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Dr KK Aggarwal
Group Editor-in-Chief, IJCP Group

"In the Path of Wellness, One Health will be My Priority this Year"

The 34th CMAAO General Assembly and 55th Council Meeting

Dear Colleague

On September 5, I took over as the President of CMAAO for the year 2019-20 during the 34th CMAAO General Assembly held in Goa.

Here are excerpts from my speech delivered on the occasion.

"Coming to a General Assembly of CMAAO, the confederation of 19 National Medical Associations in Asia and Oceania feels like homecoming and a reunion of family as it resonates with my philosophy of life as a student of Vedic literature.

"*Vasudhaiva Kutumbakam*" is a Sanskrit Vedic saying from the Rig Veda, considered the oldest of our ancient texts, which means "the whole world is my family."

The complete verse from Rig Veda is as under:

अयं निजः परो वेति गणना लघुचेतसाम् |
उदारचरितानां तु वसुधैव कुटुम्बकम् ||

"*Ayam nijo paro veti ganana laghuchetasam,*
Udaracharitanam tu vasudhaiva kutumbakam"

"यह मेरा है, यह उसका है; ऐसी सोच संकुचित चित्त वोले व्यक्तियों की होती है; इसके विपरीत उदारचरित वाले लोगों के लिए तो यह सम्पूर्ण धरती ही एक परिवार जैसी होती है ।"

The English translation of this is "for narrow-minded people, things belong to him or others, but a person with a broad mind does not differentiate. For him the universe is a big family, so everybody belongs to one family where everything is shared."

Most religions also propound the same philosophy.

Carl Gustav Jung, the Founder of Analytical Psychology, classified this under the category of archetypal experience of "Unus Mundus", which is Latin for "one world".

"Vasudhaiva Kutumbakam" imparts the basic message of unconditional love and oneness of the soul. Without the soul, a person would be like an outcast.

"I am not my physical body, as I know, once my body dies, nobody wants to touch it" (Adi Shankaracharya in the Bhaja Govindam). Such is the significance of soul that the wife who all her life has loved her husband does not even want to touch his body after the soul has left (Bhaja Govindam Sutra 3).

"Vasudhaiva Kutumbakam" (the whole world is one family, where you and I carry the same spirit) together with another saying "*Ekam sat viprah bahudevanti*" (truth is one and the wise may call it by different names) forms the basis of Vedanta.

The six "*Maha-vakyas*" or the "Great Sayings" are the essence of the teachings of the Upanishads.

"Tat Tvam Asi" or "You are that" is one of the six "*Maha-vakyas*". It comes from the Chandogya Upanishad in Samveda and signifies that the consciousness present in you is similar to the consciousness present in me. And, if the same consciousness lies in you, me and others, this means that we are part of the same family.

So, if the aforesaid is true and if the whole world is one, then it is also true that the same consciousness is also present in the environment, plants, animals and birds. This is in harmony with the concept of One Health, which recognizes that the health of the people is connected to the health of animals, plants and the environment that we all share.

"Yatha pinde tatha brahmande, yatha brahmande tatha pinde" is another Vedic Saying from the Yajur Veda, which means that as is the microcosm, so is the macrocosm. To put it simply, "as is the individual, so is the universe; as is the universe, so is the individual". In relation to health and science, this denotes that the human body is a replica of the universe.

So, in the path of wellness, "One Health" will be my priority this year.

Coming back to CMAAO, since it was established in 1956, the objective of CMAAO has been to promote academic exchange of information on health issues and also to cultivate ties of friendship between member medical associations.

Dr Gro Harlem Brundtland, the first woman Prime Minister of Norway and former Director-General of the World Health Organization (WHO) wrote in the European Journal of Public Health in 2005, *"**Public health challenges are no longer just local, national or regional.** They are global. They are no longer just within the domain of public health specialists. They are among the key challenges to our societies. They are political and cross-sectoral. They are intimately linked to environment and development. They are key to national, regional and global security."*

As an organization, we too share several public health challenges such as vector-borne diseases such as dengue, malaria; air pollution; communicable and non-communicable diseases (NCDs); antimicrobial resistance (AMR); tobacco use; HIV/AIDS, to name a few.

Violence against doctors and inequity in health are few other issues that are a concern. Attaining universal health coverage, which is affordable, accessible, available, appropriate and accountable, still remains a distant goal for many of us.

All these have a bearing on the socioeconomic progress of our countries. Therefore, it becomes our collective responsibility to make certain that these issues are prioritized. Some of these issues are global concerns and we should try to solve them as a family and set an example for the world. In the event of any outbreak or public health crisis, we can share our health models besides knowledge and experiences of a similar situation.

I will briefly touch upon few such issues:

THE CHALLLENGES

Antimicrobial Resistance

Antimicrobial resistance (AMR) is a major global public health threat. Common infections such as typhoid, pneumonia, tuberculosis and gonorrhea have become difficult to treat. It is now clear that only an intersectoral collaboration and action will help to contain the spread of AMR and its further emergence.

India has one of the highest burdens of AMR. It was the discovery of New Delhi metallo-β-lactamase 1 (NDM-1) in 2008, which catapulted AMR to the forefront in India.

Over the years, several steps have been taken to tackle the rising AMR crisis in the country. Most notable of these have been the setting up of a National Task Force on AMR Containment in 2010, the Jaipur Declaration in 2011, the Chennai Declaration in 2012, Red Line campaign in 2016 and more recently, the Delhi Declaration and a National Action Plan on AMR (NAP-AMR) in 2017.

In addition to the 5 priorities listed in the Global Action Plan on AMR (GAP-AMR), India's National Action Plan has a sixth priority that deals with strengthening India's leadership on AMR, including international, national and subnational collaborations.

The biggest reasons for the misuse of antibiotics are self-prescription and over-prescription. So, before prescribing antibiotics, always ask yourself: "Is antibiotic necessary? What is the most effective antibiotic? What is the most affordable antibiotic? What is the most effective dose? What is the most effective duration for which the antibiotic should be administered?"

Violence Against Doctors

Violence against doctors is not a new or recent phenomenon.

"No physician, however conscientious or careful, can tell what day or hour he may not be the object of some undeserved attack, malicious accusation, black mail or suit for damages…" These lines from an article published

more than a century ago in *JAMA (Assaults upon medical men. JAMA. 1892;18:399-400)* seemed to foretell what lay ahead.

Violence against doctors is now a grim reality and health workers are at high risk of violence all over the world. Health workers may also become the targets of collective or political violence in disaster and conflict situations.

A survey conducted by the Indian Medical Association (IMA) found that 75% of doctors in India have faced some kind of violence at their work place. Another IMA study showed that 68% of incidents of violence are caused by family members, friends or other persons accompanying the patient.

Violence against health workers is unacceptable and needs to be condemned by all, especially the general public who are direct stakeholders in this.

The Government of India is drafting a legislation on violence against doctors. According to the draft bill, violence against doctors is punishable with imprisonment and fine.

Autonomy of the Medical Profession

We cannot compromise with the autonomy of the medical profession, whether in clinical practice or in institutions.

Noncommunicable Diseases

Noncommunicable diseases (NCDs), mainly cardiovascular diseases, diabetes, chronic respiratory diseases and cancer, are the major cause of death in the South-East Asia Region (SEAR). An estimated 8.5 million deaths that occur annually in the region are attributed to NCDs; one-third of these deaths are premature and occur before the age of 70 years.

These NCDs share four modifiable behavioral risk factors: tobacco use, unhealthy diet, insufficient physical activity and harmful use of alcohol. Urbanization, sedentary lifestyles and increased life expectancy are the other major contributory factors for the epidemic of NCDs.

Traditionally considered diseases of old age, NCDs are now becoming prevalent in the younger age group, thus affecting the economically productive individuals.

India too is not untouched by this. Due to rapid urbanization, India is in the midst of an epidemiological transition, moving away from a predominantly communicable to a predominantly NCD pattern.

Air Pollution

Air pollution is considered by WHO as the greatest environmental risk to health in 2019.

India is home to seven of the world's 10 most polluted cities and 22 of 30 cities with the worst air pollution, according to the IQAir AirVisual 2018 World Air Quality Report. So, there is much we can learn from other countries.

This year, the Government of India has launched the National Clean Air Programme (NCAP) to control the rising air pollution levels across the country. The tentative target has been set for 20-30% reduction in particulate matter (PM)10 and PM2.5 levels by 2024, with 2017 as the base year for comparison.

Universal Health Care

Universal health care is the need of the hour. It ensures that all people receive the health services they need without suffering financial hardship when paying for them *(WHO Online Q&A, December 2014).*

Universal health care provides Affordable, Adequate, Accessible, Available, Appropriate and Accountable quality and safe health care to the public.

In India, the private sector provides 80% of health care today, while only 20% is provided by government sector. India also has one of the highest out of expenditures on health in the world, which is over 60%. Many people are pushed below poverty line on account of the high medical expenses in what has been termed as "the medical poverty trap".

But, now India has **"Ayushman Bharat – Pradhan Mantri Jan Arogya Yojana"** or the "National Health Protection Scheme", possibly the world's largest government funded health care program. It provides a cover of up to Rs. 5 lakhs per family per year, at any government or empanelled private hospital, for secondary and tertiary care hospitalization. The amount of 5 lakh would cover all investigations, medicine, pre-hospitalization expenses, etc. All pre-existing conditions are covered. More than 10 crore vulnerable entitled families – approximately 50 crore beneficiaries – will benefit from the scheme. There is no restriction on family size, age or gender.

Malaysia has its **B40:M40:T20 scheme**, wherein the entire population of Malaysia has been divided into three income groups: Top 20% (T20), Middle 40% (M40), and Bottom 40% (B40). The Malaysian government has announced a free national health scheme for the B40 group from this year.

SUCCESS STORIES

Nevertheless, many of our member countries have successfully met some public health challenges. These achievements should not only inspire us to accomplish these goals, but also to help each other to attain them.

Let me share with you few of these success stories.

- Emergency medical teams (EMTs) provide timely emergency medical care and transport in emergencies. As the first responders, they constitute an important part of the health care delivery system. In July this year, **Thailand became the first in WHO SEAR to get WHO classification for its EMT.** This classification makes Thailand EMT, the 26th team in the international roster of WHO classified, internationally deployable medical teams *(http://www.searo.who.int/about/administration_structure/hse/Thai_first_SEAR_EMT_WHO_classified/en/, July 31, 2019).*
- **Bangladesh, Nepal and Thailand** (*along with Bhutan*), have become **the first countries in WHO SEAR to achieve Hepatitis B control,** with less than 1% prevalence of hepatitis B among 5-year-old children. All four countries have consistently recorded over 90% coverage with hepatitis B vaccine doses provided during infancy for past many years *(SEAR/PR/1714, July 26, 2019).*
- **Elimination of malaria in Sri Lanka**. The elimination of malaria in Sri Lanka is a public health success story that is almost 8 decades in the making. The country reported its last case of measles caused by an indigenous virus in May 2016 *(SEAR/PR/1712, July 9, 2019).*

  And, the mantra for this success: *"If we learned of a case of malaria we would search for the patient's house and trap the infected mosquitoes in the surrounding areas. We had to spend days, sometimes weeks in the jungle, without passable roads".* The anti-malaria campaign made a paradigm shift from mosquito control to parasite control. *"That's how we differ to other countries. We have gotten rid of malaria by eliminating the parasite, not the vector..." (http://www.searo.who.int/srilankadefeatsmalaria.pdf?ua=1, September 2016)*
- **China's war on pollution:** Like many other countries, China too has been battling air pollution since the infamous "airpocalypse" in Beijing in 2013, when PM peaked at 35 times the WHO recommended limit. The strategies adopted are: New standards and targets for air pollution levels; revisions to China's Environmental Protection Law designed to increase penalties for polluters and repeated government inspection campaigns, coupled with heavy fines for violators. Although the battle is far from being won, air quality has improved. The average level of PM2.5 in the 50 most populous Chinese urban areas has dropped by nearly one-third, from 71.2 μg per cubic meter in 2013 to 47.9 in 2017.
- The Singapore Civil Defence Force (SCDF) provides **round-the-clock emergency medical services (EMS) in Singapore** for all types of life-threatening emergencies. SCDF operates a fleet of ambulances, "fast response paramedics" on motorcycles as well as first response fire-bikers in a fire-based system activated by a centralized dispatching. Dispatchers are predominantly firefighters, but also include paramedics and dispatch nurses. The ambulance service is staffed by salaried personnel, provided free of charge, and is publicly funded. In 2018, SCDF handled more than 1,87,000 emergency medical service calls amounting to 500 calls daily in 2018 *(https://www.channelnewsasia.com/news/singapore/scdf-will-no-longer-take-non-emergency-patients-to-hospitals-11393350, Mar 29, 2019).*

  This year, the Indian Council of Medical Research (ICMR) has launched **'Mission DELHI'** (Delhi Emergency Life Heart-Attack Initiative), an emergency medical service under which a pair of motorcycle-borne trained paramedic nurses would be the first responders for a person suffering heart attack or chest pain. The pilot project is linked with Centralized Ambulance Trauma Services (CATS) and has been launched in a radius of 3 kms (1.8 mils) around All India Institute of Medical Sciences (AIIMS), a premier tertiary care hospital in New Delhi.
- **Japan has universal public health care:** All Japanese citizens are required by law to have health insurance. Medical treatment in Japan is provided through universal health care. The health care system in Japan provides free screening processes for certain diseases, infectious disease control and prenatal care. Thirty percent of the medical costs are borne by the Japanese citizens and the remaining 70% by the government.

  The four characteristics of Japanese universal health insurance coverage system as mentioned in the website of the Japan Ministry of Health are:

  1. Covering all citizens by public medical insurance

2. Freedom of choice of medical institution (free access)
3. High-quality medical services with low costs
4. Based on the social insurance system, spending the public subsidy to maintain the universal health insurance coverage.

- **India has become a preferred medical tourism destination today.** Millions of patients from abroad have so far availed the best medical facilities in India. A medical tourism report considering data for the year 2015-16 suggests that a majority of Indian medical visa was issued to patients from Bangladesh, followed by other regions such as Afghanistan, African countries, other Asian countries, Iraq and Nigeria. Sri Lanka, Kenya, Pakistan and Commonwealth of Independent States (CIS) countries also rank among some of the leading nations from where a maximum number of patients come to avail the best medical facilities in India.

  The high quality hospital infrastructure, latest technology, affordability, world class treatment, less waiting time, a large English-speaking population are some of the USPs that make India a hotspot for medical and wellness travel destination. India is already on the tourist map. Last year, the Indian Government launched a dedicated health care tourism portal to streamline the travel and to promote medical and wellness tourism.

PATH TO WELLNESS

The theme of this General Assembly is "Path to Wellness".

Traditionally, health care has focused on treating diseases and not preventing them. But, with the escalating incidence of lifestyle diseases, health care is now shifting from sickness to wellness care.

Wellness is not just for the sick, it applies to healthy people too, who have no evident or overt disease, yet may be unwell due to depression, anxiety or other such conditions.

Wellness is defined as "*the sense that one is living in a manner that permits the experience of consistent, balanced growth in the physical, spiritual, emotional, intellectual, social and psychological dimensions of human existence.*"

This means that wellness takes care of the overall quality-of-life and well-being and not just physical health.

My Formula of 80 to Live up to 80 Years without a Lifestyle Disease

All the major lifestyle disorders share modifiable risk factors; so, instead of advocating a lifestyle for individual disease, patients should be advised a common lifestyle, which will prevent all lifestyle disorders.

Keeping this in mind, I have devised a 'Formula of 80', which I teach and recommend to all my patients. They are evidence-based and as most recommendations are to keep the values below 90, I have chosen the 80 as the number common to all risk factors so that it is easy for patients to remember.

Here is my Formula of 80 to live up to the age of 80:

- Keep your lower (systolic) blood pressure, LDL "bad" cholesterol, fasting sugar, resting heart rate and abdominal circumference all below 80.
- Keep the lung functions and eGFR above 80.
- For this, walk 80 minutes a day; brisk walk 80 minutes a week; walk with a speed of at least 80 steps per minute; for cardiac walk, achieve 80% of target heart rate.
- Keep the levels of PM1, PM2.5, PM10 and noise pollution all less than 80.
- Do not take alcohol and if you take and there is no contraindication, limit it to less than 80 mL (40% 80 proof whisky) a day or less than 80 grams a week.
- Eat in moderation and variety with no more than 80 grams of caloric food or 80 mL of caloric liquid in one meal. To reduce insulin resistance, adopt to low refined carb diet 80 days in a year.
- To shift from resting sympathetic to para-sympathetic mode, do 80 cycles of parasympathetic breathing (slower and deeper breathing).
- To reduce the harm of vitamin D deficiency, sit in the sunlight for 80 days a year.
- Donate blood 80 times in lifetime.
- To reduce chances of AMR by 80%, avoid self antibiotic medication and ask yourself before prescribing an antibiotic: is it necessary?
- Do not start tobacco and if you take, then quit; if you cannot stop, switch to less harmful non-tobacco alternatives or you will end up coughing out 80K Indian rupees on treatment.
- With this there are 80% chances you will not get a heart attack. And if you still get it, ask for 80 mg aspirin and 80 mg atorvastatin.

- And if you get an angiography and your blockage is less than 80% or FFR is more than 0.8, you do not need an intervention.
- With this there are 80% chances you will not have a sudden cardiac arrest. AND even if you get a sudden cardiac arrest, there are 80% chances that some bystander will give you compression-only CPR and revive you by using the Formula of 10 (within 10 minutes of death, at least for the next 10 minutes, compress the chest of the victim effectively and continuously with a speed of at least 10 × 10 = 100 per minute).

I add another today to this list, "**For the success of CMAAO let us give 80 seconds every day to the CMAAO and share one idea with me to make this year, one of the most vibrant years in the history of CMAAO**".

I welcome you all to India.

Atithi Devo Bhava (vfrfFknok Hko:) or "The guest is God" has been a tradition for us in India for centuries.

This mantra is from the Taittiriya Upanishad, Shikshavalli I.11.2 that says: *matrudevo bhava, pitrudevo bhava, acharyadevo bhava, atithidevo bhava.* It literally means that treat the mother, father, teacher and guests as God.

I bow before all our International and National guests present on the dais and off the dais and seek your blessings and good wishes.

And let us all clap 80 times for them.

Long Live CMAAO!

Long Live IMA!

■■■■

Consensus Statement of Padma Awardee Doctors' Forum Regarding Exclusion of Medical Professionals from the Consumer Protection Act

India International Centre (IIC), New Delhi | August 28, 2019

KK AGGARWAL, AK BHALLA, AK GROVER, ANOOP MISRA, ARVIND LAL, AS SOIN, ASHOK SETH, BN SAHI, DS GAMBHIR, GANESH MANI, GK KHATRI, HARSH MAHAJAN, KALYAN BANERJEE, KK SETHI, KK TALWAR, M KHALILULLAH, M WALI, MADAN MOHAN, MAHESH VERMA, MALVIKA SABHARWAL, NEELAM KLER, NIKHIL TANDON, NITISH NAIK, NK PANDEY, NM SHROFF, NP GUPTA, P LAL, P VENUGOPAL, RAMAN KAPOOR, RANDHIR SUD, RK GROVER, SANJEEV BAGAI, SAUMITRA RAWAT, SC MANCHANDA, TS KLER, UPENDRA KAUL, YASH GULATI

The Consumer Protection Bill, 1986 was passed by both the Houses of Parliament and it received the assent of the President on 24th December 1986. It came on the Statutes Book as The Consumer Protection Act, 1986 (68 of 1986). The Legislature while drafting the Bill, 1986 had specifically not included the services provided by the medical professionals in the term of services. Also, there is no mention of medical professionals, doctors, etc., anyplace in the Consumer Protection Act, 1986.

The fact that there is a distinction between a profession and an occupation was the main reason for not including the medical professionals under the purview of Consumer Protection Act, 1986. A person engaged in an occupation renders service, which falls within the ambit of Section 2(1)(o) of the Consumer Protection Act, 1986; however, the service rendered by a person belonging to a profession does not fall within the ambit of the said provision. Accordingly, medical practitioners who belong to the medical profession are not covered under the Consumer Protection Act.

But, in the matter of "**Indian Medical Association versus V P Shantha, AIR 1996 SC 550**", the Hon'ble Supreme Court of India held that the Consumer Protection Act, 1986 is applicable to services rendered by doctors and hospitals. The Apex Court also held that the services rendered to a patient by a medical professional are "service" within the meaning of the Consumer Protection Act, 1986 and the persons who hire or avail such services are therefore, consumers as defined under the Act *with the exception* that where the doctor/hospital renders service free of charge to every patient or under a contract of personal service, a patient availing of such free of charge services will not be a consumer.

CONSUMER PROTECTION ACT, 2019

The Consumer Protection Bill, 2019 has been passed by both Houses of Parliament i.e. Lok Sabha (30th July 2019) and Rajya Sabha (6th August 2019). Thus, a new law on consumer protection has been enacted i.e. the Consumer Protection Act, 2019. The new act does not include services rendered by medical professionals.

Earlier, when amendments to the Consumer Protection Act were introduced in 2015, **there was no mention of "health care" in the list of examples of as to what constitutes "service".** The Bill said "service" means service of any description made available to potential users and includes, but is not limited to, the provision of facilities relating to banking, financing, insurance, transport, processing, supply of electrical or other energy, telecom, board or lodging or both, housing construction, entertainment, amusement or the purveying of news or other information. It does not include the rendering of any service free of charge or under a contract of personal service.

The Bill had gone through the parliamentary committee. But in 2019, when the new Consumer Protection Bill was introduced in the Lok Sabha, "health care" was included in the list after telecom.

But later "health care" was removed from the list of services which had been specifically mentioned earlier under the definition of services in the draft Consumer Protection Bill.

Now, in the new Act of 2019, the terms "medical profession", "health care", "doctors", etc. are not mentioned.

LEGISLATIVE INTENT

While enacting both the Consumer Protection Act, 1986 and Consumer Protection Act, 2019, the draftsmen of the Legislature had specifically and intentionally not included the services rendered by medical professionals. In 2019, when the new Bill was presented, the term "health care" was included in the draft of the Consumer Protection Bill; however, the same was later removed from the Bill.

Even though, the landmark precedents as laid down by the Hon'ble Supreme Court of India cover the medical profession/health care under the purview of Consumer Protection Act, the Legislature never intended to cover the services rendered by the medical professionals under Consumer Protection Act.

It is also to mention that medical professional services are not covered under GST.

LAWYERS DO NOT COME UNDER THE PURVIEW OF CONSUMER PROTECTION ACT

In the matter titled as "**D. K. Gandhi versus M. Mathias**", the State Commission of Consumer Disputes Redressal Forum, Delhi, held that services rendered by a Lawyer would not come within the ambit of Section 2(1)(o) of the Consumer Protection Act, 1986, as the client executes the power of attorney authorizing the Counsel to do certain acts on his behalf and there is no term of contract as to the liability of the lawyer in case he fails to do any such act. The State Commission held that it is a unilateral contract executed by the client giving authority to the lawyer to appear and represent the matter on his behalf without any specific assurance or undertaking.

However, this verdict of the State Commission was reversed by the National Consumer Disputes Redressal Commission (NCDRC) in the Revision Petition titled as **D. K. Gandhi versus M. Mathias** on the ground that lawyers are rendering a service. They are charging fees. It is not a contract of personal service and that there was no reason to hold that they are not covered by the provisions of the Consumer Protection Act, 1986. It was held that though a lawyer may not be responsible for the favorable outcome of a case as the result/outcome does not depend only on lawyers' work, but, if there was deficiency in rendering services promised, for which consideration in the form of fee is received by him, then the lawyers can be proceeded against under the Consumer Protection Act.

However, the said judgment of the NCDRC has now been stayed by the Hon'ble Supreme Court in the matter titled as "**Bar of Indian Lawyers vs. D. K. Gandhi**". The said case is still pending adjudication before the Hon'ble Supreme Court of India.

Thus, the question whether the lawyers are covered under the Consumer Protection Act or not is still pending before the Hon'ble Supreme Court of India. However, as on date, the lawyers do not come under the purview of Consumer Protection Act.

POLICY RECOMMENDATIONS/CLARIFICATION

The Padma Awardee Doctors Forum and the Heart Care Foundation of India (HCFI) would seek clarification and would also encourage the Government of India to issue clarification that the services rendered by the medical professionals are not covered under the Consumer Protection Act.

Also, if required, the Padma Awardee Doctors Forum and HCFI would seek clarification from the Hon'ble Supreme Court of India, Hon'ble High Courts of various states of the country that the services rendered by medical professionals are not covered under the Consumer Protection Act.

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Evaluation of the Prevalence of Cardiovascular Disease in Urban Delhi Using a Handheld ECG Device

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ABSTRACT

Background: Cardiovascular diseases (CVD) have now become the leading cause of mortality in India. However, there is a gap in prevalence data or national representative surveillance data. **Aim:** The aim of this cross-sectional study was to evaluate the prevalence of CVD in the urban population of Delhi and the usability of a handheld smartphone-based ECG device "SanketLife" in detecting heart ailments. **Material and methods:** The study was conducted among 1,521 participants visiting the Perfect Health Mela conducted by Heart Care Foundation of India (HCFI) from 23rd to 27th October, 2018. Known cases of myocardial infarction, hypertension and diabetes were also seen during the study. **Results:** Of the 1,521 persons screened, 324 (21.3%) were found to have 15 types of abnormalities on ECG after review by an ECG analyst. Tachycardia was detected in 105 (32.4%) persons. Other common findings were intraventricular conduction delay (17.9%; n = 58), premature ventricular contraction (12.6%; n = 41), premature atrial contraction (7.72%; n = 25) and left bundle branch block (6.17%; n = 20). The results also showed a high prevalence of coronary artery blockage (indicative of atherosclerotic CVD) among the study population. **Conclusion:** The results showed the high prevalence of CVD, particularly in the younger age group and also demonstrated the usability of the device as a point of care test in detecting heart disease in the general population. The effectiveness of such a handheld device can aid in further prevention of avoidable cardiac events and help in better monitoring of CVD.

Keywords: Cardiovascular disease, prevalence, hypertension, diabetes, ECG, handheld ECG device, Perfect Health Mela, Heart Care Foundation of India

India is witnessing an epidemic of noncommunicable diseases (NCDs)[1] with an alarming rise in their incidence. Accounting for nearly 61% of total deaths, NCDs have emerged as the leading causes of deaths in India.[2] Along with diabetes mellitus and respiratory disorders, cardiovascular diseases (CVD) are among the top 10 causes of death in India.[3] The average age of people presenting with NCDs in India is a decade early (≥45 years of age) as compared with people in developed countries (55 years or older).[4]

Among CVD, ischemic heart disease and stroke are the predominant causes and are responsible for more than 80% of CVD deaths in India. Despite wide heterogeneity in the prevalence of cardiovascular risk factors across different regions, CVD has emerged as the leading cause of death in all parts of India, including poorer states and rural areas. The Global Burden of Disease study estimated age-standardized CVD death rate as 272 per 1,00,000 population in India, which is higher than the global average of 235 per 1,00,000 population. Premature mortality in terms of years of life lost because of CVD in India has increased by 59%, from 23.2 million in 1990 to 37 million in 2010.[5]

CVD tend to affect patients in the most productive years of their lives and lead to disastrous social and economic consequences.[6] Early age of onset, high case fatality rate and rapid progress are some features particular to CVD in India.[5]

High CVD mortality in the South Asian region and India can be attributed to four factors, including lack of policies related to social determinants of CVD for control of primordial risk factors such as smoking, smokeless tobacco, alcohol, physical inactivity and

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unhealthy diet; poor-quality preventive management; low availability and substandard acute coronary heart disease management and lack of appropriate long-term care of these patients and absent cardiovascular rehabilitative and secondary prevention programs.[7]

Even though the burden of CVDs is increasing in India, there is a lack of systematic understanding of its distribution and time trends across all the states.[8]

Keeping in view the above gap in prevalence data, the present study aimed at evaluating the prevalence of CVD in the population and usability of a handheld, smartphone-based ECG device in detecting heart ailments.

MATERIAL AND METHODS

This is a cross-sectional study conducted during the MTNL Perfect Health Mela from 23rd to 27th October, 2018 at New Delhi. A dedicated booth for heart health screening was set up at the Mela venue.

Perfect Health Mela is an annual flagship event of the Heart Care Foundation of India (HCFI) aimed at generating all-round awareness on health using infotainment as the mass awareness module. The Mela organizes seminars, conclaves, lifestyle exhibitions, workshops, lectures, competitions and free health check-ups on issues of public health importance.

During the study, participants were screened at the event with the help of a handheld ECG device "SanketLife". The data collection team comprised of 10 members including one ECG analyst and 9 volunteers to organize and conduct the ECG recordings at the booth during the event.

Before collecting the data, patients were allowed to sit down for 2 minutes to bring their body to optimal condition. The patients were informed about the procedure and asked to fill in the following details in a prescribed format: age, gender, contact information, pre-existing health conditions such as diabetes, hypertension and lifestyle habits such as smoking or alcohol consumption. After the data was collected, the ECG was performed on the people visiting the booth for the same.

A total of 1,521 individuals participated in the study; necessary permissions were taken from the administration to perform the ECG screening at the venue. Before performing the ECG, informed consent was taken from all participants. ECG screening was conducted free of cost.

The participants with significant findings were immediately referred to their physicians.

All of the participants were aware of their ailment and were already being monitored by a doctor.

RESULTS

Among 1,521 participants who voluntarily participated in the study, 324 (21.3%) were found to have significant cardiac findings on the ECG as analyzed by the ECG analyst (Table 1).

Among the participants screened, 18.61% had hypertension and were aware of their condition; 14% of people were diagnosed with diabetes, who were also aware of their condition.

Eighty-one percent of the participants were males while the remaining 19% were females.

The majority of the study participants belonged to the age group 40-70 years. The age-wise distribution of individuals screened at the booth is shown in Figure 1.

DISCUSSION

The prevalence of CVD is constantly rising in India and is higher in urban areas. CVD mortality rates vary from 75 to 100 per 1,00,000 in the sub-Himalayan states of Nagaland, Meghalaya, Himachal Pradesh and

Table 1. Total Cardiac Events Observed During the Study

ECG finding	Prevalence
Tachycardia	105 (32.41%)
Intraventricular conduction delay (IVCD)	58 (17.9%)
Premature ventricular contraction (PVC)	41 (12.65%)
Premature atrial contraction (PAC)	25 (7.72%)
Old myocardial infarction (MI)	25 (7.72%)
Bradycardia	22 (6.79%)
Left bundle branch block (LBBBB)	20 (6.17%)
First-degree AV block	10 (3.08%)
Right bundle branch block (RBBB)	5 (1.54%)
Multifocal PVCs	5 (1.54%)
Atrial fibrillation	3 (0.92%)
Dual chamber paced rhythm	2 (0.62%)
Atrial flutter	1 (0.31%)
Second-degree AV block, Mobitz-1	1 (0.31%)
Acceleration junctional rhythm	1 (0.31%)
Total	**324 (21.3%)**

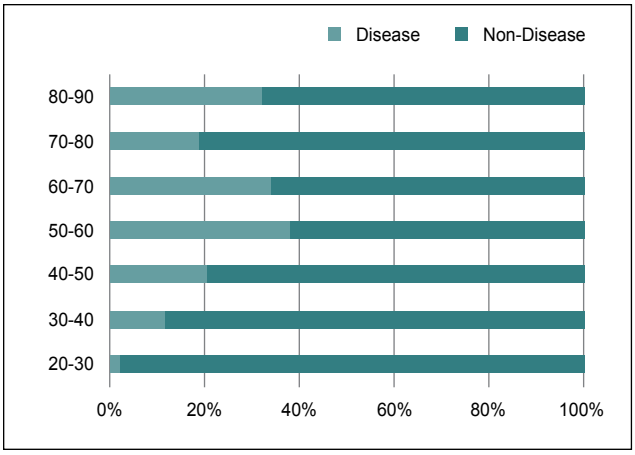

Figure 1. Age ratio and disease prevalence.

Sikkim to 360 to 430 per 1,00,000 in Andhra Pradesh, Tamil Nadu, Punjab and Goa.[9]

A systematic review of studies on CVD in Asian Indians from January 1969 to October 2012 revealed that the prevalence in urban areas was 2.5-12.6% and 1.4-4.6% in rural areas.[9,10]

The overall prevalence of CVD in South Indian population has been estimated to be 11%, a 10-fold increase as compared to the prevalence in urban India in the 1970s.[9,11]

A previous study conducted in Delhi found the prevalence of coronary heart disease to be 14.8% in urban areas.[12] Our study too found a high prevalence of coronary artery blockage (7.72%) among the study population.

In the urban areas of India, the prevalence of diabetes mellitus has almost doubled in nearly 20 years from 9% to 17%.[5] The Global Burden of Diseases study reports that hypertension associated mortality and morbidity in India is one of the highest in the world and is increasing.[13] Our results also showed high prevalence of hypertension (18.61%) and diabetes (14%) among the study group.

Social determinants of hypertension are vital and it has been noted that states with greater human and social development and urbanization have more hypertension. This is in contrast to developed countries, such as the United States, where hypertension is more in less developed states.[13] Cardiovascular risk factors - hypertension, hypercholesterolemia, low high-density lipoprotein cholesterol, hypertriglyceridemia and tobacco use are highly prevalent in the urban Indian middle class. There is low awareness, treatment and control of hypertension and hypercholesterolemia in patients with diabetes.[14]

The handheld ECG device SanketLife was able to effectively evaluate cardiac-related conditions in the population. It provides complete ECG and its ease of use in home monitoring as well as in clinical setup to get a quick ECG at the desk of clinician and hence in making clinical judgments cannot be denied.

CONCLUSION

CVD is growing faster than predicted and is also occurring in younger section of the population. Region-specific data on CVD is quite less and needs to be studied more. The effectiveness of such a handheld device as a "point of care" test can aid in further prevention of avoidable cardiac events and help in better monitoring of CVD. The burden from the leading CVD in India varies widely between the states and their increasing prevalence and that of several major risk factors in every part of India indicates the need for urgent health system response appropriate to different locations.

Acknowledgment

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Conflict of Interest

The authors would like to state that there are no conflicts of interest.

REFERENCES

1. Banerjee A. Noncommunicable diseases in India: challenges and the way forward. J Postgrad Med 2019;65(1):5-6.
2. Pati S, Sinha R, Mahapatra P. Non-communicable disease risk reduction teaching in India: a curricular landscape. Front Public Health. 2019;7:133.
3. CDC Global Health - India [Internet]. Cdc.gov. 2019 [cited 13 August 2019]. Available at: https://www.cdc.gov/globalhealth/countries/india/.
4. Arokiasamy P. India's escalating burden of non-communicable diseases. Lancet Glob Health. 2018;6(12): e1262-e1263.
5. Prabhakaran D, Jeemon P, Roy A. Cardiovascular diseases in India: current epidemiology and future directions. Circulation. 2016;133(16):1605-20.
6. Abdul-Aziz AA, Desikan P, Prabhakaran D, Schroeder LF. Tackling the burden of cardiovascular diseases in India: The essential diagnostics list. Circ Cardiovasc Qual Outcomes. 2019;12(4):e005195.
7. Gupta R, Mohan I, Narula J. Trends in coronary heart disease epidemiology in India. Ann Glob Health. 2016;82(2):307-15.

8. India State-Level Disease Burden Initiative CVD Collaborators. The changing patterns of cardiovascular diseases and their risk factors in the states of India: the Global Burden of Disease Study 1990-2016. Lancet Glob Health. 2018;6(12):PE1339-PE1351.
9. Shrivastava U, Mishra A, Mohan V, Unnikrishnan R, Bachani D. Obesity, diabetes and cardiovascular diseases in India: public health challenges. Curr Diabetes Rev. 2016;13(1):65-80.
10. Rao M, Xavier D, Devi P, Sigamani A, Faruqui A, Gupta R, et al. Prevalence, treatments and outcomes of coronary artery disease in Indians: a systematic review. Indian Heart J. 2015;67(4):302-10.
11. Mohan V, Deepa R, Rani SS, Premalatha G; Chennai Urban Population Study (CUPS No. 5). Prevalence of coronary artery disease and its relationship to lipids in a selected population in South India: The Chennai Urban Population Study (CUPS No. 5). J Am Coll Cardiol. 2001;38(3):682-7.
12. Chauhan S, Aeri BT. The rising incidence of cardiovascular diseases in India: assessing its economic impact. J Preventive Cardiol. 2015;4(4):735-40.
13. Gupta R, Gaur K, S Ram CV. Emerging trends in hypertension epidemiology in India. J Hum Hypertens. 2019;33(8):575-87.
14. 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:e000048.

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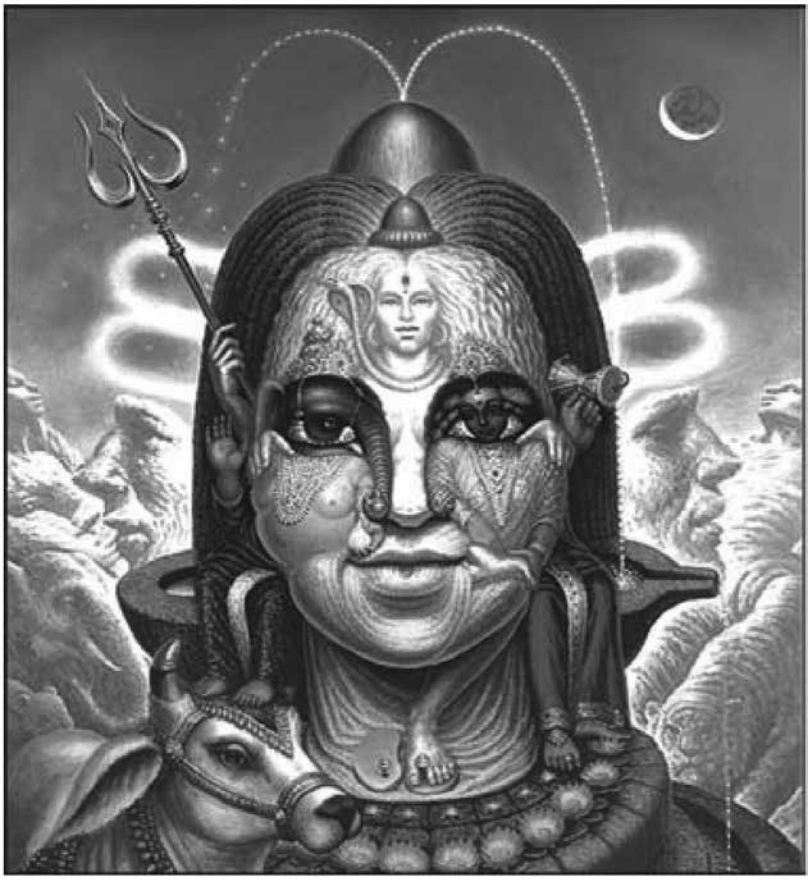
Different Perspectives of Life



Different perceptions of Lord Shiva – multiple faces.

Indian Journal of Clinical Practice, Vol. 30, No. 4, September 2019

Thyroid Abnormality: A Hospital-based Retrospective Study

AMIT KUMAR*, SUDHIR CHANDRA JHA†, JITENDRA KUMAR SINGH‡

ABSTRACT

Introduction: Endocrine disorders are common among Indian population, out of which, thyroid disorders represent an important subset of these endocrine disorders. **Aims and objectives:** To study the prevalence of thyroid abnormality in outpatients. **Material and methods:** The study was conducted on outpatient basis and analyzed the holistic medical reports of a sample of 200 outpatients to study the prevalence of thyroid abnormality. **Results:** Thyroid abnormality was found in 10% of persons in Darbhanga Medical College and Hospital (DMCH) as compared to Indian prospective (~20%). **Conclusion:** The fractional prevalence of thyroid disorders, observed at the DMCH, is lower than national average.

Keywords: Hypothyroidism, hyperthyroidism, TSH, T3, T4

Thyroid abnormality is a generic term used to refer to a set of disorders pertaining to functioning of the thyroid gland and levels of thyroid secretions in the body.

Projections from various studies on thyroid disease estimate that about 42 million people in India suffer from thyroid diseases.[1]

Thyroid disorders can range from a small, harmless goiter (enlarged gland) that needs no treatment, to, life-threatening cancer.

The most common thyroid problems involve abnormal production of thyroid hormones. Hypothyroidism and hyperthyroidism refer to sub-requisite and surplus activity of the thyroid gland, respectively. Both of these varieties have several unique, nuanced subtypes, attributed to various causatives. Additionally, cancer of the thyroid gland is quite rare and occurs in about 5% of thyroid nodules.[2]

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Hyperthyroidism is a physiological phenomenon characterized by the excessive production of thyroid hormone, owing to overactivity of the thyroid gland.[3] Typical symptoms albeit subject to interpersonal variation, mainly comprise of one or many of: sleep irregularities, an irritable demeanor, general fatigue, muscle weakness, tachycardia, diarrhea, thyroid-gland enlargement, heat intolerance, trembling of hands, and loss of weight. Graves' disease is causative in about 50-80% of the cases in the United States of America. Other causes include multinodular goiter, thyroid inflammation, toxic adenoma, consumption of excessive iodine and surplus intake or administration of the synthetic thyroid hormone. A significantly less prevalent cause is pituitary adenoma. The diagnosis may be suspected based on signs and symptoms and then confirmed with blood tests, which typically depict a low thyroid-stimulating hormone (TSH) and raised triiodothyronine (T3) or thyroxine (T4). Measuring radioiodine uptake by the thyroid, performing a thyroid scan and thyroid-stimulating immunoglobulin (TSI) antibody-analyses may help ascertain the cause.[4]

There are three main treatment options: radioiodine therapy, i.e., oral ingestion of iodine-131 isotope, anti-thyroid medications and/or β-blockers, and thyroid surgery.[4] Surgical intervention is only appropriate in drastic cases, typically with hyper-enlargement or cancer-risk emergencies.

The ailment is fairly commonplace, estimated to be affecting roughly 1 in a 100 people. Its observed

frequency is 2-10 times greater in females than in males.[4] Onset is commonly between 20 and 50 years of age.[5] Broadly hyperthyroidism is more common in persons with age over 60 years.[4]

Hypothyroidism (underactive thyroid) is a condition in which the thyroid gland doesn't produce enough of certain crucial hormones. Hypothyroidism may not cause noticeable symptoms in the early stages. Over time, untreated hypothyroidism can cause a number of health problems, such as obesity, joint pain, infertility and heart disease.

Hypothyroidism encompasses a broad clinical spectrum that may range from an overt state of myxedema, end-organ effects and multiorgan failure to an asymptomatic or subclinical state that presents with normal levels of T4 and T3 and mildly elevated levels of serum thyrotropin.[6-10] The prevalence of hypothyroidism in the developed world is about 4-5%.[11,12] The prevalence of subclinical hypothyroidism in the developed world is about 4-15%.[11,13]

Thyroid diseases are different from other diseases in terms of their ease of diagnosis, accessibility of medical treatment, and the relative visibility that even a small swelling of the thyroid offers to the treating physician. Early diagnosis and treatment remain the cornerstone of management.

MATERIAL AND METHODS

The study was conducted upon a sample of 200 outpatients coming to hospital from July 2018 to August 2018. The patients were >10 years of age. The TSH level was checked for all the patients.

RESULTS

Out of 200 patients included, 180 had no abnormality of the thyroid gland (Table 1 and Fig. 1). Figure 2 shows a comparison of prevalence of thyroid disorder in our study with that of control Indian data.[14]

CONCLUSION

The fractional prevalence of thyroid disorders, observed at Darbhanga Medical College and Hospital (DMCH), is lower than the estimated national average. Fractional prevalence of thyroid disorder in the population was 10% but that of another Indian data was about 20%.[14] Thyroid diseases are, arguably, among the commonest endocrine disorders worldwide. India too is no exception. Thyroid diseases are different from other diseases in terms of their ease of diagnosis, accessibility of medical

Table 1. TSH Levels of Study Population

Normal TSH	180 (90%)
Hypothyroidism (TSH >10)	14 (7%)
Hypothyroidism (TSH <10)	4 (2%)
Hyperthyroidism	2 (1%)

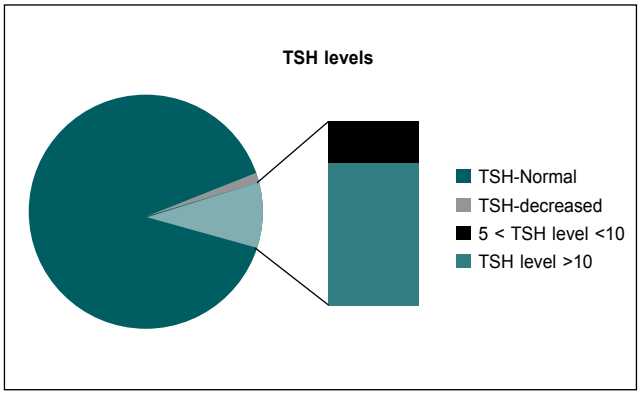

Figure 1. TSH levels of study population.

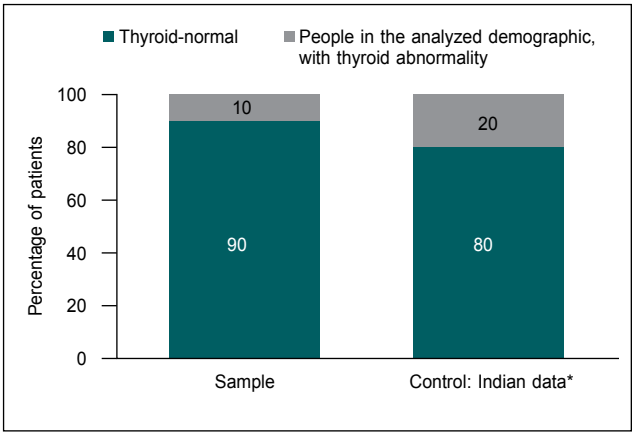

Figure 2. Comparison of prevalence of thyroid disorder in our study with that of control Indian data.

*Approximate value.

treatment and the relative visibility that even a small swelling of the thyroid offers to the treating physician. Early diagnosis and treatment remain the cornerstone of management.

REFERENCES

1. Unnikrishnan AG, Menon UV. Thyroid disorders in India: An epidemiological perspective. Indian J Endocrinol Metab. 2011;15(Suppl 2):S78-81.
2. Thyroid problems. Available at: https://www.webmd.com/women/guide/understanding-thyroid-problems-basics#2
3. Bahn Chair RS, Burch HB, Cooper DS, Garber JR, Greenlee MC, Klein I, et al; American Thyroid Association;

American Association of Clinical Endocrinologists. Hyperthyroidism and other causes of thyrotoxicosis: management guidelines of the American Thyroid Association and American Association of Clinical Endocrinologists. Thyroid. 2011;21(6):593-646.

4. Hyperthyroidism. Available at: https://www.niddk.nih.gov/health-information/endocrine-diseases/hyperthyroidism.
5. Pokhrel B, Bhusal K. Graves Disease. [Updated 2019 Jun 3]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2019 Jan-. Available at: https://www.ncbi.nlm.nih.gov/books/NBK448195/.
6. Cooper DS. Clinical practice. Subclinical hypothyroidism. N Engl J Med. 2001;345(4):260-5.
7. Roberts CG, Ladenson PW. Hypothyroidism. Lancet. 2004;363(9411):793-803.
8. Biondi B, Klein I. Hypothyroidism as a risk factor for cardiovascular disease. Endocrine. 2004;24(1):1-13.
9. Krassas GE, Poppe K, Glinoer D. Thyroid function and human reproductive health. Endocr Rev. 2010;31(5):702-55.
10. Modala S, Dhar U, Thimmaraju KV, Baghe M, Hari Krishna B. Haematological profile and body composition in hypothyroid patients. IJCMR. 2017;4(3):661-5.
11. Hollowell JG, Staehling NW, Flanders WD, Hannon WH, Gunter EW, Spencer CA, et al. Serum TSH, T(4), and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III). J Clin Endocrinol Metab. 2002;87(2):489-99.
12. Hoogendoorn EH, Hermus AR, de Vegt F, Ross HA, Verbeek AL, Kiemeney LA, et al. Thyroid function and prevalence of anti-thyroperoxidase antibodies in a population with borderline sufficient iodine intake: influences of age and sex. Clin Chem. 2006;52(1):104-11.
13. Bemben DA, Hamm RM, Morgan L, Winn P, Davis A, Barton E. Thyroid disease in the elderly. Part 2. Predictability of subclinical hypothyroidism. J Fam Pract. 1994;38(6):583-8.
14. Usha Menon V, Sundaram KR, Unnikrishnan AG, Jayakumar RV, Nair V, Kumar H. High prevalence of undetected thyroid disorders in an iodine sufficient adult south Indian population. J Indian Med Assoc. 2009;107(2):72-7.

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A Great Monarch

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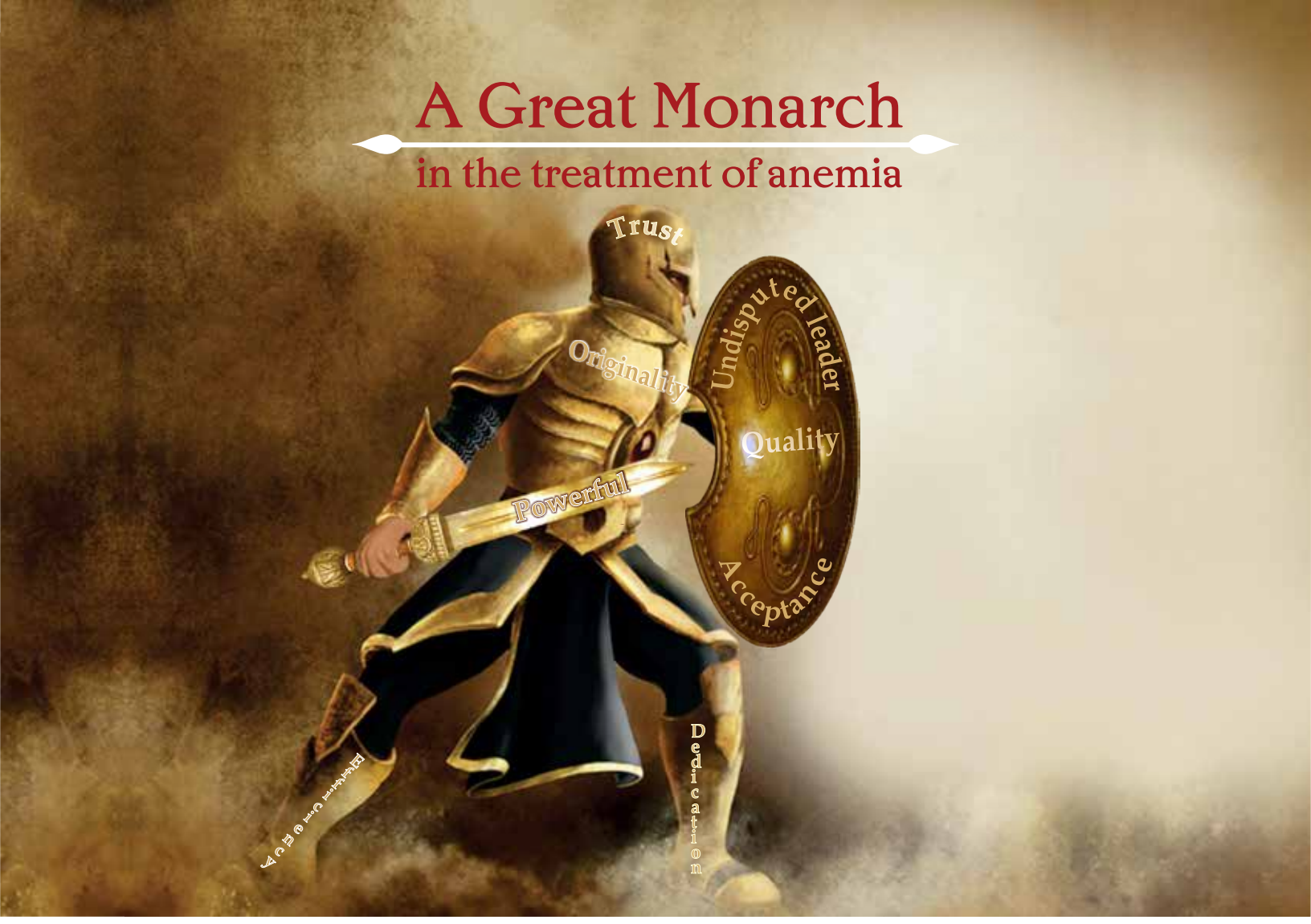

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Warning Signs of Heart Attack

Is There Any Silver Bullet?

MV RAGHAVENDRA RAO*, SATEESH ARJA†, SIREESHA BALA ARJA‡, KUMAR PONNUSAMY#

ABSTRACT

India has become the world capital for heart disease. Furthermore, in comparison with the West, Indians are affected by cardiovascular-related problems at a significantly younger age. Cardiovascular disease (CVD) is the world's leading cause of morbidity and mortality. The present review discusses the risk factors associated with myocardial infarction, advances in research and lifestyle changes to manage CVD.

Keywords: Myocardial ischemia, epicardial coronary artery, gastroesophageal reflux disease, coronary artery disease, C-reactive protein

"Every soul shall taste death. Sometimes you will never know the value of a moment until it becomes a memory."

In the last few decades, India has emerged as the world capital for heart disease, with more people with heart problems in this country than anywhere else in the world and that's not all; in comparison with the West, Indians are affected by cardiovascular-related problems at a significantly younger age. The average age at which a person may suffer a heart attack has now come down from 40 years to 30 years. When such a high proportion of Indians are being affected at a young and productive age, it will certainly have an alarming impact not only on the finances of an affected individual family but also on the nation's economy. Women are far more worried about breast cancer than they are about heart disease. But women have a greater risk of dying from heart disease than from all cancers combined. This is true for women of all races and ethnicities. Yet only about 50% of women realize that they are at greater risk from heart disease than from anything else. It is the myth of the 'widow maker'. Even in women with breast cancer, dying from heart disease is a leading cause of death.

Is there any silver bullet?

The heart has always represented a cornerstone of current discipline. Cardiovascular disease (CVD) is now the world's leading cause of morbidity and mortality. Don't go under the knife yet!

Approximately 12% of patients presenting with chest pain are found to have ischemic heart disease (IHD). Sudden cardiac death (SCD) is a major public health problem because of its frequency and demographics with numeric estimates in range of 3,00,000-3,75,000 deaths per year in the United States alone accounting for half of all cardiovascular deaths.

Acute myocardial infarction (AMI) is among the most common diseases in the industrialized countries. AMI occurs when myocardial ischemia overcomes myocardial cellular repair mechanisms that maintain normal operating function and homeostasis. The incidence of myocardial infarction in the world varies to a great extent. In the United States and the United Kingdom, about 6,50,000 and 1,80,000 patients get AMI every year, respectively. Indians are four times more likely to develop AMI as compared to people of other countries owing to a combination of genetic and lifestyle factors promoting metabolic dysfunction.

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The worldwide incidence of SCD is difficult to estimate because numbers vary as a function of the prevalence of coronary heart disease in different countries.

The most common serious cause of acute chest discomfort is myocardial ischemia or infarction, which occurs when the supply of myocardial oxygen is inadequate for the demand.

Myocardial infarction, also known as a **heart attack**, occurs when blood flow decreases or stops to a part of the heart, causing damage to the heart muscle. The most common symptom is chest pain or discomfort which may travel into the shoulder, arm, back, neck or jaw. Often, it occurs in the center or left side of the chest and lasts for more than a few minutes. The discomfort may occasionally feel like heartburn.

Heart disease (including coronary heart disease, hypertension and stroke) remains to be the number 1 cause of death in the US. Coronary heart disease accounts for 1 in 7 deaths in the US, killing over 3,60,000 people a year. Nearly 7,90,000 people in the US have heart attacks each year. Of these, about 1,14,000 will die.

Reversal of Atherosclerosis with Aggressive Lipid-lowering (REVERSAL) study randomized patients with coronary artery disease (CAD) to high-dose atorvastatin or moderate dose of pravastatin. In the atorvastatin arm, low-density lipoprotein cholesterol (LDL-C)-lowering to levels well below what was considered normal led to a halt of atherosclerotic progression.

The percentage of patients who present to the emergency department with AMI or unstable angina who are not hospitalized is low, but the discharge of such patients may be associated with increased mortality. Failure to hospitalize is related to race, sex and the absence of typical features of cardiac ischemia. There is a need for efforts to reduce the number of missed diagnoses.

Numerous studies in several different hospital environments have proven the utility of the chest pain centers (CPCs) and have strived to evaluate the patients for these possible conditions.

Coronary artery calcification (CAC) is almost invariably associated with atherosclerotic plaque formation. Patients with intermittent left bundle branch block will frequently develop chest discomfort at the onset of the dysrhythmia. This is thought to be related to paradoxical cardiac movement at the onset of the bundle branch block.

Risk factors include hypertension, cigarette smoking, type 2 diabetes mellitus, increased cholesterol concentration and obesity. Atherosclerosis, the formation of plaque inside the arteries, is the main cause of CAD. Emergency physicians will increasingly encounter clinical situations involving patients with cardiac devices, in particular, pacemakers and automatic implantable cardiac defibrillators in emergency department.

The World Health Organization (WHO) criteria developed in the 1970s, defined AMI as the presence of 2 of the following 3 characteristics: i) acute ischemia (chest pain), ii) Q waves in electrocardiogram (ECG) and iii) increase of enzymes in the blood (combination of total creatine kinase [CK], CK-myocardial band [MB], aspartate aminotransferase [AST] and lactate dehydrogenase [LDH]).

HISTORY

CVD research dates back to at least the 18th century. In 1893, Einthoven developed the ECG and transmitted an ECG over 1.5 km by telephone cable. He received Nobel Prize in 1924. The first defibrillation report was published by Paul Zoll in 1956.

The term "primordial prevention" was first coined by Strasser. The first coronary percutaneous transluminal coronary angioplasty (PTCA) was performed by Andreas Grunt Zig in 1977, in Switzerland. In the early 1990s, the Medical College of Virginia (Now Virginia Commonwealth University) had medical emergency room (ER). In 1887, the first transcutaneous tracing of human cardiac electrical activity was published by Augustus Walter, founding the field of electrocardiograph.

AMI is a life-threatening condition that needs emergency diagnosis and early treatment in the ER. The mid-1990s led to the usage of cardiac-specific troponins (I and T) for the risk stratification of patients with acute coronary syndrome (ACS), while CK-MB mass was considered to be a proven marker for diagnosis of AMI.

Cardiac ultrasound was first described in the emergency medicine in the 1880s, as a diagnostic tool for the identification of pericardial effusions.

The first clinical use of CPB (cardiopulmonary bypass) was performed by Gibbon in 1953, during successful correction of an atrial septal defect.

The evaluation of patients with chest pain presenting to the ED warrants a focused strategy because of the clinical volume and the potential consequences for the patient, physician liability and the burden of payer. Elevated blood pressure (BP) is a major risk factor for

coronary heart disease, atrial fibrillation, heart failure, cerebrovascular disease, peripheral artery disease and renal failure. On a global level, 7.6 million premature deaths (13.5% of all premature deaths) have been attributed to high BP. Of the major cardiovascular events, about 54% of all strokes and 47% of all IHD cases can be attributable to high BP. CAC was previously thought to be a benign process, and the calcified lesion increases in accordance with aging. Subsequently, studies determined that medial calcification is associated with arterial stiffness, which increases risk for adverse cardiovascular events.

IDEAS WHERE THE RESEARCH GOES NEXT?

Cardiac stress testing is used to assess cardiac function and to disclose evidence of exertion-related cardiac hypoxia. Radionuclide testing using thallium or technetium can be used to demonstrate areas of perfusion abnormalities. With a maximal stress test, the level of exercise is increased until the person's heart rate will not increase any higher, despite increased exercise. A fairly accurate estimate of the target heart rate, based on extensive clinical research, can be estimated by the formula 220 beats/minute minus patient's age.

This linear relation is accurate up to about age 30, after which it mildly underestimates typical maximum attainable heart rate achievable by healthy individuals. Other formula exist, such as that by Miller (217 - [0.85 × Age]) and others. Achieving a high enough heart rate at the end of the exercise is critical to improving the sensitivity of the test to detect high-grade heart artery stenosis. High-frequency analysis of the QRS complex may be useful for detection of CAD during an exercise stress test.

Prevention of CVD involves improving risk factors through healthy eating, exercise, avoidance of tobacco smoke and limiting alcohol intake. Treating risk factors, such as high BP, blood lipids and diabetes is also beneficial. Treating people who have strep throat with antibiotics can decrease the risk of rheumatic heart disease.

Different strategies, including pharmacological and gene therapeutic approaches, directed at blocking viral replication or stimulating the antiviral-directed immune response are under investigation in experimental and clinical studies.

Cardiomyocyte necrosis tends to activate an inflammatory response that helps clear the injured myocardium from dead cells, and facilitates repair. However, it could also extend injury. Research suggests that the cell types involved in the process play an important role. Namely, monocyte-derived macrophages tend to induce inflammation while inhibiting cardiac regeneration, while tissue resident macrophages may help in the restoration of tissue structure and function.

Magnetic resonance imaging (MRI) with gadolinium enhancement reveals spotty areas of injury through the myocardium, but the correlation with endomyocardial biopsy results have been poor. There may be no symptoms and if symptoms occur, they occur usually a few weeks after viral infection. Most patients recover, although a few die of congestive heart failure or arrhythmias.

Viral myocarditis is unusually severe in infants and pregnant women. There is no specific treatment, only supportive measures are the rule. Despite the resolution of the active phase of this disease, a functional impairment may persist for years and progress to cardiomyopathy. Current evidence suggests that there are at least 4 potential sources of cells that account for new cardiomyocytes after birth.

The overall goal of performing an ECG is to obtain information about the electrical function of the heart. Medical uses for this information are varied and often need to be combined with knowledge of the structure of the heart and physical examination signs to be interpreted. Some indications for performing an ECG include the following: Chest pain or suspected myocardial infarction (heart attack), such as ST elevated myocardial infarction (STEMI) or non-ST elevated myocardial infarction (NSTEMI); symptoms such as shortness of breath, murmurs, fainting, seizures or arrhythmias, including new onset palpitations or monitoring of known cardiac arrhythmias.

Recent advances have extended the importance of ECG. It is vital to test for determining the presence and severity of acute myocardial ischemia.

MAJOR ADVANCES AND DISCOVERIES

- According to large prospective population studies, the systemic level of inflammatory markers may also be predictive of the risk of future cardiovascular events in otherwise well individuals.
- Patients who develop heart failure have markedly decreased quality-of-life and physical functioning, and approximately 50% of patients will die within 5 years of their diagnosis.
- In men and women followed-up for 18 years in the

Framingham study, diabetes was associated with a twofold increase in heart failure in men and a five-fold increase in women. The risk persisted after adjustment for age, CAD and hypertension.

- Chest pain is discomfort, typically in the front of the chest. It may be described as sharp, dull, pressure, heaviness or squeezing. Associated symptoms may include pain in the shoulder, arm, upper abdomen or jaw, or nausea, sweating or shortness of breath. It can be divided into heart-related and non-heart-related pain. Pain due to insufficient blood flow to the heart is also called angina pectoris. Those with diabetes or who are old may have less clear symptoms.
- Human immunodeficiency virus (HIV) is becoming a more prevalent cause of myocarditis, either alone or in association with other viruses.
- All calcium channel blockers (CCBs) lower the BP. CCBs are a class of medications used to treat high BP. They're also called calcium antagonists. They're as effective as angiotensin-converting enzyme (ACE) inhibitors in reducing BP.
- Atherosclerosis is a major cause of heart attack and stroke. Observations that cholesterol is an important component of arterial plaques paved way for the cholesterol hypothesis for the pathogenesis of atherosclerosis.
- Nitroglycerin sublingual tablet is used to stop or prevent angina (chest pain). A sublingual tablet is one that dissolves under the tongue or inside the cheek. Nitroglycerin also comes as a spray, aerosol solution, transdermal patch and ointment. It comes in an injectable form that's only given by a health care provider.
- Angina suit offers relief for chest pain. Is your angina pain so severe that you've been considering surgery?

Don't go under the knife yet. Another option may be available - a pulsating body suit. The suit isn't likely to win you any fashion contests. In fact, you probably would never leave the house in it. But, it seems to be a safe and effective way to treat angina pain.

The "suit" actually consists of cuffs that wrap around your arms, legs and buttocks. When your heart expands, the cuff fills with air and squeezes extra blood to your heart which is just what your heart needs if you have angina. When your heart contracts, the cuff deflates.

That helps the heart to do its job of pumping blood back to the rest of your body. The suit has been approved by the Food and Drug Administration (FDA) and is marketed by Future Medical Products Inc. of Hauppauge, NY. Its cost is about one-sixth that of surgery and about a third of angioplasty.

LIFESTYLE CHANGES FOR A HEALTHY HEART

In the USA, CVD is still responsible for almost 1 million fatalities every year and more than half of all deaths. Fortunately, research focusing on causes, diagnosis, treatment and prevention of heart disease, is moving ahead rapidly. Angina doesn't permanently damage your heart.

But even if it's not a medical emergency, angina is a warning sign that your heart isn't getting enough oxygen, and you could get a heart attack someday soon if you don't take care of yourself. When you've been diagnosed with angina, you need to make a few lifestyle changes to control your condition. Sometimes, these changes can make the difference between getting rid of angina completely or having to undergo surgery.

- Even a small amount of exercise-walking at a moderate pace for 30 minutes, 2-3 days a week - can make a big difference to your health.
- Stop smoking! Smoking makes it harder for the heart to do its work, namely, to pump blood throughout your body.
- Control your BP.
- Avoid over-the-counter drugs that may raise your heart rate and BP, such as diet pills and decongestants.
- You can also lower your BP with a low-fat, high-fiber and low-salt diet.
- Eat small meals. Large meals make your digestive system and your heart work harder.
- Eat several small meals rather than three big meals a day. Take it easy after eating and try not to overdo it.

CURRENT DEBATE

The raised lipids, chiefly cholesterol, in the blood, are linked to an increased risk of heart disease has been an established fact. It has been proven that lowering blood lipid levels by statins significantly reduces the risk of heart disease. Obesity is also linked to heart disease and preventing obesity will lower the rates of heart disease.

Many genetic variants are likely to exert their effects on the walls of arteries, making them more susceptible to

the common heart disease risk factors such as cigarette smoking, diabetes and cholesterol.

A number of preventative strategies target the vessel wall (control of BP and smoking cessation), but the large majority of existing drug treatments for lowering CAD risk operate through manipulation of circulating lipid levels and few direct target vessel wall processes.

In modern medicine, there is a generally negative feeling about sodium, the element found in salt. Excessive sodium intake is linked to water retention, and it is also a risk factor for high BP. Both excessive sodium intake and high BP are major risk factors for developing heart failure, and for causing complications in those with existing heart failure.

CONCLUSION

Ischemia is a result of the effects of atheroma, causing narrowing or occlusion of one or more branches of the coronary arteries. Athermatous plaques cause narrowing.

Occlusion may be by plaques alone, or plaques complicated by thrombosis. The overall effect depends on the size of the coronary artery involved and whether it is only narrowed or completely blocked. Narrowing of an artery leads to angina pectoris and occlusion to myocardial infarction.

When atheroma develops slowly, collateral arterial blood supply may have time to develop and effectively supplement or replace the original. This consists of the dilatation of normally occurring anastomotic arteries joining adjacent arteries. When sudden severe narrowing or occlusion of an artery occurs, the anastigmatic arteries dilate but may not be able to supply enough blood to meet myocardial needs.

It is perhaps the most beneficial immediate treatment that can be administered to the patient with myocardial ischemia and can be given promptly and with confidence to all suspected patients without aspirin sensitivity contraindications. Nitroglycerin is another frequently used medication in the care of patients with chest discomfort. Nearly all patients with chest pain considered to be of possible cardiac origin should receive at least one sublingual nitroglycerin.

SUGGESTED READING

1. Tello M (Ed.). Heart disease and breast cancer: Can women cut risk for both? Harvard Health Publishing, Harvard Medical School. 2019.
2. Raghavendra Rao MV, Meka Balaramiah, Sireesha Bala A. Is myocarditis like a hot knife through butter? Int J Curr Med Pharm Res. 2018;4(2-A):2988-92.
3. Myerburg RJ, Castellanos A. Cardiac arrest and sudden cardiac death (Chap 39). Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine. Volume 2, Elsevier; 2015. p. 821.
4. Cayley WE Jr. Diagnosing the cause of chest pain. Am Fam Physician. 2005;72(10):2012-21.
5. Rathore V, Singh N, Mahat R. Risk factors for acute myocardial infarction: A review. EJMI. 2018;2(1):1-7.
6. Priori SG, Aliot E, Blomstrom-Lundqvist C, Bossaert L, Breithardt G, Brugada P, et al. Task Force on Sudden Cardiac Death of the European Society of Cardiology. Eur Heart J. 2001;22(16):1374-450.
7. Nigam PK. Biochemical markers of myocardial injury. Indian J Clin Biochem. 2007;22(1):10-7.
8. Benjamin EJ, Blaha MJ, Chiuve SE, Cushman M, Das SR, Deo R, et al; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics-2017 update: a report from the American Heart Association. Circulation. 2017;135(10):e146-e603.
9. What are the signs and symptoms of coronary heart disease?" www.nhlbi.nih.gov. September 29, 2014. Archived from the original on 24 February 2015. Retrieved 23 February 2015.
10. Nissen SE, Tuzcu EM, Schoenhagen P, Brown BG, Ganz P, Vogel RA, et al; REVERSAL Investigators. Effect of intensive compared with moderate lipid-lowering therapy on progression of coronary atherosclerosis: a randomized controlled trial. JAMA. 2004;291(9):1071-80.
11. Pope JH, Aufderheide TP, Ruthazer R, Woolard RH, Feldman JA, Beshansky JR, et al. Missed diagnoses of acute cardiac ischemia in the emergency department. N Engl J Med. 2000;342(16):1163-70.
12. Amsterdam EA, Lewis WR, Kirk JD, Diercks DB, Turnipseed S. Acute ischemic syndromes. Chest pain center concept. Cardiol Clin. 2002;20(1):117-36.
13. Storrow AB, Gibler WB. Chest pain centers: diagnosis of acute coronary syndromes. Ann Emerg Med. 2000;35(5):449-61.
14. McCarthy JH, Palmer FJ. Incidence and significance of coronary artery calcification. Br Heart J. 1974;36(5):499-506.
15. Virtanen KS, Heikkilä J, Kala R, Siltanen P. Chest pain and rate-dependent left bundle branch block in patients with normal coronary arteriograms. Chest. 1982;81(3):326-31.
16. Hertzeanu H, Aron L, Shiner RJ, Kellermann J. Exercise dependent complete left bundle branch block. Eur Heart J. 1992;13(11):1447-51.
17. Robert Wahl, Sridevi Pitta, Robert J. Zaluski. Cardiac emergencies. Tata McGraw Hill. Edn. P-269.
18. Hansson GK. Inflammation, atherosclerosis, and coronary artery disease. N Engl J Med. 2005;352(16):1685-95.
19. Wang CZ, Mehendale SR, Calway T, Yuan CS. Botanical flavonoids on coronary heart disease. Am J Chin Med. 2011;39(4):661-71.
20. Mythili S, Malathi N. Diagnostic markers of acute myocardial infarction. Biomed Rep. 2015;3(6):743-8.

21. Strasser T. Reflections on cardiovascular disease. Interdisc Sci Rev.1978;3(3):225-30.
22. Gibbs HR. History of cardiovascular disease. In: Walker HK, Hall WD, Hurst JW (Eds.). Clinical Methods: The History, Physical, and Laboratory Examinations. 3rd Edition, Boston: Butterworth Publishers; 1990.
23. Maghamiour N, Safaie N. High Creatine kinase (CK)-MB and lactate dehydrogenase in the absence of myocardial injury or infarction: a case report. J Cardiovasc Thorac Res. 2014;6(1):69-70.
24. Mayron R, Gaudio FE, Plummer D, Asinger R, Elsperger J. Echocardiography performed by emergency physicians: impact on diagnosis and therapy. Ann Emerg Med. 1988;17(2):150-4.
25. Gibbon JH Jr. Application of a mechanical heart and lung apparatus to cardiac surgery. Minn Med. 1954;37(3): 171-85; passim.
26. Selker HP, Zalenski RJ, Antman EM, Aufderheide TP, Bernard SA, Bonow RO, et al. An evaluation of technologies for identifying acute cardiac ischemia in the emergency department: a report from a National Heart Attack Alert Program Working Group. Ann Emerg Med. 1997;29(1):13-87.
27. Ronksley PE, Brien SE, Turner BJ, Mukamal KJ, Ghali WA. Association of alcohol consumption with selected cardiovascular disease outcomes: a systematic review and meta-analysis. BMJ. 2011;342:d671.
28. Sobernheim JF. Praktische Diagnostik der Inneren Krankheiten mit Vorzueglicher Ruecksicht auf Pathologische Anatomic. Berlin: Hirschwald; 1837. p. 117.
29. Lawes CM, Vander Hoorn S, Rodgers A; International Society of Hypertension. Global burden of blood-pressure-related disease, 2001. Lancet. 2008;371(9623):1513-8.
30. Kalra SS, Shanahan CM. Vascular calcification and hypertension: cause and effect. Ann Med. 2012;44 Suppl 1: S85-92.
31. Lee TH. Measurement and improvement of quality of cardiovascular care. In: Bonow RO, Mann DL, Zipes DP, Libby P (Eds.). Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine. pp. 42-8.
32. Mendis S, Puska P, Norrving B. Global Atlas on Cardiovascular Disease Prevention and Control (PDF). World Health Organization in collaboration with the World Heart Federation and the World Stroke Organization. 2011. pp. 3-18. ISBN 978-92-4-156437-3. Archived (PDF) from the original on 2014-08-17.
33. Schultheiss HP, Kühl U, Cooper LT. The management of myocarditis. Eur Heart J. 2011;32(21):2616-25.
34. Frangogiannis NG. Inflammation in cardiac injury, repair and regeneration. Curr Opin Cardiol. 2015;30(3):240-5.
35. Masters, Jo; Bowden, Carole; Martin, Carole. Textbook of veterinary medical nursing. Oxford: Butterworth-Heinemann; 2003. p. 244.
36. Bonow RO, Mann DL, Zipes DP, Libby P (Eds.). Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine.
37. Kannel WB, Hjortland M, Castelli WP. Role of diabetes in congestive heart failure: the Framingham study. Am J Cardiol. 1974;34(1):29-34.
38. Johnson K, Ghassemzadeh S. Chest Pain. [Updated 2019 Mar 13]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2019 Jan-. Available at: https://www.ncbi.nlm.nih.gov/books/NBK470557/.
39. Nordqvist C. How to spot and treat a heart attack. Medical News Today. 2017. Available at: https://www.medicalnewstoday.com/articles/151444.php
40. Barbaro G, Di Lorenzo G, Grisorio B, Barbarini G. Incidence of dilated cardiomyopathy and detection of HIV in myocardial cells of HIV-positive patients. Gruppo Italiano per lo Studio Cardiologico dei Pazienti Affetti da AIDS. N Engl J Med. 1998;339(16):1093-9.
41. Treating hypertension with calcium channel blockers. 2018. Available at: https://www.healthline.com/health/heart-disease/calcium-channel-blockers.
42. Linton MRF, Yancey PG, Davies SS, Jerome WG, Linton EF, Song WL, et al. The Role of Lipids and Lipoproteins in Atherosclerosis. 2019 Jan 3. 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/books/NBK343489/
43. Nitroglycerin: Side effects, dosage, uses, and more – healthline. Available at: https://www.healthline.com/health/nitroglycerin-sublingual-tablet.
44. Sandoiu A. Blood test may predict cardiovascular disease. Available at: https://www.medicalnewstoday.com/articles/325083.php.
45. American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines; American Society of Echocardiography; American Society of Nuclear Cardiology; Heart Rhythm Society; Society of Cardiovascular Anesthesiologists; Society for Cardiovascular Angiography and Interventions; Society for Vascular Medicine; Society for Vascular Surgery, Fleisher LA, Beckman JA, Brown KA, Calkins H, Chaikof EL, Fleischmann KE, et al. 2009 ACCF/AHA focused update on perioperative beta blockade incorporated into the ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery. J Am Coll Cardiol. 2009;54(22):e13-e118.
46. Grines CL, Bonow RO, Casey DE Jr, Gardner TJ, Lockhart PB, Moliterno DJ, et al; American Heart Association; American College of Cardiology; Society for Cardiovascular Angiography and Interventions; American College of Surgeons; American Dental Association; American College of Physicians. Prevention of premature discontinuation of dual antiplatelet therapy in patients with coronary artery stents: a science advisory from the American Heart Association, American College of Cardiology, Society for Cardiovascular Angiography and Interventions, American College of Surgeons, and American Dental Association, with representation from the American College of Physicians. J Am Coll Cardiol. 2007;49(6):734-9.

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False Localizing Signs in Neurology

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ABSTRACT

False localizing neurological signs reflect dysfunction distant from the site of the pathology. They pose considerable difficulties to the treating neurologist as they are unreliable when attempting to localize the lesion, which challenges the traditional clinicoanatomical correlation. It is important to be aware of false localizing signs and the situations in which they occur as they may be indicative of a serious, even life-threatening, pathology for appropriate and timely investigations and management.

Keywords: False localizing signs, raised ICP, intracranial pathology

Neurological signs are described as 'false localizing' if they reflect dysfunction distant or remote from the expected anatomical locus of pathology and challenge the traditional clinicoanatomical correlation paradigm that forms the basis of neurological examination.

HISTORY

The notion false localizing signs was first described by James Collier in 1904 based on clinical examination during life and subsequent postmortem studies. Gassel noted false localizing signs to be more common in patients with raised intracranial pressure (ICP). Structural imaging, especially magnetic resonance imaging (MRI), which gives an opportunity to study pathological anatomy concurrent with clinical examination, has provided some new insight into the causes of these signs.

PATHOGENESIS

The pathogenesis of false localizing signs remain uncertain. False localizing signs occur in two contexts: As a consequence of raised ICP, which is symptomatic of intracranial pathology (tumor, hematoma, abscess) or idiopathic (idiopathic intracranial hypertension [IIH]) and with spinal cord lesions. Associated lesions may be intra- or extraparenchymal. The course of the associated disease may be acute (cerebral hemorrhage) or chronic (IIH, tumor). Disturbance of higher mental functions, cranial nerve palsies, hemiparesis, sensory features and muscular atrophy, may all occur as false localizing signs.

FALSE LOCALIZING SIGNS

Cortical Functions

Signs traditionally thought to be of cortical origin, such as aphasia and inattention, may some times occur with exclusively subcortical pathology; conversely exclusively cortical lesions may result in dysarthria.

Hemineglect is much commoner with right rather than left parietal lobe lesions. False localizing ipsilateral hemineglect has been reported in patients with posterior fossa tumors like meningioma causing left pontine compression, despite normal imaging of cerebral hemispheres.

Cranial Nerves

Oculomotor nerve

Unilateral fixed dilated pupil (Hutchinson's pupil) may occur with an ipsilateral lesion such as an intracerebral hemorrhage, due to transtentorial herniation of the brain compressing the oculomotor nerve against the free edge of the tentorium. Because of the fascicular organization of the fibers within the oculomotor nerve, the externally placed pupillomotor fibers are most vulnerable. Very occasionally, fixed pupil

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may occur contralateral, and hence false localizing, to cranial pathology. The exact mechanism for this clinical observation is not known. The mechanism for this third nerve palsy has traditionally been ascribed to extrinsic compression of the third nerve on the margin of the tentorium. An alternative explanation, possibly relevant to false localizing third nerve palsy, is that raised ICP causes kinking of the nerve over the clivus, just posterior to the clinoid. Another suggestion is that a central mechanism might be responsible, supratentorial pressure causing the brainstem to buckle as it descends because of caudal tethering of the neuraxis at the first dentate ligament (dynamic axial brainstem distortion).

Divisional third nerve palsy is usually associated with lesions at the superior orbital fissure or anterior cavernous sinus, where the superior division of the oculomotor nerve passes to the superior rectus and levator palpebrae, and the inferior division to the medial and inferior recti and inferior oblique muscles. Divisional third nerve palsies may sometimes occur with more proximal lesions, presumably as a consequence of the topographic arrangement of the fascicles within the nerve, for example with intrinsic brainstem disease (e.g., stroke) or with pathology in the subarachnoid space where the nerve rootlets emerge from the brainstem (e.g., malignant infiltration).

Trochlear nerve

False localizing fourth nerve palsies, causing diplopia on downward and inward gaze, have occasionally been described in the context of IIH. Trochlear nerve palsy might be overlooked in cases in which other cranial nerves are affected (sixth, third) because the signs are subtle.

Trigeminal nerve

Trigeminal nerve hypofunction (trigeminal sensory neuropathy) or hyperfunction (trigeminal neuralgia) may on occasion be false-localizing, for example in association with IIH or with contralateral pathology, often a tumor. For example, trigeminal neuralgia has been associated with a contralateral chronic calcified subdural hematoma, which caused rotational displacement of the pons, with resolution after removal of the hematoma.

This dysfunction may be hypoactive or hyperactive, manifesting with negative or positive Jacksonian symptoms, respectively; hence, there may be trigeminal neuropathy or trigeminal neuralgia. Gassel found motor involvement in only 2 of 8 patients with false localizing fifth nerve involvement. Arsava et al reported both clinical and electrophysiological evidence of left trigeminal neuropathy in a patient with IIH. Examining the blink reflex, no response was elicited either ipsi- or contralaterally when stimulating the left supraorbital nerve, and although trigeminal motor function was clinically intact, no response was elicited from the left masseter muscle when measuring the latency of the jaw reflex.

As with the idiopathic condition, there has been debate about the pathophysiology of trigeminal neuralgia associated with contralateral tumors. Some favor vascular compression of the nerve root as the proximate cause of paroxysmal ephaptic transmission, whereas others implicate angulations and distortion of the nerve root entry/exit zone as a consequence of displacement of brain tissue caused by an expanding mass lesion in the posterior fossa. In favor of the latter explanation, two cases have been reported in which trigeminal neuropathy was 'converted' to trigeminal neuralgia (hence, a lesser degree of dysfunction) following removal of a contralateral posterior fossa tumor. However, other cases have been presented in which trigeminal neuralgia did not resolve after tumor removal alone. Matsuura and Kondo implicate adherence of arachnoid membrane to the nerve as a contributing factor and advocate its resection in order to straighten the nerve axis.

Abducens nerve

Sixth nerve palsies are the most common false-localizing sign of raised ICP. In one series of 101 cases of IIH, 14 cases were noted, 11 unilateral and three bilateral. Stretching of the nerve in its long intracranial course or compression against the petrous ligament or ridge of the petrous temporal bone have been suggested as the mechanism for false-localizing sixth nerve palsy.

Facial nerve

Lower motor neuron type facial weakness has been described in the context of IIH, sometimes occurring bilaterally to cause facial diplegia, usually with concurrent sixth nerve palsy or palsies. Hemifacial spasm has rarely been described with contralateral posterior fossa lesions.

Vestibulo cochlear nerve

Hearing loss has on occasion been reported as a complication of IIH.

Multiple Lower Cranial Nerve involvement

Concurrent false-localizing involvement of multiple cranial nerves has been noted on occasion, for example, trigeminal, abducens and facial nerves with a contralateral acoustic neuroma, and trigeminal, glossopharyngeal and vagus nerves with a contralateral laterally-placed posterior fossa meningioma.

Motor System

Kernohan's notch syndrome: False-localizing hemiparesis

A supratentorial lesion, such as acute subdural hematoma, may cause transtentorial herniation of the temporal lobe, with compression of the ipsilateral cerebral peduncle against the tentorial edge; since this is above the pyramidal decussation, a contralateral hemiparesis results.

Occasionally; however, the hemiparesis may be ipsilateral to the lesion, and hence false-localizing; this occurs when the contralateral cerebral peduncle is compressed by the free edge of the tentorium. This is the Kernohan-Woltman notch phenomenon, or Kernohan's notch syndrome. There may be concurrent homolateral third nerve palsy, ipsilateral to the causative lesion.

Brainstem compression: False-localizing diaphragm paralysis

Hemidiaphragmatic paralysis with ipsilateral brainstem (medullary) compression by an aberrant vertebral artery has been described, in the absence of pathology localized to the C_3-C_5 segments of the spinal cord where phrenic motor neurones originate, hence it is a false-localizing sign.

Foramen magnum/upper cervical cord

Paresthesia in the hands with intrinsic hand muscle wasting and distal upper limb areflexia, with or without long tract signs, suggestive of a lower cervical myelopathy may occur with lesions at the foramen magnum or upper cervical cord (remote atrophy).

Lower cervical/upper thoracic cord

Compressive lower cervical or upper thoracic myelopathy may produce spastic paraplegia with a mid-thoracic sensory level (or 'girdle sensation'). In one case a spastic paraplegia with a sensory level at T10 was associated with cervical compression from a herniated disc at C5/C6.

Radiculopathy

False-localizing radiculopathy may occur in the context of IIH and cerebral venous sinus thrombosis, manifesting as acral paresthesias, backache and radicular pain, and less often with motor deficits, which on occasion may be sufficiently extensive to mimic Guillain-Barré syndrome (flaccid-areflexic quadriplegia). The postulated mechanism for such radiculopathy is mechanical root compression due to elevated cerebrospinal fluid (CSF) pressure.

Cerebellar syndrome

Frontocerebellar pathway damage, for example, as a result of infarction in the territory of the anterior cerebral artery, may result in incoordination of the contralateral limbs, mimicking cerebellar dysfunction. Suboccipital exploration to search for cerebellar tumors based on these clinical findings was known to occur before the advent of brain imaging.

Pseudo-internuclear ophthalmoplegia

False localizing terminology has also been used to describe internuclear ophthalmoplegia, usually indicative of medial longitudinal fasciculus dysfunction, in patients with myasthenia gravis; this 'pseudo-internuclear ophthalmoplegia' has also been observed in dermatomyositis.

Pseudoathetosis

Pseudoathetosis or abnormal writhing movements, usually of the fingers, is caused by a failure of joint position sense (proprioception). It indicates disruption of the proprioceptive pathway, from peripheral nerve to parietal cortex. It may be mistaken for choreoathetosis. However, these abnormal movements are relatively constant irrespective of whether the eyes are open or closed and occur in the absence of proprioceptive loss.

Pseudosyringomyelia

Pseudosyringomyelia has been used to describe a selective loss of pain and temperature sensation with relative preservation of vibration and position sense seen in amyloid polyneuropathy and Tangier disease, (a small fiber sensory neuropathy), in the absence of any spinal cord pathology, and hence false localizing.

DISCUSSION

False localizing neurological signs have presented significant challenges to clinical neurologists. In the

era before neuroimaging, operations were sometimes performed on, and treatments administered to, the wrong side based on these signs.

For the practicing neurologist, an awareness of the possibility of false localizing signs, and knowledge of the situations in which they are most likely to occur, is necessary to heighten the index of clinical suspicion, so that the possible pathological import of false localizing signs is not missed. The pathophysiology of many false localizing signs is still poorly, if at all, understood. The preponderant association with extrinsic mass lesions, such as intracranial tumors (especially meningioma), subdural hematoma, and intervertebral disc prolapse, has long been noted, although intrinsic lesions may certainly be responsible on occasion. Some of these pathologies exert their effects acutely, whereas for others (for example, meningiomas) it is their slow growth which is implicated. The possibility of multifactorial pathophysiology therefore seems likely.

Most importantly, since false localizing signs may be indicative of serious, even life threatening, pathology within neural pathways, awareness of the signs and the situations in which they occur, will facilitate appropriate and timely investigation and management.

SUGGESTED READING

1. Larner AJ. A dictionary of neurological signs: Clinical Neurosemiology. Kluwer Academic Publishers; October 2001.
2. Collier J. The false localising signs of intracranial tumour. Brain. 1904;27(4):490-508.
3. Gassel MM. False localizing signs. A review of the concept and analysis of the occurrence in 250 cases of intracranial meningioma. Arch Neurol. 1961;4:526-54.
4. Marshman LA, Polkey CE, Penney CC. Unilateral fixed dilation of the pupil as a false-localizing sign with intracranial hemorrhage: case report and literature review. Neurosurgery. 2001;49(5):1251-5; discussion 1255-6.
5. Ksiazek SM, Repka MX, Maguire A, Harbour RC, Savino PJ, Miller NR, et al. Divisional oculomotor nerve paresis caused by intrinsic brainstem disease. Ann Neurol. 1989; 26(6):714-8.
6. Larner AJ. Proximal superior division oculomotor nerve palsy from metastatic subarachnoid infiltration. J Neurol. 2002;249(3):343-4.
7. Lee AG. Fourth nerve palsy in pseudotumor cerebri. Strabismus. 1995;3(2):57-9.
8. Speer C, Pearlman J, Phillips PH, Cooney M, Repka MX. Fourth cranial nerve palsy in pediatric patients with pseudotumor cerebri. Am J Ophthalmol. 1999; 127(2):236-7.
9. Arsava EM, Uluc K, Nurlu G, Kansu T. Electrophysiological evidence of trigeminal neuropathy in pseudotumor cerebri. J Neurol. 2002;249(11):1601-2.
10. Matsuura N, Kondo A. Trigeminal neuralgia and hemifacial spasm as false localizing signs in patients with a contralateral mass of the posterior cranial fossa. Report of three cases. J Neurosurg. 1996;84(6):1067-71.
11. Kondoh T, Tamaki N, Takeda N, Shirataki K, Mastumoto S. Contralateral trigeminal neuralgia as a false localizing sign in calcified chronic subdural hematoma: a case report. Surg Neurol. 1989;32(6):471-5.
12. Maurice-Williams RS. Multiple crossed false localizing signs in a posterior fossa tumour. J Neurol Neurosurg Psychiatry. 1975;38(12):1232-4.
13. Davenport RJ, Will RG, Galloway PJ. Isolated intracranial hypertension presenting with trigeminal neuropathy. J Neurol Neurosurg Psychiatry. 1994;57(3):381.
14. Ro LS, Chen ST, Tang LM, Wei KC. Concurrent trigeminal, abducens, and facial nerve palsies presenting as false localizing signs: case report. Neurosurgery. 1995;37(2): 322-4; discussion 324-5.
15. Michelucci R, Tassinari CA, Plasmati R, Rubboli G, Forti A, Tognetti F, et al. Trigeminal neuralgia associated with contralateral intracranial tumour: a false localising sign caused by vascular compression? Report of two cases. J Neurol Neurosurg Psychiatry. 1989;52(10):1202-3.
16. Grigoryan YA, Onopchenko CV. Persistent trigeminal neuralgia after removal of contralateral posterior cranial fossa tumor. Report of two cases. Surg Neurol. 1999;52(1):56-60; discussion 60-1.
17. Round R, Keane JR. The minor symptoms of increased intracranial pressure: 101 patients with benign intracranial hypertension. Neurology. 1988;38(9):1461-4.
18. Larner AJ. False localising signs. J Neurol Neurosurg Psychiatry. 2003;74(4):415-8.
19. Davie C, Kennedy P, Katifi HA. Seventh nerve palsy as a false localising sign. J Neurol Neurosurg Psychiatry 1992;55(6):510-1.
20. Kiwak KJ, Levine SE. Benign intracranial hypertension and facial diplegia. Arch Neurol. 1984;41(7):787-8.
21. Dorman PJ, Campbell MJ, Maw AR. Hearing loss as a false localising sign in raised intracranial pressure. J Neurol Neurosurg Psychiatry. 1995;58(4):51.
22. Kernohan JW, Woltman HW. Incisura of the crus due to contralateral brain tumor. Arch Neurol Psychiatry 1929;21:274-87.
23. Cohen AR, Wilson J. Magnetic resonance imaging of Kernohan's notch. Neurosurgery. 1990;27(2):205-7.
24. Schulz R, Fegbeutel C, Althoff A, Traupe H, Grimminger F, Seeger W. Central sleep apnoea and unilateral diaphragmatic paralysis associated with vertebral artery compression of the medulla oblongata. J Neurol. 2003;250(4):503-5.
25. Sonstein WJ, LaSala PA, Michelsen WJ, Onesti ST. False localizing signs in upper cervical spinal cord compression. Neurosurgery. 1996;38(3):445-8; discussion 448-9.

26. Adams KK, Jackson CE, Rauch RA, Hart SF, Kleinguenther RS, Barohn RJ. Cervical myelopathy with false localizing sensory levels. Arch Neurol. 1996;53(11):1155-8.
27. Ochiai H, Yamakawa Y, Minato S, Nakahara K, Nakano S, Wakisaka S. Clinical features of the localized girdle sensation of mid-trunk (false localizing sign) appeared in cervical compressive myelopathy patients. J Neurol. 2002;249(5):549-53.
28. Pego-Reigosa R, Trobajo de las Matas JE, Branas F, Martinez-Vazquez F Cortes-Laino JA. Dorsal sensory level as a false localizing sign in cervical myelopathy. Rev Neurol. 1998;27(155):86-8.
29. Moosa A, Joy MA, Kumar A. Extensive radiculopathy: another false localising sign in intracranial hypertension. J Neurol Neurosurg Psychiatry. 2004;75(7):1080-1.
30. Obeid T, Awada A, Mousali Y, Nusair M, Muhayawi S, Memish S. Extensive radiculopathy: a manifestation of intracranial hypertension. Eur J Neurol. 2000;7(5): 549-53
31. Gado M, Hanaway J, Frank R. Functional anatomy of the cerebral cortex by computed tomography. J Comput Assist Tomogr. 1979;3(1):1-19.
32. Bakheit AM, Behan PO, Melville ID. Bilateral internuclear ophthalmoplegia as a false localizing sign. J R Soc Med. 1991;84(10):627.
33. Cohen L. Tumors in the region of the foramen magnum. In: Handbook of Clinical Neurology. Volume 17, Tumours of the brain and skull. Part II. Vinken PJ, Bruyn GW (Editors), Amsterdam: North-Holland; 1974. pp. 719-30.

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Study on Correlation Between MELD Score and Hematological Abnormalities in Predicting Prognosis in Patients with Chronic Liver Disease

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ABSTRACT

Abnormalities in hematological indices are frequently encountered in cirrhosis of liver. Multiple causes contribute to the occurrence of hematological abnormalities. Recent studies suggest that the presence of hematological cytopenias is associated with a poor prognosis in cirrhosis. This study was conducted on 43 patients with chronic liver disease to assess the hematological abnormalities. We found 37 (90%) patients had hemoglobin <12 g/dL. Macrocytic anemia was the predominant type, followed by normocytic normochromic and microcytic type. Twenty-four patients had platelets <1.5 lakh/dL; 28 patients had prolonged prothrombin time (PT) and international normalized ratio (INR). Twelve patients showed peripheral smear picture suggestive of pancytopenia. We observed patients with anemia had model of end-stage liver disease (MELD) score above 15% compared to patients without anemia. We also observed patients with MELD score above 20% had mean platelets of 1.5 lakh/dL compared to lower score. Thirty-eight patients had splenomegaly. We also observed that mean platelet count in patients with hepatic encephalopathy was low and they also had prolonged PT.

Keywords: Anemia, cirrhosis, hematological spectrum in cirrhosis

The liver is the largest organ in the body and amongst the most complex organs that has a wide range of functions. It has a major role to play in the metabolism of carbohydrates, proteins and lipids, inactivation of various toxins, metabolism of drugs, hormones, synthesis of plasma proteins and maintenance of immunity. The liver has a significant role in maintenance of blood homeostasis - from being a primary site of hematopoiesis in fetal life to maintenance of hematological parameters in postnatal life. It stores iron, folic acid and vitamin B12, and secretes clotting factors and inhibitors. Therefore, a range of hematological abnormalities are encountered in association with liver diseases.[1]

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Decompensated chronic parenchymal liver disease is one of the most common diseases encountered in day-to-day practice. Because of chronic disease many hematological abnormalities are present in these patients. The hematological abnormalities in a chronic disease add morbidity to the primary pathology and increase the mortality. Hence, it becomes necessary to investigate the hematological abnormalities and hemostatic abnormalities to decrease the comorbidity. Abnormalities in hematological parameters are commonly seen in patients with cirrhosis. Abnormal hematological indices (HIs) in cirrhosis have a multifactorial pathogenesis that includes sequestration due to portal hypertension, altered bone marrow stimulating factors, bone marrow suppression due to viruses, toxins or excess alcohol consumption, etc.[2-4]

Abnormalities in HIs are associated with an increased risk of complications such as bleeding and infection.[4]

Various studies on patients with varying stages of cirrhosis have shown a prevalence of hematological abnormalities ranging from 6% to 77%.[4-6]

In an analysis of homogenous patients with compensated Child-Pugh Class A/B cirrhosis, 84% were found to have abnormalities in the HIs, defined as a platelet count of ≤150 × 10^9/L, white blood cell (WBC)

count of ≤400 × 10^9/L or hemoglobin level ≤135 g/L for men and 115 g/L for women. Thirty-two percent of these patients had a combination of cytopenias.[7] Thrombocytopenia was the most common single abnormality and thrombocytopenia and leukopenia was the most common combined abnormality.[8]

The study was conducted at RajaRajeswari Medical College and Hospital, Bangalore. The study was conducted to assess the hematological abnormalities and derangements and the nature of hematological abnormalities mainly to reduce the morbidity. Broadly the hematological abnormalities are viewed under abnormalities in red blood cells (RBCs), WBCs, platelets and coagulation profile.

MATERIAL AND METHODS

This study was conducted at RajaRajeswari Medical College and Hospital, Bangalore. Institutional Ethical Committee clearance was obtained before the study. Informed consent was obtained from all patients who met with inclusion criteria.

Inclusion Criteria

- Patients above 18 years.
- Patients presenting with signs and symptoms of chronic liver disease.
- Patients with ultrasound evidence of chronic liver disease with portal hypertension.

Exclusion Criteria

- Patients with underlying malignancy or known primary hepatocellular carcinoma.
- Patients with primary coagulation disorder or primary abnormalities of hemostatic function.
- Patients with acute hepatic failure.
- Patients with pre-existing anemia due to other causes.
- Patients suffering from end-stage medical diseases like chronic obstructive pulmonary disease, coronary artery disease, cardiac failure, chronic kidney disease.

All patients who met with inclusion criteria were evaluated with detail history and clinical examination. Blood sample was taken for assessment of liver function tests, complete hemogram, coagulation profile, peripheral blood smear, renal function tests and ultrasound abdomen and baseline upper gastrointestinal (GI) endoscopy were done for all patients. Results were analyzed with statistics.

RESULTS

We conducted the study on 43 patients with clinical and sonological diagnosis of chronic liver disease with various etiologies. In all, data were available for 41 patients. Hematological parameters, including anemia, leukocyte count, prothrombin time (PT) and platelet count were assessed in the subjects and were categorized under the different groups of model of end-stage liver disease (MELD) score. The relationship of these variables with MELD score was studied and statistical analysis was done.

This was an observational noninterventional correlational clinical study. Maximum number of patients was in 41-50 years and 30-40 years of age groups. Only 6 patients were above 50 years. Eighty-eight percent of patients were males and 12% were females. Alcohol consumption (38 patients) was common etiology for all these patients and 3 patients had cirrhosis of cryptogenic origin. Fifty percent of patients had history of alcohol consumption for more than 10 years. Ascites, jaundice, generalized weakness and edema of limbs were common symptoms at admission.

Nine patients had bleeding manifestations and 37 patients had hemoglobin <12 g/dL (Table 1). Macrocytic anemia was predominant type. Thirteen patients had leukopenia, 8 patients had leukocytosis and 20 patients had normal leukocyte count. Thrombocytopenia was observed in 24 patients. Twenty-eight patients had prolonged PT and international normalized ratio (INR) (Table 2). Elevated total bilirubin was observed in 16 patients; 36 patients had serum albumin <3 g. Enlarged spleen of more than 10 cm was observed in 38 patients (Table 3). We also observed peripheral smear suggestive of pancytopenia in 12 patients. We found 16 patients with upper GI evidence of varices. Most of patients with platelets <1.5 lakhs/dL had findings of upper GI bleed, but only 2 patients with platelets above 1.5 lakh had upper GI bleed. There was significant drop in hemoglobin and in platelets in patients with MELD score above 20%. Mean corpuscular volume (MCV) was prolonged in patients with MELD score above 20%. This finding was statistically significant. In our study, only 2 patients had MELD score <9%. Most other patients had score above 20% and about 7 patients had very high score (Table 4).

We also found there was increase in PT in patients who had MELD score above 15%. Mean duration of alcohol consumption was also >15 years in patients

Table 1. Clinical Investigations

Variables	No. of patients (n = 41)	Percentage (%)
MCV		
<80	3	7.3
80-95	15	36.6
>95	23	56.1
Hemoglobin (g/dL)		
<10	25	61.0
10-12	12	29.3
12-14	2	4.9
>14	2	4.9
PS		
Macrocytic	23	56.1
Microcytic	7	17.1
Normocytic	11	26.8
Total count		
<4000	13	31.7
4000-11000	20	48.8
>11000	8	19.5
Platelets		
<0.50	2	4.9
0.50-1.50	22	53.7
>1.50	17	41.5
ESR		
<35	11	26.8
35-60	26	63.4
>60	4	9.8

MCV = Mean corpuscular volume; PS = Peripheral smear; ESR = Erythrocyte sedimentation rate.

Table 2. Coagulation Profile

	No. of patients (n = 41)	Percentage (%)
PT, INR		
<20	13	31.7
20-40	27	65.9
>40	1	2.4
Raised INR		
<3 sec	0	0.0
3-5 sec	22	53.7
>5 sec	19	46.3

PT = Prothrombin time; INR = International normalized ratio.

Table 3. Spleen Size in Patients Studied

	No. of patients (n = 41)	Percentage (%)
Spleen		
No	1	2.4
<10	2	4.9
10-15	34	82.9
>15	4	9.8

Table 4. MELD Score Distribution of Patients Studied

MELD	No. of patients	Percentage (%)
1-9%	2	4.9
10-19%	11	26.8
20-29%	21	51.2
30-39%	7	17.1
Total	**41**	**100.0**

with MELD score above 20%. There was significant rise in MELD score with fall in hemoglobin. Mean platelet count was <1.5 lakhs/dL in patients with MELD score above 15%. We observed low mean serum albumin and total protein among patients with high MELD score; this observation was statistically significant (Table 5). Only 2 patients had MELD score <10%. Rest all patients had high score. MELD score above 30% was observed in 7 patients. We observed Child-Pugh score of Category B in 19 patients and category C was seen in 7 patients. Most of the patients with high MELD score presented with jaundice, ascites and edema. Few patients had bleeding symptoms. There was significant correlation between high MELD score and hepatic encephalopathy in our patients.

DISCUSSION

The vital functions of many organs in the body depend directly or indirectly on the liver. The hematopoietic system is an exception. Beginning early in fetal life, it exerts a profound influence on the formation and maintenance of blood. It acts as a hematopoietic organ and after birth it plays an active and important role in the production of many elements necessary for homeostasis and hematopoiesis. Indirectly, when the liver is damaged by either acute or chronic disease, the effect on these functions may be catastrophic. Liver plays a major role in carbohydrate, lipid and protein metabolism. Its role in hematological manifestations is also important. Loss of liver function can manifest as subtle metabolic abnormalities and derangements

Table 5. Comparison of Clinical Variables According to MELD Score of Patients Studied

Variables	MELD				P value
	1-9%	10-19%	20-29%	30-39%	
Age (years)	47.00 ± 0.00	52.00 ± 14.30	48.90 ± 12.43	45.29 ± 10.64	0.731
Duration	15.00 ± 0.00	18.36 ± 10.22	14.19 ± 10.25	9.14 ± 8.01	0.294
MCV	87.00 ± 0.00	95.09 ± 3.86	94.33 ± 12.34	93.71 ± 13.73	0.808
Hemoglobin (g/dL)	12.50 ± 0.00	10.23 ± 1.91	9.32 ± 2.30	10.74 ± 2.96	0.187
Total count	5700.00 ± 424.26	7514.55 ± 5256.15	6200.00 ± 3932.43	10500.00 ± 6318.49	0.222
Platelets	2.63 ± 0.33	1.72 ± 0.95	1.52 ± 0.87	1.59 ± 1.07	0.440
ESR	42.50 ± 17.68	48.64 ± 13.42	46.09 ± 14.49	48.43 ± 16.83	0.948
PT INR	16.00 ± 0.00	21.36 ± 3.61	23.65 ± 6.00	28.43 ± 27.45	0.521
INR	1.11 ± 0.01	1.69 ± 0.48	1.95 ± 0.57	2.51 ± 2.52	0.348
Total bilirubin	1.40 ± 0.00	2.95 ± 1.75	6.06 ± 4.37	17.23 ± 14.96	0.001**
OT	23.00 ± 0.00	57.18 ± 19.43	79.48 ± 55.37	117.71 ± 55.73	0.034**
PT	13.00 ± 0.00	21.55 ± 6.85	31.81 ± 19.65	66.00 ± 46.35	0.002**
Total protein	8.20 ± 0.00	6.36 ± 0.84	6.15 ± 0.74	6.03 ± 0.85	0.008**
Albumin	3.90 ± 0.00	2.24 ± 0.54	2.25 ± 0.41	2.49 ± 0.82	0.001**
Sodium (mEq/L)	133.00 ± 7.07	135.73 ± 4.52	131.81 ± 3.54	127.57 ± 1.51	0.001**
Potassium	4.60 ± 0.00	4.27 ± 0.45	4.05 ± 0.52	3.81 ± 0.54	0.142

**Statistically significant.

in hematological parameters, which can ultimately culminate in grave complications. Liver plays a major role in maintaining the hematological parameters and maintain the homeostasis. Liver stores iron, vitamin B12 and folic acid, which are necessary for normal hematopoiesis. Liver also secretes the clotting factors and inhibitors, and keeps the homeostasis in equilibrium. Chronic liver disease is usually accompanied by hypersplenism. Diminished erythrocyte survival is frequent. Dietary deficiencies, alcoholism, bleeding and difficulties in hepatic synthesis of proteins used in blood formation or coagulation add to the complexity of the problem.

In our study, we found anemia and thrombocytopenia as two major hematological abnormalities. And presence of these abnormalities can affect prognosis of patients which was observed by elevated MELD score. And thus, these abnormalities can contribute to patient's mortality.

We also observed significant relation between prolonged PT and increase in MELD and Child-Pugh score. Once again, presence of thrombocytopenia and prolonged PT can contribute to development of hepatic encephalopathy and adverse prognosis. We observed most of the patients with thrombocytopenia and prolonged PT had evidence of upper GI bleed, which could lead to the development of hepatic encephalopathy and anemia.[9,10]

Hence, identification and treatment of all abnormal HIs are a vital part of the management of patients with chronic liver disease. Similar results were observed is previous studies by Selvamani et al. Among the 100 patients, 52 patients had normochromic and normocytic anemia, 30 patients had microcytic anemia and 16 patients had macrocytosis. Two had dimorphic anemia and thrombocytopenia was found in 46 patients.[9]

Rajkumar Solomon et al, in their study, found 50% of the patients had thrombocytopenia (<1 lakh). Out of the 13 patients who had an upper GI bleed, 3 patients had normal platelet counts and the remaining had counts <1 lakh. They also found that most of the patients with thrombocytopenia had prolonged PT.[1]

CONCLUSION

Apart from serum protein, albumin, which reflects synthetic function of liver, alteration in hematological parameters are telltale signs of chronicity of liver disease. Efforts can be made to normalize the hematological parameters, so that we can reduce the mortality and morbidity of these patients effectively.

REFERENCES

1. Rajkumar Solomon T, Aravind A, Caroline Selvi K, Balamurali R, Ramkumar G, Muthukumuran K, et al. A study on hematological abnormalities in chronic liver diseases. IOSR-JDMS. 2017;16(6):38-44.
2. Aster RH. Pooling of platelets in the spleen: role in the pathogenesis of "hypersplenic" thrombocytopenia. J Clin Invest. 1966;45(5):645-57.
3. Peck-Radosavljevic M. Hypersplenism. Eur J Gastroenterol Hepatol. 2001;13(4):317-23.
4. Qamar AA, Grace ND. Abnormal hematological indices in cirrhosis. Can J Gastroenterol. 2009;23(6):441-5.
5. Morlock CG, Hall BE. Association of cirrhosis, thrombocytopenia and hemorrhagic tendency. Arch Intern Med. 1943;72(1):69-77.
6. Bashour FN, Teran JC, Mullen KD. Prevalence of peripheral blood cytopenias (hypersplenism) in patients with nonalcoholic chronic liver disease. Am J Gastroenterol. 2000;95(10):2936-9.
7. Qamar AA, Grace ND, Groszmann RJ, Garcia-Tsao G, Bosch J, Burroughs AK, et al; Portal Hypertension Collaborative Group. Incidence, prevalence, and clinical significance of abnormal hematologic indices in compensated cirrhosis. Clin Gastroenterol Hepatol. 2009;7(6):689-95.
8. Peck-Radosavljevic M. Thrombocytopenia in liver disease. Can J Gastroenterol. 2000;14 Suppl D:60D-66D.
9. Selvamani S, Thomas S. Evaluation of haematological abnormalities in decompensated chronic liver disease patients. IOSR-JDMS. 2017;16(8):16-21.
10. Laffi G, Marra F, Gresele P, Romagnoli P, Palermo A, Bartolini O, et al. Evidence for a storage pool defect in platelets from cirrhotic patients with defective aggregation. Gastroenterology. 1992;103(2):641-6.

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Acute Encephalitis Syndrome – A Presentation of Ascaris Toxin

AVINASH SHANKAR*, SHUBHAM†, AMRESH SHANKAR‡, ANURADHA SHANKAR#

ABSTRACT

Acute encephalitis syndrome (AES) is primarily caused by virus; but other pathogens cannot be ignored as prompt and correct clinical acumen saves many lives. This study represents the evaluation and treatment of 147 cases of AES admitted at our center who were managed based on previous experience of similar AES prevalence in 1985, in nutritionally deprived patients of poor socioeconomic status with history of passing round worms. We saved all 147 cases without any adversity or adjuvant required or mortality and all patients passed round worms on deworming (albendazole and ivermectin) in therapeutic dose for 3 consecutive days, after 7th day of discharge. Majority of the patients regained consciousness within 48 hours of therapy while seizures ceased in all cases by 12 hours of therapy. Thus, consider round worm encephalopathy in nutritionally deprived patients of AES in addition to other pathogens as right approach will save life, time and cost of therapy. Round worms cause encephalopathy due to competitive inhibition of pyridoxal 5 phosphate coenzyme, a prime coenzyme for gamma-aminobutyric acid synthesis and metabolism in brain by its polypeptide secretion in adverse situation.

Keywords: Acute encephalitis syndrome, round worm encephalopathy, pyridoxal 5 phosphate, gamma-aminobutyric acid

Febrile convulsion is not a new presentation but continuing since long and the disease gravity is increasing progressively. Initially, acute encephalitis syndrome (AES) was claimed to be solely due to viral infection and was termed Japanese encephalitis but these days the presentation is being termed as AES. In spite of available therapeutics and advanced diagnostic tools, the mortality remains the same even at higher centers.

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Acute encephalitis is clinically diagnosed in children with acute onset of symptoms and signs of inflammatory lesions in the brain. Changes in sensorium, seizures and upper motor neuron type of altered muscle tone are suggestive of cerebral dysfunction.

The clinical picture involves a prodromal phase of 1-3 days that includes fever, malaise and headache and an encephalitic phase with continued fever, decreasing level of consciousness, seizures, abnormal movements or paralysis. Signs of meningeal inflammation are absent or minimal.

In summary, all that presents with fever and cerebral dysfunction is not acute encephalitis.

Acute encephalitis is usually caused by any of the several neurotrophic viruses. A large number of these are vector-transmitted (arthropod-borne) arboviruses. In India, Japanese encephalitis (JE) virus is the commonest.

Clinical neurologic manifestations are caused by a wide range of viruses, bacteria, fungi, parasites, spirochetes, chemicals and toxins. Correct management will depend on the correct diagnosis.

Considering a similar disease prevalence among the downtrodden and nutritionally deprived children in 1985 that proved to be a manifestation of

Ascaris lumbricoides toxin and majority were saved, similar line of treatment was evaluated in patients with AES in this study who presented at RA Hospital & Research Centre, Warisaliganj (Nawada), Bihar with the prime motive of ensuring cure in the majority.

OBJECTIVE OF THE STUDY

The objective of the study was to ensure cure in majority of the patients and to ascertain the cause of presentation.

MATERIAL AND METHODS

Patients with complaints of AES attending Medical Emergency of RA Hospital & Research Centre from May to July 5, 2019 were considered for the study.

Parents of the admitted patients were thoroughly interrogated for onset of the disease and its progression. Patients were clinically evaluated, investigated and provided basic life support and were administered:

- Oxygen inhalation
- Ryle's tube intubation for feeding (bland, sweet, liquid oral) and antacid with oxetacaine 2.5 mL every 6 hours
- IV mannitol 10% with glycerine 10% in dose of 10 mL/kg every 12 hours
- Injection sodium valproate with pediatric IV solution
- Injection amikacin 7.5 mg/kg every 12 hours
- IV pediatric solution *plus* methylcobalamin, pyridoxine and nicotinamide ½-1 mL slow infusion
- Herbal ointment (constituting of pure ghee, *Mentha piperita*, *Cinnamomum camphora*, oil of *Caryophyllus aromaticus*, oil of *Cinnamomum zeylanicum*) for local chest application
- Herbal composite syrup through feeding tube 1.25-2.5 mL every 12 hours
- Frequent change of posture
- Cold sponging.

Patients were observed for:

- Fever
- Convulsion
- Consciousness status
- Any evident paresis
- Any unusual presentation.

On discharge on 5th day, patients were advised:

- Suspension of aluminum hydroxide, magnesium hydroxide, simethicone, oxetacaine 2.5 mL three times daily
- Herbal composite syrup 1.25-2.5 mL every 12 hours
- Syrup sodium valproate 1.25-2.5 mL every 8 hours
- Syrup B complex 2.5 mL twice-daily
- Bland, simple and sweet oral liquid diet.

After a week, for deworming, patients were advocated:

- Albendazole *plus* ivermectin suspension in dose of 5-10 mL at bed time for 3 consecutive days.

After deworming patients were advised:

- Herbal composite syrup 1.25-2.5 mL every 12 hours for 2 months
- Syrup B complex 2.5-5 mL twice-daily for 2 months
- Deworming every month for 3 days for 3 consecutive months every year
- High protein diet
- Restrict biscuits, Kurkure, etc.

OBSERVATIONS AND RESULTS

Overall, 147 patients were selected for the study in the age group of 2-14 years and majority (38.8%) were in the age group of 5-8 years. Nearly 10.9% were in the age group of 11-14 years (Table 1). Out of the 147 patients, 99 were males and 48 were females (Fig. 1).

Majority (45.6%) of the patients were suffering for 6-12 hours while 7.4% patients were suffering for more than 24 hours (Fig. 2).

Majority (55.8%) patients attended the center after 12-18 hours of onset of disease while 9.5% after >24 hours (Fig. 3).

Out of all, 44.9% were having temperature >102°F, 95.2% each had tonic-clonic convulsions and unconsciousness, 70.7% had pot belly abdomen. There was history of

Table 1. Distribution of Patients as per Age and Sex

Age group (in years)	Number of patients			
	Male	Female	Total	Percentage
2-5	31	17	48	32.7
5-8	40	17	57	38.8
8-11	17	09	26	17.6
11-14	11	05	16	10.9

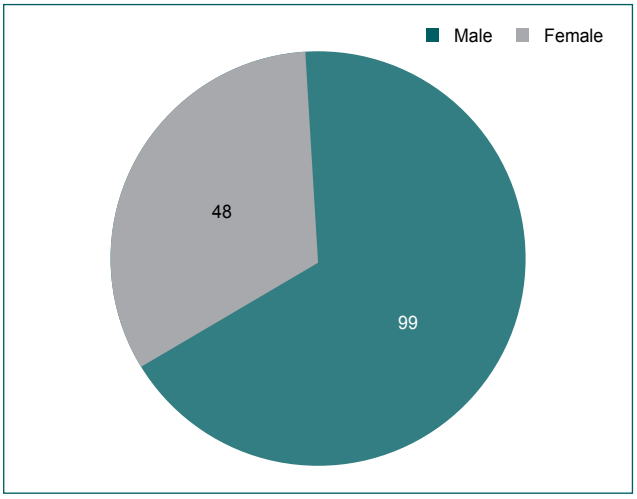

Figure 1. Number of male and female patients.

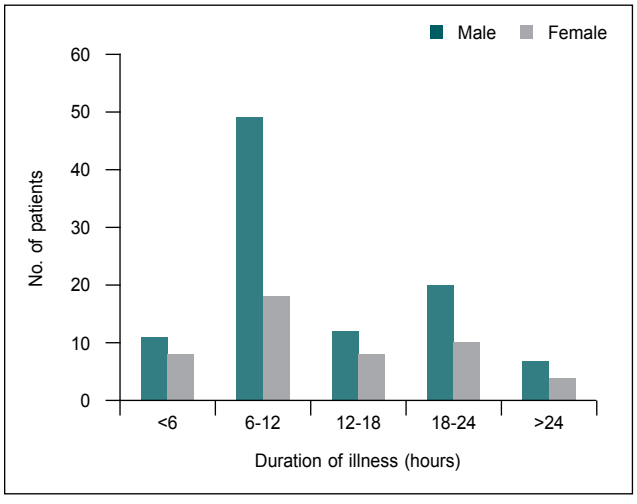

Figure 2. Distribution of patients as per duration of illness.

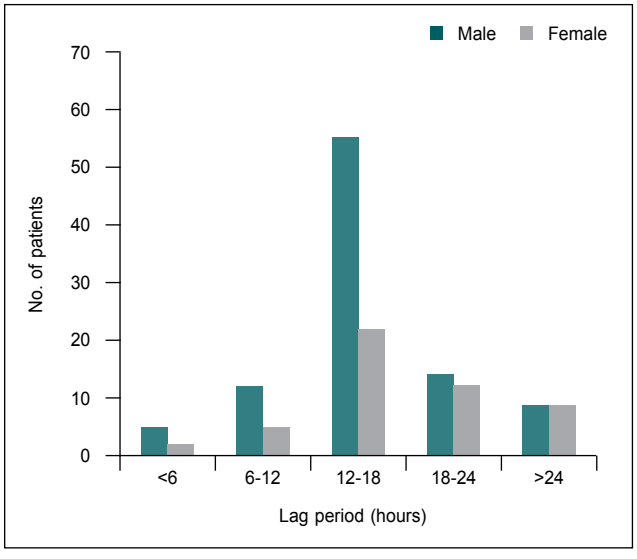

Figure 3. Distribution of patients as per lag period in attending our center.

passing round worm and urticarial rashes in past in 59.2%. About 72.8% showed hemoglobin <10 gram%. Signs of malnutrition and raised eosinophil count were present in all the cases (Table 2).

Table 2. Distribution of Patients as per their Presenting Features

Particulars	Number of patients
Fever	
>102ºF	66
<102ºF	81
Convulsions	
Tonic-clonic	140
Mild jerks	07
Loss of sensation	147
Consciousness	
Unconscious	140
Conscious	07
Abnormal behavior	07
History of helminthiasis	87
Recurrent loose motion	147
Abdominal distension	147
Urticarial rash	87
Clinical examination	
Pot belly abdomen	104
Signs of malnutrition	147
Palpable liver	90
Investigations	
CBC shows raised eosinophil	147
Hemoglobin:	
<10 gm%	107
>10 gm%	40
CSF	No abnormality seen
X-ray chest	No abnormality detected
X-ray abdomen	Distended intestinal loop
Blood for malarial antigen	None
Widal	Nonreactive
Blood and CSF for viral analysis	No virus detected
EEG	No evident pathology
CT brain	No evident pathology

CBC = Complete blood count; CSF = Cerebrospinal fluid; ECG = Electroencephalogram; CT = Computed tomography.

Majority of the patients regained consciousness in 12 hours, though 27 cases took 40 hours to regain consciousness. Convulsion seized within 12 hours in all the cases irrespective of their age or lag period.

Feeding tube was removed after 48 hours in all the cases. No patients presented with any residual paresis or neuropsychiatric changes.

After a week, administration of albendazole with ivermectin suspension at bedtime for 3 consecutive days ensured passage of round worms in all the cases. Post-therapy 2-week follow-up revealed no untoward effects or withdrawal manifestation. Repeat basic bioparameters in all cases showed no alteration in any of the cases.

DISCUSSION

Nutritionally deprived patients with AES admitted at our center having history of passing round worm in past, vomiting and diarrhea, occasional urticarial rash, fever, were treated conventionally on the line of round worm encephalopathy evident during 1985 and showed complete recovery within 48 hours and passed round worms on deworming on 7th day after discharge.

Figure 4 summarizes the pathogenesis of round worm encephalopathy.

Round worm causes encephalopathy due to competitive inhibition of pyridoxal 5 phosphate coenzyme, a prime coenzyme for gamma-aminobutyric acid synthesis and metabolism in brain by its polypeptide secretion in adverse situation.

Table 3 summarizes the plan of therapy and its effect.

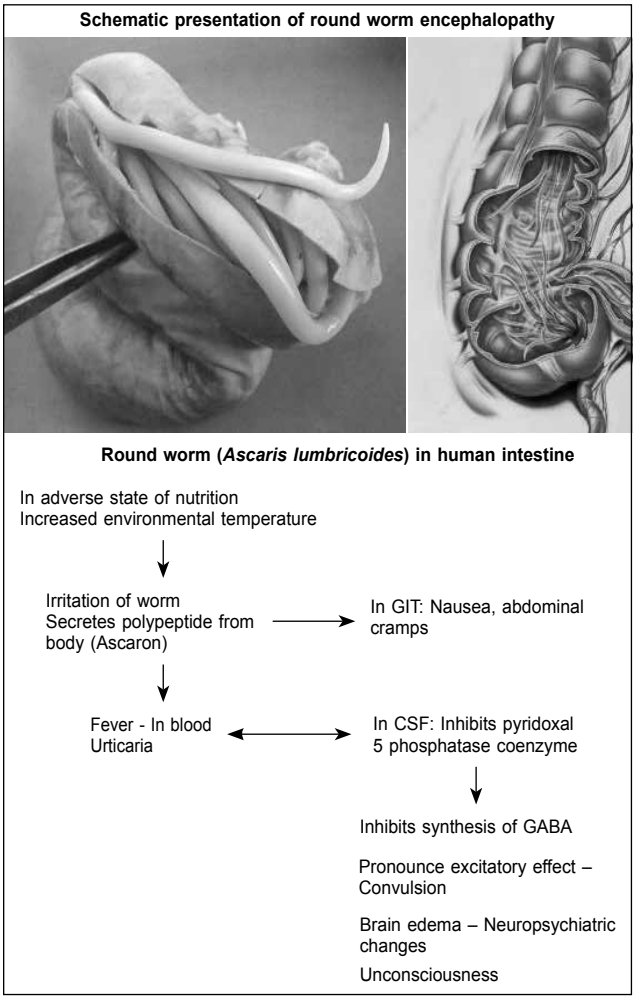

Figure 4. Pathogenesis of round worm encephalopathy.

GIT = Gastrointestinal tract; GABA = Gamma-aminobutyric acid.

Table 3. Plan of Therapy and its Effect

Oxygen inhalation	To ensure appropriate energy need of brain cells and check hypoxic degeneration.
IV mannitol 10% with glycerine 10%	To reduce brain edema.
IV pyridoxine	To facilitate pyridoxal 5 phosphatase coenzyme responsible for formation of GABA from glutamic acid and its metabolism by activating enzyme glutamate decarboxylase and GABA transaminase.
IV sodium valproate	To control seizure
Through Ryle's tube antacid with oxetacaine	Antacid solution coats intestinal mucosa, checks toxin absorption, intestinal irritation. Oxetacaine acts as local anesthetic on round worm body, calms the worm, check its irritation and secretion of polypeptide.
Herbal neurogen	Revitalize damaged neural cells, energize the brain cells and preserve neural cell function.
Bland, simple, sweet liquid oral diet	To facilitate nutrition to child.
Antimicrobial therapy	To check super infection.
Herbal chest application	To facilitate reabsorption of lung fluid and check respiratory infection
Cold sponging	To decrease body temperature and prevent neural cell integrity.

IV = Intravenous

CONCLUSION

All cases of AES responded well to the regime with 100% survival without any untoward effects or sequelae and proved to be due to *Ascaris lumbricoides* toxin. Thus, in AES in nutritionally deprived patients, round worm encephalopathy must be kept in mind.

SUGGESTED READING

1. Prober CG, Srinivas NS, Mathew R. Central nervous system infections. In: Kliegman RM, Stanton BF, St. Geme JW, Schor NF (Eds.). Nelson Textbook of Pediatrics. 20th Edition, New Delhi: Reed Elsevier India Pvt. Ltd; 2016. pp. 2936-48.
2. Shah AB, John TJ. Recurrent outbreaks of hypoglycaemic encephalopathy in Muzaffarpur, Bihar. Curr Sci. 2014;107(4):570-1.
3. Joshi R, Kalantri SP, Reingold A, Colford JM Jr. Changing landscape of acute encephalitis syndrome in India: a systematic review. Natl Med J India. 2012;25(4):212-20.
4. Jain P, Jain A, Kumar A, Prakash S, Khan DN, Singh KP, et al. Epidemiology and etiology of acute encephalitis syndrome in North India. Jpn J Infect Dis. 2014;67(3):197-203.
5. Kakkar M, Rogawski ET, Abbas SS, Chaturvedi S, Dhole TN, Hossain SS, et al. Acute encephalitis syndrome surveillance, Kushinagar district, Uttar Pradesh, India, 2011-2012. Emerg Infect Dis. 2013;19(9):1361-7.
6. John TJ, Verghese VP, Arunkumar G, Gupta N, Swaminathan S. The syndrome of acute encephalitis in children in India: Need for new thinking. Indian J Med Res. 2017;146(2):158-61.
7. Shankar A. Round worm encephalopathy. Antiseptic. 1987. pp. 595-8.
8. Bayoumi RA, Kirwan JR, Smith WR. Some effects of dietary vitamin B6 deficiency and 4-deoxypyridoxine on γ-aminobutyric acid metabolism in rat brain. J Neurochem. 1972;19(3):569-76.
9. Coursin DB. Vitamin B6 and brain function in animals and man. Ann N Y Acad Sci. 1969;166(1):7-15.
10. Gale K. Mechanisms of seizure control mediated by gamma-aminobutyric acid: role of the substantia nigra. Fed Proc. 1985;44(8):2414-24.
11. Kaufman DL, Houser CR, Tobin AJ. Two forms of the gamma-aminobutyric acid synthetic enzyme glutamate decarboxylase have distinct intraneuronal distributions and cofactor interactions. J Neurochem. 1991;56(2):720-3.
12. Martin DL, Martin SB, Wu SJ, Espina N. Cofactor interactions and the regulation of glutamate decarboxylase activity. Neurochem Res. 1991;16(3):243-9.
13. Martin DL, Rimvall K. Regulation of gamma-aminobutyric acid synthesis in the brain. J Neurochem. 1993;60(2):395-407.
14. Miller LP, Walters JR, Martin DL. Post-mortem changes implicate adenine nucleotides and pyridoxal-5' -phosphate in regulation of brain glutamate decarboxylase. Nature. 1977;266(5605):847-8.
15. Tews JK. Pyridoxine deficiency and brain amino acids. Ann N Y Acad Sci. 1969;166(1):74-82.

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Indian Journal of Clinical Practice, Vol. 30, No. 4, September 2019

Prevalence of Undiagnosed COPD in Western Indian Population

ANAND YANNAWAR*, DAMANJIT DUGGAL, RAM CHOPRA

ABSTRACT

As per World Health Organization (WHO) data, chronic obstructive pulmonary disease (COPD) ranks amongst the top five causes of death in developed as well as in developing countries. Early identification of COPD is critical for preventive care and for instituting therapy. It is widely recognized that many people with COPD are undiagnosed, including some with significant airflow obstruction. A retrospective study was conducted in a Western Indian hospital to find out undiagnosed COPD patients in all admitted and outdoor patients from year 2008 till end of year 2010 for any cause, respiratory or nonrespiratory and also to grade the severity by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines.

Keywords: Chronic obstructive pulmonary disease, spirometry, FEV_1, FVC, GOLD criteria

As per World Health Organization (WHO) data, chronic obstructive pulmonary disease (COPD) ranks amongst the top five causes of death in developed as well as in developing countries. Three million people die every year due to COPD and it ranks as 3rd largest cause of death in world. Half a million people die every year due to COPD in India, which is over 4 times the number of people who die due to COPD in USA and Europe.

Early identification of COPD is critical for preventive care and for instituting therapy. Majority of COPD cases are undiagnosed although magnitude of this problem is very large. Prevalence of COPD in different studies ranges from 2% to 22% in men and 1.2% to 19% in women.

Both smokers and nonsmokers, males and females in rural and urban areas bear the brunt of progressive obstructive airways disease, which, if diagnosed earlier, can be prevented and treated to a larger extent with newer long-acting β_2-adrenergic receptor agonists (LABAs) and long-acting muscarinic receptor antagonists (LAMAs). Indian rural women still use Chullas (kind of wood burning cooking stove) leading to continuous smoke exposure, resulting in airways inflammation and COPD.

AIMS OF STUDY

To find out undiagnosed COPD patients in all admitted and outdoor patients in our hospital from year 2008 till end of year 2010 for any cause, respiratory or nonrespiratory, and also to grade the severity by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines.

MATERIAL AND METHODS

Spirometry data of all indoor patients and outdoor patients from year 2008 till end of year 2010 was retrieved and analyzed for missed out COPD diagnosis by GOLD criteria, i.e., forced expiratory volume in 1 second/forced vital capacity (FEV_1/FVC) ratio <70%. A total of 6,066 patients (3,964 males and 2,102 females) were included in this retrospective study. Previous COPD diagnosed cases were excluded. Demographic, health behavior and quality-of-life data was obtained from spirometry report and indoor records of the patients.

RESULTS

A total of 895 patients (14.75%) were found to meet COPD criteria in our study. Six hundred twenty-nine (70.27%) patients were males and 266 (29.72%) patients were females and all females patients were

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nonsmokers and probably they were exposed to bio fuel/wood burning smoke (Chulla smokers) (Figs. 1 and 2). Table 1 and Figures 3-5 give further analysis of our study.

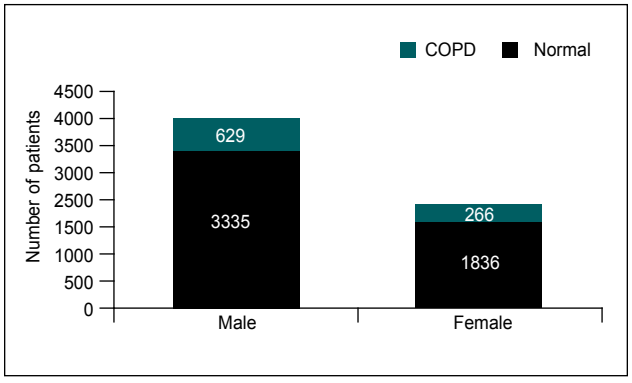

Figure 1. Number of patients diagnosed with COPD

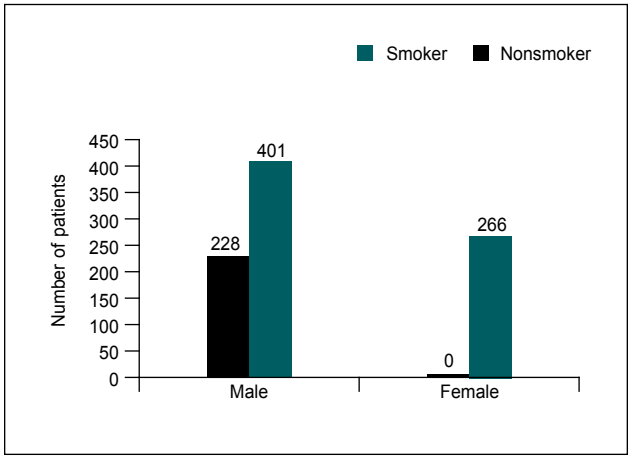

Figure 2. Smokers and nonsmokers who developed COPD.

Table 1. Demographic Profile of COPD Patients

Sex	Smoking status	Severity of obstruction
Male	Smokers 228 (36.24%)	Mild 3 (1.31%)
		Moderate 68 (29.82%)
		Severe 95 (41.66%)
		Very severe 62 (27.19%)
	Nonsmokers 401 (63.75%)	Mild 12 (2.99%)
		Moderate 191 (47.63%)
		Severe 146 (36.40%)
		Very severe 52 (12.96%)
Female	All are nonsmokers 266	Mild 5 (1.87%)
		Moderate 109 (40.97%)
		Severe 112 (42.10%)
		Very severe 40 (15. 03%)

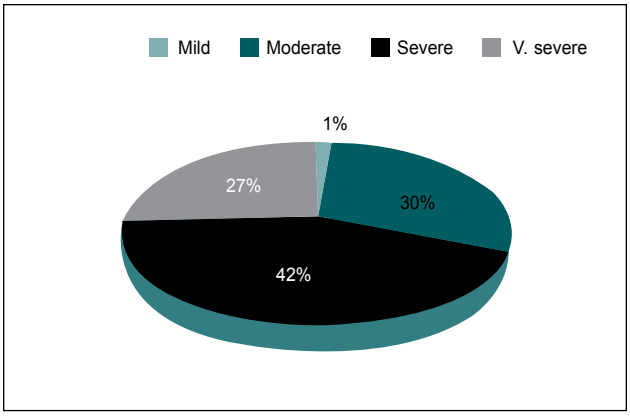

Figure 3. Severity of COPD in smokers.

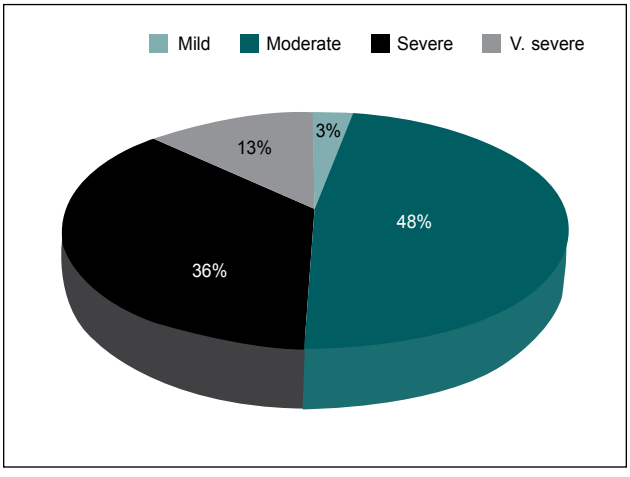

Figure 4. Severity of COPD in males.

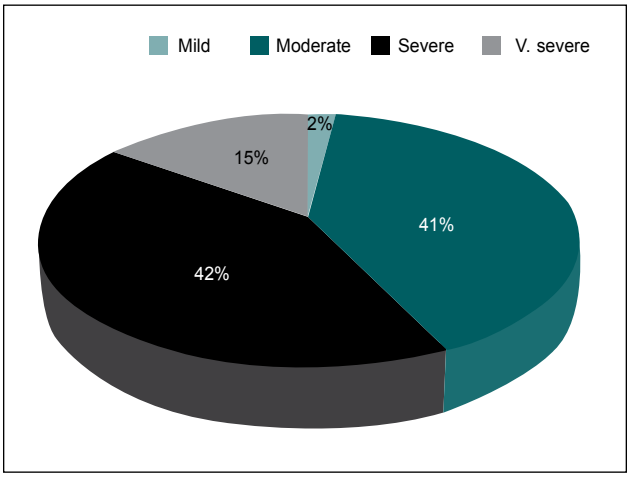

Figure 5. Severity of COPD in females.

DISCUSSION

It is widely recognized that many people with COPD are undiagnosed, including some with significant airflow obstruction. Tobacco smoking is the most important and traditionally famous risk factor for developing

COPD. Indian families use wood and animal dung for cooking food and making water warm for bath and it is the major risk factor for developing COPD in India and developing countries. During her lifetime, every woman who spends 2-3 hours for cooking every day inhales a volume of 25 million liters of highly polluted air, thereby exposing herself to extremely high levels of particulate matter and gaseous air pollutants. Burning one mosquito coil in the night emits as much particulate matter pollution, as that which is equivalent to around 100 cigarettes.

Other causes of COPD are chronic poorly treated persistent asthma, history of tuberculosis, occupational lung diseases and chemical use for killing mosquito and bed bugs. Making a diagnosis of COPD and its differentiation from other diseases presents an important challenge for primary care practitioners and in higher referring centers. Making diagnosis of COPD on the basis of clinical history and examination can underestimate diagnosis.

In our study, incidence of COPD in nonsmoker males was found to be higher (63.75%). Various studies found the prevalence of undiagnosed COPD between 4-18.2%. Even though total patients who visited this tertiary care center were 1,22,750, the PET was done in only 6,066 (4.94%) patients. Spirometry is a useful tool to diagnose serious respiratory diseases like COPD. This 14.75% undiagnosed COPD patients of our study seems to be tip of iceberg.

CONCLUSION

- 14.75% COPD patients were undiagnosed even after suffering from long time.
- Significant number of females were undiagnosed (i.e., 29.72%).
- All females were nonsmokers and biomass exposure was the main factor for developing COPD.
- More smokers were suffering from severe COPD as compared to nonsmokers.
- Diagnosing undiagnosed COPD early and treatment are necessary to prevent repeated admission and early deaths.
- Chulla smoking is one of the major culprit for nonsmokers COPD in developing countries like India.

SUGGESTED READING

1. Salvi S. COPD: the neglected epidemic. In: Jindal SK (Ed.). Textbook of Pulmonary and Critical Care Medicine. Volume 2, New Delhi: Jaypee Brothers Medical Publishers; 2011. pp. 971-4.
2. Lopez AD, Shibuya K, Rao C, Mathers CD, Hansell AL, Held LS, et al. Chronic obstructive pulmonary disease: current burden and future projections. Eur Respir J. 2006;27(2):397-412.
3. Jindal SK, Aggarwal AN, Gupta D. A review of population studies from India to estimate national burden of chronic obstructive pulmonary disease and its association with smoking. Indian J Chest Dis Allied Sci. 2001;43(3):139-47.
4. Anderson DO, Ferris BG Jr. Role of tobacco smoking in the causation of chronic respiratory disease. N Engl J Med. 1962;267:787-94.
5. Salvi S, Barnes PJ. Is exposure to biomass smoke the biggest risk factor for COPD globally? Chest. 2010;138(1):3-6.
6. Liu W, Zhang J, Hashim JH, Jalaludin J, Hashim Z, Goldstein BD. Mosquito coil emissions and health implications. Environ Health Perspect. 2003;111(12): 1454-60.
7. Salvi SS, Barnes PJ. Chronic obstructive pulmonary disease in non-smokers. Lancet. 2009;374(9691):733-43.

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FDA Approves New Add-on Drug to Treat Off Episodes in Adults with Parkinson's Disease

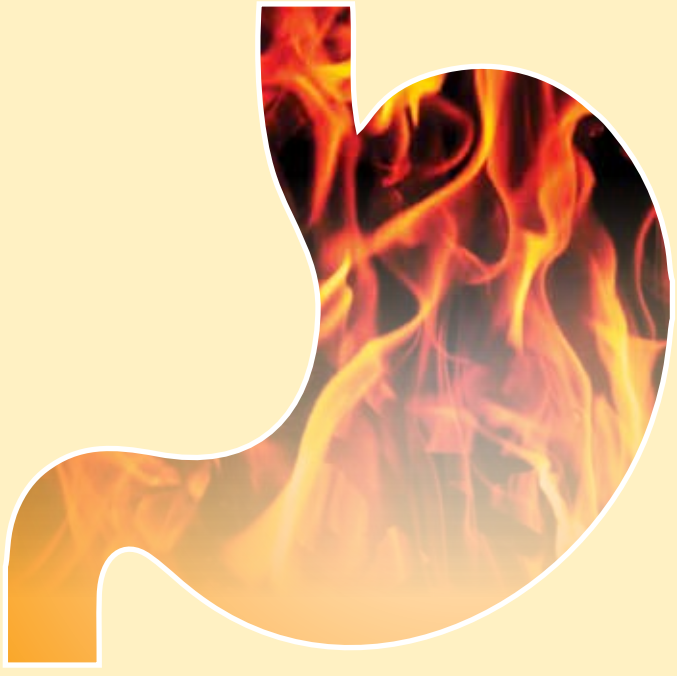
The US Food and Drug Administration approved istradefylline tablets as an add-on treatment to levodopa/carbidopa in adult patients with Parkinson's disease (PD) experiencing "off" episodes. An "off" episode is a time when a patient's medications are not working well, causing an increase in PD symptoms, such as tremor and difficulty walking… (*FDA*)

USPSTF Recommends All Adults Receive HCV Screening

The US Preventive Services Task Force (USPSTF) has posted new draft recommendations advising that essentially all US adults aged 18-79 years should be screened for hepatitis C virus (HCV) (B recommendation).

This recommendation represents a major change from 2013 guidelines, which recommended screening in high-risk individuals and baby boomers (who are at high risk for HCV). The draft recommendation was posted on the USPSTF website and will be open to public comment through September 23… (*Medscape*)

In GERD



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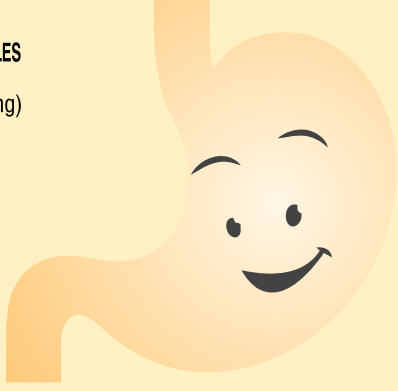

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Indian Journal of Clinical Practice, Vol. 30, No. 4, September 2019

A Case of Leptospirosis Presenting as Multiorgan Failure

AK BADRINATH*, K SURESH†, R RAGHUNATHAN†, SURESH BABU S‡

ABSTRACT

Leptospirosis, an infection of worldwide distribution, has come to international attention as a re-emerging infectious disease. It is caused by spirochetes of the genus Leptospira, which infect most of the domestic and wild animals and spread to humans by the infected urine of animals. Patients with leptospirosis may present with acute febrile illness to life-threatening multiorgan failure. Here we present the case of a 25-year-old female with fever, jaundice and altered sensorium, admitted as a case of sepsis with multiple organ dysfunction syndrome who was later diagnosed as a case of leptospirosis.

Keywords: Leptospirosis, icterus, renal failure, meningitis

CASE REPORT

A 25-year-old female presented with complaints of fever for 7 days; there was continuous high-grade fever, no chills or rigor, with generalized body pain. Patient had altered sensorium since 1 day. Patient had one episode of seizure (generalized tonic-clonic seizure [GTCS]) with frothing from mouth and post-ictal confusion a few hours prior to admission in the hospital. There was no history of vomiting or cough with expectoration. No history of decreased urine output or abdominal pain was given. Patient was not a diabetic and had no history of pulmonary tuberculosis in the past. Patient was married, had 2 children and had no menstrual irregularities at present.

On examination, patient was irritable, not obeying oral commands, responded to pain. Patient's general physical examination revealed patient febrile - 100.6°F with pallor++; icterus+ and subconjunctival hemorrhage. Pulse - 126/min and regular; blood pressure (BP) - 100/60 mmHg; cardiac examination - normal; respiratory system - patient tachypneic, normal vesicular breath sounds present with scattered crepitations and per abdomen - soft, hepatomegaly present. Central nervous system - patient had altered sensorium, agitated, responded to pain, moved all limbs, reflexes diminished bilaterally and bilateral plantars extensor. Bilateral pupils equal and reacting to light and terminal neck rigidity was present. Patient was admitted with the provisional diagnosis of meningitis with multiorgan dysfunction syndrome and was evaluated.

Her complete hemogram revealed anemia with hemoglobin - 9.9 g/dL, total leukocyte count - 8,400/mm^3, differential count: polymorphs - 67% and lymphocytes - 24%, with severe thrombocytopenia - platelets 24,000/mm^3. She had hypoglycemia with random blood glucose of 60 mg/dL. Her renal function tests and serum electrolytes were normal. Her liver function was deranged: total bilirubin - 4.6 mg/dL, SGOT - 430 IU/L, SGPT - 190 IU/L, ALP - 190 IU/L, total protein - 7.0 g/dL and albumin - 3.7 g/dL. Her urine examination showed microalbuminuria with plenty of RBCs and hemogranular casts suggestive of acute tubular necrosis. Arterial blood gas analysis revealed metabolic acidosis. ECG showed sinus tachycardia but was otherwise normal and chest X-ray revealed increased bronchovascular markings.

Patient was started on intravenous (IV) fluids, Ryle's tube feeding, nasal O_2, antipyretics and IV antibiotics (injection ceftriaxone 1 g IV b.i.d. and injection vancomycin 1 g IV b.i.d.). Treatment was continued with glucose and platelet monitoring in intensive care

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unit. Since, patient had altered sensorium, a computed tomography (CT) brain was done that showed multiple small calcifications, but was otherwise normal. A lumbar puncture was done for cerebrospinal fluid (CSF) analysis - cytology showed moderate cellularity with 240 cells predominant of neutrophils - 70% and monocytes - 20%. However, CSF protein was normal - 25 mg/dL, glucose - 55 mg/dL and lactate dehydrogenase (LDH) - 80.

Dengue serology, scrub typhus and viral markers were negative. Blood, urine and CSF culture were negative and peripheral smear was normal. On Day 2 of admission, her platelets decreased to 12,000/mm^3 and prothrombin time was prolonged. The patient was transfused with 4 units of platelet concentrate and 2 units of fresh frozen plasma. On Day 3 of admission, we had a suspicion of leptospirosis and serum leptospirosis antibody test (IgM) was negative. A serum microagglutination test (MAT) for leptospirosis was positive - 1:160 dilution (significant >1:80 dilution). Patient was continued on injection ceftriaxone 1 g IV b.i.d. and injection vancomycin 1 g IV b.i.d. for 7 days. Patient gradually improved over a period of 7 days; sensorium improved, no fever spikes, platelets returned to normal and liver function improved. After 10 days of intensive care treatment patient was discharged. Final diagnosis - Leptospirosis with multiorgan failure.

DISCUSSION

Leptospirosis is a re-emerging infectious disease of worldwide distribution but more commonly seen in the tropical countries and outbreaks occur in the rainy season. The causative organism is *Leptospira interrogans*, a Gram-negative, thin and motile bacterium, 6-20 μm in length with flagella and it includes around 250 serovars. It is the most common zoonosis and humans are accidental hosts, infected from body fluids, especially urine, of infected animal and rodents are the most common source worldwide.

Leptospirosis presents after an incubation period of 5-14 days. Often a good clinical history is needed to suspect and diagnose leptospirosis. Studies have shown that most of the patients (around 90%) present with acute febrile illness due to bacteremia (anicteric leptospirosis), which is often self-limiting. Patients typically present with fever associated with headache and muscle ache (typically calf pain) and conjunctival suffusion. Also, patients may have symptoms of vomiting, diarrhea and pharyngitis. Inspite of fever being the cardinal symptom, studies have shown that about 5% of cases have no history of fever.

The second phase (immune stage) of illness occurs after 1-3 days of symptom free period or after the initial bacteremic phase. The exact pathogenesis of this immune phase remains unclear. This is probably due to the host immune response to the leptospiral antigens and protein. The two phases are often indistinguishable in icteric leptospirosis. Renal manifestations include oliguric acute tubular necrosis due to hypovolemia and decreased renal perfusion, direct tissue injury, presence of vasoconstrictor agents and some studies suggest rhabdomyolysis, but could not prove it. Acute renal failure is associated with increased mortality. Patients present with jaundice and deranged liver function because of hepatic necrosis. Acalculous cholecystitis, though rare, is clinically significant. Weil's syndrome, the severe form of leptospirosis, manifests with hepatic, renal and pulmonary dysfunction and is associated with increased mortality.

The pulmonary complications are life-threatening; these include acute respiratory distress syndrome and massive hemoptysis. Aseptic meningitis is seen in patients in anicteric immune stage and cranial nerve palsies, encephalitis and altered sensorium are uncommon. Our patient had meningitis with icterus and altered sensorium. Conjunctival hemorrhage is common in immune stage and uveitis may be observed and persist for a year.

The complications of leptospirosis are Weil's disease, disseminated intravascular coagulation, meningoencephalitis, massive hemoptysis, acute renal failure, myocarditis, acalculous cholecystitis and pancreatitis. Thus, leptospirosis can involve most of the vital organs in the body.

Diagnosis is made by rapid diagnostic kits by detecting antibodies IgM and IgG but are negative during first week of illness. Limitation of serology is that antibodies are lacking in the acute phase of the disease. In recent years, several real-time polymerase chain reaction assays have been described. Culturing the bacteria in the blood during first week of illness and in urine from Day 7 of illness is diagnostic but it takes weeks for diagnosis. The MAT represents growth of battery of serovars of 26 leptospiral groups. Detection of agglutination by dark field microscopy is definitive of diagnosis but it usually is negative in first week of illness and is done in specialized centers.

Most of the antibiotics are sensitive in leptospirosis and the drugs commonly used are doxycycline, penicillins and macrolides. Some studies suggest no definite role of antibiotics in milder form of disease. But early

antibiotic treatment has been found to reduce mortality in some studies. Patients with Weil's disease require IV antibiotics. Cefotaxime and ceftriaxone have replaced penicillin in the treatment of leptospirosis. Patients with Weil's disease should be treated in intensive care unit. Renal failure requires dialysis and other supportive care should be given.

Patients should be carefully monitored for the pulmonary complications, which are life-threatening. Few studies showed that oliguria, hypotension and abnormal chest auscultations were important prognostic factors in leptospirosis. There are few case reports of patients with Weil's disease managed successfully with plasma exchange.

CONCLUSION

To conclude, physicians should be aware of complicated leptospirosis. A high-degree of clinical suspicion is required to diagnose leptospirosis. If any patient presents with multiorgan dysfunction, leptospirosis should be ruled out as earlier the diagnosis and treatment, better the prognosis.

SUGGESTED READING

1. Vijayachari P, Sugunan AP, Shriram AN. Leptospirosis: an emerging global public health problem. J Biosci. 2008;33(4):557-69.
2. Bharti AR, Nally JE, Ricaldi JN, Matthias MA, Diaz MM, Lovett MA, et al; Peru-United States Leptospirosis Consortium. Leptospirosis: a zoonotic disease of global importance. Lancet Infect Dis. 2003;3(12):757-71.
3. Togal T, Sener A, Yucel N, Demirbilek S, Akgun FS, Aydogan M, et al. Intensive care of a Weil's disease with multiorgan failure. J Clin Med Res. 2010;2(3):145-9.
4. Aydemir S, Ustundag Y, Borazan A, Sekitmez N, Ozdemir H. A case with jaundice, acute renal failure and thrombocytopenia: Weil's disease. Acad Gastroenterol J. 2004;3(1):42-5.
5. Abdulkader RC. Acute renal failure in leptospirosis. Ren Fail. 1997;19(2):191-8.
6. Thammakumpee K, Silpapojakul K, Borrirak B. Leptospirosis and its pulmonary complications. Respirology. 2005;10(5):656-9.
7. Pappas MG, Ballou WR, Gray MR, Takafuji ET, Miller RN, Hockmeyer WT. Rapid serodiagnosis of leptospirosis using the IgM-specific Dot-ELISA: comparison with the microscopic agglutination test. Am J Trop Med Hyg. 1985;34(2):346-54.
8. Kee SH, Kim IS, Choi MS, Chang WH. Detection of leptospiral DNA by PCR. J Clin Microbiol. 1994;32(4): 1035-9.
9. Trivedi SV, Vasava AH, Bhatia LC, Patel TC, Patel NK, Patel NT. Plasma exchange with immunosuppression in pulmonary alveolar haemorrhage due to leptospirosis. Indian J Med Res. 2010;131:429-33.
10. Tse KC, Yip PS, Hui KM, Li FK, Yuen KY, Lai KN, et al. Potential benefit of plasma exchange in treatment of severe icteric leptospirosis complicated by acute renal failure. Clin Diagn Lab Immunol. 2002;9(2):482-4.

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PM Launches 'Fit India Movement', Says it will Lead India Towards Healthy Future

Prime Minister Narendra Modi launched the 'Fit India' Movement', saying the initiative is the need of the hour and will take the country towards a healthier future. At a colourful ceremony, which included a presentation of India's indigenous martial art forms, dances and sports, Modi said technology has contributed to a sedentary lifestyle.

"Fitness has always been an integral part of our culture. But there is indifference towards fitness issues now. A few decades back, a normal person would walk 8-10 km in a day, do cycling or run," Modi said at the event. "But with technology, physical activity has reduced. We walk less now and the same technology tells us that we are not walking enough," he added.

The launch was also attended by Sports Minister Kiren Rijiju and this year's National Sports Awards winners among others. "We will take this movement to new heights with the cooperation of my fellow Indians. I am so glad that this movement is being launched on the birth anniversary of Major Dhyan Chand, our hockey wizard," Rijiju said at the launch.

Indian Journal of Clinical Practice, Vol. 30, No. 4, September 2019

Senior-Loken Syndrome Complicated by Panuveitis: A Diagnostic Challenge

VK KATYAL*, DEEPAK JAIN†, ISHITA GUPTA‡, SANDHYA RANI PN‡, DEEPAK YADAV‡, JAY PRAKASH KUMAR‡

ABSTRACT

Senior-Loken syndrome (SLS) is a rare autosomal recessive syndrome affecting eyes and kidneys. The kidney condition nephronophthisis, classified as medullary cystic kidney disease, begins in childhood with symptoms of polydipsia and polyuria, which are secondary to defective urinary concentrating ability. Nephronophthisis progresses to end-stage renal disease during the second decade. The retinal lesions are variable, ranging from severe infantile onset retinal dystrophy to more typical retinitis pigmentosa. Other associated features observed in this entity are cerebellar, skeletal and dermatological anomalies. Here, we report a case of SLS in which eye involvement is complicated, rather masqueraded, by panuveitis, causing diagnostic dilemma. There may be a role of autoimmunity in the pathophysiology of the syndrome.

Keywords: Panuveitis, nephronophthisis, retinitis pigmentosa, Senior-Loken syndrome

Senior-Loken syndrome (SLS) is a rare autosomal recessive disorder described by Senior and Loken in 1961 in children. It is broadly a ciliopathy and consists of retinopathy and nephronophthisis. Retinopathy in SLS is variable, including retinitis pigmentosa, retinal dystrophy, Leber amaurosis.[1] Nephronophthisis is a chronic tubulointerstitial nephritis leading onto inability to concentrate urine due to which polyuria and polydipsia occur initially and finally leads to end-stage renal disease (ESRD) by second decade.[2] Clinically, it is diagnosed on the basis of ocular examination and renal assessments. Ocular examination includes fundus examination, refraction testing, visual acuity examination, color testing, electroretinography; whereas renal assessment includes urine analysis, renal function test, ultrasonography and kidney biopsy.[3]

Here, we report a case of SLS involving kidneys in the form of ESRD and eyes in the form of retinitis pigmentosa with other manifestations including skeletal defects and bilateral sensorineural hearing loss. What makes the case different is associated bilateral panuveitis which created the diagnostic dilemma along with an extensive search for the autoimmune etiology, which could not be ascertained.

CASE REPORT

A 19-year-old female presented with history of progressive loss of vision for the last 6 years and progressive hearing loss for last 2 years. For eye condition, she was diagnosed as a case of idiopathic panuveitis in another hospital and was given treatment in the form of steroids, which she stopped 1 year back on her own. She also had multiple seizure episodes of generalized tonic-clonic in type followed by loss of consciousness. There was no history of fever, headache, loose stool, vomiting, jaundice and head trauma.

On examination, she was confused, dyspneic, pale with puffy face and edema over both feet. She was hypertensive with blood pressure of 170/100 mmHg. Lab investigations revealed deranged renal parameters with blood urea of 215 mg/dL and serum creatinine of 8.1 mg/dL, with severe anemia (hemoglobin - 4.6 g/dL), hypocalcemia (serum calcium <5.0 mg/dL), hyperphosphatemia (serum phosphorus - 6.0 mg/dL), metabolic acidosis with pH - 7.11, PCO_2 - 25.5 mmHg and bicarbonate - 7.9 mmol/L. Her serum sodium level was 128 mEq/L and had hyperkalemia with serum potassium >6.0 mEq/L. Her ECG showed sinus tachycardia with

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tall T waves secondary to hyperkalemia. Her chest X-ray revealed bilateral symmetrical opacities suggestive of uremic lung with scoliosis of thoracic spine (Fig. 1).

On ultrasonography, her kidneys were found to be contracted with size of right kidney measuring 6.2 × 2.7 cm and left kidney measuring 6.0 × 2.5 cm with loss of corticomedullary differentiation. Urine complete examination revealed albuminuria without red blood cell cast or dysmorphic red cells. She was treated as a case of ESRD with uremic lung with hypocalcemic seizure. Patient was managed with regular hemodialysis and showed significant improvement in metabolic derangements including metabolic acidosis, hyperkalemia, renal function tests and clinical improvement with relieved shortness of breath and no recurrence of seizure. Her ophthalmologic examination at our institute revealed changes suggestive of retinitis pigmentosa in both eyes with old uveitis (Fig. 2 a and b).

To further evaluate, magnetic resonance imaging (MRI) brain was done, which was suggestive of mild cerebral atrophy. Pure-tone audiometry was done which suggested mild-to-moderate sensorineural hearing loss. Cardiac and hepatic involvement was ruled out with the help of echocardiography and ultrasonography abdomen, respectively. She was advised antinuclear antibody (ANA), c-ANCA, p-ANCA, rheumatoid arthritis factor and C-reactive protein to look for small vessel vasculitis, which turned out to be negative. Mantoux test for tuberculosis, Venereal Disease Research Laboratory (VDRL) for syphilis were also negative. Hence, other possible causes of bilateral panuveitis were ruled out.

To summarize, this was a case of SLS where eye involvement in the form of retinitis pigmentosa which was masquerading as bilateral panuveitis with progressive vision loss despite steroid therapy and progressive kidney disease, which remained undiagnosed until ESRD.

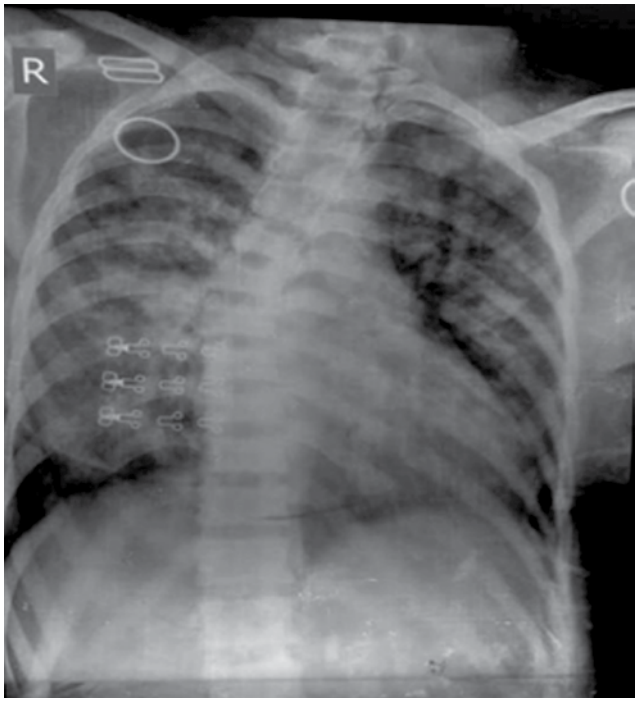

Figure 1. Chest X-ray showing bilateral pulmonary infiltrate with scoliosis.

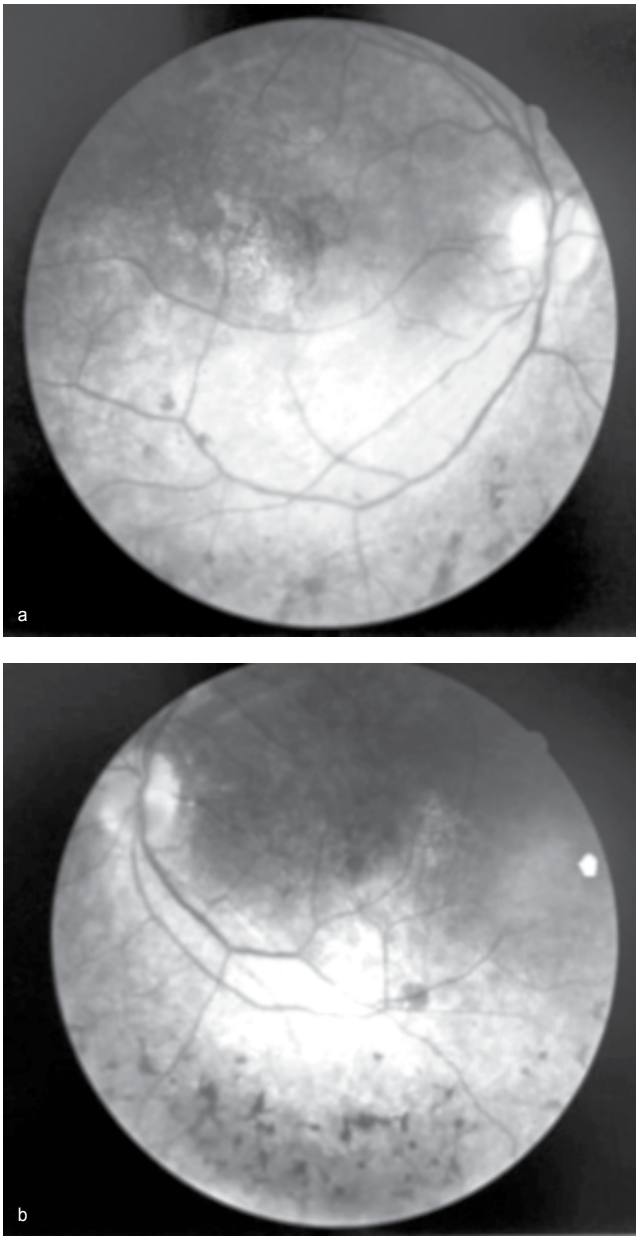

Figure 2 a and b. Fundus of right and left eye, respectively, showing retinitis with bony spicules.

DISCUSSION

Senior-Loken syndrome is a rare autosomal disease with incidence of 1/1,00,000 population and is more common in consanguineous marriage. Other synonyms for this disease are juvenile nephronophthisis with Leber amaurosis, renal retinal syndrome and renal dysplasia and retinal aplasia. Renal nephronophthisis is a ciliopathy due to genetic mutation of *NPHP* gene, which leads to renal cystic dysplasia or cystic kidney. On the basic of median age of presentation, nephronophthisis is categorized into three variants: 'Infantile' at the age of 1 year, 'juvenile' at the age of 13 years and 'adolescent' at the age of 19 years.[4]

It has been shown that SLS is caused due to mutations in several genes known as nephrocystins, which encode proteins that are presented in the primary cilium of kidney cells and in the connecting cilium of photoreceptor cells.[5] Various identified genetic variants as cause of SLS include *NPHP* 1-6, *NPHP10, NPHP13, NPHP15, TRAF3IP1* and the recently identified heterozygous splice site sodium channel and clathrin linker 1 (*SCLT1*) variants.[6] Gene responsible for infantile variant *NPHP2* is localized on chromosome 9q22-q31, for juvenile variant *NPHP1* on chromosome 2q12-q13 and for adolescent variant *NPHP3* is localized on chromosome 3q21-q22.[7] A triad of renal interstitial fibrosis, interstitial infiltration and renal tubular cell atrophy with cyst development is found on histology of renal tissue.[8] Ocular involvement presents as variable forms like tapetoretinal degeneration, Leber's congenital amaurosis, retinitis pigmentosa, Coat's disease, keratoconus, cataract, retinal dystrophy.[9] Other eye manifestations include nystagmus, vision loss in infancy or childhood, hyperopia and photophobia.[3] Other than renal and ocular involvement there are dermatological manifestations as well, like madarosis, skeletal manifestations like small hands, scoliosis and cerebellar involvement, obesity, liver fibrosis.[3,10] For end-stage renal failure, patient should undergo hemodialysis; however, renal replacement therapy appears to be the best option for end-stage renal failure and also there is poor prognosis for ocular manifestations.[11]

In our case, lack of cyst does not exclude the diagnosis of nephronophthisis. Hyperechogenic kidneys with reduced or normal size are consistent with the diagnosis of nephronophthisis.[12] Bilateral sensorineural hearing loss in our case favors underlying ciliopathy; scoliosis of spine is also a positive finding. This case remained undiagnosed due to coexistent panuveitis and patient presented to us with ESRD. Coexistent panuveitis and retinitis pigmentosa are rare though, can occur. In this case, association of SLS with idiopathic panuveitis, with some improvement in vision with steroid therapy, may indicate role of autoimmunity in pathogenesis and thus the role of immunosuppressive therapy for the treatment of this genetic disorder.

REFERENCES

1. Hemachandar R. Senior- Loken syndrome - A ciliopathy. J Clin Diagn Res. 2014;8(11):MD04-MD05.
2. Madhura S, Sowrabha, Manjunath, Savitha MR. Senior Loken syndrome with atypical retinitis pigmentosa: a rare manifestation of rare disease. Int J Contemp Pediatr. 2018;5(2):651-3.
3. Abeshi A, Zulian A, Beccari T, Dundar M, Colombo L, Bertelli M. Genetic testing for Senior-Loken syndrome. Euro Biotech J. 2017;1(S1):99-101.
4. Kaur A, Dhir SK, Goyal G, Mittal N, Goyal RK. Senior Loken syndrome. J Clin Diagn Res. 2016;10(11): SD03-SD04.
5. Ronquillo CC, Bernstein PS, Baehr W. Senior-Løken syndrome: a syndromic form of retinal dystrophy associated with nephronophthisis. Vision Res. 2012;75:88-97.
6. Katagiri S, Hayashi T, Yoshitake K, Murai N, Matsui Z, Kubo H, et al. Compound heterozygous splice site variants in the SCLT1 gene highlight an additional candidate locus for Senior-Løken syndrome. Sci Rep. 2018;8(1):16733.
7. Omran H, Sasmaz G, Häffner K, Volz A, Olbrich H, Melkaoui R, et al. Identification of a gene locus for Senior-Løken syndrome in the region of the nephronophthisis type 3 gene. J Am Soc Nephrol. 2002;13(1):75-9.
8. Giridhar S, Padmaraj R, Senguttuvan P. Twins with Senior-Loken syndrome. Indian J Pediatr. 2006;73(11):1041-3.
9. AlFadhel M, AlAmir A. Senior-Loken syndrome in a Saudi child. Saudi J Kidney Dis Transpl. 2008;19(3):443-5.
10. Aggarwal HK, Jain D, Yadav S, Kaverappa V, Gupta A. Senior-loken syndrome with rare manifestations: a case report. Eurasian J Med. 2013;45(2):128-31.
11. Marafie MJ, Mulla FA. Senior-Loken syndrome: A novel NPHP5 gene mutation in a family from Kuwait. Egypt J Med Hum Genet. 2014;15(2):203-7.
12. Blowey DL, Querfeld U, Geary D, Warady BA, Alon U. Ultrasound findings in juvenile nephronophthisis. Pediatr Nephrol. 1996;10(1):22-4.

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Every citizen of India should have the right to accessible, affordable, quality and safe heart care irrespective of his/her economical background

HEART CARE FOUNDATION OF INDIA
A Not-For-Profit Organisation

Sameer Malik Heart Care Foundation Fund

An Initiative of Heart Care Foundation of India

E-219, Greater Kailash, Part I, New Delhi - 110048 E-mail: heartcarefoundationfund@gmail.com Helpline Number: +91 - 9958771177

"No one should die of heart disease just because he/she cannot afford it"

About Sameer Malik Heart Care Foundation Fund

"Sameer Malik Heart Care Foundation Fund" it is an initiative of the Heart Care Foundation of India created with an objective to cater to the heart care needs of people.

Objectives

- Assist heart patients belonging to economically weaker sections of the society in getting affordable and quality treatment.
- Raise awareness about the fundamental right of individuals to medical treatment irrespective of their religion or economical background.
- Sensitize the central and state government about the need for a National Cardiovascular Disease Control Program.
- Encourage and involve key stakeholders such as other NGOs, private institutions and individual to help reduce the number of deaths due to heart disease in the country.
- To promote heart care research in India.
- To promote and train hands-only CPR.

Activities of the Fund

Financial Assistance

Financial assistance is given to eligible non emergent heart patients. Apart from its own resources, the fund raises money through donations, aid from individuals, organizations, professional bodies, associations and other philanthropic organizations, etc.

After the sanction of grant, the fund members facilitate the patient in getting his/her heart intervention done at state of art heart hospitals in Delhi NCR like Medanta – The Medicity, National Heart Institute, All India Institute of Medical Sciences (AIIMS), RML Hospital, GB Pant Hospital, Jaipur Golden Hospital, etc. The money is transferred directly to the concerned hospital where surgery is to be done.

Drug Subsidy

The HCFI Fund has tied up with Helpline Pharmacy in Delhi to facilitate patients with medicines at highly discounted rates (up to 50%) post surgery.

The HCFI Fund has also tied up for providing up to 50% discount on imaging (CT, MR, CT angiography, etc.)

Who is Eligible?

All heart patients who need pacemakers, valve replacement, bypass surgery, surgery for congenital heart diseases, etc. are eligible to apply for assistance from the Fund. The Application form can be downloaded from the website of the Fund. http://heartcarefoundationfund.heartcarefoundation.org and submitted in the HCFI Fund office.

Important Notes

- The patient must be a citizen of India with valid Voter ID Card/ Aadhaar Card/Driving License.
- The patient must be needy and underprivileged, to be assessed by Fund Committee.
- The HCFI Fund reserves the right to accept/reject any application for financial assistance without assigning any reasons thereof.
- The review of applications may take 4-6 weeks.
- All applications are judged on merit by a Medical Advisory Board who meet every Tuesday and decide on the acceptance/rejection of applications.
- The HCFI Fund is not responsible for failure of treatment/death of patient during or after the treatment has been rendered to the patient at designated hospitals.
- The HCFI Fund reserves the right to advise/direct the beneficiary to the designated hospital for the treatment.
- The financial assistance granted will be given directly to the treating hospital/medical center.
- The HCFI Fund has the right to print/publish/webcast/web post details of the patient including photos, and other details. (Under taking needs to be given to the HCFI Fund to publish the medical details so that more people can be benefitted).
- The HCFI Fund does not provide assistance for any emergent heart interventions.

Check List of Documents to be Submitted with Application Form

- Passport size photo of the patient and the family
- A copy of medical records
- Identity proof with proof of residence
- Income proof (preferably given by SDM)
- BPL Card (If Card holder)
- Details of financial assistance taken/applied from other sources (Prime Minister's Relief Fund, National Illness Assistance Fund Ministry of Health Govt of India, Rotary Relief Fund, Delhi Arogya Kosh, Delhi Arogya Nidhi), etc., if anyone.

Free Diagnostic Facility

The Fund has installed the latest State-of-the-Art 3 D Color Doppler EPIQ 7C Philips at E – 219, Greater Kailash, Part 1, New Delhi.
This machine is used to screen children and adult patients for any heart disease.

Free Education and Employment Facility

HCFI has tied up with a leading educational institution and an export house in Delhi NCR to adopt and to provide free education and employment opportunities to needy heart patients post surgery. Girls and women will be preferred.

Laboratory Subsidy

HCFI has also tied up with leading laboratories in Delhi to give up to 50% discounts on all pathological lab tests.

Help Us to Save Lives

The Foundation seeks support, donations and contributions from individuals, organizations and establishments both private and governmental in its endeavor to reduce the number of deaths due to heart disease in the country. All donations made towards the Heart Care Foundation Fund are exempted from tax under Section 80 G of the IT Act (1961) within India. The Fund is also eligible for overseas donations under FCRA Registration (Reg. No 231650979). The objectives and activities of the trust are charitable within the meaning of 2 (15) of the IT Act 1961.

Donate Now...

About Heart Care Foundation of India

Heart Care Foundation of India was founded in 1986 as a National Charitable Trust with the basic objective of creating awareness about all aspects of health for people from all walks of life incorporating all pathies using low-cost infotainment modules under one roof.

HCFI is the only NGO in the country on whose community-based health awareness events, the Government of India has released two commemorative national stamps (Rs 1 in 1991 on Run For The Heart and Rs 6.50 in 1993 on Heart Care Festival- First Perfect Health Mela). In February 2012, Government of Rajasthan also released one Cancellation stamp for organizing the first mega health camp at Ajmer.

Objectives

- Preventive Health Care Education
- Perfect Health Mela
- Providing Financial Support for Heart Care Interventions
- Reversal of Sudden Cardiac Death Through CPR-10 Training Workshops
- Research in Heart Care

Heart Care Foundation Blood Donation Camps

The Heart Care Foundation organizes regular blood donation camps. The blood collected is used for patients undergoing heart surgeries in various institutions across Delhi.

Committee Members

Chief Patron

Raghu Kataria

Entrepreneur

President

Dr KK Aggarwal

Padma Shri, Dr BC Roy National & DST National Science Communication Awardee

Governing Council Members

Sumi Malik
Vivek Kumar
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Raj Kumar Daga
Shalin Kataria
Anisha Kataria
Vishnu Sureka
Rishab Soni

This Fund is dedicated to the memory of **Sameer Malik** who was an unfortunate victim of sudden cardiac death at a young age.

- HCFI has associated with Shree Cement Ltd. for newspaper and outdoor publicity campaign
- HCFI also provides Free ambulance services for adopted heart patients
- HCFI has also tied up with Manav Ashray to provide free/highly subsidized accommodation to heart patients & their families visiting Delhi for treatment.

http://heartcarefoundationfund.heartcarefoundation.org

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A Case Report of Pancreatic Lipomatosis

N JEEVA*, S ARUN KUMAR†, JOGA VEERA BALAJI‡, DEEPA JAMES#

ABSTRACT

Total fat replacement of the pancreas is rare. Focal fatty replacement is the most common degenerative lesion of pancreas. Focal fatty deposits have no major clinical significance; however, extreme fat replacement is of pathologic significance, as it is associated with marked reduction in exocrine function of pancreas, resulting in malabsorption due to pancreatic enzyme insufficiency. Here we are presenting a case with nonalcoholic fatty liver disease and pancreatic lipomatosis, which is a incidental finding for which we found that aging is the only etiological factor in this case.

Keywords: Exocrine function, malabsorption, nonalcoholic fatty liver disease, pancreatic lipomatosis

In pancreatic lipomatosis, there will be complete replacement of pancreas by fat usually associated with pancreatic insufficiency. It is speculated that nonalcoholic fatty liver disease begets pancreatic lipomatosis. However, in this case, pancreatic lipomatosis was associated with nonalcoholic steatohepatitis in early cirrhosis. Higher incidence of pancreatic lipomatosis had been observed in obese but in our case the patient was thin.

CASE REPORT

A 75-year-old woman presented with the complaints of abdominal pain on and off, bilateral lower limb swelling and generalized fatigue since 15 days. History of loss of appetite was present; not a known case of hypertension, diabetes mellitus, tuberculosis, coronary artery disease.

Clinical examination revealed pallor and bilateral pitting pedal edema. Body mass index (BMI) was 19.2. Vital signs were within normal limits. Systemic examination revealed no abnormality. Laboratory investigations: Hemoglobin (Hb) - 6 g/dL, peripheral smear showed microcytic hypochromic anemia. Prothrombin time (PT) - 19.1, international normalized ratio (INR) - 2.02; routine blood tests, renal function tests were normal.

Lipid profile - normal; blood sugar - normal; Echo - within normal limits; USG abdomen showed chronic parenchymal liver disease. CT abdomen showed diffuse parenchymal liver disease with heterogeneous fatty infiltration. There was mild nodular surface with complete fatty replacement of pancreas, and few perigastric collaterals and degenerative changes in spine. Liver biopsy revealed early cirrhosis. Upper gastrointestinal endoscopy showed no abnormality. Serum amylase and lipase were normal.

DISCUSSION

Incidence of pancreatic lipomatosis is unknown. Several predisposing factors have been suggested. These include age, obesity, diabetes mellitus, chronic pancreatitis, hereditary pancreatitis, pancreatic duct obstruction by calculus or tumor and cystic fibrosis.

In normal individuals, only 10% of parenchyma is sufficient for maintenance of normal exocrine function.

Even though the total parenchyma of pancreas was replaced by fat in our patient, she had no exocrine and endocrine deficiency symptoms.

The subtypes are even pancreatic lipomatosis and uneven pancreatic lipomatosis. Uneven pancreatic lipomatosis may present as:

- **Type 1a**: Preferential fatty replacement of head.

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- **Type 1b:** Preferential fatty replacement of head, neck and body.
- **Type 2a:** Preferential fatty replacement of head and uncinate process.
- **Type 2b:** Fatty replacement of most of pancreas except peribiliary region.

The role of ultrasound in the diagnosis of pancreatic lipomatosis is very limited. However, CT has an important role in evaluation of pancreatic disease.

SUGGESTED READING

1. Reddy OJ, Gafoor JA, Reddy GM, Prasad PO. Total pancreatic lipomatosis: A rare presentation. J NTR Univ Health Sci. 2015;4(4):272-4.
2. Anand R, Narula MK, Chaudhary V, Agrawal R. Total pancreatic lipomatosis with malabsorption syndrome. Indian J Endocrinol Metab. 2011;15(1): 51-3.
3. Prachayakul V, Aswakul P. Pancreatic steatosis: what should gastroenterologists know? JOP. J Pancreas (Online). 2015;16(3):227-31.

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Different perceptions on a flower.

Indian Journal of Clinical Practice, Vol. 30, No. 4, September 2019

A Rare Case of Hemophagocytic Lymphohistiocytosis in an 18-year-old Patient

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ABSTRACT

Hemophagocytic lymphohistiocytosis (HLH) is a rare and potentially fatal syndrome characterized by multisystem inflammation resulting in an uncontrolled and ineffective immune response. It usually presents in children less than 1 year of age as unexplained peripheral blood pancytopenia with history of fever and presence of hepatosplenomegaly. We present a rare case of an adolescent, 18-year-old patient who presented with fever, pancytopenia and hepatosplenomegaly. Bone marrow aspirate showed marked hemophagocytosis. After diagnosing the condition as HLH according to the established criteria of International Histiocytic Society, she was treated with corticosteroids, etoposide and cyclosporine followed by good response. The prompt diagnosis of HLH may be an important strategy to optimizing the clinical approach and outcome.

Keywords: Hemophagocytic lymphohistiocytosis, familial hemophagocytic lymphohistiocytosis, treatment, diagnosis

Hemophagocytic lymphohistiocytosis (HLH) is a generalized, nonmalignant histiocytic proliferation with prominent phagocytosis of formed blood cells resulting in pancytopenia. The prolonged and excessive activation of T-lymphocytes and antigen presenting cells with subsequent hypercytokinemia leads to systemic manifestations and progressive organ dysfunction. It presents with fever and symptoms of anemia, thrombocytopenia and neutropenia. On clinical examination, there is typically splenomegaly, hepatitis and lymphadenopathy and evidence of central nervous system (CNS) involvement. Pathologically, there is accumulation of hemophagocytic histiocytes in the bone marrow, spleen, lymph nodes and CNS.[1]

HLH can be divided into two forms which are difficult to distinguish from one another, primary (genetic) and secondary (acquired) form. The primary form can be inherited in an autosomal recessive fashion or X-linked manner, also called as familial hemophagocytic lymphohistiocytosis (FHL). FHL is a rare and rapidly fatal disorder presenting in infancy and early childhood with the typical features of HLH. The acquired/secondary forms are associated with a variety of viral, bacterial, fungal, parasitic causative organisms as well as collagen vascular diseases and malignancies. The diagnosis of HLH requires either molecular diagnosis of FHL or the demonstration of hemophagocytic histiocytes in tissue biopsies in association with pancytopenia, fever and hepatosplenomegaly, and may be supported by the demonstration of hypofibrinogenemia, hypertriglyceridemia, decreased NK cell function and increased concentrations of soluble CD25. Raised cerebrospinal fluid (CSF) protein concentrations and CSF pleocytosis are found in 50% of patients.[2,3]

CASE REPORT

An 18-year-old girl presented with 15 days of generalized weakness, fatigue and high-grade fever with chills and rigor since 1 day. It was not accompanied by upper respiratory or urinary complaints. There was no history of jaundice or blood transfusion. On presentation, she was conscious, oriented to time, space and person. Temperature of 103°F, pulse of 130/min, blood pressure of 130/72 mmHg with respiratory rate of 18 cycles/min were noted. Findings on examination were presence of pallor with pronounced hepatosplenomegaly (liver - 3 cm below costal margin, spleen - 5 cm below costal

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margin), there was no icterus or lymphadenopathy and systemic examination was within normal limits.

On the day of admission (Day 1), her complete blood count (CBC) findings were: hemoglobin concentration was 3.7 g/dL, white blood cell count was 0.90 × 10^3/uL, red blood cell count was 1.23 × 10^6/uL, platelets were 51 × 10^3/uL, differential white cell count was - neutrophils - 38%, lymphocytes - 51%, monocytes - 10%, eosinophils - 0% and basophils - 1%. On peripheral blood film, smear showed marked anisopoikilocytosis, red cells being hypochromic, both microcytic and macrocytic, with few tear drop cells and macro-ovalocytes. Also, 2 nucleated red blood cells/100 white blood cells were seen. There was marked leukopenia but no immature white blood cells were seen; platelets were markedly reduced on smear. No hemoparasite was seen.

Serum bilirubin total was 2.3 mg% (normal, 0.1-1.2 mg%), serum bilirubin direct was 1.2 mg% (normal, 0.0-0.3 mg%), SGOT and SGPT were 80 U/L and 38 U/L, respectively. Serum alkaline phosphatase was 123 U/L, lactate dehydrogenase was 1,430 IU/L, triglyceride levels were 168.4 mg%. Malarial antigen test and hepatitis B surface antigen (HBsAg) were negative, test for human immunodeficiency virus (HIV) was nonreactive, anti-HCV antibodies (spot test) was nonreactive, VDRL (TRUST) was negative, Widal for typhoid was negative, dengue immunoglobulin M (IgM) antibody was weakly positive, scrub typhus IgM was negative. Blood culture was sterile, potassium hydroxide (KOH) mount was negative.

Chest radiograph was normal, abdominal ultrasound showed bilateral pleural effusion with ascites, no obvious lymph nodes were evident. Computerized tomography (CT) of chest showed evidence of bilateral pleural effusion with minimal pericardial effusion. Pleural fluid examination was normal.

The clinical spectrum of fever, hepatosplenomegaly, unexplained cytopenias and elevated liver enzymes indicated an underlying cytokine storm, possibly due to macrophage activation.

Further tests were done to confirm the possibility of hemophagocytic syndrome. Serum ferritin was elevated up to >500 μg/L (normal, 15-200 μg/L) and fibrinogen was reduced to 0.5 g/L (normal, 2-4 g/L).

A bone marrow aspirate from the posterior superior iliac spine was normocellular with erythroid hyperplasia. Erythroid series showed hyperplasia with dual maturation, both megaloblastic and normoblastic. Myeloid series showed normal maturation, no evidence of toxic granulation or atypia seen. Megakaryocytic series was adequate in number and morphology, with hypersegmentation of megakaryocytes seen at few places. There was increase in marrow macrophages, and a few of these macrophages showed engulfed numerous cells of various hemopoietic lineage like platelets, red cells, white cells and myeloid and erythroid precursor cells called hemophagocytes (Figs. 1 and 2). On screening, occasional mononuclear, and very occasional binucleated, Reed-Sternberg like cells were seen. Bone marrow biopsy findings were similar to that of aspirate findings with sighting of histiocytes and

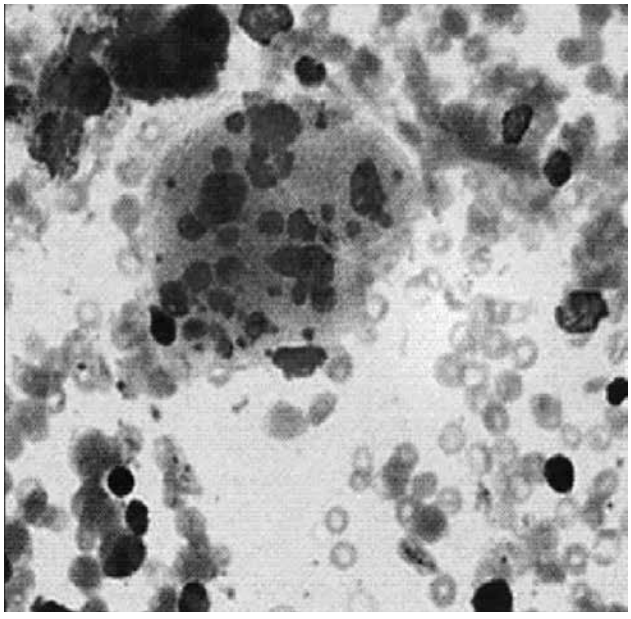

Figure 1. Photomicrograph of the bone marrow aspirate showing macrophage with marked hemophagocytic activity. (Giemsa stain × 100X).

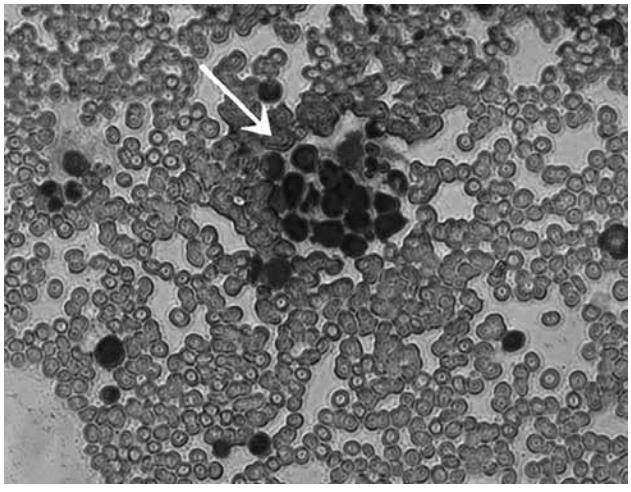

Figure 2. Photomicrograph showing nuclei of RBCs and WBC precursor cells within cytoplasm of macrophage (Giemsa stain × 100X).

Table 1. Review of CBC Findings

	Day 2	Day 4	Day 5	Day 7
WBC (10^3/uL)	0.90	2.25	7.71	10.37
RBC (10^6/uL)	1.23	1.95	2.99	3.12
Hb (g/dL)	3.7	5.8	8.9	9.3
HCT (%)	11.2	17.6	27.1	29.4
Platelet (10^3/uL)	51	53	67	80
RDW-CV (%)	31.4	24.5	22.9	24.7
Neutrophil (%)	38	38	73	86
Lymphocyte (%)	51	52	20	10
Monocyte (%)	10	8	6	4
Eosinophil (%)	0	2	1	0
Basophil (%)	1	0	0	0

WBC = White blood cell; RBC = Red blood cell; Hb = Hemoglobin; HCT = Hematocrit; RDW-CV = Red blood cell distribution width.

hemophagocytes. However, immunohistochemistry findings were negative for lymphomas.

As the criterion required for the diagnosis of HLH was fulfilled according to HLH 2009 diagnostic criteria, she was started on chemotherapy protocol of HLH 2004 trial. The patient responded to initial treatment with decrescendo course of dexamethasone 8 mg/twice-daily (10 mg/m^2) and cyclosporine along with vitamin B_{12}. On Day 7, the counts were raised to - hemoglobin concentration - 9.3 g/dL, white blood cell count - 10.37 × 10^3/uL, red blood cell count - 3.12 × 10^6/uL and platelets - 80,000/uL. Differential count being (neutrophils - 86%, lymphocytes - 10%, monocytes - 4%) (Table 1).

Patient was discharged on Day 8.

On follow-up, the patient developed a continuous headache, non-relieved by symptomatic treatment along with seizures. On further examination, her CT of brain, electroencephalography and CSF examination were normal. Cyclosporine levels were detected to be normal, so as to rule out drug-induced seizures. The patient was taken off cyclosporine and started with etoposide 150 mg/m^2 twice-daily with tapering dose of dexamethasone. She developed neutropenia with the advent of etoposide, so was again put on cyclosporine. However, persistence of headaches with cyclosporine led to the withdrawal of cyclosporine and introduction of etoposide again.

Now on weekly follow-ups, there is evidence of gradual clinical improvement and normalization of hematological abnormalities.

DISCUSSION

Hemophagocytic lymphohistiocytosis (HLH) is a life-threatening condition, which is characterized by multisystem inflammation.[4] It is a rare disorder in which hereditary and sporadic cases are reported primarily in children;[5] a crude annual incidence of 1.2 cases of FHL per million children has been reported in Sweden.[6]

HLH is a reactive process resulting from prolonged and excessive activation of antigen presenting cells (macrophages, histiocytes) and CD8+ T cells leading to hypersecretion of pro-inflammatory cytokines. This exaggerated inflammatory response is responsible for necrosis and organ failure and results in uncontrolled proliferation and phagocytic activity of histiocytes, leading to extensive systemic damage.[7] This disorder is divided into primary/genetic hemophagocytic syndrome (FHL), and secondary/reactive hemophagocytic syndrome. The HLH, whether familial or acquired, share one common feature, namely a highly stimulated but ineffective immune response that threatens the life of the patient and may lead to death unless arrested by prompt and appropriate treatment.[8]

Until recently, it was widely believed that symptoms of FHL generally arose during infancy and early childhood. With the more widespread availability of genetic testing, it is apparent that the first significant episode of FHL can occur throughout life, including *in utero* (Table 2[9-16]).[17]

Table 2. The Genetic Causes of HLH[9-16]

HLH related to defects in the perforin/granule-mediated pathway of cytotoxicity
• FHL 2 - Perforin (PRF1) AR
• FHL 3 - MUNC 13-4 AR
• FHL4 - STX11 AR
• Griscelli s. type 2 - Rab27A AR
• Chediak Higashi s. - LYST1 AR
• Hermansky Pudlak s. type II - AP3B1 AR
X-linked syndromes associated with HLH
• XLP1 - SH2D1A (SAP) X
• XLP2 - BIRC4 (XIAP) X

AR indicates autosomal recessive; X indicates X-linked.

Table 3. Proposed HLH Diagnostic Criteria, 2009[22]

Molecular diagnosis of HLH or X-linked lymphoproliferative syndrome (XLP).
Or at least 3 of 4:
• Fever
• Splenomegaly
• Cytopenias (minimum 2 cell lines reduced)
• Hepatitis
And at least 1 of 4:
• Hemophagocytosis
• ↑ Ferritin
• ↑ Soluble IL-2Rα (age-based)
• Absent or very decreased NK function
Other results supportive of HLH diagnosis
• Hypertriglyceridemia
• Hypofibrinogenemia
• Hyponatremia

The secondary or acquired HLH can have a constellation of causes. First described in adults with a viral infection following organ transplantation,[18] later it was established that most patients had no underlying immune defect and that also nonviral agents such as bacteria, fungi, parasites could trigger HLH. Epstein-Barr virus infection is an important trigger of both FHL and acquired HLH.[19] Cytomegalovirus, herpes simplex virus, HIV, bacteria and parasitic agents have also been implicated. Non-Hodgkin's lymphoma, leukemia, connective tissue diseases and autoimmune diseases may also be associated with HLH. However, the identification of an infectious organism does not help to discriminate between genetic and acquired forms of HLH, since many episodes in genetic HLH can be triggered by infections.[20]

Because of financial constraints of the patient, a conclusive cause of the hemophagocytic syndrome could not be determined. However, as the blood culture and KOH mount were found to be negative and bone marrow biopsy was negative for any malignancy by immunohistochemistry, it was thought to be of viral origin because of the presence of atypical mononuclear cells. The predominant clinical findings of HLH are fever (often hectic and persistent), pancytopenia, hepatitis and splenomegaly, which were consistent in our patient. To assist with the rapid diagnosis of HLH, the Histiocyte Society has developed a set of diagnostic guidelines that encompass both clinical and laboratory findings.[21] With additional experience these diagnostic criteria have been modestly modified as HLH diagnostic criteria 2009 (Table 3).[22] The patient fulfilled the criteria and was diagnosed as HLH.

Due to the life-threatening implications of the diagnosis of HLH, chemotherapy protocol of HLH 2004 trial consisting of steroids, etoposide or antithymocyte globulin (ATG), should be instituted promptly, along with treatment of the underlying etiology in cases of secondary HLH or followed by curative hematopoietic cell transplantation in FHL.[23-25] As seen in our case, when a patient presents with fever and unexplained cytopenias, it is important to consider the possibility of HLH and do the required follow-up with further investigations for a prompt diagnosis and rapid recovery.

REFERENCES

1. Henter JI, Aricò M, Elinder G, Imashuku S, Janka G. Familial hemophagocytic lymphohistiocytosis. Primary hemophagocytic lymphohistiocytosis. Hematol Oncol Clin North Am. 1998;12(2):417-33.
2. Janka GE, Schneider EM. Modern management of children with haemophagocytic lymphohistiocytosis. Br J Haematol. 2004;124(1):4-14.
3. Janka G, Imashuku S, Elinder G, Schneider M, Henter JI. Infection- and malignancy-associated hemophagocytic syndromes. Secondary hemophagocytic lymphohistiocytosis. Hematol Oncol Clin North Am. 1998;12(2):435-44.
4. Janka G. Hemophagocytic lymphohistiocytosis: when the immune system runs amok. Klin Padiatr. 2009;221(5): 278-85.
5. Aricò M, Janka G, Fischer A, Henter JI, Blanche S, Elinder G, et al. Hemophagocytic lymphohistiocytosis. Report of 122 children from the International Registry.

FHL Study Group of the Histiocyte Society. Leukemia. 1996;10(2):197-203.

6. Henter JI, Elinder G, Söder O, Ost A. Incidence in Sweden and clinical features of familial hemophagocytic lymphohistiocytosis. Acta Paediatr Scand. 1991;80(4): 428-35.
7. Jordan MB, Hildeman D, Kappler J, Marrack P. An animal model of hemophagocytic lymphohistiocytosis (HLH): CD8+ T cells and interferon gamma are essential for the disorder. Blood. 2004;104(3):735-43.
8. Janka G, zur Stadt U. Familial and acquired hemophagocytic lymphohistiocytosis. Hematology Am Soc Hematol Educ Program. 2005:82-8.
9. Bizario JC, Feldmann J, Castro FA, Ménasché G, Jacob CM, Cristofani L, et al. Griscelli syndrome: characterization of a new mutation and rescue of T-cytotoxic activity by retroviral transfer of RAB27A gene. J Clin Immunol. 2004;24(4):397-410.
10. Enders A, Zieger B, Schwarz K, Yoshimi A, Speckmann C, Knoepfle EM, et al. Lethal hemophagocytic lymphohistiocytosis in Hermansky-Pudlak syndrome type II. Blood. 2006;108(1):81-7.
11. Rigaud S, Fondanèche MC, Lambert N, Pasquier B, Mateo V, Soulas P, et al. XIAP deficiency in humans causes an X-linked lymphoproliferative syndrome. Nature. 2006;444(7115):110-4.
12. Feldmann J, Callebaut I, Raposo G, Certain S, Bacq D, Dumont C, et al. Munc13-4 is essential for cytolytic granules fusion and is mutated in a form of familial hemophagocytic lymphohistiocytosis (FHL3). Cell. 2003;115(4):461-73.
13. Stepp SE, Dufourcq-Lagelouse R, Le Deist F, Bhawan S, Certain S, Mathew PA, et al. Perforin gene defects in familial hemophagocytic lymphohistiocytosis. Science. 1999;286(5446):1957-9.
14. zur Stadt U, Schmidt S, Kasper B, Beutel K, Diler AS, Henter JI, et al. Linkage of familial hemophagocytic lymphohistiocytosis (FHL) type-4 to chromosome 6q24 and identification of mutations in syntaxin 11. Hum Mol Genet. 2005;14(6):827-34.
15. Arneson LN, Brickshawana A, Segovis CM, Schoon RA, Dick CJ, Leibson PJ. Cutting edge: syntaxin 11 regulates lymphocyte-mediated secretion and cytotoxicity. J Immunol. 2007;179(6):3397-401.
16. Westbroek W, Adams D, Huizing M, Koshoffer A, Dorward H, Tinloy B, et al. Cellular defects in Chediak-Higashi syndrome correlate with the molecular genotype and clinical phenotype. J Invest Dermatol. 2007;127(11):2674-7.
17. Malloy CA, Polinski C, Alkan S, Manera R, Challapalli M. Hemophagocytic lymphohistiocytosis presenting with nonimmune hydrops fetalis. J Perinatol. 2004;24(7):458-60.
18. Risdall RJ, McKenna RW, Nesbit ME, Krivit W, Balfour HH Jr, Simmons RL, et al. Virus-associated hemophagocytic syndrome: a benign histiocytic proliferation distinct from malignant histiocytosis. Cancer. 1979;44(3):993-1002.
19. Imashuku S. Clinical features and treatment strategies of Epstein-Barr virus-associated hemophagocytic lymphohistiocytosis. Crit Rev Oncol Hematol. 2002;44(3):259-72.
20. Henter JI, Ehrnst A, Andersson J, Elinder G. Familial hemophagocytic lymphohistiocytosis and viral infections. Acta Paediatr. 1993;82(4):369-72.
21. Henter JI, Horne A, Aricó M, Egeler RM, Filipovich AH, Imashuku S, et al. HLH-2004: Diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. Pediatr Blood Cancer. 2007;48(2):124-31.
22. Filipovich AH. Hemophagocytic lymphohistiocytosis (HLH) and related disorders. Hematology Am Soc Hematol Educ Program. 2009:127-31.
23. Shuper A, Attias D, Kornreich L, Zaizov R, Yaniv I. Familial hemophagocytic lymphohistiocytosis: improved neurodevelopmental outcome after bone marrow transplantation. J Pediatr. 1998;133(1):126-8.
24. Jordan MB, Allen CE, Weitzman S, Filipovich AH, McClain KL. How I treat hemophagocytic lymphohistiocytosis. Blood. 2011;118(15):4041-52.
25. Horne A, Janka G, Maarten Egeler R, Gadner H, Imashuku S, et al; Histiocyte Society. Haematopoietic stem cell transplantation in haemophagocytic lymphohistiocytosis. Br J Haematol. 2005;129(5):622-30.

■■■■

Weak Systems and Funding Gaps Jeopardize Drinking-water and Sanitation in the World's Poorest Countries

The World Health Organization (WHO) and UN-Water sounded the alarm for an urgent increase in investment in strong drinking-water and sanitation systems.

The call came as the international water sector met in Stockholm for its annual conference during World Water Week (25-30 August 2019). It is triggered by a new report published by WHO on behalf of UN-Water that reveals that weak government systems and a lack of human resources and funds are jeopardizing the delivery of water and sanitation services in the world's poorest countries – and undermining efforts to ensure health for all… (*WHO*)

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Is Health and Timely Treatment Really a Fundamental Right?

KK AGGARWAL*, IRA GUPTA†

"Body is instrument for all (good) deeds"
शरीरमाद्यं खलु धर्मसाधनम्

In a welfare State, it is the obligation of the State to ensure the creation and the sustaining of conditions congenial to good health. Is the government ensuring and providing conditions congenial to good health?

Recently, in the month of August 2019, one minor patient aged about 12 years namely Rashmi Rao approached the national public charitable trust Heart Care Foundation of India (HCFI) for assistance. She was suffering from transposition of the great arteries (TGA), multiple ventricular septal defect (VSD) with severe pulmonary stenosis (PS). After reviewing all the medical records of the patient, HCFI came to know that the patient had visited AIIMS, New Delhi for treatment on 18th January, 2019 (UHID No. 104254537) and the doctor had suggested the father of the patient (Mr Ramesh Kumar) to get Echo test, blood tests, X-ray and other tests done. The father of the patient got all her tests done.

After all relevant tests and check-ups, the doctors at AIIMs confirmed that the patient Baby Rashmi Rao was suffering from single ventricle (SV) physiology aortopulmonary collaterals (APC) and she needed to undergo surgery for the same. The Senior Resident/ Consultant of AIIMS hospital also gave the estimated cost of the surgery as Rs. 46,000/- on 1st May, 2019. However, the hospital gave the date for surgery for 8th September, 2023. Further, the hospital advised the patient and her father to get separate estimate for Coil Embolization from Cardiac Radiology Department.

Further, the reason for giving such a long date of surgery was that the surgery cannot be done earlier because of huge rush of patients. The said reason has been mentioned in the OPD card. Also, in the OPD card, the AIIMS hospital has asked the patient to contact some other government hospital for early surgery.

As the patient belonged to the Economically Weaker Section (EWS) category and the patient required immediate surgery, so HCFI wrote a letter dated 12th August, 2019 to AIIMS thereby requesting the hospital to take immediate action within a period of 48 hours and get the surgery of Baby Rashmi Rao done immediately as the patient cannot wait for 4 years.

In the said letter, HCFI had also mentioned that if the hospital cannot do the surgery itself, then the hospital should refer the patient to some other government hospital or any empanelled private hospital.

In response to the said letter, Dept. of CTVS, CT Centre, AIIMS, New Delhi in a reply dated 20th August, 2019 stated that more than 1,800 patients are waiting for cardiac surgery till date, who have been scheduled for surgery up to September, 2024. Most of them are seriously ill and may need early surgical intervention for which AIIMS hospital is helpless because of emergency cases coming to AIIMS casualty on daily basis. However, these emergency surgeries are performed without any delay though it increases the waiting period for the other successive patients like Rashmi Rao.

Instead of providing early medical treatment, AIIMS Hospital suggested/informed HCFI that the cases like Rashmi Rao can also be operated in any Govt. hospital like Safdarjung Hospital, RML Hospital, GB Pant Hospital, etc. in Delhi. These hospitals have reputed CTVS departments, which can safely do all kinds of complex heart surgeries.

Also, vide reply dated 20th August, 2019 the Dept. of CTVS, AIIMS Hospital had informed HCFI that a high-power committee had constituted under the chairmanship of Director, AIIMS to address long waiting list in the Dept. of CTVS, AIIMS (copy attached).

The Minutes of Meeting held on 15.06.2018 to discuss the problem of overcrowding in CT Centre OPD and long waiting list for operations at AIIMS, New Delhi

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clearly reveals that the following possible solutions were suggested for discussion:

- Expand the infrastructure and increase the manpower to enhance the operating capacity.
- As a stop gap measure, limit the number of referrals to the Dept. of CTVS. This can be effectively done by putting a cap to the number of new patients registered in the Dept. of Cardiology.

At the same time, all those patients who can be operated at other public sector hospitals should also be referred to these hospitals.

However, even after the constitution of the high-powered committee, AIIMS hospital has till date not expanded the infrastructure and increased the manpower to enhance the operating capacity. The situation remains the same even after a period of 1 year of such meeting.

Is health really a fundamental right of a citizen when even a hospital like AIIMS, which is a premier institute of the country, is not able to provide timely and immediate medical care?

In the year 2017 also, one patient named Meena Devi had approached HCFI for immediate surgery as she was also refused immediate surgery owing to lack of infrastructure. HCFI adopted the patient and got her treatment done in GB Pant Hospital. At the same time, the said patient Meena Devi had also approached the Hon'ble High Court of Delhi. After the notice in the said case, the Delhi Government announced its quality health scheme as per which if the poor or EWS patient requiring urgent attention is given a date for surgery beyond a period of 30 days by any government hospital in Delhi, then the government hospital should refer such patient to any empanelled private hospital or to some other government hospital.

It is the duty of the said government hospital to refer the patient to any empanelled private hospital or any other government hospital for immediate surgery and treatment free of cost. However, in reality government hospitals like AIIMS are neither providing immediate surgery or treatment nor referring the patient.

In a series of cases dealing with the substantive content of the right to life, the Court has found that the right to live with human dignity includes the right to good health:

- Vincent Panikurlangara v. Union of India, (1987) 2 SCC165
- Paschim Banga Khet Mazdoor Samity versus State of WB, (1996) 4 SCC 37
- Murli S. Deora v. Union of India, (2001) 8 SCC 765
- Consumer Education and Research Centre v. Union of India, (1995) 3 SCC 42
- M.C. Mehta vs. Union of India, (1999) 6 SCC 9
- Mr 'X' v. Hospital 'Z', (2003) 1 SCC 500
- Parmanand Katara vs. Union of India, (1989) 4 SCC 286).

It was held that Article 21 of the Constitution casts an obligation on the State to take every measure to preserve life. The Court found that it is the primary duty of a welfare State to ensure that medical facilities are adequate and available to provide treatment.

In **Consumer Education and Research Centre vs. Union of India**, and in **Kirloskar Brothers Ltd. vs. Employees State Insurance Corporation**, the Supreme Court held that right to health and medical care is a fundamental right under Article 21 read with Article 39(e), 41 and 43.

In **Association of Medical Super Speciality Aspirants and Residents & Ors. Versus Union of India & Ors**, Writ Petition (Civil) No. 376 of 2018, the Hon'ble Supreme Court held that *"Right to health is integral to the right to life. Government has a constitutional obligation to provide health facilities. The fundamental right to life which is the most precious human right and which forms the ark of all other rights must therefore be interpreted in a broad and expansive spirit so as to invest it with significance and vitality which may endure for years to come and enhance the dignity of the individual and the worth of the human person. The right to life enshrined in Article 21 cannot be restricted to mere animal existence. It means something much more than just physical survival."*

In in the case of **"Paschim Banga Khet Mazdoor Samity vs. State of W.B. & Another**" 1996 (4) SCC 37, their Lordships of the Hon'ble Supreme Court have held that Constitution envisages the establishment of a welfare State at the federal level as well as the State level. In a welfare State, the primary duty of the Government is to secure the welfare of the people. Providing adequate medical facilities for the people is an essential part of the obligations undertaken by the Govt. in a welfare State. **Article 21** imposes an obligation on the State to safeguard the right to life of every person. Preservation of human life is thus of paramount importance. Failure on the part of a government hospital to provide timely medical treatment to a person in need of such treatment results in violation of his right to life guaranteed under Article 21.

But the reality is that patients are not getting proper and timely medical care and treatment as enshrined in Article 21 of the Constitution of India and also as held by Hon'ble Supreme Court in numerous landmark judgments.

In a catena of cases, the Hon'ble Supreme Court has held that the failure to provide timely medical care amounts to violation of the fundamental right to life. The State has an obligation to provide medical facilities in such circumstances, and financial inability or lack of infrastructure is no justification to avoid this obligation.

ANNEXURE

Letter sent to AIIMS, New Delhi by HCFI

Date: 12.08.2019

To,

The Medical Superintendent, AIIMS
Sri Aurobindo Marg, Ansari Nagar
Ansari Nagar East, New Delhi – 110029
ms.aiims@aiims.edu

Head of Department
Department of Cardiology, AIIMS
Sri Aurobindo Marg, Ansari Nagar
Ansari Nagar East, New Delhi – 110029

Subject: Immediate Surgery Required for the Patient Namely Rashmi Rao Who is Given a Date for 08.09.2023.

Dear Sir,

The patient 12 years old namely Rashmi Rao resident of 97 Ailwal Post Sadar Dist Azamgarh, UP has approached the Heart Care Foundation of India for assistance. She is suffering from TGA, Multiple VSD with Severe PS.

The patient visited AIIMS for treatment on 18th January, 2019 (UHID No. 104254537) and the doctor suggested the father of the patient (Mr Ramesh Kumar) to her Echo test, blood test, X-ray and other test. The father of the patient Baby Rashmi Rao got all her tests done. The report of the blood test, X-ray report are with the hospital only. The copy of the OPD card, Echo report are annexed herewith.

After all relevant test and check-up, the doctors in AIIMs confirmed that the patient Baby Rashmi Rao is suffering from SV physiology APCs and she needs to undergo surgery for the same. The Senior Resident/ Consultant of AIIMS hospital also gave the estimated cost of the surgery being Rs. 46,000/- on 1st May, 2019. However, the hospital has given the date for surgery for 8th September, 2023. Further the hospital advised the patient and her father to get separate estimate for Coil Embolization from Cardiac Radiology Department. The copy of the estimate certificate is annexed herewith.

Further, the reason for giving such a long date of surgery is that because of huge rush of patients the surgery cannot be done early. The said reason has been mentioned in the OPD card. Also, in the OPD card, the hospital has asked the patient to contact some other government hospital for early surgery.

The Legal Cell of Heart Care Foundation of India has reviewed the medical condition of the baby Ms. Rashmi Rao and has also reviewed all the reports and documents of Baby Ms. Rashmi Rao. After thorough examination and review, the Legal Cell of Heart Care Foundation of India feels that the patient needs urgent medical attention and the surgery needs to be done at the earliest.

Also, it is submitted that if patients requiring urgent attention is given a date for surgery beyond a period of 30 days, then the government hospital should refer such patient to any empanelled private hospital or to some other government hospital.

The patient and her family members cannot be asked to keep running from one hospital to another.

It is humbly requested that Baby Ms. Rashmi Rao requires immediate surgery and the patient cannot wait for 4 years for her surgery.

The addressees herein are requested to take immediate action within a period of 48 hours and get the surgery of Baby Rashmi Rao done immediately. If the hospital cannot do the surgery itself, then the hospital should refer the patient to some other government hospital or any empanelled private hospital. In case, the hospital does not take any immediate action within a period of 48 hours, the Legal cell of Heart Care Foundation of India will be constrained to seek appropriate legal action as every citizen of this country has the fundamental right to health and living as enshrined in the Constitution of India.

The undersigned are looking forward for immediate action and response with a copy marked to us of the action taken.

With regards,

Ira Gupta
Advisor - HCFI Legal Cell

About Heart Care Foundation of India

HCFI is a registered charitable trust incorporated in the year 1986 for creating awareness about all aspects of health using innovative low-cost informative ways. In two of its events, Run for the Heart in 1991 and Perfect Health Mela in 1993, Government of India has released National Commensurate Postal Stamps. Also, in 2012 Government of Rajasthan released Cancellation Stamps for organizing first ever telemedicine camp. Also, for organizing Mega CPR Camp, HCFI's name has been recorded in Limca Book of Records.

About Sameer Malik Heart Care Foundation Fund

It is one of the initiatives of HCFI which financially assists people for heart surgery who have no other means of reimbursement.

About HCFI Legal Cell

Legal team of HCFI scrutinizes and reviews all the documents, history of the patient and decide whether the patient can be funded under Sameer Malik Heart Care Fund or not. Also, the HCFI Legal Cell reviews whether the patient is eligible for reimbursement under any existing scheme of the State as well as Central Government. If HCFI Legal Cell finds that the patient is eligible for any scheme/policy of the State or Central Government under which the patient can get benefit, then HCFI Legal Cell helps such patients in getting the benefit under such scheme/policy.

Enclosure: The copy of the OPD card, Echo report, the copy of the estimate certificate.

Replies Received

Department of CTVS, C.T. Centre
All India Institute of Medical Sciences
Ansari Nagar, New Delhi-110029
Dated: 20th August 2019

To,

Ms. Ira Gupta
Advisor-HCFI Legal Cell,
Heart Care Foundation of India
A-344, Asiad Village, K.P. Thakkar Block
New Delhi-110049

Ref: Your letter dated 12.8.2019 addressed to the Medical Superintendent, AIIMS, New Delhi & HOD, Cardiology, AIIMS, New Delhi, regarding a patient namely Rashmi Rao, age 12 years resident of Azamgarh, UP.

Madam, Under my care, more than 1800 patients are waiting for cardiac surgery till date, who have been scheduled for surgery up to September, 2024. Most of them are seriously ill and may need early surgical intervention for which we are helpless because of emergency cases coming to AIIMS casualty on daily basis. However, these emergency surgeries are performed without any delay though it increases the waiting period for the other successive patient like Rashmi Rao.

With the existing facilities and resources, we operate approximately 10-16 cases per day, throughout the year depending on bed availability in the CTVS ICU. Still we are having very long waiting list, for which we are helpless because Cardiac surgeries generally take longer duration and longer stay in the Wards/Hospitals. On the days of OPD also i.e. Monday, Wednesday and Friday, which starts at 2.00 PM onwards, all the Doctors in the CTVS, are carrying out life saving cardiac surgeries just to reduce the waiting list and to save the life of many under privileged citizens of India, which serves the protection of fundamental right to health & living of citizen as enshrined in the Constitution of India.

In view of the facts mentioned above, I would like to inform you that the cases like Rashmi Rao can also be operated in any Govt. hospital like Safdarjung Hospital, RML Hospital, GB Pant Hospital, etc. in Delhi. These hospitals consist of reputed department of CTVS, which can do safely all kinds of complex heart surgeries. This has also been explained to the patients.

As mentioned in your letter, no enclosures were found (copy of OPD card, Echo Report, Estimate certificate).

Thanking you,

(Dr. P. Rajashekhar)
Assoc. Professor of CTVS,

Copy for information to :

2. The Medical Superintendent

3. The Chief, C.T. Centre, AIIMS, New Delhi

4. The HoD, CTVS, AIIMS, New Delhi

Reply to the Letter Dated 12.08.2019 Received from AIIMS Hospital

Department of CTVS, C.T. Centre
All India Institute of Medical Sciences
Ansari Nagar, New Delhi – 110029
Dated: 20th August, 2019
F.No.10-2019-20/CTVS/0018

To,

Ms. Ira Gupta,
Advisor- HCFI Legal Cell,
A-344, Asiad Village
K.P. Thakur Block,
New Delhi-110049

Dear Ms. Ira Gupta,

I am receipt of your letter dated on 12th August, 2019 which we have received on 19.08.2019. The letter has been forwarded to the concerned consultation Dr. P. Rajashekar, Assoc. Professor of CTVS for the needful.

In this regard, would like to bring to your notice that a high-power committee was constituted under the chairmanship of Director, AIIMS to address long waiting list in the department of CTVS, AIIMS to address long waiting list in the department of CTVS (copy attached).

At the same time, as your letter raised important policy related issues, your letter has also been forwarded to Director, AIIMS for policy decisions.

Thanking you,

Yours sincerely,

(Dr. S. K. Chauhan)
Professor & Head of CTVS

All India Institute of Medical Sciences
Ansari Nagar, New Delhi – 110029

F.No.20-1/2016(PGI)-Dir.Advt.04/16/Estt-I

Dated the:19.07.2018

Subject: Meeting to discuss the problem of overcrowding in CT Centre OPD and long waiting list for operations at AIIMS-regarding.

A copy of the minutes of the meeting of the aforesaid committee held on 15.06.2018 to discuss the problem of overcrowding in CT Centre OPD and long waiting list for operations at AIIMS, New Delhi is forwarded to all the concerned officers for perusal and compliances of the decision of the committee.

(B.K. Singh)
Admn. officer

Encl: As above

Distribution

1. Prof. Randeep Guleria
Director, AIIMS

2. Sh. Subhashish Panda
Deputy Director

3. Prof. V. K. Sharma
Chief, C.T. Centre

4. Dr. D. K. Sharma
Medical Superintendent

5. Dr. Nikhil Tandon
Prof. & Head, Dept. of Endo & Metabo

6. Dr. Shiv Kumar Chaudhary
Prof. & Head, Dept. of CTVS, C.T. Centre

7. Dr. Sanjay Kumar Arya
Prof. of Hospital Admn & Chief Admn. Officer (Actg.)

Copy to:-

The PPS to Director
The PS to Dean (Academic)
The PS to Dy. Director (Admn.)

Minutes of the Meeting to Discuss the Problem of Overcrowding in CT Centre and Long Waiting List of Operations in Department of CTVS.

A. Background

The department of CTVS at AIIMS provides excellent care to patients suffering from a variety of diseases related to the specialty of Cardiothoracic and Vascular Surgery. These patients are referred from all over India and belong to a wide range of socioeconomic strata.

More than three decades have passed since the inception of the current CT Centre and during this period, the number of patients visiting the outpatients and those undergoing surgery have grown significantly. Currently, the Department is performing around 4000 operations every year. With the current infrastructure, there is no scope for increasing the numbers any further. However, the number of patients who come for surgery has increased exponentially and is still increasing.

Despite operating with maximum capacity, the gap between the number of operations being performed and number of patients who come for surgery is increasing. This has resulted in long waiting list. The current waiting list extends up to the year 2023.

Under the Chairmanship of Director, AIIMS, a meeting was held on 15th June 2018 in Director's Committee Room to discuss and find a solution of the problem. Following Members attended the meeting:

Dr Randeep Guleria: Chairman
Director, AIIMS

Sh. Subhashish Panda: Member
Deputy Director (Admin)

Dr V K Bahl: Member
Chief, CT Centre

Dr D K Sharma: Member
Medical Superintendent

Dr Nikhil Tandon: Member
Prof. & Head, Dept. of Endo & Metabo

Dr Shiv Kumar Choudhary: Member
Prof & Head, Dept. of CTVS, CT Centre

Dr Sanjay Kumar Arya
Chief Admin Officer

B. Proceedings and Discussion

In the beginning, Dr Shiv Kumar Choudhary apprised the committee members of the current situation. He informed that, in CT Centre, new patients are registered in the Department of Cardiology. Every month, nearly 4000 new cases are registered in the Department of Cardiology. Approximately, 10% of these cases (390-410) require surgery and are referred to the Department of CTVS. Besides these OPD Patients, Departments of CTVS operates 100-120 cases as "emergency". About 50 patients are referred directly to the Department of CTVS from other resources. Thus, every month, 550 to 570 patients come to Department of CTVS for surgery.

Currently, all the CTVS consultants operate every day. The Department operates to its maximum capacity, and perform 310-350 operations in a month. This number cannot be increased further with existing infrastructure and manpower. This is creating a backlog of 200 to 250 patients every month and adds to the ever-growing pool of patients with extended waiting list.

Dr Choudhary also informed that as per AIIMS ethos, the Department of CTVS makes all possible efforts to provide treatment for underprivileged section of society, emergency cases, and complex clinical problem not amenable for treatment elsewhere.

ii. Three possible solutions were suggested for discussion:

Expand the infrastructure and increase the manpower to enhance the operating capacity.

As a stop gap measure, limit the number of referrals to the Department of CTVS. This can be effectively done by putting a cap to the number of new patients registered in the Department of Cardiology.

At the same time, all those patients who can be operated at other public sector hospitals should also be referred to these hospitals.

iii. Each option was discussed in detail.

1. Expand the infrastructure and increase the manpower to enhance the operating capacity.

Dr. V K Bahl stressed the need for expansion of infrastructure and manpower. He informed the members that there was no scope to increase the number of operations with existing infrastructure. He requested Director, AIIMS to take immediate steps to enhance the capacity of CT Centre. Director, AIIMS promised to look for the possible options. However, it was felt that it will take time to increase the capacity, and alternative measures to reduce the waiting list should be worked out.

2. As a stop gap measure, limit the number of referrals to the Department of CTVS.

Director, AIIMS was of the opinion that as there are only few public sector hospitals in NCR Delhi that can perform emergency cardiac surgery, the current practice for emergency cases should be maintained.

It was felt that the majority of patients come by way of OPD referral from the Department of Cardiology, putting a cap to the number of new patients registered in the Department of Cardiology can effectively reduce the number of patients referred to the CTVS. This practice is in vogue in several other departments also. Dr Nikhil Tandon pointed out that certain procedures are carried out at AIIMS only, and a blanket cap on the number may deprive these patients of optimum treatment. After detailed discussion, the idea of limiting the number of new registrations was accepted in principle, and the decisions to cap the number and modalities of implementations were left to the Chief, CT Centre.

Dr D K Sharma suggested initiation of a screening OPD for the Department of Cardiology. Dr V K Bahl explained that, though a screening OPD would decrease the patients load in the Department of Cardiology, it would not decrease the number of surgical cases for CTVS.

3. All those patients who can be operated at other public sector hospitals should be referred to these hospitals.

Dr Shiv Kumar Choudhary apprised the committee about the existing facilities and the spectrum of cardiac surgical operations available in public sector hospital in NCR, Delhi.

Director, AIIMS and all the members were unanimous that the CTVS faculty members must give the earliest available date of admission. The patients should be explained about the reasons for long waiting list, and should be advised to seek treatment at other public-sector hospital in NCR Delhi. Director, AIIMS desired that the date of admission and advisory should be in a standard format and can be provided by way of a stamp or printed form.

Dr D K Sharma suggested that, similar to the Department of Neurosurgery patients should be categorized into 'emergency', 'priority' and 'elective'. There should be separate waiting list for 'priority' and 'elective' categories.

Dr Nikhil Tandon mentioned that the priority should be decided on the basis of clinical factors and availability of its treatment in other public-sector hospitals in NCR, Delhi.

C. Decisions

1. Options for capacity enhancement of CT Centres would be explored on priority.
2. The idea of limiting the number of new registrations was accepted in principle, and the decisions to cap the number and modalities of implementations were left to the Chief, CT Centre.
3. The current practice for emergency cases should be maintained.

4. Similar to the Department of Neurosurgery, patients should be categorized into 'emergency', 'priority' and 'elective'. There should be separate waiting list for 'priority' and 'elective' categories. The Priority should be decided on the basis of clinical factors and availability of its treatment in other public-sector hospitals in NCR, Delhi.
5. The CTVS faculty members must give the earliest available date of admission in each category. The patients should be explained about the reasons for long waiting list, and should be advised to seek treatment at other public-sector hospital in NCR, Delhi. The date of admission and advisory should be in a standard format and should be provided by way of a stamp or a printed form.

(Dr. Randeep Guleria)
Director, AIIMS

(Sh. Subhashish Panda)
Dy. Director (Admn.)

(Dr. V. K. Bahl)
Chief, CT Centre

(Dr D K Sharma)
Medical Superintendent

(Dr Nikhil Tandon)
Prof. & Head, Dept. of Endo. & Metabo

(Dr. Shiv Kumar Choudhary)
Prof. & Head, Dept. of CTVS, CT Centre

(Dr. Sanjay Kumar Arya)
Chief Administrative Officer

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Indian Journal of Clinical Practice, Vol. 30, No. 4, September 2019

Non-narcotic Methods of Pain Management: A Neurosurgeon's Point of View

AMIT AGRAWAL*, LUIS RAFAEL MOSCOTE-SALAZAR†, RAVISH KENI‡

Acute pain can be one cause to visit emergency services;[1] chronic pain can be the cause to seek medical attention. Acute pain can be sequel of surgical intervention and poorly managed postoperative pain can become chronic pain.[2,3] Neurosurgical interventions (cranial/spinal) can be performed for acute/chronic pain syndromes and these interventions can lead to acute pain and chronic pain syndromes.[3-5] It is being increasingly recognized that effective and aggressive control of postoperative pain avoids the risk of increase in intracranial pressure[2] and development of chronic pain.[4] One study suggested that cyclooxygenase-2 (COX-2) inhibitors provide better pain control and avoid the side effects associated with narcotic uses.[4] The article provides a generalized overview of pain, emphasizes the importance of pain relief by nonpharmacological methods and judicious use of narcotics and other medications.[1] Depending on etiology of pain and patient related factors there is a need to further explore effectiveness of preoperative behavioral interventions to reduce pain medications and risk of chronic pain.

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Faculty of Medicine - University of Cartagena, Cartagena de Indias, Bolivar
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REFERENCES

1. Finnerup NB. Nonnarcotic methods of pain management. N Engl J Med. 2019;380(25):2440-8.
2. Saha P, Chattopadhyay S, Rudra A, Roy S. Pain after craniotomy: A time for reappraisal? Indian J Pain. 2013;27(1):7-11.
3. Vadivelu N, Kai AM, Tran D, Kodumudi G, Legler A, Ayrian E. Options for perioperative pain management in neurosurgery. J Pain Res. 2016;9:37-47.
4. Rahimi SY, Vender JR, Macomson SD, French A, Smith JR, Alleyne CH Jr. Postoperative pain management after craniotomy: evaluation and cost analysis. Neurosurgery. 2006;59(4):852-7; discussion 857.
5. Rahimi SY, Alleyne CH, Vernier E, Witcher MR, Vender JR. Postoperative pain management with tramadol after craniotomy: evaluation and cost analysis. J Neurosurg. 2010;112(2):268-72.

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Childhood Cancer Survivors Face Variety of Heart Risks

Childhood cancer survivors' risks for heart problems may be broader than what was previously recognized, say researchers.

It's been known for years that some treatments for childhood cancer increase the risk of heart failure. But in a new study of more than 43,000 children, Canadian researchers found young cancer survivors had as much as a threefold increased risk of developing a variety of other cardiovascular problems, too, according to the report published in *Circulation*. Researchers found that even at relatively young ages, cancer survivors had a threefold increased risk for any type of heart event and as much as a 10-fold increased risk for heart failure compared to their peers… (*Reuters*)

Indian Journal of Clinical Practice, Vol. 30, No. 4, September 2019

Medtalks with Dr KK Aggarwal

Dangerous Drug Interactions More Common in Women and the Elderly

A new study led by researchers at Indiana University has found that women and older adults who use multiple prescription drugs are significantly more likely to be prescribed pills whose combination produces dangerous side effects. The analysis, conducted in the Brazilian health care system and recently published in the journal *npj Digital Medicine*, revealed a 60% increased risk for adverse drug reaction in women compared to men - and a 90% increased risk in cases of medicines whose interaction is known to produce dangerous reactions. In older people, one in every four people prescribed multiple medicines over age 55 received drugs with an interaction - reaching one in every three for ages 70-79. The drugs identified as most commonly prescribed in dangerous combinations were standard medications - such as omeprazole, fluoxetine and ibuprofen as well as some less common drugs, such as erythromycin.

Asians Sleep the Least Due to Higher Work and Educational Demands, Says Study

A new study indicates that young and middle-aged adults in Asia had the shortest sleep duration, and it may be due to high cultural demands. "Higher work and educational demands in Asian countries compared to the West likely explain the latter's shorter sleep duration," said M Gradisar from Flinders University in Australia.

According to the researchers, **young adults in Asia had the shortest sleep duration of 6 hours 30 minutes,** whereas those in Oceania had 7 hours 14 minutes, and **Europe had the longest at seven hours 7 minutes.** Young adults in Central and Southern America and the Middle East also reported short sleep of 6 hours 40 minutes. "Our findings suggest that cultural factors likely impinge upon the sleep opportunity of young people around the world," Gradisar said.

For the study published in the journal *Sleep Medicine*, researchers compared the sleeping habits of 17,335 people who were asked to wear fitness trackers through which their 14-day sleep patterns were tracked … (*Indian Express*)

Arrest of Health Professionals Deplored

The arrest of four Turkish health professionals for providing medical care to a wounded child in Turkey during a curfew has been deplored by the World Medical Association (WMA) and the Standing Committee of European Doctors (CPME).

The four health staff - a physician Dr Nesim Sayın and three nurses - were detained and arrested by Turkish authorities earlier this month following a police raid on their homes.

According to information from their lawyers, they provided care to a 12-year-old wounded child in 2015 at a time when there was a curfew and access to health services was almost impossible. They have now been detained in Şırnak Prison on charges of providing support to terrorist activity.

In a letter to the Turkish President, Dr Frank Ulrich Montgomery, Chair of the WMA and CPME President, protested about "the brutal arrest" of the four. He said: "There is a remarkable disproportionality between the alleged facts and the measures taken by the Turkish authorities. We are very sceptical that providing care to a 12-year-old wounded child constitutes a crime that poses a threat to public order justifying such a police raid."

These health professionals have done nothing more than perform their duties in line with the ethical principles of health care. According to our code of conduct, it is a physician's obligation to maintain the utmost respect for human life. It is therefore our responsibility to extend health care to all who need it, anywhere and even in emergency situations. "Penalizing those providing health care to injured people is an aberration and a flagrant infringement of medical ethics, humanitarian and human rights."

Dr Montgomery added: "International humanitarian law, ratified by Turkey, requires health professionals to provide health care and assistance to all in need and in all circumstances. To criminalize these actions is appalling."

"We urge the Turkish authorities to recognize this fact and to immediately drop the charges and release these health professionals."

No Country is 100% Free of Risk of Import of Potential Ebola Virus Disease

No country, regardless of how far or remote from the current Ebola outbreak in the Democratic Republic of the Congo (DRC), can be considered 100% free of the risk of importation of a potential Ebola virus disease case. However, WHO's current assessment finds the overall risk in the European Region to be low.

The risk remains very high in the DRC and the WHO African Region. The current Ebola outbreak in the DRC was declared a public health emergency of international concern (PHEIC) under the International Health Regulations (IHR) (2005) on 17 July 2019. A PHEIC represents an extraordinary event that poses a public health risk to other countries through international spread, and that potentially requires a coordinated international response.... (*WHO Europe*)

Lefamulin, A New Antibiotic to Treat Community-acquired Bacterial Pneumonia

The US Food and Drug Administration (FDA) has approved a new antibiotic, lefamulin to treat adults with community-acquired bacterial pneumonia. It will be available for oral (600 mg every 12 hours) and IV (150 mg every 12 hours) administration with a short 5- to 7-day course of therapy.

Lefamulin is a first-in-class semisynthetic pleuromutilin antibiotic indicated for community-acquired bacterial pneumonia caused by the following susceptible microorganisms: *Streptococcus pneumoniae, Staphylococcus aureus* (methicillin-susceptible isolates), *Haemophilus influenzae, Legionella pneumophila, Mycoplasma pneumoniae* and *Chlamydophila pneumoniae.*

Adverse effects: Diarrhea, nausea, reactions at the injection site, elevated liver enzymes and vomiting. The drug has the potential to cause a change on an ECG reading (prolonged QT interval).

Contraindications: Patients with known hypersensitivity to lefamulin or any other members of the pleuromutilin antibiotic class, or any of the components of lefamulin; patients with prolonged QT interval, patients with certain irregular heart rhythms (arrhythmias), patients receiving treatment for certain irregular heart rhythms (antiarrhythmic agents) and patients receiving other drugs that prolong the QT interval.

Precaution: Pregnant women and women who could become pregnant should be advised of the potential risks of lefamulin to a fetus. Women who could become pregnant should be advised to use effective contraception during treatment with lefamulin and for 2 days after the final dose.

(Source: US FDA, Medscape)

Green Spaces Good for Mental Health and Well-being

Living within 300 m of urban green space such as parks, nature reserves or play areas is associated with greater happiness, sense of worth and life satisfaction, according to a new study by researchers at the University of Warwick, Newcastle University and the University of Sheffield published in the August issue of *Applied Geography.*

The study applied new geospatial research techniques to create an accurate measure of the relationship between green space and the 3 different aspects of mental well-being (life satisfaction, worth, happiness). Survey responses from 25,518 participants in the UK government's Annual Population Survey (APS) were combined with data on the shape, size and location of London's 20,000 public green spaces. Researchers were able to more accurately model green space distribution in relation to where each of the 25,518 survey participants lived, and explore how that influenced their mental well-being as revealed in their survey answers.

Key findings of the study were:

- Overall there is a very strong relationship between the amount of green space around a person's home and their feelings of life satisfaction, happiness and self-worth.
- Green space within 300 m of home had the greatest influence on mental well-being.
- An increase of 1 hectare within 300 m of residents was associated with an increase of 8 percentage points in life satisfaction, 7 in worth and 5 in happiness.
- Green space was less important for mental well-being in Central London and East London.

Adequate Sleep and Limited Screen Time can Reduce Impulsivity in Children

A study "24-Hour Movement Behaviors and Impulsivity", published online in the journal *Pediatrics* has found that children who met the sleep, screen time and physical activity recommendations reported lower levels of impulsivity. **Adequate sleep and limited screen time had the largest association with reduced impulsivity.**

According to the authors, these findings could be important for pediatricians, educators, parents and policy makers as they consider opportunities to limit screen time, while also promoting early, routine bedtimes; especially as it relates to prevention and treatment of impulsivity-related psychiatric disorders such as Attention Deficit-Hyperactivity Disorder (ADHD).

The guidelines recommend 9-11 hours sleep each night, no more than 2 hours of daily recreational screen time, and at least 60 minutes of moderate-to-vigorous physical activity each day.

WHO Calls for More Research into Microplastics and a Crackdown on Plastic Pollution

The WHO has called for a further assessment of microplastics in the environment and their potential impacts on human health, following the release of an analysis of current research related to microplastics in drinking-water. The Organization also calls for a reduction in plastic pollution to benefit the environment and reduce human exposure.

According to the analysis, which summarizes the latest knowledge on microplastics in drinking-water, microplastics larger than 150 mm are not likely to be absorbed in the human body and uptake of smaller particles is expected to be limited. Absorption and distribution of very small microplastic particles including in the nano size range may, however, be higher, although the data is extremely limited.

WHO recommends drinking-water suppliers and regulators prioritize removing microbial pathogens and chemicals that are known risks to human health, such as those causing deadly diarrheal diseases. This has a double advantage: waste-water and drinking-water treatment systems that treat fecal content and chemicals are also effective in removing microplastics… (*WHO*)

AHA Advisory Backs Prescription Omega-3s for Triglycerides

Prescription omega-3 fatty acids - products containing eicosapentaenoic acid (EPA) *plus* docosahexaenoic acid (DHA) or EPA alone - are an "effective and safe" way to reduce elevated triglyceride levels when used alone or with other lipid-lowering therapy, according to a science advisory from the American Heart Association (AHA) published online in *Circulation*. Dietary supplements containing omega-3 fatty acids, which are not regulated by the US FDA, should not be used in place of prescription medication for the long-term management of high triglyceride levels. Prescription omega-3 fatty acids at the FDA-approved dose of 4 g/day are safe and are generally well-tolerated, the advisory states.

Updated USPSTF Recommendations on BRCA1/2 Testing in Women

For women with a personal or family history of breast, ovarian, tubal or peritoneal cancer or an ancestry associated with BRCA1/2 gene mutation, the US Preventive Services Task Force (USPSTF) recommends that primary care clinicians assess women with a personal or family history of breast, ovarian, tubal or peritoneal cancer or who have an ancestry associated with breast cancer susceptibility 1 and 2 (BRCA1/2) gene mutations with an appropriate brief familial risk assessment tool.

Women with a positive result on the risk assessment tool should receive genetic counseling and, if indicated after counseling, genetic testing (Grade B).

For women whose personal or family history or ancestry is not associated with potential harmful BRCA1/2 gene mutations, the USPSTF recommends against routine risk assessment, genetic counseling or genetic testing for women whose personal or family history or ancestry is not associated with potentially harmful BRCA1/2 gene mutations (Grade D).

Knowledge Alone is Insufficient to Change Behavior

Teacher training followed by classroom education with information, activities and emotional support improves lifestyles in teachers and students, according to research from Brazil presented at ESC Congress 2019 together with the World Congress of Cardiology. The study suggests that knowledge alone is insufficient to change behavior. In the study, **junk food intake in children reduced by health education that addresses emotional issues.**

The Happy Life, Healthy Heart program randomly allocated 10 public schools (473 students aged 6-12 and 32 teachers) in the city of Frederico Westphalen, Brazil, to the intervention group (five schools) or control group (five schools). The intervention had two stages: teacher training followed by students in the classroom.

Teachers attended four meetings over a 4-month period, were given a booklet and had access to video lessons. The material was in seven chapters: 1) risk factors for cardiovascular diseases in childhood; 2) choice of healthy foods; 3) food labeling; 4) sodium, sugars and fats; 5) emotional health and quality-of-life; 6) physical activity and 7) healthy practices and changes in habits. Each section contained theory *plus* suggestions for classroom

activities based on the theme, age of the children and intended goals. The researcher visited the intervention schools to stimulate teachers and offer guidance. For the control group schools, teachers did not participate in the training course and students attended the school's usual classes about health and healthy eating based on the curriculum.

Both students and teachers benefitted from the intervention. The proportion of students following Brazilian Food Guide advice to avoid pizza/hamburgers and soft drinks increased significantly by 15% and 20%, respectively. In addition, there was a 28% increase in the number of teachers who were physically active.

Men should be Included in Clinical Trials of Breast Cancer Drugs, Says US FDA

Breast cancer is rare in males, with less than one percent of all breast cancer cases occurring in male patients. Hence, they have been usually excluded from clinical trials. The US FDA has published draft guidance for including men in clinical trials of breast cancer drugs. It recommends that eligibility criteria for clinical trials of breast cancer drugs should allow for inclusion of both males and females. It further recommends that "Scientific rationale should be included in the protocol when proposing to exclude males from breast cancer trials. FDA does not intend to consider low expected accrual rates of male patients with breast cancer to be a sufficient scientific rationale for excluding them from a clinical trial".

When males have not been included or when inclusion of males is very limited in clinical trials for a specific breast cancer drug

- It may be possible to extrapolate findings to include male patients in the FDA approved indication for the drug where no difference in efficacy or safety is anticipated between males and females based on the mechanism of action of a drug. The use of extrapolation should be supported by data from earlier stages of development (e.g., nonclinical testing), literature or both.
- Further data may be necessary to support extrapolation of findings to support an FDA-approved indication for male patients with breast cancer where there is a concern for differential efficacy or safety between males and females.

(Source: FDA)

5 Hidden Dangers in International Travel

1. **Vaccination:** Ensure that your patients are up to date on all routine vaccines, including measles, mumps and rubella (MMR); varicella (chickenpox); and the seasonal flu vaccine or other specific vaccines advised for the destinations your patient will be visiting.
2. **Insect bites:** Encourage patients to use insect repellents (DEET, picaridin, IR3535, oil of lemon eucalyptus, para-menthane-3, 8-diol or 2-undecanone); advise use of mosquito nets, especially for rooms without screens or air conditioning. Insect bites can transmit mosquito-borne diseases (Zika, dengue, yellow fever or malaria), tick-borne diseases (Lyme disease, spotted fevers), fly-borne diseases (leishmaniasis, sleeping sickness) and flea-borne diseases (typhus, plague).
3. **Food and water safety:** Encourage patients to choose food that is cooked and served hot, food from sealed packages, peeled fruits and vegetables, and pasteurized dairy. Travelers should avoid drinking tap water or using ice. Bottled and canned drinks are safer choices.
4. **Deep vein thrombosis (DVT):** Long-distance travelers should be counseled about associated risks that increase their chances of developing DVT. People at higher risk include those who were recently hospitalized or had recent surgery, pregnant women, and those in the postpartum period (up to 3 months after childbirth). Other risk factors include history of previous DVT; family history of DVT; obesity; increased estrogen; indwelling catheters; cancer and certain chronic medical illnesses, such as heart or lung disease. Remind patients to move their legs frequently and to walk around every 2-3 hours while traveling. Educate them about the symptoms and what to do.
5. **Road and traffic risks:** Patients should always wear seat belts; avoid riding in a car in a developing country at night, if possible; avoid riding motorcycles; know local traffic laws before driving; ride only in marked taxis that have seat belts and avoid overcrowded buses.

(Source: 5 hidden dangers in international travel - Medscape)

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Indian Journal of Clinical Practice, Vol. 30, No. 4, September 2019

DERMACON International 2019 – India

17TH JANUARY 2019 | CLARKS EXOTICA CONVENTION RESORT & SPA, BENGALURU

STEROID TOPICAL PRESCRIPTION BY DOCTORS

Dr P Narsimha Rao, Hyderabad

- Topical corticosteroid misuse is a very important issue related to our specialty.
- The topical corticosteroid is a key player in dermatology therapy.
- The sale of topical steroid creams in India accounts for 82% sale of all topical drugs in India.
- Topical steroid preparations are available as stand alone topical steroid preparations; 2-drug combinations of topical steroids cream and 3-drug Kligman' formula creams.
- Although evidence shows that combination antifungal/corticosteroid topical are more expensive and less effective than single-agent antifungals, still practitioners prescribe them.
- Unfortunately, it was also observed that even trained physicians and some dermatologists are prescribing either the wrong strength of topical corticosteroids or for the wrong indication.
- Pediatric dermatologists have long warned of the hazards of use of combination steroid cream for children.

Practice sutra: *It is easy to keep away from steroid-antifungal combination while treating dermatophyte infection.*

HILLS AND VALLEYS AROUND THE EYE

Dr Milind Naik, Hyderabad

- Under eye fat bags are compartmentalized and limited by orbital rim whereas fluid bags are diffuse, and extend beyond the rim.
- Fat bags worsen on looking up, and improve on looking down; fluid bags stay the same with gaze. Fat bags can be removed with blepharoplasty. Fluid bags are hard to treat.
- Assessment of vision (pocket charts/mobile apps) is prudent before and after an under eye/glabellar filler injection.
- Lower lid blepharoplasty is best done by scarless transconjunctival approach.

PLATELET RICH PLASMA

Dr Shuken Dashore, Indore

- Platelet rich plasma (PRP) is an efficacious, cost-effective and simple technique, which doesn't need expensive instruments.
- In this era, where side effects have become a concern and litigation is on the rise, autologous treatments like PRP are bound to find an important place in our treatment armamentarium.
- Growth of stem cells is proportional to the concentration or dose of growth factors as shown in various studies; hence, PRP must have platelets in high enough concentration to be effective.

APREMILAST

Dr KN Sarveswari, Chennai

- Orally administered apremilast is an effective generally well-tolerated and convenient option for the treatment of many chronic inflammatory dermatoses. It does not cause immune suppression but acts by targeting the central inflammatory signalling pathways.
- Hence, it has an added advantage over conventional treatment modalities available.
- It is not associated with an increased risk of infection or malignancy and no lab monitoring is required.
- However, a low drug survival beyond 6-8 months as reported in real-world studies limits its use as a long-term maintenance therapy.
- Availability of 10 mg and 20 mg dosage may widen the scope of its use in various other dermatological diseases. Safety and efficacy in pediatric age group should also be proven.

ACNE SURGERY

Dr Pushpa KR, Bengaluru

- Acne surgery is only an adjunct to medical therapy.
- Combination of various techniques gives better results.

- Prevents scarring and hastens recovery.
- Useful in patients who have restrictions to medical therapy and in patients who want faster results.

ROLE OF CHEMICAL PEELS

Dr Rasya Dixit, Bengaluru

- Chemical peels are the first step towards rejuvenation.
- It is an easy office procedure and cost-effective.
- It can help with color and improving texture.
- It can easily combine with other treatments.
- It cannot improve laxity or volume loss or muscular ageing.

MANAGEMENT OF PSORIASIS IN SPECIAL SCENARIOS

Dr Raghunatha Shivanna, Bengaluru

Management of psoriasis is based on children, pregnant and lactating women, elderly and comorbid conditions. The determinants of psoriasis are primary morphology, progression of disease, severity of disease, triggers, impact on quality-of-life, family history of psoriasis and involvement of joints.

Practice sutra: *We need to depend on thorough assessment of scenario, careful monitoring of disease progression and potential adverse events, and critical analysis of available data till proper evidences are generated through appropriately designed studies.*

AXILLARY DERMATOSES - HIDRADENITIS SUPPURATIVA AND HAILEY-HAILEY DISEASE

Dr Vidya Kharkar, Mumbai

Hidradenitis suppurativa (HS) is a chronic, painful, follicular occlusive disease that affects the folliculopilosebaceous unit. The treatment goals are to treat existing lesions, to reduce the frequency of new lesion and to prevent disease progression. Emerging therapies for severe and refractory HS include ustekinumab, anakinra, canakinumab, MABp1 (bermekimab). Hailey-Hailey disease (HHD) is an AD inherited genodermatosis caused by dysregulation of calcium hemostasis in the keratinocytes that leads to acantholysis in the epidermis. There is no specific therapy for HHD; therapeutic approach to HHD involves the control of exacerbating factors, secondary infections and cutaneous inflammation. Emerging therapies for HHD include oral magnesium chloride and low-dose oral naltrexone. The most important aspect of treatment is the psychosocial considerations; hence, counseling should be done for every patient.

RITUXIMAB IN DERMATOLOGY

Prof (Dr) Krina Bharat Patel, Ahmedabad

- Rituximab is one of the most talked about medicine in dermatology in recent era of biological drugs and targeted molecules. It is used in day-to-day practice for large number of indications including pemphigus group of disorders and other autoimmune diseases.
- Due to its greater efficacy and large safety profile, the drug is becoming the most used medicine for indications as diverse as pemphigus, SL, vitiligo and melanoma.
- Relative low cost of the drug as compared to other biological drugs is an added advantage of this wonder molecule.

MINIATURE PUNCH GRAFTING IN VITILIGO

Dr Koushik Lahiri, Kolkata

- Mini grafting in vitiligo remains the easiest, fastest and cheapest of all surgical options in vitiligo.
- Stability must be assured before opting for surgical options in vitiligo.
- Cobblestoning and polka dotting remains the main complication if larger punches are used, but with time or intervention this diminishes gradually.
- NB-UVB after mini grafting evokes encouraging results.

CRYOTHERAPY AND INTRALESIONAL INJECTIONS

Dr Pavan Raj R, Bengaluru

- Cryotherapy and intralesional injections are simple, safe and inexpensive office procedures which are an integral part of the dermatological therapeutic armamentarium.
- When used judiciously and cautiously by a trained dermatologist, they provide good cosmetic result with minimal complications.

CUTANEOUS WINDOW IN THYROID AND DIABETES

Dr A Bhattacharyya, Bengaluru

- There are pathologic correlations between skin and thyroid disorders like pretibial myxedema, onycholysis, hyperpigmentation while infective disorders of the skin predominate in diabetes.

- In the latter case, both treatment of the skin condition and good control of diabetes are important.
- Problems escalate when steroids for various bullous disorders of the skin have to be used.

Practice sutra: *A good correlation between dermatologist and medical specialist is the key to success in such cases.*

HEPATIC AND RENAL PRURITUS

Dr Asit Kumar Mittal, Udaipur

- In recent years, there is an attempt to better understand mechanism of itch in systemic itch.
- Disturbance in endogenous opioids both at the central and peripheral level is one of the proposed mechanisms.
- Drugs-like gabapentin and pregabalin in low doses have shown maximum efficacy in itch of chronic kidney disease (CKD).
- Antagonist such as naltrexone and agonist such as nalfurafine have shown efficacy in itch arising out of both kidney and liver disorders.
- Other pharmacotherapies that have been attempted in hepatobiliary itch are rifampicin, cholestyramine and sertraline.
- Ileal bile acid transporter inhibitors are some of the exciting new developments in treating hepatobiliary itch.

STABILITY ISSUES IN VITILIGO

Dr Koushik Lahiri, Kolkata

- When ultrastructural investigation facilities are available, an attempt should be made to clearly fathom stability, not merely on clinical grounds but along with electron microscopy and histoenzymological analysis of the perilesional and nonlesional skin of vitiligo patients.
- Growth factors responsible for both mitogenic and melanogenic stimulation of melanocyte should also be taken into account.
- The understanding of the area based variable status and limited period of inertia or activity might necessitate test grafting at various sites at different time interval.

Practice sutra: *Till the unexplored areas are chartered, we should not refrain from choosing the surgical option. Judging every patient as a unique one and logical application of clinical knowledge may be very important.*

HAIR LOSS IN CHILDREN

Dr Manish K Shah, Mumbai

- Androgenic hair loss can occur quite early in childhood and is not always associated with premature puberty.
- Adrenal tumors are a rare cause of poorly responsive androgenic hair loss. Alopecia areata incognita can sometimes cause diffuse hair loss in children.
- Loose anagen syndrome is probably being missed in Indian children. It responds quite well to topical minoxidil.
- Transient neonatal hair loss can present as occipital alopecia, frontotemporal hair loss or diffuse thinning.

GENETICS AND HAIR LOSS

Dr Saumya Panda, Kolkata

- New technologies have made unraveling genetic pathways in hair loss a practical proposition.
- Recent genetic analysis is providing evidence of activity of immune response-related genes in androgenic alopecia (AGA) provides long-awaited explanation of microinflammation in the follicular bulge.
- The most comprehensive genetic studies of alopecia areata were performed on Caucasian populations, and it is possible that the genetic component in this condition is different in other ethnic groups.

BIOLOGICALS: OFF LABEL INDICATION

Dr Brijesh Nair, Jaipur

Biologicals are cutting edge molecules which have added to the armamentarium of the treating dermatologist. The biologicals/biosimilars available in India include TNF-α inhibitors, IL-17 inhibitors, T-cell costimulatory blockers, B-cell depletion therapies like rituximab, IL-6R blockers (tocilizumab) and CD6 blocker (itolizumab). These molecules are currently approved in diseases like psoriasis, psoriatic arthritis, hidradenitis (TNFi all) and pemphigus and AAV (rituximab) among others. Off-label indications of biologicals include pustular psoriasis, autoinflammatory diseases, subepidermal bullous disorders, connective tissue diseases, non-AAV vasculitis, neutrophilic dermatoses, lepra reactions and even severe syndromic follicular occlusion disorders like acne.

Practice sutra: *The dermatologists must derive immunological insights about various innate and adaptive*

immune pathways and must use these agents judiciously for off-label indications with risk benefit ratio assessment and adequate monitoring and screening.

PERIORBITAL LASER

Dr Namitha Prabhu, Bengaluru

- The choice of laser depends on the etiology of periorbital melanosis (POM). Q-switched lasers and fractionated lasers are useful in treating pigmentary causes of POM.
- Vascular conditions can be treated with long pulsed lasers. Fractionated lasers are used to treat skin laxity.
- Low fluence treatment with subthermolytic Q-switched lasers (1,064 nm) is associated with less side effects but requires multiple sessions weekly.
- A multimodal treatment approach offers best results for periorbital hyperpigmentation.

MINOR MALE GENITAL SURGERY AND CYST REMOVAL

Dr Hanuamnathaiah HC, Bengaluru

- Common conditions requiring surgical interventions are median raphe cysts of penis, short frenulum, paraphimosis, phimosis, steatocystoma multiplex/simplex of scrotum, angiokeratoma of scrotum.
- Multiple cysts of scrotum are not rare, with radiosurgery using cutting mode being the best option.
- Frenuloplasty is done in patients with short frenulum.
- Electrodesiccation or electrofulguration is the best treatment option in case of benign dilated capillary lesions or angiokeratoma of scrotum.

EXCESS ANDROGENS AND SKIN

Dr Ganapathi B, Bengaluru

- Hyperandrogenism/hyperandrogenemia is the most common endocrinopathy among women of the reproductive age.
- It refers to classical androgen-dependent signs, such as hirsutism, acne, AGA and seborrhea.
- Pharmacologic therapy of PCOS (hirsutism) includes various agents such as combination estrogen-progestin, antiandrogens and biguanides.
- Other agents include glucocorticoids, 5α-reductase inhibitors, ornithine decarboxylase inhibitors, minoxidil and ketoconazole.

ATOPIC DERMATITIS: WHAT'S NEW IN THERAPY?

Dr Thomas Ruzicka, Germany

Atopic eczema has high incidence, increasing in frequency, predominantly seen in children and shows a diminished quality of life. Basic dermatological therapy comprises of skin care, corticosteroids/tacrolimus and antihistamines. New therapeutic approaches include anti-IL-4 (dupilumab), anti-IL-31RA (nemolizumab), retinoids (alitretinoin), skin barrier improvement and early intervention to stop atopic march.

CHRONIC BALANITIS

Dr (Prof) H Hanumanthappa, Mysore

- Balanitis is inflammation of "Glans penis" and "Posthitis" is inflammation of "prepuce".
- Both the areas are often affected together and the term commonly used as 'Balanoposthitis' commonly seen in uncircumcised males.
- Treatment consists of saline wash/potassium permanganate wash.
- Specific treatment includes topical/oral antibiotics/antifungals/antivirals/antihelminthics/antiparasitic drugs.

CHEMICAL PEELS FOR BODY REJUVENATION

Dr KB Kavitha, Karur, Tamil Nadu

- Nonfacial are confined to light and medium depth peel.
- Conservative - less pilosebaceous units, thin skin, large surface area, dry. It requires more number of sessions and application in expedited fashion.
- Black acne peel varies in degreasing, concentration of peel, time.
- Area of peeling <25% in one session to avoid toxicity.
- Correct technique, indication, limitations, complications is paramount. Multiple sessions needed to achieve desired results.

EMERGING SYSTEMIC THERAPY: JAK INHIBITORS

Dr Yashpal Manchanda, New Delhi

- Janus kinase inhibitors also known as jakinibs, inhibit the kinase component of JAKs, thereby preventing them from phosphorylating and stopping the transduction of intercellular signalling.
- First-generation jakinibs, which include the drugs tofacitinib and ruxolitinib inhibit multiple JAKs.

- Second-generation jakinibs are still under investigation and more selective target only one JAK isoform, thereby inhibiting a narrower range of cytokines.
- The dermatological uses of jakinibs include atopic dermatitis, psoriasis and psoriatic arthritis.
- Several case reports and preclinical evidence suggest that JAK inhibitors may be useful in the treatment of other inflammatory, autoimmune and malignant skin conditions. These include cutaneous lupus, cutaneous T-cell lymphoma, melanoma, allergic contact dermatitis and lichen planus.

MANAGEMENT OF BULLOUS PEMPHIGOID

Dr Muralidhar Rajagopalan, Chennai

- Bullous pemphigoid: Localized/limited disease with mild activity.
- First choice: Super potent topical corticosteroids; in mild disease, on whole body except the face. In localized disease, on lesions only.
- Second choice: Oral corticosteroids (validated for prednisone); tetracycline + nicotinamide (nonvalidated); dapsone, sulfonamides (nonvalidated) and topical immunomodulation (e.g., tacrolimus) (nonvalidated).
- Third choice: Gaining more acceptance higher up in the ladder now - Combination with and/or introduction of: Anti-CD20 or anti-IgE monoclonal antibody; intravenous immunoglobulins; immunoadsorption; plasma exchange and cyclophosphamide.

EMERGING INTERVENTIONAL THERAPIES FOR WARTS

Dr Deepak Jakhar, New Delhi

- Infection of the keratinocyte by human papilomavirus (HPV) is one of the most common skin diseases worldwide. It is spread by direct contact or via environment. Spontaneous resolution can occur.
- Salicylic acid, citric acid, formic acid, topical sodium nitrate, vit D analogs, topical vit A, 5-fluorouracil, glycolic acid, pyruvic acid, 2% povidone-iodine, etc. are used in the treatment.
- Cryotherapy, photodynamic therapy, hyperthermia, Nd:YAG, photodynamic therapy, intralesional MMR, intralesional immunotherapy, intralesional Candida antigen and intralesional BCG are other therapies used in the treatment.
- HPV vaccine has also brought down the incidence of genital warts.
- Factors affecting treatment are age and immune status, site of the warts, recalcitrant warts and recurrent warts.

RECOGNIZING TARGET LESIONS IN THE EMERGENCY ROOM

Dr Ronni Wolf, Israel

- According to the consensus classification, categorization of these diseases is determined essentially by the percentage of skin detachment and by the semiology of the typical individual "EM-like" or "target" lesions.
- In addition to their presenting with lesions whose characteristics are compatible with the consensus classification, we have noticed that patients of the SJS/TEN group sometimes also have typical targets that are flat and have a flat ring around their center.
- We have added an additional type of lesions to the nomenclature, namely "flat typical target", and call the original typical targets "raised typical target".
- The new classification includes: raised typical targets, flat typical target, raised atypical targets, flat atypical targets, macules ± blisters.

Practice sutra: *The above classification will help you to differentiate EM from SJS/TEN. Remember, raised lesions wwwww= post-infection erythema multiformae; flat lesions = drug-induced SJS/TEN.*

CLINICAL BEDSIDE INVESTIGATIONS AND LIGHT MICROSCOPY FOR HAIR

Dr Yasmeen Jabeen Bhat, Srinagar

- Clinical bedside investigations should be practiced routinely in the evaluation of hair disorders.
- Their use may avert semi-invasive or invasive techniques like scalp biopsy or microarray analysis.

MASSETER HYPERTROPHY

Dr KC Nischal, Bengaluru

- Botulinum toxin injection for masseter hypertrophy is a simple, quick procedure that can change the outlook of an individual.
- Results of botulinum toxin for masseter have residual effect leading to decremental doses of toxin in subsequent treatments.
- Right dosage and right technique can prevent complications like paradoxical bulging, disappearance of dimple and Candy-in-mouth deformity.

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News and Views

PM Wants App for Disabled, Check on Modicare Frauds

Prime Minister Narendra Modi has asked all states to establish anti-fraud units and to take strict action against culprits involved in frauds relating to Ayushman Bharat scheme. PM has also directed the department dealing with disabled persons under social justice ministry to develop a mobile application where the disabled can upload pictures of the problems that they face.

Modi asked the Department of Empowerment of Persons with Disabilities (DEPwD) to develop the app so that persons with disabilities can share their difficulties and the department concerned can be directed to take quick action… (*ET Healthworld – TNN*)

Hajj Health and Safety Boosted by New Health Early Warning System

Authorities in Saudi Arabia deployed a new health surveillance system to help keep people protected from communicable diseases during the annual hajj pilgrimage.

For the first time, the Global Centre for Mass Gatherings Medicines of the Saudi Ministry of Health used the Health Early Warning System (HEWS), which ensures the early detection of and timely response to health threats and emergencies related to mass gatherings. The new system monitors clinical reporting to identify clusters of unusual health events… (*WHO*)

LVAD Patients More Active, Fit Than Counterparts with Heart Failure

Patients with left ventricular assist devices (LVAD) are more physically active than matched patients with advanced chronic heart failure (CHF), and have higher peak oxygen consumption (VO_2 peak), according to new findings.

The LVAD group averaged 19.7 kJ/kg/day, versus 11.6 kJ/kg/day in the control group ($p = 0.001$). They engaged in a median of 26 minutes of moderate-intensity physical activity per day versus 12 minutes for the advanced CHF patients ($p = 0.001$). The findings were published online in *Medicine and Science in Sports and Exercise*.

Supermarkets Near Home, Fast-Food Along Commute Tied to Obesity

People with more supermarkets and grocery stores close to home and workers who pass more fast food restaurants on their commute have higher odds of being overweight or obese, a US study suggests.

Investigators noted that people who passed more fast-food restaurants during their commute had higher body mass index (BMI) than those who encountered fewer outlets.

Surprisingly, people who had more supermarkets - the bigger retailers that typically have a wider variety of fresh produce - and smaller grocery stores near home had higher average BMIs than people who had fewer places to purchase groceries, the study found. The findings are reported in *PLoS ONE*, online August 7.

FDA Warns Consumers About Dangerous and Potentially Life-threatening Side Effects of Miracle Mineral Solution

The US Food and Drug Administration (FDA) has warned consumers not to purchase or drink a product sold online as a medical treatment due to a recent rise in reported health issues. Since 2010, the FDA has warned consumers about the dangers of Miracle or Master Mineral Solution, Miracle Mineral Supplement, MMS, Chlorine Dioxide (CD) Protocol, Water Purification Solution (WPS) and other similar products. Miracle Mineral Solution has not been approved by the FDA for any use, but these products continue to be promoted on social media as a remedy for treating autism, cancer, HIV/AIDS, hepatitis and flu, among other conditions… (*FDA*)

Scientists Hail Promise of First Effective Ebola Treatments in Congo Trial

Scientists are a step closer to finding the first effective treatments for the deadly Ebola hemorrhagic fever after two potential drugs showed survival rate of as much as 90% in a clinical trial in Congo.

Two experimental drugs - REGN-EB3 and a monoclonal antibody called mAb114 - were both developed using antibodies harvested from survivors of Ebola infection. The treatments are now going to be offered to all

patients in the Democratic Republic of Congo (DRC), according to US National Institute of Allergy and Infectious Diseases… (*Reuters*)

Little Progress Seen in Diabetes Care in Past 15 Years

There have been few improvements in diabetes diagnosis, linkage of patients to care, or achievement of treatment targets in the United States since 2005 despite advances in care, new research suggests.

The findings, from 2,488 participants in the National Health and Nutrition Examination Survey (NHANES) cycles covering 2005 to 2016, were published online August 12 in *JAMA Internal Medicine*. The data suggest that gaps in the diabetes care "cascade", defined as the sequence of diagnosis, linkage to care, and achievement of treatment targets, essentially remained the same from 2005 through 2016.

New Data on Antidepressants and Stroke Risk

Use of antidepressants that strongly inhibit serotonin is associated with a somewhat lower risk for ischemic stroke compared to agents that weakly inhibit the neurotransmitter, suggests a large, population-based study. Investigators found a 12% reduced risk for ischemic stroke among study participants who were currently taking a stronger selective serotonin-reuptake inhibitor (SSRI) or third-generation antidepressant compared to those taking a weaker inhibitor of serotonin. The study was published online in *Neurology*.

Only 6% Mothers in India Okay with Public Breastfeeding Places, Says Survey

Breastfeeding in public is still a challenge in India, with only 6% of mothers finding designated areas to comfortably nurse their children, according to a pan-India survey by Momspresso.com.

In a 5-minute, web-link based survey, 900 mothers were surveyed. Women have fed their babies in their own car (90%), public transport (78%), restaurants (56%), car parking (49%), trial rooms (47%), washrooms (44%), religious places (41%), parks (32%) and breastfeeding rooms (6%). The most awkward places are a broom closet room in an airport, under a tree, the waiting room of the passport office, bank queues, washrooms, a bench in a mall and a bus stop. Around 81% mothers are not comfortable feeding their children in public due to the lack of proper breastfeeding places… (*The Hindu*)

Social Media Use may Harm Teens' Mental Health by Disrupting Positive Activities, Study Says

Social media use has been linked to depression, especially in teenage girls. But a new study argues that the issue may be more complex than experts think.

The research, published in the journal *The Lancet Child & Adolescent Health*, found that social media may harm girls' mental health by increasing their exposure to bullying and reducing their sleep and physical exercise… (*CNN*)

ESRD: Extreme Heat Tied to Risk for Hospitalization, Death

Even a single day of extreme heat is associated with an increased risk for same-day hospital admission and same-day mortality in patients with end-stage renal disease (ESRD), new research suggests.

Extreme heat events were found to be associated with a 27% increase in the rate of same-day hospital admission (95% confidence interval [CI], 1.13-1.43) and a 31% increase in the rate of same-day mortality (95% CI, 1.01-1.70) among patients with ESRD. The findings are published online in *JAMA Network Open*.

Superbug *E. coli* Strains in Healthy Women Raise Risk of Resistant UTIs

Fluoroquinolone-resistant (FQR) strains of *Escherichia coli* may persist in the gut of healthy women and subsequently invade the urinary system, researchers say.

FQR *E. coli* were found in feces of 8.8% of healthy adult women, with most bacteria belonging to pandemic multi-drug resistant ST131-H30R or ST1193 clonal groups, note Dr Evgeni Sokurenko of the University of Washington in Seattle and colleagues. "Moreover, these highly uropathogenic clonal groups demonstrate an especially prolonged gut persistence and high rate of bacteriuria without documented urinary tract infection (UTI)," stated the researchers in *Clinical Infectious Diseases*.

Eating More Gluten Early in Life is Tied to Children's Higher Risk of Celiac Disease, Says Study

A study published in the journal *JAMA* suggests that eating higher-than-normal levels of gluten during the first 5 years of life can increase a child's likelihood of developing celiac disease.

Higher gluten intake was associated with a 6.1% increased risk of celiac disease autoimmunity, an immunological response to gluten, and a 7.2% increased

risk of celiac disease per each additional gram of gluten per day, according to the study… (*CNN*)

Fewer Parents Smoke When Pediatricians Offer Tobacco Screening, Treatment

Parents who smoke may be more likely to quit when they receive tobacco screening and smoking cessation treatment from their child's pediatrician than when they don't get this support, a new study suggests.

According to a report in *JAMA Pediatrics*, over two years, the proportion of parents who were current smokers declined 2.7% when practices offered tobacco screening and treatment but rose 1.1% with usual care… (*Reuters*)

Common ADHD Medication may Affect Brain Development

Treatment with methylphenidate (multiple brands) may affect the development of the brain's signal-carrying white matter in boys with attention deficit/hyperactivity disorder (ADHD), suggests new research.

Results of a randomized placebo-controlled study conducted in treatment-naive boys and men with ADHD showed that 4 months of treatment with methylphenidate affected specific tracts in brain white matter in boys but not in their adult counterparts. The researchers found no changes in the brains of boys who received placebo. The study was published online in *Radiology*.

Physically Active People have Lower Colon Cancer Risk

People who exercise regularly may be less likely to develop precursors to colorectal cancers, suggests a research review published in the *British Journal of Sports Medicine*.

Compared to people who get the smallest amount of physical activity, individuals who get the most exercise are 23% less likely to develop precancerous neoplasias that can sometimes progress into full-blown colorectal cancer. Regular exercisers are also 27% less likely than sedentary people to develop the most aggressive types of precancerous neoplasias with the most potential to progress to full-blown cancer.

Burundi Launches Ebola Vaccination Campaign for Health and Frontline Workers

On 13th August, the Ministry of Public Health and AIDS Control kicked off the vaccination campaign for front-line staff against the Ebola virus disease. The campaign started at the Gatumba entry point at the Border with the DRC.

The Ebola vaccination campaign is part of Burundi's preparation for a possible case of Ebola. The campaign will be implemented under the leadership of the Ministry of Public Health and AIDS Control, with the support of the World Health Organization (WHO). Financial support is provided by GAVI, the Vaccine Alliance… (*WHO*)

PAHO Warns of the Complex Situation of Dengue in Latin America and the Caribbean

The Pan American Health Organization (PAHO) has warned of the complex situation of dengue in Latin America and the Caribbean, a Region that is currently experiencing a new epidemic cycle of the disease after 2 years of low incidence. According to the latest PAHO epidemiological update, published on August 9, during the first 7 months of 2019, more than 2 million people contracted the disease and 723 died. The number of cases exceeds the total number of cases reported in 2017 and 2018, although so far, it remains lower than the number recorded in 2015-2016… (*PAHO*)

Good Sleep Plus Limits on Screen Time Help with Impulse Control

Adequate sleep paired with limits on screen time helps reduce impulsivity in children, a study suggests.

The authors studied the effect of adequate sleep, limited screen time and physical activity on impulsivity in children. Sleep and screen limits together had a particularly strong association with impulse control. The study, published online in *Pediatrics*, is the first to demonstrate the combined association, say researchers.

Air Pollution can Damage Even Healthy Lungs

The more exposure people have to air pollution, especially ozone, the more lung damage they develop over time, a US study suggests. The new study shows that even among people without lung disease, long-term exposure to air pollution even in relatively 'clean' areas can lead to signs of chronic lung disease, said Dr Joel Kaufman, a co-author of the study and an environmental health researcher at the University of Washington in Seattle. The findings are published online in *JAMA*.

Health Ministry Asks States to Create Intelligence Cells to Crackdown Against Spurious Drugs

With an aim to check illegal practices of manufacturing spurious drugs, the Health Ministry

has directed states to create intelligence cells to expose and bust such rackets. These intelligence cells will work in coordination with the officers of state drug departments and the Central Drug Control Standard Organization (CDCSO) to unearth the illegal activities of spurious drugs and their manufacturing units. The intelligence cells will also look for any contravention of the Drug and Cosmetic Act… (*ET Healthworld – ANI*)

WHO Launches Global Registry on Human Genome Editing

A WHO expert advisory committee has approved the first phase of a new global registry to track research on human genome editing. The 18-member committee also announced an online consultation on the governance of genome editing.

Dr Tedros Adhanom Ghebreyesus, WHO's Director-General, emphasized that countries should not allow any further work on human germline genome editing in human clinical applications until the technical and ethical implications have been properly considered… (*WHO*)

Global Measles Cases Three Times Higher Than Last Year: WHO

Every region in the world, except the Americas, is experiencing an increase in the number of cases of measles, the World Health Organization (WHO) said.

The WHO's Kate O'Brien put the blame on weak health systems and misinformation about vaccines, and called on social media outlets and communities to make sure information about preventing the highly contagious disease was accurate. Nearly three times as many cases were reported from January to July this year than in the same period in 2018, the WHO said… (*Reuters*)

As the Climate Shifts, Central America Confronts a Deadly Dengue Outbreak

Central America is grappling with its worst outbreak of dengue fever in decades - and scientists say the disease is likely to spread and become more frequent in the future due to climate change.

Worst hit is Honduras where about 109 deaths from the mosquito-borne disease have been recorded, many among children, making this year's dengue fever outbreak the deadliest on record in the Central America nation, the United Nations noted. Also hard hit in Central America are Nicaragua, El Salvador, and Guatemala, with other Latin American nations such as Brazil, Paraguay, Colombia and Belize also affected, according to the PAHO… (*Medscape*)

AAN Releases New Guideline About Immunization and Multiple Sclerosis

Most multiple sclerosis (MS) patients should receive recommended vaccinations, including yearly flu shots, according to an updated American Academy of Neurology (AAN) guideline about immunization and MS.

The guideline was published in *Neurology*. The new guidance updates one from 2002 and incorporates new evidence, vaccines and disease-modifying therapies (DMTs).

Statins Make Economic Sense for Borderline-risk Patients

A cost-effectiveness analysis provides economic justification for the 2018 American guideline recommendation to consider statin treatment in certain patients with borderline risk, investigators showed.

Adding preventive statins to such patients - who have predicted 10-year absolute risk of atherosclerotic cardiovascular disease in the 5.0-7.4% range and elevated low-density lipoprotein (LDL) cholesterol - would make sense at currently accepted willingness-to-pay thresholds, according to findings published in *JAMA Cardiology*.

Pre-op Aflibercept Ups Response in High-risk Rectal Cancer

The addition of aflibercept to modified fluorouracil, leucovorin and oxaliplatin (FOLFOX6) induction chemotherapy increased the rate of pathologic complete response among patients with high-risk rectal adenocarcinoma, the randomized GEMCAD 1402 trial found.

In the phase II study of 180 patients, the pathologic complete response rate was 22.6% among patients assigned aflibercept compared with 13.8% for those assigned mFOLXFOX6 alone ($p = 0.15$), reported Carlos Fernández-Martos, MD, of Fundación Instituto Valenciano de Oncología in Spain, and colleagues in *JAMA Oncology*.

Ebola Death Toll in East Congo Outbreak Climbs Above 2,000

The death toll from DRC's year-long Ebola outbreak has climbed above 2,000, government data showed, as

responders battle to overcome community mistrust and widespread security problems.

The death in neighboring Uganda of a 9-year-old girl who had tested positive for the virus after entering the country from Congo underscored the challenge medical teams face containing the disease in border territory with a highly mobile population… (*Reuters*)

No "Gay Gene" can Predict Sexual Orientation, Says Study

Sexual orientation cannot be predicted by a single "gay gene", new research indicates.

Instead, a host of genetic and environmental factors play a role, according to a study published in *Science Magazine*. The findings provide insight into the complex genetics underlying human sexuality. But they do not explain it, wrote the international team of researchers who analyzed genetic data gathered from almost half a million people… (*CNN*)

Filter-based Kits Developed for TB Diagnosis, Drug-resistance Testing

To address the tuberculosis (TB) diagnostic challenges, a multi-institutional team has developed three cost-effective kits that improve the sensitivity of smear microscopy, enable transport of sputum samples at ambient temperature without using bio-safe containers and extract DNA for diagnosing drug-resistant TB. The three kits are - TB Detect, TB Concentration & Transport and TB DNA Extraction. The TB Detect kit currently costs Rs. 100 per sample, Rs. 100 for the TB transport kit and Rs. 85 for the DNA extraction kit… (*The Hindu*)

DAPA HF: Dapagliflozin Offers New HF Therapy, Even Sans Diabetes

The diabetes drug dapagliflozin provides substantial benefits among patients with chronic heart failure with reduced ejection fraction (HFrEF) - even in those without diabetes, according to the DAPA HF trial.

The sodium-glucose cotransporter 2 (SGLT2) inhibitor reduced the relative risk for the primary outcome - a composite of time to first cardiovascular (CV) death or HF hospitalization or urgent HF visit requiring intravenous therapy - by 26% when added to standard therapy, compared with standard care alone (hazard ratio [HR], 0.74; 95% CI, 0.65-0.85; p = 0.00001). The findings were presented at the European College of Cardiology (ESC) Congress 2019.

Blood Test Promising for Detecting Mild Concussion

Blood levels of glial fibrillary acidic protein (GFAP) identified mild traumatic brain injury (TBI) in patients even when a CT scan did not detect it, the TRACK-TBI study showed. In people with negative CT findings, GFAP levels distinguished patients who were MRI-positive for intracranial lesions from patients who were MRI-negative, reported Geoffrey Manley, MD, of the University of California San Francisco, and co-authors, in *Lancet Neurology*. The best performance - when the area under the receiver operating curve (AUC) was 0.852 - was in samples taken 9-16 hours after injury.

WHO Updates Cardiovascular Risk Charts

WHO has updated the cardiovascular risk charts through the WHO Cardiovascular disease risk chart working group. Updated charts are published in the *Lancet Global Health*.

Widespread use of these charts could enhance the accuracy, practicability and sustainability to reduce the burden of cardiovascular diseases worldwide… (*WHO*)

Microplastics Turning up in Human Stool

Tiny bits of plastic may be getting into our bodies via the air we breathe and the food we eat, a new study suggests. Researchers who examined stool samples from eight people from diverse geographic locations found that all contained bits of plastic, according to a report in *Annals of Internal Medicine*.

"This small prospective case series showed that various microplastics were present in human stool, and no sample was free of microplastics," wrote the team of scientists, led by Dr Philipp Schwabl of the Medical University of Vienna… (*Reuters*)

ESC Diabetes and CVD Guideline: "Unprecedented" New Evidence

The ESC in collaboration with the European Association for the Study of Diabetes (EASD) has released new guidelines for the management and prevention of cardiovascular disease (CVD) in patients with diabetes or prediabetes.

Recommendations in the document reflect recent positive findings from large cardiovascular outcome trials (CVOTs) of new classes of diabetes drugs and other new developments. The guidelines were presented at the ESC Congress 2019, and the document was simultaneously published online in *European Heart Journal* and on the ESC website.

Weight Loss Cuts Hospital Stays for Obese TKA Patients

Morbidly obese patients who lost 20 lbs before total knee arthroplasty (TKA) cut their hospital stays by about 1 day, and were 76% less likely to have an extended hospital stay, research showed.

However, morbidly obese patients who lost between 5 and 10 lbs before the surgical procedure did not have shorter hospital stays, according to David S Jevsevar, MD, MBA, of Dartmouth-Hitchcock Medical Center in Lebanon, New Hampshire and colleagues. The findings were published in the *Journal of Bone & Joint Surgery*.

Anti-stigma Campaign "Let's Talk About Dementia" Marks Beginning of World Alzheimer's Month in the Americas

An Americas-wide campaign launched by Alzheimer's Disease International (ADI) and the PAHO aims to get people talking more comfortably and openly about Alzheimer's disease and dementia.

1 September marks the beginning of the month of awareness. "Let's Talk About Dementia" is based on the understanding that talking about dementia helps tackle the stigma, normalizes language and encourages people to find out more about the disease and seek help, advice and support for it… (*PAHO*)

Six WHO South-East Asia Countries Felicitated for Public Health Achievements

Ministers of Health of 6-Member countries of WHO South-East Asia Region were felicitated for public health achievements in recent months such as measles elimination, hepatitis B control and elimination of mother-to-child transmission of HIV and syphilis.

Sri Lanka was recognized for eliminating measles; Bangladesh, Bhutan, Nepal and Thailand for becoming the first four countries from the Region to control Hepatitis B; and Maldives for eliminating mother-to-child transmission of HIV and syphilis. Citations were presented to the Ministers for their public health achievements at a side event during the 72nd Session of WHO Regional Committee of South-East Asia in New Delhi… (*WHO*)

New York City Measles Outbreak has Ended, Health Officials Say

A massive measles outbreak that spread across parts of Brooklyn since October has ended, New York City health officials announced. This marks the end of the largest measles outbreak New York City has seen in nearly three decades.

No new cases have been reported since mid-July, the city's health department said, but officials will continue keeping track and may add cases retrospectively as they are identified… (*CNN*)

Inflammation in Adolescence Linked to Early Mortality

Inflammation during late adolescence may be associated with early death from cancer and cardiovascular disease (CVD), a large study published online in *JAMA Pediatrics* suggests.

The investigators used erythrocyte sedimentation rate (ESR) data as a nonspecific marker of inflammation. During a mean follow-up of 35 years (maximum age 57 years), 4835 of the men died; underlying causes of death included cancer, CVD, alcohol or drugs and suicide, traffic accidents or falls. After adjusting for potential confounders, ESR was associated with overall mortality (high vs. low ESR: multivariable-adjusted HR, 1.36; 95% CI, 1.11-1.67; p for trend < 0.001).

Intense Step Training may Improve Walking, Balance After Stroke

High-intensity step training that mimics real-world conditions could better promote walking ability after a patient experiences a stroke compared with traditional, low-impact training, new research suggests.

In a study of 90 patients who had weakness on one side of the body after experiencing a stroke 6 months previously, high-intensity step training was associated with greater improvements in both walking ability and gait symmetry than low-intensity training, with potentially greater improvements in balance confidence. The findings were published online in *Stroke*.

Parliamentarians: Climate Crisis One of the Most Critical Threats to Health in the Asia-Pacific Region

Parliamentarians from 20 Asian and Pacific nations delivered a clear message, naming the climate crisis as one of the region's most critical threats to human health.

Hosted by the Parliament of Fiji, the 20-22 August 5th Asia-Pacific Parliamentarian Forum on Global Health brought together Parliamentarians from various jurisdictions and sectors to discuss solutions, actions and opportunities for collaboration, to protect health from climate change. Participants discussed ways to identify and address the health impacts of climate change, and to protect vulnerable communities… (*WHO*)

Venezuelan Migrants to Get Regional Vaccination Cards Under 10-nation Pact

Venezuelan migrants will be provided with a regional vaccination card beginning in October, health officials from 10 countries agreed in an effort to ensure they receive needed vaccines and are not given double doses.

Health officials from the United States, Colombia, Ecuador, Panama, Canada, Haiti, the Dominican Republic, Argentina, Peru and Paraguay unanimously approved the measure in a meeting in the Colombian border city of Cucuta.

The vaccination card will "accompany migrants from the middle of October and have the support of international agencies for its printing, distribution and training for its use," Colombian Health Minister Juan Pablo Uribe told journalists… (*Reuters*)

The US is Throwing Away at Least 3,500 Donated Kidneys Every Year, Study Finds

There are currently 93,000 people in the United States on a waiting list for a donated kidney, yet at least 3,500 donated kidneys are discarded every year, according to a study published in the journal *JAMA Internal Medicine*.

In this study, researchers looked at the number of deceased donors with organs offered to kidney transplant centers between 2004 and 2014. Over that time period, 156,089 kidneys were donated; 128,102 were transplanted; 27,987 were discarded. That means more than 17% of kidneys donated in the United States were discarded… (*CNN*)

Close Relatives of Celiac Disease Patients at Higher Risk

First-degree relatives of people who have celiac disease (CD) are at elevated risk of developing the condition - although they may have no symptoms - and could benefit from screening, according to results of a study published online in *Mayo Clinic Proceedings*.

Of 477 first-degree relatives of the 104 patients, 360 individuals had been screened for CD and of these 160 (44%) were diagnosed and tested positive for anti-TTG titer. Of the 160 diagnosed relatives, 148 presented with clinical features of CD, but only nine (6%) had classic symptoms, whereas 97 (66%) had nonclassic symptoms and 42 (28%) reported no symptoms.

WHO Revision of Pain Management Guidelines

The WHO announces the revision process for two recently discontinued documents, "Ensuring balance in national policies on controlled substances: Guidance for availability and accessibility of controlled medicines" (2011) and "WHO guidelines on the pharmacological treatment of persisting pain in children with medical illnesses" (2012).

WHO has in place robust procedures concerning the quality of its norms and standards. Both of the discontinued guidelines referenced above will be updated according to these standard procedures, as detailed in the "WHO Handbook for Guideline Development" (2nd edition)… (*WHO*)

Alternate-Day Fasting in Short-term Safe, Has Metabolic Benefits

Alternate-day fasting (ADF) had positive effects on body weight, cardiovascular measures, and molecular markers of aging when assessed in a randomized controlled trial among healthy adults without obesity or diabetes, suggested a study published online in *Cell Metabolism*.

No adverse effects were seen among participants in the ADF group. Their caloric intake dropped from baseline by 37.4% (95% CI, –48.3% to –24.4%), compared with 8.2% (95% CI, –32.2% to 3.6%) in the control group. BMI among the 4-week fasters fell by 1.2 kg/m^2 (95% CI, –1.515 to –0.875; $p < 0.0001$) and the average reduction in belly fat was 14.5% ± 6.4% ($p < 0.0001$).

FDA: Serious Liver Injury Possible with Some HCV Tx

Patients with advanced liver disease taking certain medications for hepatitis C virus (HCV) infection may be at risk for serious liver complications, including liver failure, the FDA said.

In a statement, the agency said it had received reports linking the use of three agents for treating chronic HCV infection - glecaprevir/pibrentasvir, elbasvir/grazoprevir and sofosbuvir/velpatasvir/voxilaprevir - to "rare" cases of worsening liver function or liver failure in patients with moderate-to-severe liver impairment (Child-Pugh B or C)… (*Medpage Today*)

■■■■

Indian Journal of Clinical Practice, Vol. 30, No. 4, September 2019

The Science Behind Observing Shradhs

KK AGGARWAL

Shradhs are observed every year in Dakshinayana during Chaturmas in the Krishna Paksha of Ashwin month. Many rituals are performed to satisfy the unfulfilled desires of three generations of our ancestors.

According to the Vedas, every individual has three debts to be paid off, firstly, the Devtas (Dev Rin), secondly of Guru and teachers (Rishi Rin) and, thirdly, of Ancestors (Pitra Rin). From the scientific point of view, devtas represent people with Daivik qualities; teachers the ones who have taught us and Pitra, three generations of our ancestors. Rin from scientific point of view would mean unfinished desires or tasks.

The rituals scientifically would mean detaching oneself from the guilt of unfinished tasks of our ancestors by detoxifying our mind.

Debt means desires of our ancestors that had not been fulfilled during their lifetime. The responsibility to fulfil them automatically falls onto the eldest son in the family and they need to be carried out. If not, it is a sign of guilt disorder in the family and may present with loss of wealth, loss of direction and courage and health. The resultant problems faced were called Pitra Dosh in mythology.

The ritual of performing Shradhs originated to remove this guilt and the resultant illnesses. Shradh has many components.

- Tarpan (offering water to the ancestors while reciting Mantras).
- Arpan (preparing food what the ancestors used to like on the day of Shradh).
- Brahmin bhoj (offering Satvik food to Brahmins).
- Pind Daan (offering black sesame, Kusha Grass, Jwar and boiled or baked rice); observed by some.
- Observing a spiritual holiday or incubation period (taking a break from the routine worldly desires and going to a distant place like Gaya).
- Remembrance: Once the unfulfilled desires of the ancestors are over, remembering our ancestors every year on the day of their death anniversary.

Scientifically, Dakshinayana is the period of negative state of mind (nights are longer than days) and starts from 14th July and ends on 13th January. Chaturmas period (first four months) during Dakshinayana has the maximum negativity in the mind. Chaturmas includes the months of Sawan, Bhado, Ashwin and Kartik.

The negative state of mind in Sawan is related to anger and disturbed mind; in Bhado to nonfulfilment of desires and uncontrolled ego and in the month of Ashwin to guilt because of nonfulfilment of desires of others (ancestors), especially during Amavasya.

In the rituals, Tarpan of jal (water) is offered to ancestors. Jal in mythology means flow of thoughts and offering jal in mythology equates to confession and getting connected. Tarpan is always done with an aim to purify the mind and wash off the guilt.

Tarpan is always done after the desires of our ancestors have been fulfilled by the person performing the Shradh. This ritual is Arpan. Tarpan and Arpan on the day of Shradh mean getting connected to our consciousness and informing that all the unfinished tasks are over so that we can get rid of the long persisting guilt from our mind. Offering and making food which was liked by our ancestors on that day is just to remember and pay respect to them.

Confession is only possible in a Satwik state of mind, which requires eating of Satwik food for a few days. The ritual of offering Satwik food to Brahmins during the Shradh means making only Satwik food on that day so that everyone in the family is forced to eat Satwik food during Shradhs.

Pind Daan denotes medicinal ways of detaching oneself from the guilt. All the four offerings (black sesame, Kusha grass, Jwar and boiled or roasted rice) in Ayurveda have been described to detoxify the mind and making it Satwik by removing Rajas and Tamas.

If the guilt does not go by repeated Shradhs then one is required to go for a spiritual vacation during Shradh period so that he is away from the worldly desires for

Group Editor-in-Chief, IJCP Group

a few days before the Shradh and this is what going to Gaya means. This spiritual retreat works like an incubation period to the disturbed mind and gets rid of the disturbed mind and allows the undisturbed state of mind to confess and purify.

The Pitra ceremonies are usually performed either on Amavasya every month (period of most negativity in a month) or on the death anniversary or the Hindu Tithi (day) of the death of the ancestors coinciding with the day during Shradh days. If the date of death is not known then the Shradh is observed on Amavasya.

Some people perform Shradh for full 15 days and others perform it from the first day till the day of their ancestors' Shradh.

It is said that once a Shradh is successfully performed or Gaya Shradh is performed, there is no need to perform Shradh rituals thereafter. Once the guilt is over, there is no need for further detoxification of the mind. After that the only ritual that needs to be performed is remembrance, which is usually performed on the death anniversary of the deceased ancestor usually by doing some charity on their names.

One is not supposed to do auspicious things during Shradh as during this period, the mind is in a process of detoxification.

Disclaimer: The views expressed in this write up are entirely my own.

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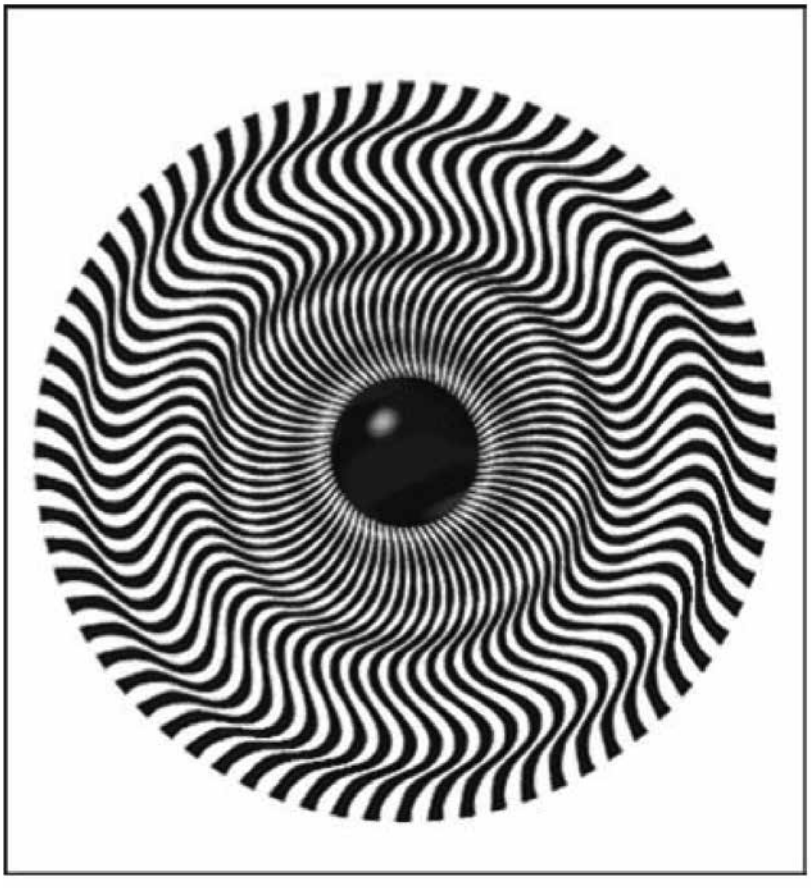
Different Perspectives of Life



The earth is moving but looks stationary. This circle is stationary but looks moving.

Indian Journal of Clinical Practice, Vol. 30, No. 4, September 2019

A Simple Gesture

A little boy selling magazines for school walked up to a house that people rarely visited. The house was very old and run down and the owner hardly ever came out. When he did come out, he would not say hello to neighbors or passers-by but simply just glare at them.

The boy knocked on the door and waited, sweating from fear of the old man. The boy's parents told him to stay away from the house, a lot of the other neighborhood children were told the same from their parents.

As he was ready to walk away, the door slowly opened. "What do you want?" the old man said. The little boy was very afraid but he had a quota to meet for school with selling the magazines.

"Uh, sir, I uh am selling these magazines and uh I was wondering if you would like to buy one." The old man just stared at the boy. The boy could see inside the old man's house and saw that he had dog figurines on the fireplace mantle. "Do you collect dogs?" the little boy asked. "Yes, I have many collectibles in my house, they are my family here, they are all I have." The boy then felt sorry for the man, as it seemed that he was a very lonely soul. "Well, I do have a magazine here for collectors, it is perfect for you, I also have one about dogs since you like dogs so much." The old man was ready to close the door on the boy and said, "No boy, I don't need any magazines of any kind, now goodbye."

The little boy was sad that he was not going to make his quota with the sale. He was also sad for the old man being so alone in the big house that he owned. The boy went home and then had an idea. He had a little dog figure that he got some years ago from an aunt. The figurine did not mean nearly as much to him since he had a real live dog and a large family. The boy headed back down to the old man's house with the figurine. He knocked on the door again and this time the old man came right to the door. "Boy, I thought I told you no magazines."

"No, sir I know that, I wanted to bring you a gift." The boy handed him the figurine and the old man's face lit up. "It is a Golden Retriever, I have one at home, this one is for you." The old man was simply stunned; no one had ever given him such a gift and shown him so much kindness. "Boy, you have a big heart, why are you doing this?" The boy smiled at the man and said, "Because you like dogs."

From that day on the old man started coming out of the house and acknowledging people. He and the boy became friends; the boy even brought his dog to see the man weekly.

This simple gesture changed both of their lives forever.

■■■■

An Optimistic Outlook "Means You Live Longer"

Optimists are more likely to live longer than those who have a more negative approach to life, a US study has found.

The study used two existing groups of people recruited for different studies - 70,000 women in the Nurses' Health Study and 1,500 men in the Veterans' Health Study. On average, the most optimistic men and women had an 11-15% longer lifespan, and were significantly more likely to live to 85 compared with the least optimistic group… (*BBC*)

Guidelines may Speed Obesity Hypoventilation Syndrome Diagnosis

Obesity hypoventilation syndrome (OHS) is a serious yet commonly misdiagnosed condition. New recommendations from a panel of the American Thoracic Society (ATS) offer clinical guidance on screening and treatment for the condition, which is likely to become more prevalent as obesity rates rise.

A key issue addressed in the recommendations involves OHS screening, during which most diagnosis mishaps occur. The guideline was published in the August issue of the *American Journal of Respiratory and Critical Care Medicine*.

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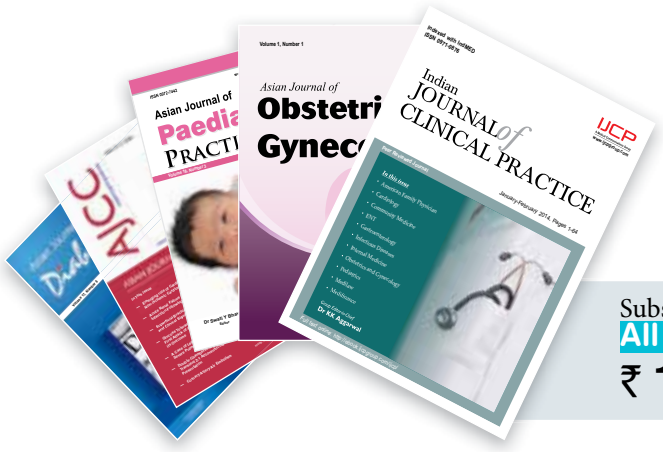

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Indian Journal of Clinical Practice, Vol. 30, No. 4, September 2019

Lighter Side of Medicine

HUMOR

HURRY UP

A wife was making a breakfast of fried eggs for her husband. Suddenly, her husband burst into the kitchen. 'Careful', he said, "CAREFUL! Put in some more butter! Oh my Gosh! You're cooking too many at once. TOO MANY! Turn them! TURN THEM NOW! We need more butter. Oh my Gosh! WHERE are we going to get MORE BUTTER? They're going to STICK! Careful. CAREFUL! I said be CAREFUL! You NEVER listen to me when you're cooking! Never! Turn them! Hurry up! Are you CRAZY? Have you LOST your mind? Don't forget to salt them. You know you always forget to salt them. Use the salt! USE THE SALT! THE SALT!"

The wife stared at him.

"What in the world is wrong with you? You think I don't know how to fry a couple of eggs?'

The husband calmly replied, "I just wanted to show you what it feels like when I'm driving."

A MAN WAS JUST WAKING

A man was just waking up from anesthesia after surgery, and his wife was sitting by his side.

His eyes fluttered open and he said, "You are gorgeous."

Then he fell asleep again. His wife had never heard him say that, so she stayed by his side.

A few minutes later, his eyes fluttered open and he said, "You are beautiful!"

Then he fell asleep again.

After a few minutes, he again opened his eyes and said, "You are cute!"

The wife was disappointed because instead of 'gorgeous' or 'beautiful,' it was now just 'Cute.'

She said, "What happened to 'gorgeous, beautiful'?"

Her husband replied, "The drugs are wearing off!"

OLD AGE SECRET

Grandpa was celebrating his 100th birthday and everybody complimented him on how athletic and well-preserved he appeared.

"Gentlemen, I will tell you the secret of my success," he cackled. "I have been in the open air day after day for some 75 years now."

The celebrants were impressed and asked how he managed to keep up his rigorous fitness regime.

"Well, you see my wife and I were married 75 years ago. On our wedding night, we made a solemn pledge. Whenever we had a fight, the one who was proved wrong would go outside and take a walk."

THREATENING LETTERS

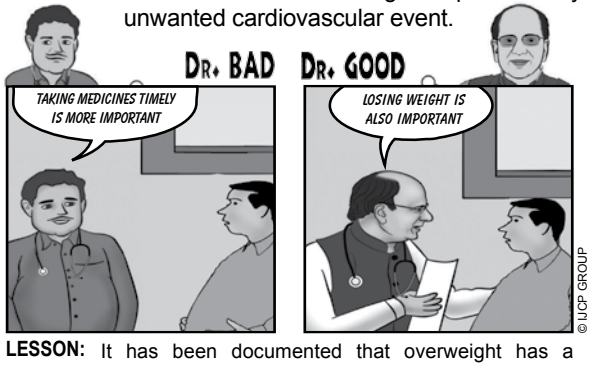
The fellow stormed into the postmaster's office in a fury. "I've been getting threatening letters in the mail for months and I want them stopped."

"Of course," said the postmaster. "Sending threatening letters through the mail is a federal offense. Do you know who's sending them?"

"Yes," shouted the man. "It's those idiots down at the Internal Revenue Service."

Dr. Good and Dr. Bad

SITUATION: An overweight male with type 2 diabetes who had preserved LV ejection fraction was advised to lose weight to prevent any unwanted cardiovascular event.



LESSON: It has been documented that overweight has a comparatively greater effect on LV longitudinal myocardial systolic function in patients with type 2 diabetes than in nondiabetic healthy individuals. Therefore, strict control of overweight in diabetic patients may help in preventing the development of heart failure with preserved ejection fraction.

Cardiovasc Diabetol. 2017;16(1):145.

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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

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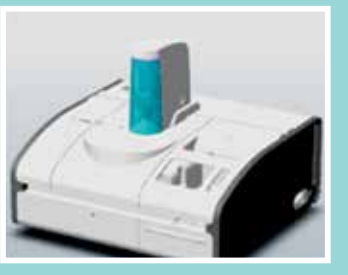

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