effect on Cardiovascular Events-Thrombolysis in Myocardial Infarction 58 (DECLARE-TIMI 58) trial evaluated the safety of dapagliflozin in over 17,000 patients with ASCVD or risk factors (including ~40% without cardiovascular disease [CVD]). Significant benefits were reported at median follow-up of 4.2 years. Treatment with dapagliflozin significantly reduced CV death or hospitalization for heart failure (HHF) compared to placebo (4.9% vs. 5.8%; hazard ratio [HR] 0.83; 95% CI, 0.73-0.95; p = 0.005). This finding was mainly driven by a reduction in HHF (HR 0.73; 95% CI, 0.61-0.88). Further, dapagliflozin was noninferior to placebo for major adverse cardiovascular events (MACE; p < 0.001 for noninferiority). The incidence of the composite of ≥40% decrease in estimated glomerular filtration rate (eGFR) to <60 mL/min/1.73 m^2, new end-stage renal disease (ESRD), or death from renal or CV causes was also in favor of dapagliflozin versus placebo (HR 0.53 95% CI 0.43-0.66). Dapagliflozin did not increase the incidence of stroke, amputations or fractures compared to placebo. However, a higher rate of diabetic ketoacidosis (excess rate <1% per year) and genital infections compared to placebo were reported.[9]

The DECLARE-TIMI 58 study also analyzed (prespecified subgroup analysis) the clinical benefits of dapagliflozin in patients with T2DM and prior myocardial infarction (MI). Dapagliflozin significantly reduced MACE in patients with a prior history of MI (HR 0.84, 95% CI 0.72-0.99) vs. those without a prior history of MI (HR 1.00, 95% CI 0.88-1.13). However, HHF and CV death did not differ irrespective of prior MI status.[36] In another subgroup analysis, Kato et al assessed the outcomes of dapagliflozin according to baseline HF status. It defined HFrEF as ejection fraction <45%. Dapagliflozin greatly reduced CV death or HHF in patients with HFrEF (HR 0.62, 95% CI 0.45-0.86), but not in patients with HF without known reduced EF (HR 0.88, 95% CI 0.66-1.17 and HR 0.88, 95% CI 0.74-1.03, respectively). Dapagliflozin did not increase the incidence of diabetic ketoacidosis and amputation. The overall safety profile was comparable to placebo.[37] In a real-world study of patients who met DECLARE-TIMI 58 inclusion criteria (n = 28,408), 21% lower risk of CV mortality or HHF (HR 0.79, 95% CI 0.69-0.92) were noted with dapagliflozin therapy compared to other glucose-lowering drugs (OGLDs) without any significant association with MACE (HR 0.90, 95% CI 0.79-1.03).[38]

The CVD-REAL study is the largest real-world comparative effectiveness study that evaluated a range of CV outcomes in patients with T2DM at high CV risk initiated on SGLT2 inhibitors vs. OGLDs. A total of 1,54,528 patients were grouped in each treatment group after propensity matching. Canagliflozin followed by dapagliflozin accounted for more drug exposure with 53% and 42%, respectively. Significant reduction of HHF (pooled HR, 0.61; 95% CI, 0.51-0.73; p < 0.001) and all-cause death (pooled HR, 0.49; 95% CI, 0.41-0.57; p < 0.001) were observed in the SGLT2 inhibitors group vs. the OGLDs group.[39] The CVD-REAL 2 study was conducted across 6 countries in the Middle East, Asia Pacific and North American regions. A total of 2,35,064 episodes of treatment were grouped in each treatment group after propensity matching (~27% had CVD). Of all SGLT inhibitors, dapagliflozin accounted for 75% of drug exposure time. The SGLT2 inhibitors were associated with a significant reduction in the risk of mortality (HR: 0.51, 95% CI 0.37-0.70; p < 0.001), HHF (HR 0.64; 95% CI 0.50-0.82; p < 0.001), mortality or HHF (HR 0.60, 95% CI 0.47-0.76; p < 0.001), stroke (HR 0.68; 95% CI 0.55-0.84; p < 0.001) and MI (HR 0.81; 95% CI 0.74-0.88; p < 0.001) compared to OGLDs.[40] The CVD-REAL 3 study conducted across five countries (Israel, Italy, Japan, Taiwan and the UK) included patients with measurements of eGFR within 3 months before and after initiation of SGLT2 inhibitor or OGLDs. After propensity matching, a total of 35,561 episodes of treatment were grouped in each of the treatment groups. In the SGLT2 inhibitor cohort, dapagliflozin and empagliflozin accounted for 58% and 34% of drug exposure time, respectively. The baseline mean HbA1c was 8.71%, and mean eGFR was 90.7 mL/min/1.73 m^2. The between-group difference in the rate of eGFR decline was 1.53 mL/min/1.73 m^2 per year favoring SGLT2 inhibitors over OGLDs (p < 0.0001). The decline in eGFR across eGFR and HbA1c subgroups was similar and consistent, regardless of CVD or concomitant treatments with antihypertensives (p < 0.0001 in favor of SGLT2 inhibition in all subpopulations). Further, SGLT2 inhibitors were associated with a lower risk for ESRD alone compared to OGLDs (HR 0.33, 95% CI 0.16-0.68; p = 0.0024).[41]

The Dapagliflozin and Prevention of Adverse-Outcomes in Heart Failure (DAPA-HF) trial evaluated the safety and efficacy of dapagliflozin in patients with HF with reduced LVEF (defined as LVEF ≤40%) regardless of T2DM status (n = 4,744). The primary endpoint (a composite of death from CV causes or worsening HF) was significantly reduced in the dapagliflozin group vs. the placebo group (16.3% vs. 21.2%; HR 0.74; 95% CI 0.65-0.85; p < 0.001). Dapagliflozin was also associated with significant reduction in the individual components of the primary endpoints: worsening HF (10.0 vs. 13.7%; HR 0.70; 95% CI: 0.59-0.83) and CV mortality (9.6 vs. 11.5%; HR 0.82; 95% CI: 0.69-0.98; p = 0.029). These CV improvements were also seen in patients with diabetes (n = 215/1,075 in the dapagliflozin group and n = 271/1,064 in placebo group) as well as patients without diabetes (n = 171/1,298 and 231/1,307); with no difference between the groups (HR 0.75 [95% CI 0.63-0.90] in diabetes and HR 0.73 [95% CI 0.60-0.88] in no diabetes). The incidence of HHF or CV mortality in the dapagliflozin group was lower compared to the placebo group (16.1 vs. 20.9%; HR 0.75; 95% CI: 0.65-0.85; p < 0.001). The total first and recurrent events with dapagliflozin was 567 (340 HHF and 227 CV mortality) compared to 742 events with placebo (469 HHF and 273 CV mortality; HR 0.75; 95% CI: 0.65-0.88; p < 0.001). Further, the incidence of death from any cause was low with dapagliflozin vs. placebo (11.6 vs. 13.9%; HR 0.83; 95% CI: 0.71-0.97).[8]

Physical function, symptom burden and quality of life in patients with HFrEF were also improved with dapagliflozin. The proportion of patients with ≥5-point improvement in the clinical summary of the Kansas City Cardiomyopathy Questionnaire (KCCQ) score was higher with dapagliflozin compared to placebo (58.3% vs. 50.9%; odds ratio [OR] 1.15, 95% CI: 1.08-1.23; p < 0.001), while significant deterioration was noted in a smaller proportion compared to placebo (25.3% vs. 32.9%; OR 0.84, 95% CI: 0.78-0.90; p < 0.001).[42] Hypoglycemia, volume depletion and renal dysfunction were the most frequent adverse events noted and were similar between the dapagliflozin and placebo arms.[8]

In an exploratory analysis of DAPA-HF patients without diabetes at baseline (n = 2,605), 6.0% of patients developed T2DM during the trial, of which 95.5% of patients had prediabetes at randomization (HbA1c 5.7-6.4%). The rate of new-onset diabetes was 4.9% with dapagliflozin compared to 7.1% with placebo, indicating a 32% reduction in risk with dapagliflozin.[43]

The DELIGHT trial was a prospective, double-blind, placebo-controlled randomized trial that assessed the effects of dapagliflozin alone or in combination with saxagliptin in patients with T2DM who were already on treatment with other glucose-lowering drugs and had moderate-to-severe CKD (n = 461). Dapagliflozin significantly reduced albuminuria by 21% (baseline eGFR of ~50 mL/min/1.73 m^2 and a mean urine albumin-to-creatinine ratio [UACR] of ~27 mg/g) and by 38% with

the combination of saxagliptin, 24 weeks post-treatment. The HbA1c reduction was three times higher with combination therapy compared to dapagliflozin monotherapy (58% vs. 16%). After adjusting for concomitant changes in HbA1c, SBP, eGFR and uric acid, dapagliflozin reduced albuminuria by 15% and by 31% with the combination therapy indicating that there was no influence of these covariates on the albuminuria-lowering effect. While minor hypoglycemia was more common with the dapagliflozin and saxagliptin combination, major hypoglycemia did not vary across the groups.

Further, volume depletion and impaired kidney function related adverse events were common with the dapagliflozin and saxagliptin combination but did not differ between dapagliflozin alone and placebo groups.[44]

DAPA-CKD is a randomized double-blind trial that assessed the safety and efficacy of dapagliflozin in reducing renal events in CKD 2-4 stage patients (n = 4,304). The primary composite endpoint was the worsening of renal function, defined as a composite of an eGFR decline of at least 50%, onset of end-stage kidney disease and death from a CV or renal cause. Overall, 197/2,152 primary endpoint events occurred with dapagliflozin, compared to 312/2,152 events with placebo (HR 0.61; 95% CI: 0.51-0.72; $p < 0.001$). The benefits of dapagliflozin were consistent regardless of T2DM status. Dapagliflozin also reduced worsening renal function or death due to kidney failure (HR 0.56; 95% CI: 0.45-0.68; $p < 0.001$); HHF or CV death (HR 0.71; 95% CI: 0.55-0.92; $p = 0.009$) and all-cause mortality (HR 0.69; 95% CI: 0.53-0.88; $p = 0.004$).[45]

Table 1 presents the expert opinions on the beneficial role of dapagliflozin concerning cardiac and renal outcomes.

CARDIORENAL REHABILITATION POST-COVID

Since its outbreak in late 2019, there has been a rapid spread of the novel coronavirus disease (COVID-19) globally.[46]

The health care system has been severely burdened by COVID-19, especially due to the absence of an approved therapeutic protocol.[47] Despite organ support, mortality is significantly high in patients receiving advanced respiratory support or dialysis or kidney transplant (65% and 78%, respectively).

Further, a prospective observational study revealed that the involvement of cardiac complications and ongoing MI in patients post-COVID recovery was independent of severity and overall course of the acute illness, pre-existing conditions and the time from the original diagnosis.[48] Since SGLT2 inhibitors have shown cardio- and renal protection among diabetes and patients without diabetes, they may offer organ support in high-risk patients. The prospective beneficial mechanisms of SGLT2 include: 1) improving ventricular load by diuresis or natriuresis; 2) improving cardiac energy metabolism and 3) reducing the risk of kidney disease progression. Further preclinical data suggest benefits on the pulmonary system as well.[49]

Expert opinion on role of dapagliflozin concerning cardiorenal rehabilitation post-COVID-19 is presented in Table 2.

Table 1. Expert Opinion

There is emerging evidence about the role of dapagliflozin in prediabetes, especially in the space of cardiac and kidney disease, irrespective of diabetes status. In this context, the majority of the experts agreed to the use of dapagliflozin in patients with metabolic syndrome irrespective of diabetes status. However, it was highlighted that this treatment would be considered off-label. The experts opined that data on mechanistic aspects of dapagliflozin in CV and renal metabolic therapy would provide deeper insights into the role of dapagliflozin concerning cardiac and renal outcomes.

With emerging data on HFrEF and data in CKD, it is evident that dapagliflozin is entering the nondiabetes arena. For now, the role of endocrinologists will largely remain in the space of T2DM with a focus on preventing HF and CKD. However, in nondiabetic patients, the experience of endocrinologists should be used, so that the product is utilized optimally by other specialists. Risk assessment tools are useful in identifying patients at risk of HF and for decision-making, in assigning specific treatment of diabetes control and prevention and or management of risk factors with SGLT inhibitors. The cardiac benefits can probably be attributed to the hematocrit mechanism. The experts suggested the need for publication and multidisciplinary academic meetings involving the endocrinologists and cardiologists' communities to have a balanced view of different specialists.

Table 2. Expert Opinion

As known, survivors of severe acute respiratory syndrome (SARS) and other pandemics have several complications related to the cardiopulmonary, vasculometabolic and neuropsychiatric systems. In this context, there is a need for a publication on vasculometabolic and cardiorenal rehabilitation post-COVID, to evaluate the role of SGLT2 inhibitors. Most complications related to post-respiratory infection are largely confined to the pulmonary system, and it would be interesting to know the role dapagliflozin/SGLT2 inhibitors play in preventing pulmonary complications. The ongoing DARE-19 (Dapagliflozin in Respiratory Failure in Patients with COVID-19) trial may provide valuable insights in this regard.[50]

CONCLUSION

In summary, there exist robust data supporting the beneficial role of dapagliflozin concerning cardiac and renal outcomes. Further, dapagliflozin was found to reduce HHF or CV death by 23% and reduce the risk of kidney disease progression by 45% independent of baseline ASCVD or history of HF.[51] Dapagliflozin substantially reduced the risk of ESRD or acute kidney injury, dialysis, transplantation or death due to kidney disease by ~30%. Renal protection was consistent across all eGFR and baseline albuminuria values.[52] Thus, the role of dapagliflozin in cardio- and nephroprotection potentially extends beyond T2DM patients.

Conflict of Interest

Bharath HS is an employee of AstraZeneca Pharma India Ltd.

Funding

This work was supported by AstraZeneca Pharma India Ltd.

Contribution Details

All authors have contributed equally towards the conception and design of the study, or acquisition of data, or analysis and interpretation of data; drafting the article or revising it critically for important intellectual content and for final approval of the version to be submitted.

Acknowledgment

The authors would like to thank AstraZeneca Pharma India Ltd for providing medical writing assistance in the development of this manuscript, in collaboration with BioQuest Solutions in accordance with GPP3 guidelines (http://www.ismpp.org/gpp3).

Key Messages: Dapagliflozin, a SGLT-inhibitor, has been shown to improve HbA1c reduction in patients with major comorbidities associated with T2DM and is expected to become a preferred drug in T2DM. Recent studies have shown that dapagliflozin also significantly reduces cardiovascular events and delays kidney disease progression irrespective of diabetes. Dapagliflozin is emerging as a choice in these populations.

REFERENCES

1. International Diabetes Federation. IDF Diabetes Atlas, 9th Edition. Brussels, Belgium: International Diabetes Federation; 2019.
2. Aschner P. New IDF clinical practice recommendations for managing type 2 diabetes in primary care. Diabetes Res Clin Pract. 2017;132:169-70.
3. Davies MJ, D'Alessio DA, Fradkin J, Kernan WN, Mathieu C, Mingrone G, et al. Management of hyperglycemia in type 2 diabetes, 2018. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care. 2018;41(12):2669-701.
4. Mishra S, Ray S, Dalal JJ, Sawhney JP, Ramakrishnan S, Nair T, et al. Management Protocols of stable coronary artery disease in India: Executive summary. Indian Heart J. 2016;68(6):868-73.
5. Chawla R, Madhu SV, Makkar BM, Ghosh S, Saboo B, Kalra S, et al. RSSDI-ESI clinical practice recommendations for the management of type 2 diabetes mellitus 2020. Int J Diabetes Dev Ctries. 2020;40(Suppl 1):1-122.
6. Kalra S, Ghosh S, Aamir AH, Ahmed T, Ameen MF, Bajaj S, et al. Safe and pragmatic use of sodium-glucose co-transporter 2 inhibitors in type 2 diabetes mellitus: South Asian Federation of Endocrine Societies consensus statement. Indian J Endocrinol Metab. 2017;21(1):210-30.
7. Dapagliflozin for treating chronic heart failure with reduced ejection fraction. NICE Guidance. Technology appraisal guidance [TA679]. Published in 24 February, 2021. Available at: https://www.nice.org.uk/guidance/ta679. Accessed March 6, 2021.
8. McMurray JJV, Solomon SD, Inzucchi SE, Køber L, Kosiborod MN, Martinez FA, et al; DAPA-HF Trial Committees and Investigators. Dapagliflozin in patients with heart failure and reduced ejection fraction. N Engl J Med. 2019;381(21):1995-2008.
9. Wiviott SD, Raz I, Bonaca MP, Mosenzon O, Kato ET, Cahn A, et al; DECLARE–TIMI 58 Investigators. Dapagliflozin and cardiovascular outcomes in type 2 diabetes. N Engl J Med. 2019;380(4):347-57.
10. Gupta A, Gupta R, Sharma KK, Lodha S, Achari V, Asirvatham AJ, et al. Prevalence of diabetes and cardiovascular risk factors in middle-class urban participants in India. BMJ Open Diabetes Res Care. 2014;2(1):e000048.
11. Pradeepa R, Mohan V. Prevalence of type 2 diabetes and its complications in India and economic costs to the nation. Eur J Clin Nutr. 2017;71(7):816-24.
12. De Cosmo S, Viazzi F, Pacilli A, Giorda C, Ceriello A, Gentile S, et al; and the AMD-Annals Study Group. Predictors of chronic kidney disease in type 2 diabetes: a longitudinal study from the AMD Annals initiative. Medicine (Baltimore). 2016;95(27):e4007.
13. Unnikrishnan RI, Rema M, Pradeepa R, Deepa M, Shanthirani CS, Deepa R, et al. Prevalence and risk factors of diabetic nephropathy in an urban South Indian population: the Chennai Urban Rural Epidemiology Study (CURES 45). Diabetes Care. 2007;30(8):2019-24.
14. Kalra S, Bantwal G, John M. The exaptation of endocrine pharmacology. Indian J Endocrinol Metab. 2012;16(3):329-30.
15. Kalra S, Jain A, Ved J, Unnikrishnan AG. Sodium-glucose cotransporter 2 inhibition and health benefits: the Robin Hood effect. Indian J Endocrinol Metab. 2016;20(5):725-9.
16. Clar C, Gill JA, Court R, Waugh N. Systematic review of SGLT2 receptor inhibitors in dual or triple therapy in type 2 diabetes. BMJ Open. 2012;2:e001007.

17. Sun YN, Zhou Y, Chen X, Che WS, Leung SW. The efficacy of dapagliflozin combined with hypoglycemic drugs in treating type 2 diabetes: protocol for meta-analysis of randomized controlled trials. Syst Rev. 2013;2:103.
18. Kalra S, Shetty KK, Nagarajan VB, Ved JK. Basic and clinical pharmaco-therapeutics of SGLT2 inhibitors: a contemporary update. Diabetes Ther. 2020;11(4):813-33.
19. Ferrannini E. Sodium-glucose co-transporters and their inhibition: clinical physiology. Cell Metab. 2017;26(1):27-38.
20. Esterline RL, Vaag A, Oscarsson J, Vora J. Mechanisms in endocrinology: SGLT2 inhibitors: clinical benefits by restoration of normal diurnal metabolism? Eur J Endocrinol. 2018;178(4):R113-25.
21. Osataphan S, Macchi C, Singhal G, Chimene-Weiss J, Sales V, Kozuka C, et al. SGLT2 inhibition reprograms systemic metabolism via FGF21-dependent and -independent mechanisms. JCI Insight. 2019;4(5):e123130.
22. Inoue MK, Matsunaga Y, Nakatsu Y, Yamamatoya T, Ueda K, Kushiyama A, et al. Possible involvement of normalized Pin1 expression level and AMPK activation in the molecular mechanisms underlying renal protective effects of SGLT2 inhibitors in mice. Diabetol Metab Syndr. 2019;11:57.
23. Sano M. Hemodynamic effects of sodium-glucose cotransporter 2 inhibitors. J Clin Med Res. 2017;9(6):457-60.
24. Filippatos TD, Liontos A, Papakitsou I, Elisaf MS. SGLT2 inhibitors and cardioprotection: a matter of debate and multiple hypotheses. Postgrad Med. 2019;131(2):82-8.
25. Li J, Gong Y, Li C, Lu Y, Liu Y, Shao Y. Long-term efficacy and safety of sodium-glucose cotransporter-2 inhibitors as add-on to metformin treatment in the management of type 2 diabetes mellitus: a meta-analysis. Medicine (Baltimore). 2017;96(27):e7201.
26. Saeed MA, Narendran P. Dapagliflozin for the treatment of type 2 diabetes: a review of the literature. Drug Des Devel Ther. 2014;8:2493-505.
27. Verma S. Potential mechanisms of sodium-glucose co-transporter 2 inhibitor-related cardiovascular benefits. Am J Cardiol. 2019;124 Suppl 1:S36-44.
28. Mazidi M, Rezaie P, Gao HK, Kengne AP. Effect of sodium-glucose cotransport-2 inhibitors on blood pressure in people with type 2 diabetes mellitus: a systematic review and meta-analysis of 43 randomized control trials with 22 528 patients. J Am Heart Assoc. 2017;6(6):e004007.
29. Ferrannini E, Ramos SJ, Salsali A, Tang W, List JF. Dapagliflozin monotherapy in type 2 diabetic patients with inadequate glycemic control by diet and exercise: a randomized, double-blind, placebo-controlled, phase 3 trial. Diabetes Care. 2010;33(10):2217-24.
30. Kinguchi S, Wakui H, Ito Y, Kondo Y, Azushima K, Osada U, et al. Improved home BP profile with dapagliflozin is associated with amelioration of albuminuria in Japanese patients with diabetic nephropathy: the Yokohama add-on inhibitory efficacy of dapagliflozin on albuminuria in Japanese patients with type 2 diabetes study (Y-AIDA study). Cardiovasc Diabetol. 2019;18(1):110.
31. Cha SA, Park YM, Yun JS, Lim TS, Song KH, Yoo KD, et al. A comparison of effects of DPP-4 inhibitor and SGLT2 inhibitor on lipid profile in patients with type 2 diabetes. Lipids Health Dis. 2017;16(1):58.
32. Kosiborod M, Gause-Nilsson I, Xu J, Sonesson C, Johnsson E. Efficacy and safety of dapagliflozin in patients with type 2 diabetes and concomitant heart failure. J Diabetes Complications. 2017;31(7):1215-21.
33. Kohan DE, Fioretto P, Tang W, List JF. Long-term study of patients with type 2 diabetes and moderate renal impairment shows that dapagliflozin reduces weight and blood pressure but does not improve glycemic control. Kidney Int. 2014;85(4):962-71.
34. Fioretto P, Del Prato S, Buse JB, Goldenberg R, Giorgino F, Reyner D, et al; DERIVE Study Investigators. Efficacy and safety of dapagliflozin in patients with type 2 diabetes and moderate renal impairment (chronic kidney disease stage 3A): the DERIVE Study. Diabetes Obes Metab. 2018;20(11):2532-40.
35. Scott R, Morgan J, Zimmer Z, Lam RLH, O'Neill EA, Kaufman KD, et al. A randomized clinical trial of the efficacy and safety of sitagliptin compared with dapagliflozin in patients with type 2 diabetes mellitus and mild renal insufficiency: the CompoSIT-R study. Diabetes Obes Metab. 2018;20(12):2876-84.
36. Furtado RHM, Bonaca MP, Raz I, Zelnikar TA, Mosenzon O, Cahn A, et al. Dapagliflozin and cardiovascular outcomes in patients with type 2 diabetes mellitus and previous myocardial infarction. Circulation. 2019;139(22):2516-27.
37. Kato ET, Silverman MG, Mosenzon O, Zelniker TA. Effect of dapagliflozin on heart failure and mortality in type 2 diabetes mellitus. Circulation. 2019;139(22):2528-36.
38. Norhammar A, Bodegård J, Nyström T, Thuresson M, Nathanson D, Eriksson JW. Dapagliflozin and cardiovascular mortality and disease outcomes in a population with type 2 diabetes similar to that of the DECLARE-TIMI 58 trial: a nationwide observational study. Diabetes Obes Metab. 2019;21(5):1136-45.
39. Kosiborod M, Cavender MA, Fu AZ, Wilding JP, Khunti K, Holl RW, et al. Lower risk of heart failure and death in patients initiated on sodium-glucose cotransporter-2 inhibitors versus other glucose-lowering drugs: the CVD-REAL study (Comparative Effectiveness of Cardiovascular Outcomes in New Users of Sodium-Glucose Cotransporter-2 Inhibitors). Circulation. 2017;136(3):249-59.
40. Kosiborod M, Lam CSP, Kohsaka S, Kim DJ, Karasik A, Shaw J, et al; CVD-REAL Investigators and Study Group. Cardiovascular events associated with SGLT-2 inhibitors versus other glucose-lowering drugs: the CVD-REAL 2 study. J Am Coll Cardiol. 2018;71(23):2628-39.

41. Heerspink HJL, Karasik A, Thuresson M, Melzer-Cohen C, Chodick G, Khunti K, et al. Kidney outcomes associated with use of SGLT2 inhibitors in real-world clinical practice (CVD-REAL 3): a multinational observational cohort study. Lancet Diabetes Endocrinol. 2020;8(1):27-35.
42. Kosiborod MN, Jhund PS, Docherty KF, Diez M, Petrie MC, Verma S, et al. Effects of dapagliflozin on symptoms, function, and quality of life in patients with heart failure and reduced ejection fraction: results from the DAPA-HF trial. Circulation. 2020;141(2):90-9.
43. Inzucchi SE, Docherty K, Kober L, Kosiborod MN, Martinez F, Ponokowski P, et al. 271-OR: ADA Presidents' select abstract: effect of dapagliflozin on the incidence of diabetes: a prespecified exploratory analysis from DAPA-HF. Diabetes. 2020;69(Suppl 1):271-OR.
44. Pollock C, Stefánsson B, Reyner D, Rossing P, Sjöström CD, Wheeler DC, et al. Albuminuria-lowering effect of dapagliflozin alone and in combination with saxagliptin and effect of dapagliflozin and saxagliptin on glycaemic control in patients with type 2 diabetes and chronic kidney disease (DELIGHT): a randomised, double-blind, placebo-controlled trial. Lancet Diabetes Endocrinol. 2019;7(6):429-41.
45. Heerspink HJL, Stefánsson BV, Correa-Rotter R, Chertow GM, Greene T, Hou FF, et al; DAPA-CKD Trial Committees and Investigators. Dapagliflozin in patients with chronic kidney disease. N Engl J Med. 2020;383(15):1436-46.
46. Dasgupta A, Kalhan A, Kalra S. Long term complications and rehabilitation of COVID-19 patients. J Pak Med Assoc. 2020;70(Suppl 3):S131-5.
47. Vellingiri B, Jayaramayya K, Iyer M, Narayanasamy A, Govindasamy V, Giridharan B, et al. COVID-19: a promising cure for the global panic. Sci Total Environ. 2020;725:138277.
48. Puntmann VO, Carerj ML, Wieters I, Fahim M, Arendt C, Hoffmann J, et al. Outcomes of cardiovascular magnetic resonance imaging in patients recently recovered from coronavirus disease 2019 (COVID-19). JAMA Cardiol. 2020;5(11):1265-73.
49. Fernandez-Fernandez B, D'Marco L, Górriz JL, Jacobs-Cachá C, Kanbay M, Luis-Lima S, et al. Exploring sodium glucose co-transporter-2 (SGLT2) inhibitors for organ protection in COVID-19. J Clin Med. 2020;9(7):2030.
50. Kosiborod M, Berwanger O, Koch GG, Martinez F, Mukhtar O, Verma S, et al. Effects of dapagliflozin on prevention of major clinical events and recovery in patients with respiratory failure because of COVID-19: design and rationale for the DARE-19 study. Diabetes Obes Metab. 2021;23(4):886-96.
51. Zelniker TA, Wiviott SD, Raz I, Im K, Goodrich EL, Bonaca MP, et al. SGLT2 inhibitors for primary and secondary prevention of cardiovascular and renal outcomes in type 2 diabetes: a systematic review and meta-analysis of cardiovascular outcome trials. Lancet. 2019;393(10166):31-9.
52. Neuen BL, Young T, Heerspink HJL, Neal B, Perkovic V, Billot L, et al. SGLT2 inhibitors for the prevention of kidney failure in patients with type 2 diabetes: a systematic review and meta-analysis. Lancet Diabetes Endocrinol. 2019;7(11):845-54.

■■■■

Young People are at Higher Health Risk from Alcohol Than Older Adults

The study published in *The Lancet* suggested that adults aged 40 and older without underlying health conditions can gain some benefits from small alcohol consumption (between 1 and 2 standard drinks/day), including a reduced risk of cardiovascular disease, stroke and diabetes. On the other hand, in young adults aged between 15 and 39, drinking alcohol does not provide any health benefits and in contrast, this may lead to several presents many health risks.

Senior author of the study, Dr Emmanuela Gakidou, Professor, Institute for Health Metrics and Evaluation (IHME) at the University of Washington, US, stated "Our message is simple: young people should not drink, but older people may benefit from drinking small amounts". In the study, the researchers observed the link between the risk of alcohol consumption and 22 health outcomes, including injuries, cardiovascular diseases and cancers. They evaluate the relationship; they collected data for 204 countries and territories using 2020 Global Burden of Disease data for males and females between the ages of 15 to 39 years from 1990 to 2020.

Based on the data analyzed, the researcher's recommended 0.136 standard drinks per day for people aged 15 to 39 before risking the loss of their health. The analysis also suggested that for adults aged 40 and older without any underlying health conditions, drinking a small amount of alcohol may provide some benefits, such as reducing the risk of ischemic heart disease, stroke, diabetes, etc.

(*Source: https://www.hindustantimes.com/lifestyle/health/young-people-at-higher-health-risk-from-alcohol-than-older-adults-study-101657863594308.html*)

hematinics with traditional root

always stay true to its values

Rx in Anaemia associated with

- Pregnancy & Lactation
- Menorrhagia
- Nutritional & Iron Deficiency
- Chronic Gastrointestinal Blood Loss
- General Weakness
- Chemotherapy-induced anaemia
- Lack of Appetite
- Chronic Kidney Disease

FRANCO-INDIAN
PHARMACEUTICALS PVT. LTD.
20, Dr. E. Moses Road, Mumbai 400 011.

CASE REPORT

Rasmussen's Encephalitis

MAHESH DAVE*, YASH SHAH†, GAURAV DAVE‡, MANASVIN SAREEN#, SAHIL KHARBANDA#, RAVI KUMAR†, RAHUL METRI¥

ABSTRACT

Introduction: Rasmussen's encephalitis (RE) is an inflammatory encephalopathy characterized by progressive refractory focal seizures, cognitive deterioration and focal neurological deficit that occur with gradual atrophy of one brain hemisphere. **Case presentation:** We report a case of an 18-year-old male with a history of abnormal body movements involving the right half of the body without loss of consciousness for the last 15 years. Noncontrast computed tomography (NCCT) head and magnetic resonance imaging (MRI) revealed hemiatrophy of the left cerebral hemisphere. **Conclusion:** RE is a rare disease; hence, diagnosing and managing such patients may be challenging. Our aim is to draw attention of the treating physicians towards this disease with the help of this case report.

Keywords: Inflammatory encephalopathy, refractory, focal, rare, abnormal body movements, epilepsia partialis continua

Rasmussen's encephalitis (RE) is a chronic inflammatory disease of unknown origin, usually affecting one-half of brain, first described by Rasmussen et al in 1958.[1] It is characterized by seizures, hemiparesis and hemiatrophy of brain. Seizures are usually focal and half of them are epilepsia partialis continua. Progressive hemiparesis and other deficits occur depending on the affected hemisphere and are usually associated with intellectual decline. Imaging of the brain shows progressive hemiatrophy.[2] It affects the age group of 3 to 15 years with mean age of 6 years, and has female preponderance.[3]

The estimated incidence is 2.4 per 10 million people aged 18 years or younger per year.[4]

The etiology is unknown although autoimmune mechanism in the form of antibodies against GluR3 subunit of glutamate receptors have been identified.[5]

In this article, we present a case of RE as it is a rare disorder and therefore it is important to draw attention towards such cases.

*Senior Professor and Unit Head
†Junior Resident (2nd Year)
‡Junior Resident
#Junior Resident (3rd Year)
¥Junior Resident (1st Year)
Dept. of General Medicine, RNT Medical College, Udaipur, Rajasthan
Address for correspondence
Dr Yash Shah
Junior Resident (2nd Year)
Dept. of Medicine, RNT Medical College, Udaipur, Rajasthan
E-mail: yashs029@gmail.com

CASE REPORT

An 18-year-old male patient was admitted to our medical ward with history of abnormal body movements of right half of body without loss of consciousness for last 15 years. These episodes were 1 to 2 per month and were not associated with tongue bite and urinary incontinence. The patient was not on any antiepileptic drugs. The last episode occurred 1 day prior to the present hospitalization, which was associated with loss of consciousness. Patient had episode of high-grade fever at the age of 3 years for which he was admitted at the District Hospital, where his mother noticed decreased movement of right half of body but it was not investigated. The weakness gradually worsened over the next 15 years to the extent that at present patient is unable to perform any activity like dressing, undressing, eating, brushing teeth, etc. with right upper limb resulting in muscle atrophy and contractures. Patient was born with normal vaginal delivery with no history of any complications following it. Patient had history of delayed development of milestones and poor scholastic performance.

On examination, patient was conscious and oriented to time, place and person. There was extension at right elbow joint; pronated forearm and flexion at wrist joint (Fig. 1). Mental status examination revealed impaired calculation and Mini-Mental State Examination (MMSE) revealed a score of 24/30. On cranial nerve examination, patient had right upper motor neuron (UMN) type of facial nerve palsy. On motor examination, patient had gross wasting in right upper and lower limbs. Tone was markedly increased on right side of body with reduced

Figure 1. Right-sided wasting with flexion deformity at wrist joint.

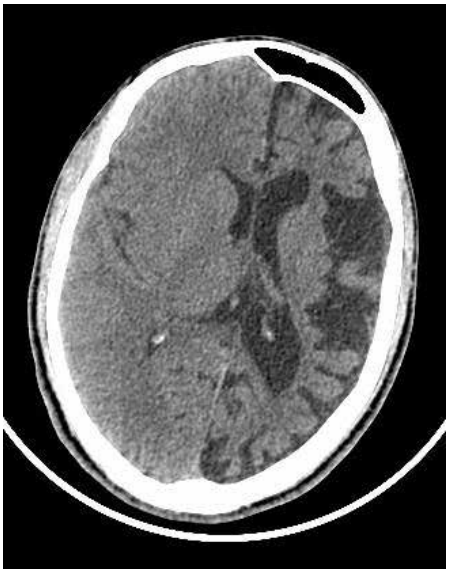


Figure 2. NCCT head showing left cerebral hemiatrophy as evidenced by reduction in volume, prominence of cerebral sulci and dilation of left lateral ventricle.

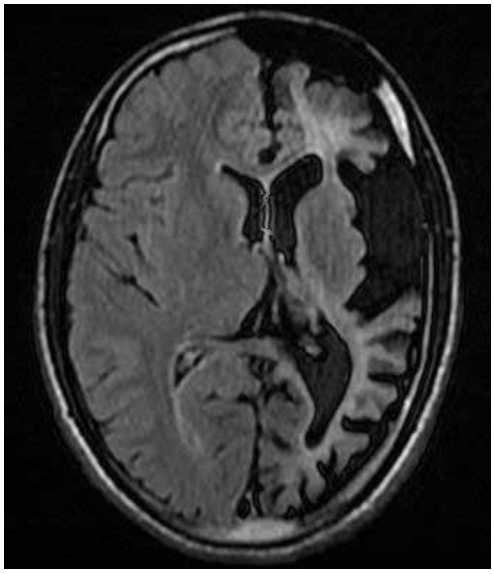


Figure 3. FLAIR transverse section showing loss of volume of white matter in left cerebral hemisphere with thinning of gyri and ex vacuo dilatation of left lateral ventricle.

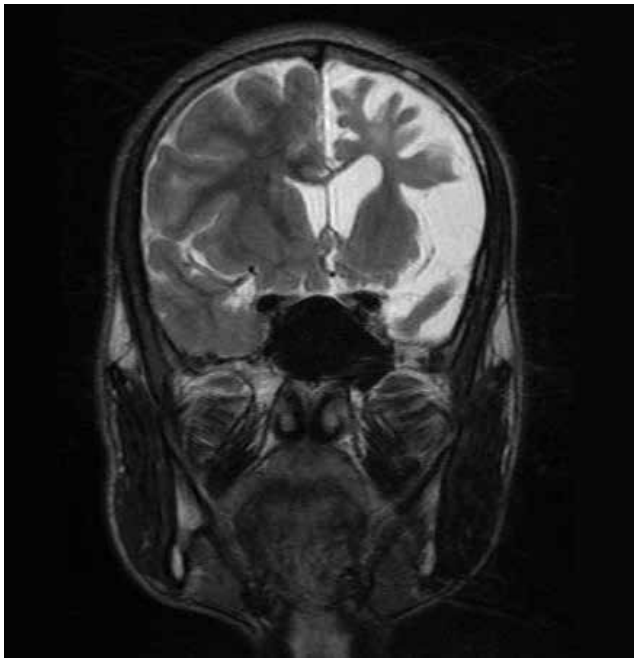


Figure 4. T2WI showing loss of volume of white matter in left cerebral hemisphere with thinning of gyri.

power (3/5), brisk deep tendon reflexes and reduced sensation to touch, pain, temperature, vibration and proprioception. Plantar response was extensor on right side. Biochemistry was unremarkable. A provisional diagnosis of insidious onset gradually progressive sensorimotor hemiparesis with focal to generalized epilepsy with mental retardation was made. Noncontrast computed tomography (NCCT) head and magnetic resonance imaging (MRI) brain was performed, which revealed left cerebral hemiatrophy as evidenced by reduction in volume, prominence of cerebral sulci and dilation of left lateral ventricle. No other bony vault abnormality or prominence of frontal and mastoid air cells were seen (Figs. 2-4). Electroencephalogram (EEG) revealed epileptiform discharges in the form of sharp and slow wave complexes. Histopathology could not be done as attendants were not willing. Patient fulfilled the diagnostic criteria of RE (Table 1). He was treated with tablet phenytoin 100 mg TDS; tablet azathioprine 50 mg OD was started to halt progression of the disease. Patient had no episode of seizure thereafter. He was advised follow-up and repeat MRI brain was planned to check for any progression.

It is essential to differentiate RE from other causes of hemiatrophy including Dyke-Davidoff-Masson syndrome, Sturge-Weber syndrome and unihemispheric cerebral vasculitis were ruled out, both through clinical and radiological features.

DISCUSSION

Rasmussen's encephalitis is a chronic inflammatory disease of central nervous system usually affecting one cerebral hemisphere. It is characterized by seizure, hemiparesis, hemiatrophy of brain and cognitive dysfunction. It affects children at ages 3 to 15 years, with mean age of 6 years, and occurs more often in females than in males.

Table 1. Diagnostic Criteria of Rasmussen's Encephalitis

Part A	
Clinical	Focal seizures (may progress to epilepsia partialis continua)
	Unilateral cortical defects
EEG	Unihemispheric slowing with or without epileptiform activity
	Unilateral seizure onset
MRI	a: Unihemispheric focal cortical atrophy
	b: Grey or white matter T2/FLAIR hyperintense signal
	c: Hyperintense signal or atrophy of ipsilateral caudate head
	(should include point 'a' and at least one among point 'b/c')
Part B	
Clinical	Epilepsia partialis continua
	Progressive unilateral cortical deficits
MRI	Progressive unihemispheric focal cortical atrophy
Histopathology	T-cell-dominated encephalitis with activated microglial cells and reactive astrogliosis

Rasmussen's encephalitis can be diagnosed if either all three criteria of Part A or 2 out of 3 criteria of Part B are present.

Our patient presented at 18 years of age, but he had developed clinical features at the age of 5 years, which is consistent with age group within which this disease usually manifests. He also presented with similar clinical features, i.e., seizures, right-sided hemiparesis and cognitive dysfunction. The MMSE score was 24 indicating cognitive dysfunction. Brain imaging revealed left-sided hemiatrophy.

The seizures in RE remain simple partial or evolve to complex partial or secondary generalized tonic-clonic seizures, with half of them having epilepsia partialis continua. Our patient presented with simple partial seizure with epilepsia partialis continua initially and until 1 day back, when he developed secondary generalized tonic-clonic seizure.

The seizures are often intractable despite aggressive medical management.[6] This is not consistent with our patient as he responded well to phenytoin.

RE has an unknown etiology, although autoimmune mechanism in the form of antibodies against GluR3 subunit of glutamate receptors has been identified.[5]

The diagnosis of RE is based on clinical, radiological and pathological features with emphasis on clinical and radiological features (Table 1).[7]

Management of RE is challenging and disappointing. Steroids, immunomodulators, plasma exchange and immunoglobulins have been used in the acute phase of the disease with limited success. Surgical treatment in the form of functional hemispherectomy is needed in resistant cases. But our patient who was started on oral antiepileptics, responded well to treatment and seizures were controlled.

This case presented with classic clinical and radiological features suggestive of RE and fulfilled the diagnostic criteria as at least two criteria from Part B were met.

CONCLUSION

Rasmussen's encephalitis is a rare disease, so diagnosing and managing such patients may pose difficulty to treating physician. With the help of this case report, our aim is to draw attention of treating physicians towards this disease. Since, it is a progressive disease; further studies need to be done for medical therapy in halting the disease process.

REFERENCES

1. Rasmussen T, Olszewski J, Lloydsmith D. Focal seizures due to chronic localized encephalitis. Neurology. 1958;8(6):435-45.
2. Abou- Khalil BW, Gallagher MJ, Macdonald RL. Epilepsies. In: Daroff RB, Jankovic J, Mazziotta JC, Pomeroy SL (Eds.). Bradley's Neurology in Clinical Practice. 7th Edition. China: Elsevier Inc; 2016. pp. 1563-614.
3. Ropper AH, Samules MA, Klein JP, Prasad S. Adams and Victor's Principle of Neurology. 11th Edition. McGraw-Hill Education; 2019. pp. 332-73.
4. Bien CG, Tiemeier H, Sassen R, Kuczaty S, Urbach H, von Lehe M, et al. Rasmussen encephalitis: incidence and course under randomized therapy with tacrolimus or intravenous immunoglobulins. Epilepsia. 2013;54(3):543-50.
5. Rogers SW, Andrews PI, Gahring LC, Whisenand T, Cauley K, Crain B, et al. Autoantibodies to glutamate receptor GluR3 in Rasmussen's encephalitis. Science. 1994;265(5172):648-51.
6. Tien RD, Ashdown BC, Lewis DV Jr, Atkins MR, Burger PC. Rasmussen's encephalitis: neuroimaging findings in four patients. AJR Am J Roentgenol. 1992;158(6):1329-32.
7. Varadkar S, Bien CG, Kruse CA, Jensen FE, Bauer J, Pardo CA, et al. Rasmussen's encephalitis: clinical features, pathobiology, and treatment advances. Lancet Neurol. 2014;13(2):195-205.

When **COUGH**
Gets **TOUGH!!!**

In Productive cough associated with Bronchospasm

℞

Grilinctus-LS® Syrup

(Levosalbutamol Sulphate 1 mg + Ambroxol Hydrochloride 30 mg + Guaiphenesin 50 mg / 5 ml)

DiLateS, LiquifieS and ExpeLS

SUGAR FREE

2022

FRANCO-INDIAN PHARMACEUTICALS PVT. LTD.
20, Dr. E. Moses Road, Mumbai 400 011.

Addressing Lower Segment Cesarean Section Hesitancy: A Patient-centered, Pragmatic Communication Guide

BHARTI KALRA*, ANJALI SHARMA†, KAMLESH DHINGRA‡, SWATI AGRAWAL#

ABSTRACT

In women in whom a normal vaginal delivery is not possible or is not indicated, delayed acceptance of lower segment cesarean section (LSCS) or outright LSCS refusal, leads to complications that can easily be avoided. Hence, it makes sense for obstetricians and other health care professionals, to address LSCS hesitancy as an integral part of obstetric care. In this article, we discuss both the communication style and communication content, that is required to manage LSCS hesitancy in women in whom the intervention is indicated. We highlight the need to analyze the reasons for hesitancy, and address them in an appropriate and affable manner, using accurate information to buttress one's points. We also encourage seeking assistance from colleagues in the health care team, utilizing audio-visual and social media aids, and offering alternatives if the patient so desires.

Keywords: Communication, delivery, labor, maternal health, person-centered care, pregnancy

Modern obstetric care has succeeded in reducing maternal morbidity and mortality levels to levels lower than ever seen in the history of womankind. One of the reasons for this has been the judicious use of lower segment cesarean section (LSCS) as a mode of delivery.[1] Data from the National Family Health Survey (NFHS) shows that the incidence of LSCS has increased over the past few years.[2] Timely LSCS, in indicated situations, improves feto-maternal pregnancy outcomes, and contributes to long-term health in both mother and child. Delayed LSCS, on the other hand, associated with childbirth trauma, may contribute to fistulae, prolapse and incontinence.[3] Birth asphyxia, which occurs if delivery is delayed, can cause behavioral or cognitive dysfunction and developmental delay in offspring.

*Consultant, Dept. of Obstetrics and Gynecology, Bharti Hospital, Karnal, Haryana
†Dept. of Obstetrics and Gynecology, Siddharth Hospital, Shahabad, Haryana
‡Consultant, Dept. of Obstetrics and Gynecology, Bansal Superspeciality Hospital, Sri Ganganagar, Rajasthan
#Dept. of Obstetrics and Gynecology, Hospital, Gwalior, Madhya Pradesh
Address for correspondence
Dr Bharti Kalra
Consultant, Dept. of Obstetrics and Gynecology, Bharti Hospital, Karnal, Haryana - 132001
E-mail: brideknl@gmail.com

There is however, poor awareness about various modes of delivery among antenatal patients.[4] In spite of the clear-cut advantages, many people continue to regard LSCS as an unnecessary or unsafe mode of delivery. The reasons for this have been explored in mixed methods studies.[5]

In a woman in whom vaginal delivery is not possible, and LSCS is clearly indicated, delayed LSCS acceptance or outright LSCS refusal, leads to complications that can easily be avoided. Hence, it makes sense for obstetricians and other health care professionals, to address LSCS hesitancy as an integral part of obstetric care. In this article, we discuss both the communication style and communication content, that is required to manage LSCS hesitancy. We highlight the need to **analyze** the reasons for hesitancy, and **address** them in an **appropriate** and **affable** manner, using **accurate** information to buttress one's points. We also encourage seeking **assistance** from colleagues in the health care team, utilizing audio-visual and social media **aids**, and offering **alternatives** if the patient so desires (Table 1).

COMMUNICATION DURING ANTENATAL CARE

- Build a good rapport with the patient, her husband and her family.
- Encourage them to ask questions and clarify doubts.

Table 1. The "10 A" Approach to LSCS Hesitancy

1.	Approach patient and her family in Affable manner
2.	Apprise them of current feto-maternal status, anticipated future trajectory of events and the indication for LSCS
3.	Articulate in BLACK (Benefits, Limitations, possible Adverse events, Cost and Knowledge required of/for LSCS) and WHITE (Warm empathy, Holistic understanding, Interests of mother and child, need for Team-based decision and Explanation of efforts made so far)
4.	Ascertain and Analyze reasons for LSCS hesitancy, if any: perceived lack of necessity, safety/tolerability or affordability
5.	Address these reasons in an empathic and firm manner
6.	Allude to the emergency/urgency/elective nature of LSCS during the discussion, and mention the time frame for decision-making
7.	Anticipate need for more information/time for decision-making, and share accurate sources of knowledge regarding the patient's diagnosis
8.	Ask for assistance from members of health care team, or use audio-visual/social media decision aids, if needed
9.	Arrive at shared and informed decision regarding the place timing and mode of delivery
10.	Accurately document the consent taking process, including LSCS hesitancy management in real time

LSCS = Lower segment cesarean section.

- Keep the patient informed about progress of pregnancy, and plans for place, time and mode of delivery, at each visit.
- Use 2D/3D models and aids to explain the female genital tract anatomy, as well as process of labor and delivery.
- Use salutogenic/positive language to encourage healthy behavior that can facilitate normal labor, (as long as there is no absolute indication for elective LSCS):
  - Exercise
  - Nutrition
  - Micronutrient supplementation
  - Yoga.
- Highlight consistently that the primary aim is a healthy mother and baby; the mode and timing of delivery is decided in such a way so as to ensure this aim.
- Clarify that the natal woman, obstetrician, family members and nursing/midwifery staff are a team, whose united objective is to ensure a healthy mother and child.
- Simultaneously, counsel women (and the family) that a normal vaginal delivery should not be viewed as a "badge of honor" or as a sign of "femininity".
- If you work in a busy, high-volume health care facility, identify and utilize alternative/complementary sources of accurate/appropriate information: colleagues, paramedical staff, visual aids, audio messages/video clips, websites.
- Ensure balanced communication regarding various modes of delivery.

COMMUNICATION IMMEDIATELY BEFORE/DURING LABOR

- Take a shared and informed decision regarding induction/augmentation and trial of labor, explaining all relevant aspects.
- Share clinical findings with patient and family during monitoring of labor.
- In case, LSCS is indicated, explain primary indication, and describe benefit to mother and child in positive language.
- Explore reason for LSCS hesitancy, if consent is not forthcoming.
- For pedagogic ease, we structure the main reasons for LSCS hesitancy as:
  - Perceived lack of necessity
  - Perceived lack of safety/tolerability
  - Perceived lack of affordability.
- History taking should be done in a hierarchal manner, to elicit the reasons mentioned in the order above.
- All communication should be documented, and may also be audio-recorded and/or video graphed as per standard of care.

PERCEIVED LACK OF NECESSITY FOR LSCS

- Explain primary indication for LSCS, inform about emergency/urgency of decision (Table 2) and list contributory factors.
- Use positive language, e.g., LSCS will ensure a healthy baby and a healthy maternal tract for future pregnancies.

Table 2. Indications for LSCS: Classification According to Urgency

Category	Feto-maternal health risk	Decision-to-delivery interval	Some indications
1: "crash" LSCS	Immediate threat to life of fetus and/or mother	As short as possible, maximum 30 minutes	Fetal bradycardia, cord prolapse, rupture uterus
2: emergency	Fetal and/or maternal distress, but no immediate threat to life	As short as possible, maximum 75 minutes	Meconium, abnormal cardiotocogram
3: emergency	No distress or threat to life, but early delivery is indicated	As short as resources allow	Poor progress of labor
4: elective	No compromise or threat to life	As per convenience of mother and health care system	Cephalopelvic disproportion, not in active labor

LSCS = Lower segment cesarean section.

- Clarify that you have best interest of mother and child at the center of your decision-making.
- Reiterate that you are part of a team, and that the captain of the team is the mother in labor (or decision maker in the family).
- Convey that it is neither the mother's fault, nor the obstetrician's fault, that normal vaginal delivery is not possible/feasible.
- Encourage the family to view LSCS as a life-saviour for the fetus/baby.
- If urgency, describe potential mishaps that may occur related to maternal and fetal outcome.
- If emergency, also explain secondary mishaps that may occur due to prolonged/obstructed/lack of progress of labor, e.g., maternal-childbirth trauma, stress urinary incontinence, prolapse, cervical incontinence and fetal - birth asphyxia sequelae.
- Reinforce the message through various members of health care team.
- Offer option of second opinion for place, mode and timing of delivery.

PERCEIVED LACK OF SAFETY/TOLERABILITY OF LSCS

- Explore specific myths and address them, e.g., inability to breastfeed/work/maintain conjugal relations/have normal vaginal delivery after LSCS.
- Use positive, non-judgmental language in patient and empathic manner, while reminding patient and family that time is of essence.
- Describe the postoperative rehabilitation process after LSCS.
- Allude to possibility of delayed rehabilitation after prolonged labor/childbirth trauma during vaginal delivery.
- Reassure the family regarding expertise and experience of operating team.
- Reinforce the message through various members of health care team.
- Offer option of second opinion for place, mode and timing of delivery.

PERCEIVED LACK OF AFFORDABILITY

- Inform differential in cost of normal vaginal delivery and LSCS, and explain the reasons for this (manpower, infrastructure and consumables).
- Encourage family to take a holistic view of cost of childbirth, including cost of neonatal and future child care, as well as future obstetric and gynecological care.
- Offer options for staggered or deferred payment, if feasible.
- Suggest economic alternatives for place of delivery if feasible.

SUMMARY

We reiterate that the decision-making regarding mode and timing of delivery is highly individualized, and must be based upon the unique combination of fetal and maternal factors at completion of pregnancy. LSCS hesitancy sometimes prevents the appropriate decision from being made in a timely manner. The points listed and tabled here provide an overview of the communication style, and communication content, which is required to manage LSCS hesitancy. We hope that this framework will encourage discussion as well as debate, which will strengthen not only our communication skills but obstetric care as well.

REFERENCES

1. Meh C, Sharma A, Ram U, Fadel S, Correa N, Snelgrove JW, et al. Trends in maternal mortality in India over two decades in nationally representative surveys. BJOG. 2022;129(4):550-61.

When treating **Skin Infections** become a **Challenge!**

Cure for Sure

In Mixed Skin Infections

℞ **SURFAZ-SN®** Cream

(Clotrimazole 1% + Beclomethasone Dipropionate 0.025% + Neomycin Sulphate 3500 Units/gm)

For Various Types of Fungal Infections

℞ **SURFAZ®**

Cream
Solution
Dusting Powder

(1% Clotrimazole)

In the Management of Superficial & Systemic Fungal Infections

℞ **SURFAZ-O®**

(Fluconazole 150 mg tablets)

In Fungal Infections with Inflammation

℞ **SURFAZ-B®**

(Clotrimazole 1 % + Beclomethasone Dipropionate 0.025 %) Cream

2022

FRANCO-INDIAN PHARMACEUTICALS PVT. LTD.
20, Dr. E. Moses Road, Mumbai 400 011.

2. Radhakrishnan T, Vasanthakumari KP, Babu PK. Increasing trend of caesarean rates in India: evidence from NFHS-4. J Med Sci Clin Res. 2017;5(8):26167-76.
3. Pergialiotis V, Bellos I, Fanaki M, Vrachnis N, Doumouchtsis SK. Risk factors for severe perineal trauma during childbirth: an updated meta-analysis. Eur J Obstet Gynecol Reprod Biol. 2020;247:94-100.
4. Saxena RK, Ansari NFT, Balan A. Factors influencing women's choice of mode of delivery in rural Bangalore, India. Indian J Obstet Gynecol Res. 2019;6(1): 71-7.
5. Ugwu NU, de Kok B. Socio-cultural factors, gender roles and religious ideologies contributing to caesarean-section refusal in Nigeria. Reprod Health. 2015;12(1):70.

■■■■

Improved Diet could Reduce the Rate of Illness among Women

A new study published in *Nutritional Neuroscience* suggests that a healthy diet, especially one rich in foods containing a high amount of carotenoids, may help reduce the incidence of sickness among women. These bright-colored fruits and vegetables are particularly important in minimizing cognitive and visual decline.

According to the study, which examined and evaluated data from earlier studies stated that women accounted for about 80% of all autoimmune diseases collectively. Therefore, women require more preventive care because of their sensitivity, which is directly related to biology.

Women's vulnerability or sensitivity is caused by the way women's body retains vitamins and minerals. Women have more body fat than males, and this body fat acts as a large sink for many dietary vitamins and minerals, creating a helpful reservoir for women during pregnancy. However, because of this, the retina and the brain receive less nutrition, making women more prone to degenerative issues.

Experts stated that dietary carotenoids work as antioxidants, hence were very much essential. It has been demonstrated that lutein and zeaxanthin, two distinct carotenoids found in particular tissues of the eye and brain, directly ameliorate central nervous system degeneration. Additionally, the role of the microbiome and the bacteria in the gut, coupled with dietary elements produce the neurotransmitters and structural components of our brain.

Thus, the study stressed that women needed more vitamins and minerals and advised them to be aware of these facts. They further added that women should take proper measures to prevent these problems later in life.

(Sources: Hindustan Times, Jul 16, 2022; https://www.hindustantimes.com/lifestyle/health/women-can-lower-their-rate-of-illness-with-improved-diet-suggests-study-101657944857729.html)

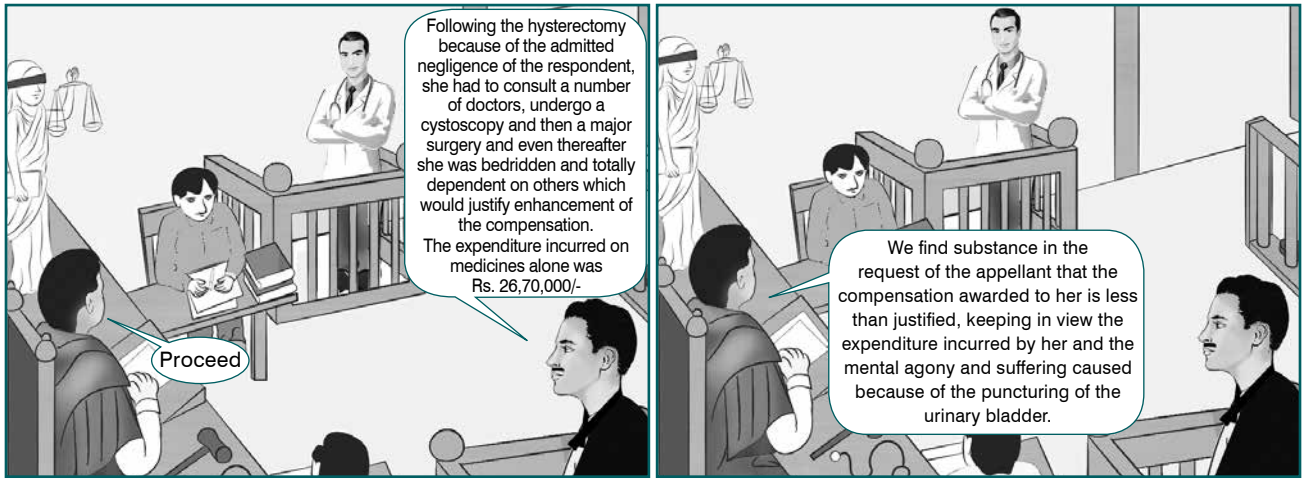
Study Suggests Simple Tests to Identify Blood Clots Related to COVID-19

In a study published in the *American Journal of Pathology*, researchers revealed the use of a minimally invasive test to find blood clots in small blood vessels in the skin of patients who had severe COVID-19. These clots appeared normal and were not present in the skin of patients who had other types of severe infectious lung diseases or in people who only had mild or moderate COVID-19.

A skin biopsy, according to the researchers, can aid in determining the extent of COVID-19-related tissue damage as well as helping in separating this blood vessel disease from other severe respiratory infections. The study also included biopsy samples from 9 hospitalized patients who had severe or critical respiratory or kidney diseases and passed away prior to the COVID-19 era. Also, MxA an antiviral protein which can stop SARS-CoV-2 growth was detected in all the 6 mild to moderate COVID-19 patients.

Microthrombi or small blood clots were seen in 13 of the 15 patients with severe or critical COVID-19 while no microthrombi were found in the biopsies of patients with mild to moderate COVID-19 or the pre-COVID-19 era patients with severe respiratory sickness or kidney disorders. The scientists stated that these microvascular changes may be a unique characteristic of COVID-19 respiratory disorder compared to other acute respiratory diseases. (*Source: Hindustan Times, Jul 15, 2022*)

Enhancement of Compensation in Case of Medical Negligence



Lesson: In the case no. 382 of 2007 NCDRC, The Commission ruled in the favor of the appellant saying that this is a fit case where the compensation is enhanced from Rs. 1 lakh to Rs. 2,50,000/- taking into account the medical expenditure incurred as also compensation for mental agony and harassment.

COURSE OF EVENTS

- Appellant approached the respondent/doctor with complaints of severe pains during her menstrual period. After examination, respondent advised her to undergo an abdominal hysterectomy for removal of uterus. She accordingly got admitted in the nursing home for the said surgery and paid the Respondent a package fee of Rs. 20,000/- which included the cost of the surgery, postoperative care as also expenditure on medicines.
- 19.11.2000: The Appellant was operated by the respondent; latter informed the appellant's spouse that the operation was successful.
- 24.11.2000: On removal of the catheter it was noted that the urine kept on dripping and this fact was immediately brought to the notice of the respondent. Appellant was thereafter referred to a urology specialist, Dr A at Nellore who after examining her opined that the urinary bladder had got punctured during the surgery and if the hole was minute it would have healed within a day or two.
- 26.11.2000: The appellant was admitted to Hospital A since this problem continued and Dr B another urology specialist advised immediate surgery.
- 29.11.2000: Cystoscopy was conducted and the problem was diagnosed as vesicovaginal fistula (VVF) for which she was initially prescribed conservative treatment.
- The appellant also consulted Dr C, a urologist in Hyderabad for a second opinion who opined that the appellant's urinary bladder had got punctured on account of negligence of the respondent while suturing the upper portion of the vagina during the hysterectomy and a surgery to repair the VVF was recommended.
- 08.02.2001: A team of doctors at Hospital A in Chennai conducted this surgery.
- 19.02.2001: The appellant was discharged with advice to take full bed rest for about 3 months and also be under regular medical supervision for another 6 weeks.
- 10.12.2001: The appellant was finally declared finally cured. During the intervening period, she had to depend on others for all her daily requirements and suffered mental agony and huge financial expenditure on account of the negligence of the respondent while conducting the hysterectomy surgery and puncturing her urinary bladder.

- Appellant filed a complaint before the State Commission on grounds of medical negligence and requested that the respondent be directed to pay her Rs. 2,67,137/- towards medical treatment and incidental expenses, Rs. 6 lakhs towards mental agony with interest @ 18% per annum from 16.02.2001 till realization.
- Respondent denied that there was any medical negligence and stated that the problem occurred because the patient did not cooperate and on the 6th day removed the catheter against medical advice. It was further stated that the appellant had already undergone two cesarean sections and during the surgery. Respondent found that the bladder was very much adherent to the uterus, which often occurs because of cesarean sections. The complication that occurred during the surgery is known to occur in respect of patients who have undergone previous surgeries and it was not because of any medical negligence on the part of the Respondent.
- The State Commission after hearing the parties and examining the evidence filed before it observed that due to the negligence on the part of respondent the appellant had suffered the problems of undergoing several clinical and diagnostic tests. Apart from that she had suffered pain and agony while undergoing hysterectomy surgery, cystoscopy and VVF surgery.
- The State Commission directed the respondent to pay Rs. 1 lakh towards medical expenses and compensation within a period of 6 weeks failing which the said sum shall carry interest @ 9% per annum till the date of payment. Rs. 3,000/- was awarded as litigation cost.
- This order was accepted by the respondent who did not file an appeal. The present first appeal has been filed by the appellant for enhancement of the compensation.

COMPLAINANT ALLEGATIONS

Counsel for appellant stated that following the hysterectomy because of the admitted negligence of the respondent, she had to consult a number of doctors, undergo a cystoscopy and then a major surgery and even thereafter she was bedridden and totally dependent on others, which would justify enhancement of the compensation. The expenditure incurred on medicines alone was Rs. 26,70,000/- for which evidence was filed.

RESPONDENT REJOINDER

Counsel for respondent on the other hand stated that there was no case for enhanced compensation and the State Commission after taking into account the expenditure incurred and assessing the appellant's contention of mental agony and harassment awarded a compensation of Rs. 1 lakh which under the circumstances is not a lesser compensation.

SOME SALIENT COURT OBSERVATIONS

- The respondent has not filed an appeal against the finding of medical negligence against him.
- On going through the evidence filed by the appellant on the expenditure incurred by her as also the undisputed fact that she had to undergo several tests and another major surgical procedure to repair the damage to her urinary bladder caused during a reasonably common surgery, i.e., hysterectomy, we find substance in the request of the appellant that the compensation awarded to her is less than justified, keeping in view the expenditure incurred by her and the mental agony and suffering caused because of the puncturing of the urinary bladder.
- We are of the view that the statement showing the medical and related expenditure incurred by the appellant of Rs. 2,67,137/- is on the higher side and is not supported by receipts.

FINAL JUDGEMENT

The Commission ruled in the favour of the appellant saying that this is a fit case where the compensation is enhanced from Rs. 1 lakh to Rs. 2,50,000/- taking into account the medical expenditure incurred as also compensation for mental agony and harassment. Respondent is therefore directed to pay the appellant, Rs. 2,50,000/- for medical expenses and compensation and Rs. 3,000/- as litigation cost within a period of 8 week from the date of receipt of this order failing which the entire amount will carry interest @ 9% per annum from the date of default till realization. The Counsel for Respondent states that Rs. 1 lakh has already been deposited by the respondent before the State Commission. If that be so, this amount be adjusted against the compensation awarded to the appellant by us and the balance be paid to the appellant within the stipulated period.

REFERENCE

1. Case no. 382 of 2007, NCDRC; Order date 11.09.2012.

HCFI Dr KK Aggarwal Research Fund

HCFI Round Table Environment Expert Zoom Meeting on "Soil Protection: For Earth Protection and Life Protection"

June 19, 2022 (Sunday, 12 noon - 1 pm)

- As per the recent State of the Environment Report 2022 released by the Centre for Science and Environment (CSE), almost 30% of India's geographical area is under degradation which means decline in productivity of land in terms of biodiversity and economy triggered by various factors such as climate change along with human factors.
- Agricultural land in India is around 36%, forest land is ~22%. These are the lands most commonly being degraded.
- This affects all of us and leads to food insecurity due to reduced yield and climate change due to release of soil carbon and nitrogen oxide.
- As per the report, 14 states have seen more than 10% rise in the share of degraded land compared to other states. Maximum land degradation has occurred in Punjab, Mizoram, Arunachal Pradesh, Tripura, Assam and Nagaland.
- Isha Foundation has initiated "Save soil movement". It is a global movement to initiate a conscious approach to soil and planet in all. As part of this movement, a journey of over 30,000 km across 24 nations will also be undertaken.
- Earth supports 8 million plant and animal species in different geographical ecosystems maintained by the soil.
- Soil holds water and conserves ground water, which maintains productivity of the soil.
- Soil has been our past; it is our present and future. Soil protection means earth protection and life protection.
- Soil is required not just for agriculture, but also for horticulture, creating meadows, etc.
- Soil is an important part of UN the Sustainable Development Goals (SDGs): Goals on zero hunger (SDG 2), climate action (SDG 13) and life on land (SDG 15).
- Environment has never been considered as "one system". Land, soil, river, oceans are all interlinked. Any problem in one is bound to alter the other natural systems.
- Soil protection has largely been ignored; hence the problem of soil degradation.
- Changes in land use pattern, terrain and slope have led to problems like floods. Lack of proper planning of cities has added to the problem.
- The most active part of the soil is humus, which is now mostly missing. It absorbs solar rays. Sunlight helps in the sequestration process in the soil. In the absence of humus, soil acts as a mirror and reflects the sunlight back in the atmosphere, which increases the overall temperature.
- About 30% of native biomass has been lost, which has greatly disturbed the biodiversity and food pattern. About 20-25% plants and animals are at risk. Five hundred fifty-nine of 6,190 domesticated mammals used for food and agriculture have been lost and 1,223 are on the verge of extinction.
- Soil represents the largest terrestrial carbon pool.
- Carbon creates, soil preserves.
- Carbon sequestration by soil minerals represents a promising strategy for climate change mitigation. Soil protection can make climate resilient.
- The carbon sequestration process occurs inside the soil. Carbon discharged in the atmosphere acts like a heater, when carbon is in the soil, it is a coolant.
- Soil carbon storage can be increased by 453% to 757% if it is cultivated according to land type and plant type.
- Conservation of agricultural crops practices such as proper management of agriculture residues, zero/reduced tillage and residue retention. Burning of agriculture residue in thermal power plants is dangerous. It should be done at site so that minerals are not lost and remain the soil.
- Soil amendment such as addition of biochar has been advocated as a promising technology for simultaneously increasing crop yield and mitigation of climate change.
- A law to conserve soil was introduced in the US in 1990 and it had some penalty clauses also. In 1996, Federal Agriculture Improvement and Reform Act

was passed for wetland conservation and regulation of soil erosion control, which had a vital impact on conservation of soil and fertility.

- The concept of crop rotation seems to be forgotten now. It is very helpful in diversifying soil conservation.
- There is a need to shift to the old agricultural practices.
- An integrated approach for soil conservation includes mitigation of resources, conservation of soil fertility by minimizing the synthetic fertilizers and pesticides, enhancing the organic manures and green manure, soil testing, reclamation and conservation and a balanced and integrated approach for good nutrients, development and conservation of water resources, crop diversification and organic farming. There are other strategies also to conserve soil – tillage of land, which is not being used frequently to sow crops. It saves soil from erosion and also increases its water holding capacity; moisture of the soil is maintained.
- Strip cropping, as a method to prevent soil erosion, is used to get some buffer from rivers or water bodies when a slope is too steep.
- Many wetlands in villages have been converted into agriculture lands, which is not good as wetlands maintain ground water balance and ground water recharge.
- Many practices such as dumping of municipal waste, tilling in a manner that allows soil erosion, have damaged the soil.
- Taking care of soil *per se* is missing in the legal framework, in contrast to air and water.
- There is a need for policies to revitalize the ecology and soil.
- Engineering efforts are necessary to see that erosion is controlled.
- Laws regarding what can be added to soil and what are the norms to be met before anything is put in the soil are needed. This is not just to take care of ground water but to also take care of soil *per se*.
- At the same time, it must be ensured that soil is conserved by preservation of erosion and by deposition of fresh soil during floods and other methods that keep soil healthy.
- Attitude of man has been to take care of natural resources. A sense of duty toward environment is missing.
- Tradition of paying high regard to these natural resources should be restored. It is a cultural effort but will empower proper attitude and actions to ensure soil conservation.
- Nitrogen and phosphorus are very important for soil. If carbon, nitrogen and phosphorus are less, biodiversity will be very less.
- Government has distributed Soil Health Cards to farmers. It is a pioneering program, but there is lack of awareness about this.
- Climate is the major factor for soil erosion. Other factors such as type of soil, type of plantation on that soil, biological activities also affect soil erosion.
- Soil erosion occurs at a faster rate on slopes, particularly steep slopes, as the speed of water is increased and its transportation capacity is also increased.
- Adoption of ridge furrow system will also help to check soil erosion.
- The direction of crops on slopes should be perpendicular to the wind to reduce erosion.
- A team of soil health volunteers must be created.
- Soil, as a resource, has been greatly misused. It has largely been a neglected area unlike air and water as it does not affect man directly.
- Mining and infrastructure development are the two major activities that are greatly affecting soil.
- The impact of infrastructure development on soil has to be assessed. At present, the only requirement is that the top soil should be preserved and used in gardens, etc.

Participants: Mr Paritosh Tyagi, Dr Dipankar Saha, Dr SK Tyagi, Dr SK Gupta, Dr Sanjeev Agrawal, Mr Neeraj Tyagi, Mr Varun Singh, Dr Anil Kumar, Dr S Sharma

HCFI Round Table Environment Expert Zoom Meeting on "Ban on Identified Single Use Plastics: A Step Towards Reducing Plastic Waste Pollution and Health Effects of Microplastics"

Speakers: Mr Amit Jain, *UNEP* and Dr Kamal Sharma, *CEO-WeCare*

July 3, 2022 (Sunday, 12 noon - 1 pm)

- Single use plastics (SUPs) are of great convenience in daily life. But they have a major effect on environment and human health.
- Open burning of plastic waste, indiscriminate dumping of single use plastics in water bodies and

sewers, plastic contamination of seafood and microplastics are why single use plastics need to be phased out.

- There is lot of ongoing research on microplastics.
- It is estimated that there are more than 1.5 million trillion microplastics in the oceans.
- The government of India has banned the manufacture, sale and use of single use plastic products effective from 1st July, 2022. The list of banned SUPs includes 19 priority products. The regulatory action had begun early this year, when advisories had been issued to State Pollution Control Boards (SPCBs).
- This mission began in 1999 by banning thin polythene bags. There were further amendments and the first Plastic Waste Management Rules came in 2016 to increase the thickness of plastic bags to 50 microns. But we have been unable to eliminate even one SUP.
- Poor enforcement may be one reason, but the major reason is poor socioeconomic status.
- Collection of plastic waste is a huge problem.
- If there are no convenient and cost-effective alternatives and if enforcement is not strong, the plastic pollution problem will remain and go on increasing.
- Plastic is found everywhere. It started in 1950s when plastic was discovered. It is a universal packaging option across all sectors.
- Because of its widespread use over the years, we are now facing a problem of plastic pollution.
- This plastic is being transported from land through rivers to seas and oceans. Seas and rivers are a major part of food chain.
- About 80% of microplastics in the ocean come from the shipping industry.
- The source of microplastics has to be identified and act to control it.
- More than 10 rivers have been identified as carriers of plastic waste. The Ganges in India is one of them.
- Plastics are being recycled, but this is not adequate. There are different types of plastics; for some there is no business sense in recycling them, so they are dumped.
- Efforts are ongoing to identify hotspots of plastic leakage in the plastic value chain – from usage point to disposal point.
- More reforms are needed to so that a lifecycle approach can be adopted. To implement the lifecycle approach, market-based instruments were designed. Products need to be designed in a way that they generate revenue.
- There is a need to produce alternate products; at the same time, our habits too have to improve.
- All stakeholders – general public, producers as well as the informal sector needs to be involved in enforcing this ban.
- Microplastics are tiny plastic particles (<5 mm) that result from both commercial product development as well as the breakdown of larger plastics.
- Microplastics cause water, air and soil pollution. Through the food chain, microplastics enter the body and affect different organs and harms human health.
- It is speculated that microparticles carry viruses and make their lifecycle longer.
- Though their concentration is not so much at present, the impact would be visible in the next three decades. This would require modification of regulations related to air/water/soil pollution.
- Microplastics are being studied, but now there is a need to make it a movement, so that all states can get their water bodies evaluated with regard to microplastics.
- The capacity and capability of research institutes should be increased so that they can identify the microplastics and analyze them.
- The policymakers too have to be aware about microplastics.
- The way out of this problem is to comply with regulations as much as possible. This will be a gradual process and will not happen overnight.
- The 3Rs (Reduce, Recycle and Recover) must be kept in mind. First reduce consumption and then move on to resource efficiency and find out alternate materials – their cost-effectiveness, circularity.
- Awareness will have a major impact so a mass movement should be started.
- There is a need to develop infrastructure to manage it in a responsible manner.
- One way of dealing with the problem can be to fix the responsibility or extended producer responsibility (EPR), i.e., they take back the plastic produced by them so that it is in safe hands for safe handling, treatment and disposal.

- Identify what can be controlled and what cannot be controlled. If responsibility cannot be fixed, then ban on such materials may be required.
- Use of other materials such as paper, glass, aluminum to replace plastic packing is not feasible as there are environment intensive. The cost of production of alternatives and their impact on the environment needs to be taken into consideration. Their compostability and biodegradability needs to be looked at. Rapid tests are not available to check compostability and biodegradability.
- Kulhad has been suggested as a replacement, but it is more carbon intensive and also requires top soil for manufacture.
- The industry is working towards sustainable packaging.
- Penalty for not complying with the ban should be imposed on the basis of the date of manufacture as the supply chain is long. This needs to be clarified from the regulators.
- A buffer time is needed for the markets.
- Instead of holding everybody accountable, the responsibility should be concentrated with the manufacturer, which is easy to identify and therefore also easy to control.
- Unless we stop manufacturing, this problem cannot be controlled.
- Currently, there is a gap between understanding, planning, mode of implementation and monitoring. These gaps need to be plugged.
- People have to be made aware that plastic is harmful. It is a derivative of phthalic acid, which is a potential carcinogen.
- The medical fraternity needs to come forward to create awareness about the harmful effects of plastic, similar to the scale of awareness that has been created about COVID-19.
- To have an effective ban, we need to learn from the past. For this, it has to be seen if the regulations are enforceable.
- SUPs have percolated down to people of lower income, so it is difficult to eliminate.
- Awareness, rational use and segregation are key.
- A behavioral change is required. We have to think and act differently.
- Research and development are necessary.
- The alternatives should be convenient, cost-effective and not hazardous to the environment.

Participants: Mr Vivek Kumar, Dr Anil Kumar, Mr Paritosh Tyagi, Dr Dipankar Saha, Mr Amit Jain, Dr Kamal Sharma, Dr SK Gupta, Dr Sanjeev Agrawal, Mr Pradeep Khandelwal, Mr Neeraj Tyagi, Dr Tripta Gupta, Dr S Sharma

■■■■

Nonalcoholic Fatty Liver Disease and Dementia

Nonalcoholic fatty liver disease (NAFLD) may increase the risk of dementia, suggests a recent study from Sweden published in the journal *Neurology.* It further says that those with heart disease and stroke are particularly at risk. Data from 2,898 patients with NAFLD, aged ≥65 years, from the Swedish National Patient Register (NPR) between 1987 and 2016 was evaluated to investigate a possible association between NAFLD and risk of new-onset dementia. A total of 28,357 matched controls, without NAFLD, were also selected. Over a follow-up period of 5.5 years (median), 145 (5%) NAFLD patients and 1,291 (4.6%) patients without NAFLD developed dementia. The rate of dementia was 38% higher among NAFLD patients after adjusting for risk factors such as diabetes, hypertension, obesity (adjusted HR [aHR] 1.38). None developed Alzheimer's disease. The incidence of vascular dementia was 44% higher in the presence of NAFLD with aHR of 1.44. Co-existing heart disease increased the risk of dementia by 50% (aHR 1.50). The risk increased by 2.5 folds among patients with NAFLD and stroke (aHR 2.60). This study has shown a link between NAFLD and all-cause dementia, mainly vascular dementia but not dementia due to Alzheimer's disease. This relationship was particularly robust in patients with comorbid heart disease. This risk was independent of the cardiometabolic risk factors. NAFLD is increasing in prevalence globally. Since it is mostly asymptomatic, the diagnosis is often missed resulting in inaccurate estimation of the interrelationship, which according to the authors is a limitation of their study.

(*Source: Shang Y, et al. Nonalcoholic fatty liver disease and risk of dementia: a population-based cohort study. Neurology. 2022:10.1212/WNL.0000000000200853.*)

AIOC 2022: 80th Annual Conference of All India Ophthalmological Society

MICROBIAL KERATITIS: EVIDENCE-BASED MEDICINE

Dr Namrata Sharma, New Delhi

The risk factors of keratitis include corneal abrasion or epithelial defect, eyelid disease, contact lens (CL) use, previous ocular surgery, ocular surface disease (OSD), compromised corneas and use of topical antibiotics, CS and TEM.

Treatment strategies include:

- Mild ulcers – <3 mm in size; not involving visual axis
  - Monotherapy – Ofloxacin (0.3%); ciprofloxacin (0.3%); gatifloxacin (0.3%); moxifloxacin (0.5%); levofloxacin (1.5%).
- Moderate ulcers – >3 mm in size; involving visual axis
  - Combination therapy – Fortified cefazolin (5%) + tobramycin (1.3%) or ciprofloxacin (0.3%); cephalosporin: Gram-positive cocci; AG: Gram-negative bacilli.

The treatment regimen comprises of sterilization phase and healing phase.

Antimicrobial resistance can be prevented by:

- Using a very low-dose or too short a duration of antimicrobial usage increase antimicrobial resistance
- Using the right antibiotic
- Rapid tests
- The use of antibiotics when proved to be a tangible benefit
- Do not taper antibiotics; stop at the therapeutic dose.

VITRECTOMY FOR MACULAR HOLES AND TRACTIONAL MACULOPATHY

Dr Unni Nair, Fort Worth, Texas

The surgeon should choose, case by case, whether a quick result is better than a slow result, which allows for avoiding the consequence of PPV.

- The target of anatomical treatment.
- Restoration of the foveal profile.
- Rectification of anomalies of the retina.
- The alteration in the foveal profile has to be treated with PPV.
- The alteration into the retinal and sclera with MB.

ENDOGENOUS ENDOPHTHALMITIS

Dr Andrew W Eller, Pittsburgh, US

- Able to provide subjective concerns:
  - Symptomatic – blurred vision, floaters, red-eye
  - Asymptomatic – fungemic patients (10% rate of endophthalmitis in asymptomatic screening).
- Unable to provide subjective concerns-but red-eye in known sepsis: bacteremic or fungemic patients.
- Triple empiric therapy while awaiting culture results.

OPTIMIZING IOL POWER CALCULATIONS

Dr Arup Chakrabarti, Thiruvananthapuram

Post-op Vision-Plano 6/6: The Holy Grail

IOL power calculation: Preoperative, intraoperative and postoperative.

It is important to identify and treat dry eye and blepharitis pre-op because these can impact:

- IOL calculations – Inaccurate keratometry can lead to the wrong IOL power
- Limbal relaxing incision (LRI) or toric IOL axis and/or magnitude – Inaccurate keratometry; inaccurate topography.

Desirable pupillary status at the time of biometry

- Some studies suggest anterior chamber depth (ACD) increases after pharmacological dilation.
- Dilation may influence the calculated IOL power when using multivariate formula.

Optimal biometry or keratometry practice

- Optimize the ocular surface in OSD patients – Repeat biometry every few weeks; accept 2 consecutive repeatable values.

- Nil touch technique of biometry – Virgin cornea; no anesthetic or mydriatic or cycloplegic drops; no prior contact procedure.

Perfecting IOL power prediction: Instruments/devices, current formulas, a constant optimization.

IOL power calculation-intraoperatively

- Precise surgery and positioning of the IOL.
- Modification of IOL design and power if standard capsule support is not feasible.

IOL power calculation-postoperatively

- Assessment of the refractive and anatomic outcome.
- Post-op Mx of unwanted residual refractive errors, which could involve – IOL rotation/exchange; Piggyback IOLs. Corneal refractive surgery, Calhoun LAL or Modification of the power of the IOL *in situ.*

Remember

- Preoperative measurements on naïve cornea
- Use validated measurements
- Work with properly optimized lens constants
- Adapt to new technologies as they present
- Employ the right formula
- Strive to use all available resources to their best advantage

PERFORMING PREMIUM CATARACT SURGERY

Dr Abhay R Vasavada, Ahmedabad

Surgery strategy that is safe, effective and PREDICTABLE.

The technique should match the type of eye/cataract, expected refractive and technical outcome. The multiple chop technique enables complete division.

Low fluid parameters led to a lower increase in central corneal thickness (CCT) 1 day and 7 days postoperatively, decreased anterior segment inflammation at 1 day and yielded clear corneas.

Femtosecond cataract surgery: Easing the steps of cataract surgery, predictable and safer in all hands, eases difficult situations.

COUNSELING AND PREOPERATIVE WORK-UP

Dr Partha Biswas, Kolkata

Need for premium IOLs

- Spectacle independence
- Correction of astigmatism

Patient profile and first glance

- Age
- Profession
- Spectacles
- Lifestyle

Patient history

- Complaint
- Past-trauma/LASER/intervention
- Family history
- General health

Vision and refractive error

- Need for immediate/delayed surgery
- Heavy dependence on intermediate vision, night vision-avoid multifocal
- In low myopes-used to excellent unaided reading vision that will be difficult to match with multifocal
- Degree of cataract not corresponding to vision-look for other pathology
- Astigmatism - Toric IOL

Dilated evaluation

- Lens subluxation
- Any retinal pathology-need for future lasers-avoid premium IOL
- Need for preoperative OCT
- Anti-VEGF if needed can be combined with Phaco.

PHACOEMULSIFICATION IN SMALL PUPIL

Dr Rajesh Sinha, New Delhi

A well-dilated pupil is a gateway to a smooth, easy and rewarding cataract surgery.

How small is a small pupil?

- Any pupil of an inadequate size that the surgeon believes he might struggle with when performing the procedure.
- Any pupil of inadequate size in which you cannot see the movement of the tip of your instrument.
- A small pupil is managed by pupillary enlargement:
  - Pharmacological
  - Surgical – Synechiolysis, iris stretching, iris cutting and iris-retracting devices.

Remember

- You must see what you are doing.
- Minimize damage to ocular tissues.

News and Views

Amyloid Clumps: A Possible Cause of Brain Fog in COVID Patients

A team of international researchers from the Swinburne University of Technology and La Trobe University in Australia and Luxembourg University in Luxembourg has uncovered the cause of the neurological conditions seen in patients with long-COVID, such as brain fog. The study published in *Nature Communications* proposed that in patients diagnosed with long-COVID symptoms, fragments of proteins from the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus led to the formation of amyloid clumps in the brain. These clumps were similar to the amyloid structure found in neurodegenerative diseases such as Alzheimer's and Parkinson's.

Hence, to have a better understanding of the impact of these amyloid clumps, the team performed biochemical flow-cytometry assays to determine the mechanism of brain cell death triggered by the amyloids.

Long-COVID is marked by neurological symptoms, such as memory loss, sensory confusion, severe headaches and even stroke. The long-COVID symptoms can persist for months after the infection is over. "While there is evidence that the virus can enter the brain of infected people, the precise mechanisms causing these neurological symptoms are unknown," stated Dr Mirren Charnley, a Postdoctoral Researcher at Swinburne University.

(*Source: https://health.economictimes.indiatimes.com/news/diagnostics/study-reveals-possible-cause-of-long-covid-brain-fog/92679192*)

Experts Call for an Update on the Current Booster Policy

The BA.2.75, the new COVID-19 sublineage has been detected in India and is said to have unique mutations, which increase the risk of infection in people. With the emergence of the new Omicron sublineage, the experts are calling for an update in booster policy in India, citing that the current policy is not making the best use of evidence and available vaccine choices.

Experts who had earlier reviewed the Christian Medical College (CMC), Vellore data had decided against the mix and match regimen of vaccines. Mr Shahid Jameel, Virologist, University of Oxford stated that Covishield is far superior to Covaxin but India continues to use 3rd dose Covaxin in people who have been administered with 2 prior Covaxin doses. The immunity increases by 5 to 6 times when the booster dose is of the same vaccine as the first two doses. However, according to clinical data, a sharp increase in the antibody levels by 58 times has been seen, when the 3rd dose of Covishield is given after two doses of Covaxin.

Meanwhile, Mr Jameel added that several global data have shown that protein vaccines produce better results after two doses of the AstraZeneca (AZ) vaccine than the 3rd dose of the AZ vaccine.

(*Source: https://health.economictimes.indiatimes.com/news/policy/current-booster-policy-needs-to-be-updated-experts/92687425*)

Can Probiotics Improve Poor Vaginal Health?

A new study from The ReproHealth Research Consortium, Zealand University Hospital found that probiotics do not improve unhealthy vaginal flora when administered vaginally in a daily capsule to patients for 10 days before fertility treatment. Dr Ida Engberg Jepsen from The Fertility Clinic at Zealand University Hospital, Denmark, stated that the 'spontaneous' improvement rate observed among patients may provide grounds for a change in approach towards *in vitro* fertilization (IVF) timing. Based on the study result, more than a third (34%) of all women who took part in the trial showed an improvement between the trial period of a month to 3 months, regardless of whether they took a probiotic or not.

The study suggested that the likelihood of pregnancy in IVF can be affected by many factors, including the type of bacteria that naturally colonize the reproductive tract. However, no significant difference was observed between women in the treatment group and placebo/control group. On this basis, the authors suggested that it may be worthwhile to postpone fertility treatment among patients with an 'unfavorable' vaginal microbiome until a normal balance is achieved. Dr Jepsen explained that the study didn't show any improvement in the suboptimal vaginal microbiome in women taking vaginal lactobacilli probiotics. Hence, she concluded that the specific vaginal probiotic tested in this study did not affect the favorability of the vaginal microbiome before IVF.

Research has shown that pregnancy and live birth rates are higher among women whose vaginal microbiota is dominated by lactobacillus, a genus of lactic-acid-producing bacteria. Results showed that the vaginal microbiome improved by 40% in the placebo group and by 29% in those taking the lactobacillus probiotic. A similar profile was observed in the menstrual cycle. The researchers claimed that the numbers represent an insignificant difference and concluded that "the broad categorization of the vaginal microbiome profile may not capture more subtle changes that could affect fertility".

(*Source: https://www.hindustantimes.com/lifestyle/health/study-shows-that-probiotics-are-inefficient-in-improving-poor-vaginal-health-101657001364774.html*)

Study Shows Krabbe Disease is Linked with the Degeneration of Neurons

In a new study conducted by Shin et al, it was reported that the gene defect underlying Krabbe disease causes degeneration of neurons directly, independent of its effects on other cell types. The study suggested that neurons may be affected independently; however, the hypothesis was difficult to test, as galactosylceramidase (GALC) is expressed ubiquitously in the brain, and its disease-related loss occurs in all cell types. GALC is an enzyme that is active in the lysosomes, and its absence leads to the build-up of the lipid psychosine. During an experimental study in a mouse model, there was no loss of oligodendrocytes, but lack of neuronal GALC expression did lead to a reduction in myelination, presumably through toxic effects on myelin sheaths from the accumulated psychosine. The results indicated that neuronal expression of GALC is essential to maintain and protect neuronal function, independent of its effects on myelin-producing oligodendrocytes. The research team concluded that a lack of the enzyme in neurons may contribute directly to the pathogenesis of Krabbe disease and that therapies for the disease may need to address the absence of neuronal expression of GALC in order to be fully effective. Mr Shin added that "Our study is the first attempt in a preclinical live animal model to directly investigate the neuronal role of the Krabbe disease gene galactosylceramidase". On generating a neuron-specific mutant of Krabbe disease in a live mouse model, the researchers found an intrinsic neuronal role for the GALC enzyme, suggesting that neuronal GALC has a primary role in neuronal homeostasis. Thus, GALC-depleted neurons can cause Krabbe disease.

(Source: https://www.hindustantimes.com/lifestyle/health/krabbe-disease-causes-degeneration-of-neurons-directly-study-101657087387988.html)

Virginity Test is Unscientific and Discriminatory, Says NMC Panel

The National Medical Commission (NMC) has decided to teach students how virginity tests are unscientific, inappropriate and discriminatory, and how to appraise the court of the same if the court orders such a test in matrimonial dispute cases. The decision was taken by the expert panel constituted by Dr Aruna Vanikar, President of UG Medical Education Board of NMC, on the orders of the Madras High Court. The expert panel was initially formed to address the issues about the LGBTQIA+ community in the MBBS curriculum.

"Virginity test has been ordered by the courts across the country in various matrimonial disputes and doctors conducted it even though there was no scientific basis. This is the first time in the history of medical education that medical undergraduate students will be taught to appraise courts about the unscientific basis of any test/signs if the court orders so. Henceforth, medical students across the country will be taught about the unscientific basis of virginity tests," explained Dr Khandekar, Professor of Forensic Medicine, MGIMS, Sevagram, who was part of the expert panel.

Dr Khandekar added that "There is no scientific way by which one can know whether the girl is virgin or not, similar to a male, whose signs of virginity were never mentioned in any medical book till date". Dr Khandekar also clarified the reason for not removing the topic from the curriculum by stating that "from the academic perspective, this topic is very crucial". However, he also added that the textbooks from the new academic year will have an additional disclaimer paragraph and reasons behind doing away with such unscientific practice.

(Source: https://www.mid-day.com/mumbai/mumbai-news/article/virginity-test-unscientific-discriminatory-says-national-medical-commission-23234583)

Skin Reaction Associated with COVID-19 Vaccines

Local injection site reactions are the most common skin reaction associated with COVID-19 vaccines, according to results of a large Spanish study, reported in the *British Journal of Dermatology*.[1] The study also identified six most common patterns of skin reactions.

A multicenter observational study was conducted with the aim to describe the clinical features of skin reactions following vaccination with any COVID-19 vaccine. All patients who had been vaccinated and developed a skin reaction within 21 days of receiving a vaccine dose, between February 16 and May 15, 2021, were enrolled

in the study. Their mean age was 50.7 years and the majority of participants were female (80.2%). An online survey was used to gather information about the skin reactions and clinical images of the skin lesions were procured via email. Patients in whom a cause could be identified and those who had injection-site reactions for less than 3 days were excluded from the study.

A total of 405 post-vaccine skin reactions were collated. Of these, 40.2% had occurred after taking the Pfizer-BioNTech vaccine, 36.3% after vaccination with Moderna vaccine, while 23.5% skin reactions were reported after the AstraZeneca vaccine.

Six major groups of skin reactions were identified: local injection site reactions or "COVID arm" (32.1%), urticaria and/or angioedema (14.6%), morbilliform rash (~9%), papulovesicular or pseudovesicular (6.4%), pityriasis rosea-like (~5%) and purpuric rashes (4%). Around 14% of skin reactions were reactivation of varicella zoster and herpes simplex virus. COVID arm was most commonly reported among women (95.4%).

When the skin reactions were categorized according to the vaccine, the most frequent skin reaction in the Moderna vaccine group was COVID arm (62%); in the Pfizer-BioNTech group, varicella zoster virus reactivation was the most common cutaneous reaction (17%), while urticaria was the commonest skin reaction encountered in the AstraZeneca group (21.1%). Most were self-resolving, while 21% were severe and very severe and 81% needed treatment.

This study has characterized the skin reactions associated with three COVID-19 vaccines. While the majority were mild to moderate in severity, few of them were severe to very severe, which required treatment. Awareness about these associations may help physicians to anticipate these skin reactions and reassure patients.

Ref: *[1]Català A, et al. Cutaneous reactions after SARS-CoV-2 vaccination: a cross-sectional Spanish nationwide study of 405 cases. Br J Dermatol. 2022;186(1):142-52.*

Gurgaon Increases Testing and Surveillance for Dengue and Malaria Cases in the City

The Gurgaon Health Department on 6th July ordered all the private hospitals to build-up a separate ward for dengue and swine flu patients as a preventative measure to tackle the anticipated surge in dengue and malaria cases in the city. Five beds each would be set aside by the government hospitals in Pataudi and Sohna for dengue patients. Additionally, 25 beds at Sector 10's Civil Hospital were set aside exclusively for dengue and malaria cases in the city in the days to come.

As diseases like dengue, malaria and swine flu are predicted to spread due to the increased humidity, the health authority has asked all hospitals to collect samples from their designated flu corners, where persons with symptoms will be tested. Additionally, there are 257 foggers in the city. In dengue clusters, the teams will check every home to ensure no breeding occurs. Doctors have requested people to take essential safety measures during the monsoon and call a health center right away if they are experiencing high temperature, nausea, joint and muscular discomfort, a red rash on their skin or extreme exhaustion. (*Source: Times of India, July 7, 2022*)

Asymptomatic COVID-19 Cases on Rise, Indicating Silent Community Transmission

According to government officials, 80% of the COVID-19 positive cases are asymptomatic and anticipated to rise in the upcoming weeks. According to experts, cases will keep rising until the Omicron subvariants BA.2.12.1, BA.4 and BA.5 become prominent. Therefore sticking to the COVID regimen is advised, particularly wearing an N-95 mask, being vaccinated, immediate isolation if tested positive and getting tested in case of suspected symptoms.

Currently, since the majority of cases are mild to moderate, symptoms usually go away 3 to 4 days after they first appear, and people recover in about 7 days.

The general director of Continental Hospitals in Hyderabad stated that community transmission was occurring silently and at a passive level. As more people stopped taking precautions after receiving their booster doses, the number of cases is increasing. The fact that the majority of patients are not informed of their COVID status and are maintaining an active social life was also contributing to the increase. (*Source: Times of India, July 7, 2022*)

Primary Cesarean Rates Increased in Recent Years

A CDC (Centers for Disease Control and Prevention) report stated that the growth in first-time C-section patients over the past few years has contributed to an increase in Cesarean deliveries in the US.

Women of all ages underwent more primary C-sections between 2019 and 2021, with the cesarean rate reaching 22.4% in that year. Primary cesarean rates rose by 4% among women in their 20s, 2% among those in their 30s to 34s and 1% among those in their 35s to 39s. But from 2016 to 2021, the annual repeat cesarean rate, which includes individuals who undergo numerous surgeries, declined gradually by about 1% (87.6-85.9%).

The National Vital Statistics System was used to collect the birth certificate data which is included in this CDC report. Further, it was observed that 97% of C-sections are medically necessary; hence, the study paves a way for the experts to understand the reason behind the increasing rate of primary C-sections. (*Source: MedPage Today, July 6, 2022*)

New Approach for Reducing Inflammation and Preventing Repigmentation in Vitiligo Patients

A new study published in the journal *JCI Insight* revealed that cell-to-cell communication networks could perpetuate irritation and help to prevent repigmentation in patients with vitiligo disease. The study was conducted by a group of researchers from the University of California, Irvine. The study "Multimodal Analyses of Vitiligo Skin Identifies Tissue Characteristics of Stable Disease" combined non-invasive multiphoton microscopy (MPM) imaging and single-cell RNA sequencing (scRNA-seq) to identify distinct subpopulations of keratinocytes in the lesional skin of stable vitiligo patients along with the changes in cellular compositions in stable vitiligo skin that result in a persistent disease condition.

Vitiligo is an autoimmune skin disease characterized by the progressive death of mature melanin-forming cells in the skin by immune cells known as autoreactive CD8 T cells, resulting in disfiguring patches of white depigmented skin. Several studies have linked vitiligo to considerable psychological discomfort in sufferers. Dr Jessica Shiu, MD, PhD, Assistant Professor of Dermatology and one of the authors of the study, stated that the role of CD8 T cells implicated in the death of melanocytes in active vitiligo was unknown, along with a lack of adequate instruments that made it difficult to analyse the interaction between immune cells, melanocytes and keratinocytes *in situ* in human skin till now.

"In this study, we coupled advance imaging with transcriptomics and bioinformatics to discover the cell-to-cell communication networks between keratinocytes, immune cells and melanocytes that drive inflammation and prevent repigmentation caused by vitiligo," stated Mr Anand K Ganesan, MD, PhD, Professor of Dermatology and Vice-Chair for Dermatology Research at the UCI School of Medicine.

(*Source: https://www.hindustantimes.com/lifestyle/health/new-way-to-reduce-inflammation-and-prevent-repigmentation-in-vitiligo-patients-study-101657175368741.html*)

Study Relates the Demise of a Loved One with an Increased Risk of Heart Failure

According to a new study, heart failure (HF) patients who are in grief or mourning after the death of a close family member are at an elevated risk of death, especially in the first week after death. Many studies have been undertaken to confirm the link between Takotsubo cardiomyopathy (popularly known as "broken heart syndrome") and extreme emotional stress.

According to the study's author, grief may activate the hypothalamic-pituitary-adrenal (HPA) axis, a critical neuroendocrine system that governs stress and emotional reaction. According to scientists, it may also cause a reaction in the renin-angiotensin-aldosterone system (RAAS) and the sympathetic nervous system, which are both important components of the neuroendocrine response in HF. Mr Hua Chen, the lead author of the study and a doctoral student at Karolinska Institutet in Stockholm, Sweden, stated, "the association between bereavement and mortality was not only observed in cases of loss due to cardiovascular disease and other natural causes but also in cases of unnatural deaths."

The relationship between bereavement and increased HF mortality risk was detected after the death of a child (10% increased risk), spouse/partner (20% increased risk), grandchild (5% increased risk) or sibling (13%), but not after the death of a parent. The risk of dying from HF after the death of any family member was highest during the first week of bereavement (78% increased risk), especially if the death was of a child (31% increased risk) or spouse/partner (113% increased risk); it was also higher in the case of two losses (35% increased risk) compared to one loss (35% increased risk).

(*Source: https://www.hindustantimes.com/lifestyle/health/death-of-a-family-member-may-increase-heart-failure-mortality-risk-101657175835655.html*)

ADHD and ASD Linked with Early Childhood Allergies

A study published in the journal *Pediatric Allergy and Immunology* suggested that young children with allergies are more likely to develop attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD) by the time they are 18. Dr Shay Nemet, MD, of the Kaplan Medical Center in Rehovot, Israel, and the lead author of the retrospective study, stated that the study provides strong evidence for the association between allergic disorders in early childhood and the development of ADHD. In the study, children who were diagnosed with one or more allergies between the ages of 0 to 9 years were found to be at a significantly

higher risk of developing ADHD (odds ratio [OR], 2.45), ASD (OR, 1.17), or both ADHD and ASD (OR, 1.56) than the children in the control group who did not have any allergies. Also, it was observed that the children diagnosed with rhinitis and conjunctivitis were the most likely to develop ADHD. Dr Jordan, MD, FAAP, an Assistant Professor of Pediatrics at UPMC Children's Hospital of Pittsburgh, Pennsylvania, stated that the study has shown a statistically significant correlation between ADHD, ASD and allergic conditions. However, the study's retrospective design and the possibility of recall bias are the major limitations of the study that can impact the study findings.

(*Source: https://www.medscape.com/viewarticle/976705*)

DCGI Approves Viralex for COVID-19 and Viral Respiratory Infections

Viralex, a drug consisting of Inosine Pranobex, has been approved by the Drugs Controller General of India (DCGI) as an effective and safe drug for the management of mild to moderate COVID-19 and other acute viral respiratory infections. A multi-center, double-blind, randomized, placebo-controlled clinical trial was conducted during the Delta wave of COVID-19. The trial showed early improvement and complete relief from mild to moderate COVID-19 symptoms. The drug developed by Themis Medicare has been approved by the DCGI for the treatment of influenza and other acute viral respiratory infections (AVRI), including COVID-19, mucocutaneous herpes, genital warts and subacute sclerosing panencephalitis (SSPE).

Inosine Pranobex is an immunomodulatory and antiviral agent that bolsters the body's defenses against viral infections by enhancing both innate and adaptive immunity. The medicine is also useful for patients with severe comorbidities and suppressed immunity due to its dual mode of action. The drug is an oral medication (500 mg tablet) available only on a prescription from a registered medical practitioner.

(*Source: https://health.economictimes.indiatimes.com/news/pharma/dcgi-approved-themis-medicares-viralex-effective-against-covid-19-viral-respiratory-infections/92727299*)

Pre-headache Symptoms of Migraine

More than 80% of people who suffer from migraine have some pre-headache symptoms warning them of the impending headache, according to a study presented at the American Headache Society 64th Annual Scientific Meeting and also published in the journal *Headache*.[1]

For the present study, researchers enrolled 12,810 participants with migraine from the Chronic Migraine Epidemiology and Outcomes (CaMEO) Study with the objective to describe the common pre-headache symptoms of migraine attacks. A pre-identified list was used to document feelings or warning of headache as reported by the participants. Pre-headache features that are not regarded as warning symptoms were also recorded.

A total of 10,800 (84.3%) had a minimum of one pre-headache and nearly 60% (n = 6129; 56.7%) viewed them as a warning symptom for an oncoming headache. More than half (51.2%) of these reported neck pain or stiffness as a pre-headache warning symptom. The other pre-headache warning symptoms were vision problems (49.2%), feeling dizzy or light-headed (41.3%), difficulty thinking or concentrating (39.6%), feeling irritable or moody (36.4%) and feeling tired or weary (32.5%). Forty-nine percent of those who reported visual problems also reported experiencing aura. The prevalence of moderate to severe anxiety or depression and interictal burden was also higher in them.

The symptoms of neck pain, vision problems, dizziness and difficulty in concentration or thinking were common between the two groups, i.e., those who considered these as warning symptoms and those who did not. Participants who reported 15 or more monthly headache days were more likely to report a warning symptom than those who had monthly headache days ranging between 0 and 3; 57.5% vs. 43.4%, respectively.

The first phase in a migraine attack is the prodrome; the phases of aura, headache and post-drome follow. The prodrome phase is also known as the pre-headache phase. People who suffer migraines often experience warning or pre-headache symptoms, but not all are aware of them as portending a headache. Recognition of these symptoms enables quick institution of treatment to either reduce the severity of headache or prevent it altogether.

Ref: *[1]Schwedt TJ, et al. P-10. Characterizing pre-headache (prodrome) features of migraine attacks: results from the CaMEO study. Headache. 2022;62(Suppl 1):11.*

Why Do We Light a Lamp During Puja?

Prayer

|| Deepajyothi Parabrahma

Deepa Jyotir Janaardanah

Deepo Harati Paapaani

Sandhyaa Deepa Namostute ||

"I prostrate to the dawn/dusk lamp; whose light is the Knowledge Principle (the Supreme Lord), which removes the darkness of ignorance and by which all can be achieved in life."

Light symbolizes knowledge, and darkness, ignorance. Knowledge removes ignorance just as light removes darkness. The purpose of any ritual is to remove internal darkness and attain knowledge.

Vedic scriptures recommend daily lighting of the lamp as a part of puja. Some do it once at dawn, others twice a day – at dawn and dusk – and some keep a lamp that is always lit (akhanda deepa). No auspicious function can commence without the lighting of a lamp.

Knowledge is the everlasting inner wealth by which all outer achievement can be accomplished. By lighting the lamp, we bow to knowledge as the greatest of all forms of wealth. Knowledge about the self is the greatest wealth. It goes around achieving inner happiness by burning the negativity of a mind that is full of lust and ego.

The traditional oil lamp defines this spiritual significance. The oil or ghee symbolizes our vaasanas (lust, negative tendencies) and the wick, the ego. When lit by spiritual knowledge, the vaasanas get slowly exhausted and the ego too finally perishes. The flame of a lamp always burns upwards signifying that the only that knowledge should be acquired, which takes us towards higher ideals.

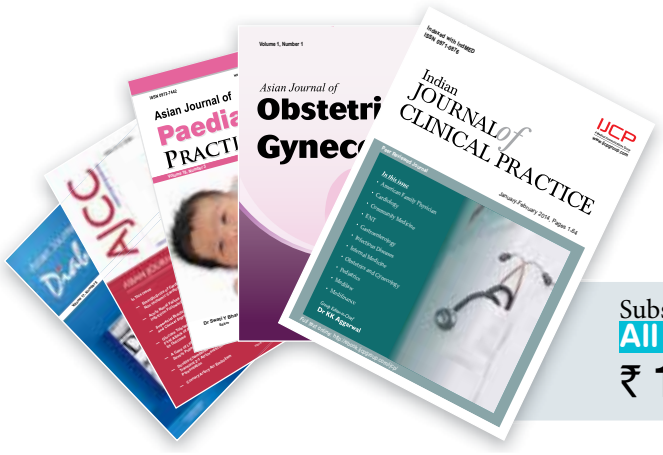
■■■■

ABHA Card will Enhance Prompt Response to Patients

Ayushman Bharat Health Account (ABHA) identity cards were introduced by the Directorate of Health Services (DHS), GVK EMRI (Emergency Management and Research Institute) 108 health services in Panaji on 15th July 2022. According to Mr Vishwajit Rane, the Health Minister, those who have used the 108 ambulance services can create "ABHA" health cards from employees working for the ambulance service. The Ayushman Bharat digital mission of the Indian government includes a statewide program called the ABHA health ID cards to build the foundation for the nation's integrated digital health infrastructure. An official from GVK EMRI stated that the cards will be generated for patients after they get critical treatment. Their ABHA card will be created with the help of an ambulance attendant and will be linked to all hospitals and make the patient's medical records available digitally. The patient information in the ABHA card will help to respond to patients more quickly and help the ambulance staff to know the patient's exact location which will be available through a mobile app. Further, ABHA cards will also be linked to Aadhaar, hence carrying their Aadhaar cards while using the ambulance service was necessary. (*Source: Times of India, Jul 16, 2022*)

Dementia Risk Increases in Elderly Patients Above 65 with Hypothyroidism

A study published in *Neurology* found that dementia risk may be much higher in older persons with a history of hypothyroidism. The study enrolled 15,686 patients with a female predominance in both the case and control (4,066 [51.8%]). For individuals who had dementia, the mean (SD) age was 74.9 (11.3) years. The experts found that individuals 65 years of age or older with a history of hypothyroidism who were taking hypothyroidism medication showed the strongest connection with an increased risk of being diagnosed with dementia. Further, it was observed that individuals older than 50 but younger than 65 and have a history of hypothyroidism were not linked to an elevated risk of dementia diagnosis. The researchers concluded that more research is required to support these findings; people should be informed that thyroid issues increase the risk factor for dementia, and also about the available medications which could slow this irreversible cognitive loss. (*Sources: MedPage Today July 6, 2022; Neurology 2022; DOI: 10.1212/WNL.0000000000200740.*)



IJCP
A Medical Communications Group

Subscription Form

Jan-Dec 2022

Subscribe to **All Journals** ₹ 10,500/-

SAVE ₹ 500/-

Special Discount on Institutional Packages

Yes, I am interested in subscribing to the *Institutional Combo package for one year (Institutional) ☐

Yes, I am interested in subscribing to the following journal(s) for one year (Institutional) ☐ (individual) ☐

JOURNALS	ISSUES	INSTITUTIONAL (₹ Amount)	INDIVIDUAL (₹ Amount)
Indian Journal of Clinical Practice	12	5,000/- ☐	1,650/- ☐
Asian Journal of Clinical Cardiology	4	1,500/- ☐	NA
Asian Journal of Diabetology	4	1,500/- ☐	NA
Asian Journal of Obs & Gynae Practice	4	1,500/- ☐	NA
Asian Journal of Paediatric Practice	4	1,500/- ☐	NA

Payment Information

Name: .....

Speciality: .....

Address: .....

.....

Country: ..... State: .....

Pincode: .....

Telephone: ..... Mobile: .....

E-mail: .....

Total ₹11,000/- for 1 year

Pay Amount: .....

Dated (dd/mm/yyyy): .....

Cheque or DD No.: .....

Drawn on Bank: .....

Cheques/DD should be drawn in favor of "M/s IJCP Publications Ltd."

IJCP
A Medical Communications Group

Mail this coupon to (HO):

IJCP Publications Ltd.

Head office: 3rd Floor, 39 Daryacha, Hauz Khas Village, New Delhi - 110 016

Telefax: 40587513 Mob.: 9891272006 E-mail: subscribe@ijcp.com

Website: www.ijcpgroup.com

We accept payments by Cheque/DD only, Payable at New Delhi. Do not pay Cash.

Online subscription: http://subscription.ijcpgroup.com/Default.aspx

Lighter Side of Medicine

INSPIRATIONAL STORY

20 WORDS TO THE WISE

1. God wants spiritual fruit, not religious nuts.
2. Dear God: I have a problem. Sometimes, it's me.
3. Growing old is inevitable, growing up is optional.
4. There is no key to happiness. The door is always open.
5. Silence is often misinterpreted, but never misquoted.
6. Do the math. Count your blessings.
7. Faith is the ability to not panic.
8. Laugh every day, it's like inner jogging.
9. If we worry, we probably didn't pray. If we pray, we probably don't worry.
10. As a child of God, prayer is kind of like calling home every day.
11. Blessed are the flexible, for they shall not be bent out of shape.
12. The most important things in our homes are the people.
13. When we get tangled up in our problems, be still. God wants us to be still so He can untangle the knots for us.
14. A grudge is a heavy thing to carry.
15. He who dies with the most toys is still dead. And who knows where he has gone?
16. We do not remember days, but moments. Life moves too fast, so enjoy your precious moments.
17. Nothing is real to you until we experience it, otherwise it's just hearsay.
18. It's all right to sit on our pity pot every now and again. Just be sure to flush when you are done.
19. Surviving and living our life successfully requires courage. The goals and dreams we seek require courage and risk-taking. Learn from the turtle — it only makes progress when it sticks out its neck.
20. Be more concerned with your character than your reputation, because your character is what you really are, while your reputation is merely what others think you are.

HUMOR

SALES PRACTICE

The out-of-work newlywed took a temporary job as a vacuum cleaner salesman to make ends meet. After 3 days of intensive training, the sales manager told him to go home and practice his pitch on his wife.

The next morning, the manager asked the novice how he made out.

"Well," the man began, "I did what you said, and after I finished, I asked her if she would buy the vacuum cleaner from me. She said 'Yes.' Then I asked her 'Why?' She replied, 'Because I love you.'"

TELL HIM I CAN'T SEE HIM

While he was talking to me, his nurse came in and said, "Doctor, there is a man here who thinks he's invisible."

The doctor said, "Tell him I can't see him."

Dr. Good and Dr. Bad

SITUATION: A woman with GDM was recently diagnosed with hypertension.

LESSON: Hypertension among women with GDM enhances the risk of macrosomia at birth and childhood overweight and obesity. Thus, it is important to control maternal hypertension in order to prevent large-for-gestational-age babies and childhood obesity.

J Hum Hypertens. 2017;31(11):731-6.

Talking Point Communications

-A Unit of the IJCP Group of Medical Communications

Brand
Launches

Start-Up
Profiling

Celebrity
Coordination

Conferences
Events

New product
& Service Launches

Media
Outreach

CEO/Leadership
Profiling

Digital
Marketing

Reputation
Management

HEART CARE FOUNDATION OF INDIA · MTNL Perfect Health Mela Since 1993 · APHRS · DR. REDDY'S · translumina therapeutics · IIC SUMMIT 2014 · afgc

For More Information call: 9582363695, E-mail naina.a@talkingpointcommunications.com
Website: http://talkingpointcommunications.com

Indian
JOURNAL of
CLINICAL PRACTICE

Information for Authors

Manuscripts should be prepared in accordance with the 'Uniform requirements for manuscripts submitted to biomedical journals' compiled by the International Committee of Medical Journal Editors (Ann. Intern. Med. 1992;96: 766-767).

Indian Journal of Clinical Practice strongly disapproves of the submission of the same articles simultaneously to different journals for consideration as well as duplicate publication and will decline to accept fresh manuscripts submitted by authors who have done so.

The boxed checklist will help authors in preparing their manuscript according to our requirements. Improperly prepared manuscripts may be returned to the author without review. The checklist should accompany each manuscript.

Authors may provide on the checklist, the names and addresses of experts from Asia and from other parts of the World who, in the authors' opinion, are best qualified to review the paper.

Covering letter

- The covering letter should explain if there is any deviation from the standard IMRAD format (Introduction, Methods, Results and Discussion) and should outline the importance of the paper.
- Principal/Senior author must sign the covering letter indicating full responsibility for the paper submitted, preferably with signatures of all the authors.
- Articles must be accompanied by a declaration by all authors stating that the article has not been published in any other Journal/Book. Authors should mentioned complete designation and departments, etc. on the manuscript.

Manuscript

- Three complete sets of the manuscript should be submitted and preferably with a CD; typed double spaced throughout (including references, tables and legends to figures).
- The manuscript should be arranged as follow: Covering letter, Checklist, Title page, Abstract, Keywords (for indexing, if required), Introduction, Methods, Results, Discussion, References, Tables, Legends to Figures and Figures.
- All pages should be numbered consecutively beginning with the title page.

Note: Please keep a copy of your manuscript as we are not responsible for its loss in the mail. Manuscripts will not be returned to authors.

Title page

Should contain the title, short title, names of all the authors (without degrees or diplomas), names and full location of the departments and institutions where the work was performed, name of the corresponding authors, acknowledgment of financial support and abbreviations used.

- The title should be of no more than 80 characters and should represent the major theme of the manuscript. A subtitle can be added if necessary.
- A short title of not more than 50 characters (including inter-word spaces) for use as a running head should be included.
- The name, telephone and fax numbers, e-mail and postal addresses of the author to whom communications are to be sent should be typed in the lower right corner of the title page.
- A list of abbreviations used in the paper should be included. In general, the use of abbreviations is discouraged unless they are essential for improving the readability of the text.

Summary

- The summary of not more than 200 words. It must convey the essential features of the paper.
- It should not contain abbreviations, footnotes or references.

Introduction

- The introduction should state why the study was carried out and what were its specific aims/objectives.

Methods

- These should be described in sufficient detail to permit evaluation and duplication of the work by others.
- Ethical guidelines followed by the investigations should be described.

Statistics

The following information should be given:

- The statistical universe i.e., the population from which the sample for the study is selected.
- Method of selecting the sample (cases, subjects, etc. from the statistical universe).
- Method of allocating the subjects into different groups.
- Statistical methods used for presentation and analysis of data i.e., in terms of mean and standard deviation values or percentages and statistical tests such as Student's 't' test, Chi-square test and analysis of variance or non-parametric tests and multivariate techniques.
- Confidence intervals for the measurements should be provided wherever appropriate.

Results

- These should be concise and include only the tables and figures necessary to enhance the understanding of the text.

Discussion

– This should consist of a review of the literature and relate the major findings of the article to other publications on the subject. The particular relevance of the results to healthcare in India should be stressed, e.g., practicality and cost.

References

These should conform to the Vancouver style. References should be numbered in the order in which they appear in the texts and these numbers should be inserted above the lines on each occasion the author is cited (Sinha[12] confirmed other reports[13,14]...). References cited only in tables or in legends to figures should be numbered in the text of the particular table or illustration. Include among the references papers accepted but not yet published; designate the journal and add 'in press' (in parentheses). Information from manuscripts submitted but not yet accepted should be cited in the text as 'unpublished observations' (in parentheses). At the end of the article the full list of references should include the names of all authors if there are fewer than seven or if there are more, the first six followed by et al., the full title of the journal article or book chapters; the title of journals abbreviated according to the style of the Index Medicus and the first and final page numbers of the article or chapter. The authors should check that the references are accurate. If they are not this may result in the rejection of an otherwise adequate contribution.
Examples of common forms of references are:

Articles

Paintal AS. Impulses in vagal afferent fibres from specific pulmonary deflation receptors. The response of those receptors to phenylguanide, potato S-hydroxytryptamine and their role in respiratory and cardiovascular reflexes. Q. J. Expt. Physiol. 1955;40:89-111.

Books

Stansfield AG. Lymph Node Biopsy Interpretation Churchill Livingstone, New York 1985.

Articles in Books

Strong MS. Recurrent respiratory papillomatosis. In: Scott Brown's Otolaryngology. Paediatric Otolaryngology Evans JNG (Ed.), Butterworths, London 1987;6:466-470.

Tables

– These should be typed double spaced on separate sheets with the table number (in Roman Arabic numerals) and title above the table and explanatory notes below the table.

Legends

– These should be typed double spaces on a separate sheet and figure numbers (in Arabic numerals) corresponding with the order in which the figures are presented in the text.

– The legend must include enough information to permit interpretation of the figure without reference to the text.

Figures

– Two complete sets of glossy prints of high quality should be submitted. The labelling must be clear and neat.

– All photomicrographs should indicate the magnification of the print.

– Special features should be indicated by arrows or letters which contrast with the background.

– The back of each illustration should bear the first author's last name, figure number and an arrow indicating the top. This should be written lightly in pencil only. Please do not use a hard pencil, ball point or felt pen.

– Color illustrations will be accepted if they make a contribution to the understanding of the article.

– Do not use clips/staples on photographs and artwork.

– Illustrations must be drawn neatly by an artist and photographs must be sent on glossy paper. No captions should be written directly on the photographs or illustration. Legends to all photographs and illustrations should be typed on a separate sheet of paper. All illustrations and figures must be referred to in the text and abbreviated as "Fig.".

Please complete the following checklist and attach to the manuscript:

1. Classification (e.g. original article, review, selected summary, etc.)_____
2. Total number of pages _____
3. Number of tables _____
4. Number of figures _____
5. Special requests _____
6. Suggestions for reviewers (name and postal address)

Indian	Foreign
1. _____	1. _____
2. _____	2. _____
3. _____	3. _____
4. _____	4. _____

7. All authors' signatures_____
8. Corresponding author's name, current postal and e-mail address and telephone and fax numbers _____

Online Submission
Also e-Issue @ www.ijcpgroup.com

For Editorial Correspondence

Indian Journal of Clinical Practice
3rd Floor, 39 Daryacha, Hauz Khas Village
New Delhi - 110 016. Tel: 40587513
E-mail: editorial@ijcp.com Website: www.ijcpgroup.com

Indian JOURNAL of CLINICAL PRACTICE

Indian Citation Index (ICI),

IndMed (http://indmed.nic.in/)

MedIND (http://medind.nic.in/)

University Grants Commission (20737/15554).

ISSN number 0971-0876

RNI number 50798/1990.

The Medical Council of India (UGC, ICI)

Indian Journal of Clinical Practice is published by the IJCP Group. A multispecialty journal, it provides clinicians with evidence-based updated information about a diverse range of common medical topics, including those frequently encountered by the Indian physician to make informed clinical decisions. The journal has been published regularly every month since it was first launched in June 1990 as a monthly medical journal. It now has a circulation of more than 3 lakh doctors.

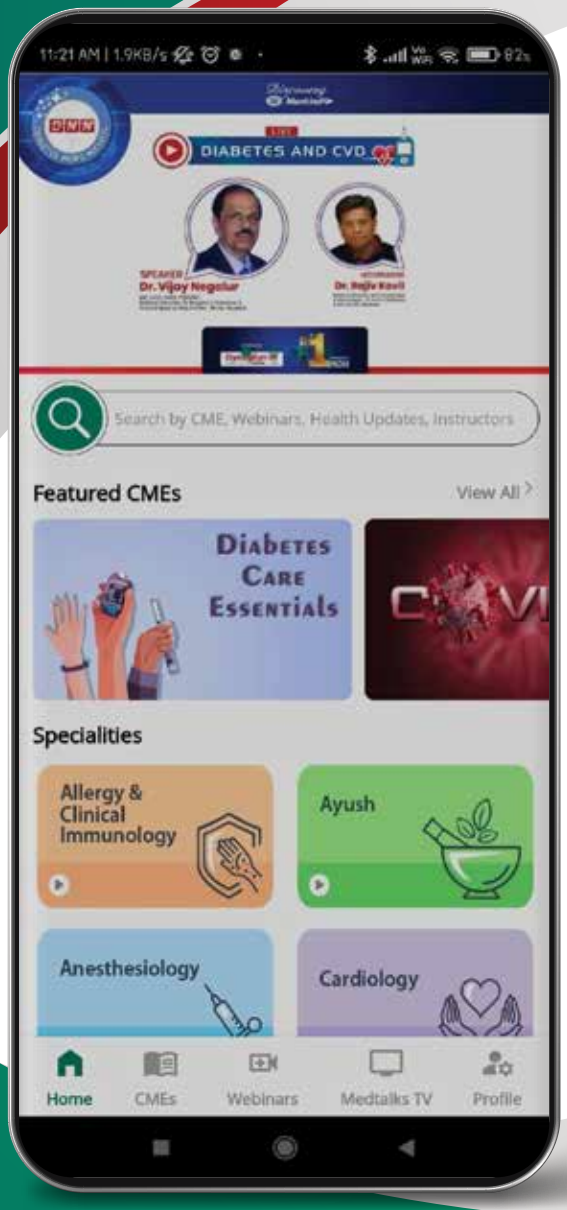
IJCP is a peer-reviewed journal that publishes original research, reviews, case reports, expert viewpoints, clinical practice changing guidelines, Medilaw, Medifinance, Lighter side of medicine and latest news and updates in medicine. The journal is available online (http://ebook.ijcpgroup.com/Indian-Journal-of-Clinical-Practice-January-2018.aspx) and also in print. IJCP can now also be accessed on a mobile phone via App on Play Store (android phones) and App Store (iphone). Sign up after you download the IJCP App and browse through the journal.

IJCP is indexed with Indian Citation Index (ICI), **IndMed** (http://indmed.nic.in/) and is also listed with **MedIND** (http://medind.nic.in/), the online database of Indian biomedical journals. The journal is recognized by the University Grants Commission (20737/15554). The Medical Council of India (MCI) approves journals recognized by UGC and ICI. Our content is often quoted by newspapers.

The journal **ISSN number** is 0971-0876 and the **RNI number** is 50798/1990.

If you have any Views, Breaking news/article/research or a rare and interesting case report that you would like to share with more than 3 lakh doctors send us your article for publication in IJCP at editorial@ijcp.com.

MEDtalks®
Discover. Learn. Discuss



CMEs
Develop and increase Knowledge and Professional Skills

MEDTALKS TV
Discussions focused on Healthcare Awareness & Treatment

CONFERENCES
Get updates about Medical Conferences in your area.

MEDBYTES
Medical and Healthcare Education

WEBINAR
Live Webinars by renowned Doctors

DOWNLOAD
Play Store

A Video Education Platform
www.medtalks.in

R.N.I. No. 50798/1990
Date of Publication 13th of Same Month
Date of Posting 13-14 Same Month

POSTAL REGISTRATION NO. DL(S)-01/3200/2021-2023
POSTED AT LPC DELHI RMS DELHI-110006

MediNexus

India's Premier Doctor Network

Free Registration

1,00,000+
REGISTERED DOCTORS

- Learn with **Interactive Clinical Content**
- Access the **Last 24 Hours in Medicine**
- **Live Conference Updates**

Instructions for App Download

1. Download eMediNexus from Play Store/iOS Store

2. After opening the app click on Register

3. Enter your details

4. Read the updates and leave your comments

Google play | Available on the App Store

www.emedinexus.com

3rd Floor, 39 Daryacha,
Hauz Khas Village, New Delhi - 110 016
Mob.: +91-9818 4212 22 | E-mail: nilesh@emedinexus.com