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A Multispecialty Journal

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Indian Journal of Clinical Practice, Vol. 30, No. 9, February 2020

Dr KK Aggarwal
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CMAAO Update 10th February on Novel Coronavirus (2019-nCoV)

40,553 confirmed cases in 28 countries; 910 deaths

Serious cases: 6,484; **New cases:** 296; **Cases severity:** 82% mild, 15% severe, 3% critical, 2% deaths

6,484 Serious cases, Mortality in admitted cases 15% (expected 972 more)

Number of deaths likely to cross 2,000

Summary: PM Modi writes to Xi Jinping, offers assistance; Kissing scenes banned in China Movies

DGCA EXEMPTS AIR CREW FROM BREATH ANALYSER TESTS IN KERALA

Thousands of people stuck on a cruise ship in Hong Kong for 5 days have been allowed to disembark after tests for coronavirus came back negative.

The virus behaves like severe acute respiratory syndrome (SARS) with 2% case fatality (15% of admitted cases), time to death 14 days, time to pneumonia 9 days, 3-4 reproductive number R_0, has its origin from bats, spreads through large droplets and predominantly from people having lower respiratory infections and hence, universal droplet precautions are the answer.

The World Health Organization (WHO) has urged countries not to impose travel and trade restrictions over the novel coronavirus, as this could increase "fear and stigma" within the international community. Some countries, including the UK, have advised their citizens to leave China altogether.

If it behaves like SARS, it will not be endemic. It most likely will be a hit and run, just like SARS. Also, if this virus follows the same path as SARS or Middle East respiratory syndrome (MERS), it won't mutate and will burn itself out in about 6 months.

The WHO has warned that "trolls and conspiracy theories" are compromising their response to the new coronavirus.

- On Russia's Channel One, the host linked the virus to US President Donald Trump, and claimed that US intelligence agencies or pharmaceutical companies are behind it.
- Another theory published in British and US tabloid media, linked the virus to a video of a Chinese woman eating bat soup. However, it has been found that the video was shot in 2016 and was in Palau, in the western Pacific Ocean, not China.
- A widely-discredited scientific study released last month has linked the new coronavirus to snakes.
- One claim advises people in the Philippines to keep the throat moist, avoid spicy food and load up on vitamin C. The information is reported to have come from the country's Department of Health but it does not match the advice on the DOH website or its official press releases on the outbreak.
- Another claim suggests avoiding cold or preserved food and drinks, such as ice cream and

milkshakes, for "at least 90 days". A Facebook page - ForChange - accompanied the post with a video of a parasite being removed from a person's lips. Altnews fact-checkers pointed out that the video is 3 months old and unrelated to the virus.

- As the United States reported its first case, several patent documents started circulating. At first glance, the documents appear to suggest that experts have been aware of the virus for years. A link to a 2015 patent filed by the Pirbright Institute in Surrey, England, was shared that discusses about developing a weakened version of coronavirus for potential use as a vaccine to prevent or treat respiratory diseases. Conspiracy theorist and YouTuber Jordan Sather used the fact that the Bill & Melinda Gates Foundation is a donor to both Pirbright and vaccine development and hinted that the current virus has somehow been manufactured to attract funding for the development of a vaccine. However, the Pirbright patent is not for the new coronavirus. On the contrary, it involves the avian infectious bronchitis virus, a member of the wider coronavirus family that infects poultry.
- Another claim suggests that the virus was part of China's secret biological weapons program and may have leaked from the Wuhan Institute of Virology. Many accounts promoting the theory quote two Washington Times articles which quote a former Israeli military intelligence officer for the claim. However, there is no evidence for the claim in the two articles, and the Israeli source is quoted as saying that "so far there isn't evidence or indication" to suggest there was a leak.
- Another claim links the virus to the suspension of a researcher at Canada's National Microbiology Laboratory. Virologist Dr Xiangguo Qiu, her husband and some of her students from China were removed from the lab following a possible policy breach, reported Canada's national broadcaster CBC last year. Police told CBC News that there was "no threat to public safety".

  Another report stated that Dr Qiu had visited the Wuhan National Biosafety Laboratory of the Chinese Academy of Sciences twice a year for 2 years.

  A tweet claimed, without any evidence, that Dr Qiu and her husband were a "spy team", had sent "pathogens to the Wuhan facility", and that her husband "specialized in coronavirus research". None of the three claims in the tweet are found in the two CBC reports and the terms "coronavirus" and "spy" do not appear even once in either of them.
- Several versions of a "whistleblower" video, allegedly taken by a "doctor" or a "nurse" in Hubei province, have gained million views on various social media platforms and have found mention in numerous online reports. The most popular version was uploaded to YouTube by a Korean user, and included English and Korean subtitles. The video; however, has been taken down.

  According to the English subtitles, the woman is a nurse in a Wuhan hospital. She does not claim to be either a nurse or a doctor in the video; however. The woman does not identify herself, and is wearing protective suit in an unknown location. The suit and mask do not match the ones worn by medical staff in Hubei.

  On account of the lockdown enforced by the authorities, it is difficult to verify videos from the province. The woman; however, makes several unsubstantiated claims about the virus, making it unlikely for her to be a nurse or a paramedic.

  She also claims that the virus has a "second mutation", which can likely infect up to 14 people. The WHO has; however, made preliminary estimates that the number of infections an individual carrying the virus can cause is 1.4 to 2.5.

CASE DEFINITION

- Fever (subjective or confirmed)

  OR signs/symptoms of lower respiratory illness (cough or shortness of breath)

  PLUS, any person (including healthcare workers) who has had close contact with a laboratory-confirmed novel coronavirus patient within 14 days of symptom onset.

  Contact refers to: Being within nearly 6 feet (2 meters) or within the room or care area of a 2019-nCoV case for a prolonged time while not wearing recommended personal protective equipment (gowns, gloves, NIOSH-certified disposable N95 respirator, eye protection); close contact may include caring for, living with, visiting or sharing a healthcare waiting area or room with a 2019-nCoV case OR having direct contact with infectious secretions of a 2019-nCoV case (such as being coughed on) while not wearing recommended personal protective equipment.

- Fever and signs/symptoms of lower respiratory illness (cough or shortness of breath) PLUS history of travel from Hubei Province, China within 14 days of symptom onset
- Fever and signs/symptoms of lower respiratory illness (cough or shortness of breath) requiring hospitalization PLUS history of travel from mainland China within 14 days of symptom onset.

Continue asking patients with suspected flu or diarrhea if they, or someone they have been in contact with, recently returned from coronavirus-affected area. [In US, in a confirmed case, 2019-nCoV RNA has been identified in a stool specimen collected on day 7 of the patient's illness.]

TAKE HOME MESSAGES

Delhi Help line number, e-mail, website: +91-11-23978046, ncov2019@gmail.com**,** https://mohfw.gov.in/node/4904

Virus: Single-strand, positive-sense RNA genome ranging from 26 to 32 kilobases in length.

Type: Beta coronavirus

Family: Corona virus family. 'Corona' means crown or the halo around the sun. Heart is considered a crown and hence the arteries that supply oxygen to the heart are also called coronary arteries. When seen under an electron microscope, the virus appears round in shape with spikes poking out from its periphery.

Virus is killed by sunlight, temperature, humidity. It can survive on stainless steel surface for 36 hours. Sunlight can diminish the virus' ability to grow in half, so the half-life will be 2.5 minutes and in the dark, it is about 13-20 m. The virus can potentially remain intact at 4° or 10° for a longer time. At 30°; however, there is inactivation. The virus cannot also tolerate high humidity. SARS stopped around May and June in 2003 probably due to more sunlight and more humidity.

The virus may not reach, Indonesia, Africa and other parts of Southern Hemisphere due to high temperature.

High-income countries: Low population density, higher level of environment control and hygiene - Low mortality.

Europe – possibility of higher transmission but environmental care is higher.

The virus can remain alive on any surface for 3-12 hours.

Types of transmission: Droplet or direct (Corona); Contact from surface (Corona), aerosol or nuclei (TB, Corona ??)

Link to ACE: 2019-nCoV might be able to bind to the angiotensin-converting enzyme 2 receptor in humans.

Origin: Wuhan, China; December 2019.

1st case informed to the world by Dr Li Wenliang who died on February 6.

Lockdown: 50 million people.

Spread: 28 countries and territories

New cases: On February 9, 31 provincial-level regions on the Chinese mainland as well as the Xinjiang Production and Construction Corps reported 3,062 cases (2618 in Hubei province).

Suspected cases on 9th: 4,008 new cases (2,272 in Hubei province).

Serious new cases on 9th: 296 new serious cases (258 in Hubei province).

Deaths on 9th Feb: 97 deaths (91 in Hubei province, 2 in Anhui province, 1 in Heilongjiang province, 1 in Jiangxi province, 1 in Hainan province and 1 in Gansu province).

Discharged on 9th: 632 cured (356 in Hubei province).

Freed from medical observation on 9th: 29,307.

Total cured: 3,281.

Suspected cases: 23,589.

Quarantine: 26,359 patients.

Serious: 6,484.

Close contacts: 3,99,487.

Medical observation: 1,87,518.

Confirmed cases: National Health Commission 40,171.

Deaths: 908.

Feb 9 – 64 confirmed infections had been reported in the Hong Kong and Macao special administrative regions and Taiwan province: 36 in Hong Kong (1 death), 10 in Macao (1 had been cured and discharged from hospital) and 18 in Taiwan (1 had been cured and discharged from hospital).

Three deadly human respiratory coronaviruses: SARS-CoV; MERS-CoV and 2019-nCoV: The virus is 75-80% identical to the SARS-CoV.

January 30, 2020 – Emergency: It is a Public Health Emergency of International Concern (It is mandatory to report to WHO human and animal cases).

Prior 5 PHEICs

April 26, 2009 Swine flu: Shift toward mortality among persons less than 65 years of age; August 10, 2010 - WHO announced that the H1N1 influenza virus has moved into the post-pandemic period. However, localized outbreaks of various magnitudes are likely to continue.

May 2014 Polio: Resurgence of wild polio after its near-eradication; Global eradication was deemed to be at risk with small numbers of cases in Afghanistan, Pakistan and Nigeria; In October, 2019, continuing cases of wild polio in Pakistan and Afghanistan, in addition to new vaccine-derived cases in Africa and Asia; The status was reviewed and remains a PHEIC. It was extended on December 11, 2019.

August, 2014 Ebola: It was the first PHEIC in a resource-poor setting.

February 1, 2016 Zika: Link with microcephaly and Guillain-Barré syndrome; This was the first time a PHEIC was declared for a mosquito-borne disease; This declaration was lifted on November 18, 2016.

2018-20 Kivu Ebola: A review of the PHEIC had been planned at the fifth meeting of the EC on October 10, 2019 and as of October 18, 2019, it continues to be a PHEIC.

Kerala: State public health emergency. Three primary cases have been reported in North, South and Central Kerala (Kasaragod district in North Kerala, Thrissur in central Kerala and Alappuzha in South Kerala). Four Karnataka districts bordering Kerala — Kodagu, Mangaluru, Chamarajanagar and Mysuru - have been put on high alert.

Median age: 59 years (2-74 years).

Male-to-female ratio: 56% male.

Link to Huanan Seafood wholesale market: 55% with onset before January 1, 2020 and 8.6% of the subsequent cases. The Chinese government has banned wildlife trade until the epidemic passes.

Mean incubation period: 5.2 days (95% confidence interval [CI], 4.1-7.0), with the 95th percentile of the distribution at 12.5 days.

Epidemic doubling time: In its early stages, every 7.4 days, with a mean serial interval of 7.5 days (95% CI, 5.3-19).

Contagiousness or basic reproductive number: 2.2 (95% CI, 1.4-3.9). The reproduction number, referred to as R_0 or "r naught" is the number of additional people that an infected person can infect. An outbreak with a reproductive number of below 1 will gradually disappear. The R_0 for the common flu is 1.3 and for SARS it was 2.0.

Comorbid conditions: 71%, deaths in comorbid cases. SARS affected people in their 30 or 50 years and MERS affected people with comorbidity. The China data indicate that it's those with the comorbidity that are most at risk, like seasonal influenza.

0-15 years age: Just like SARS, it mostly does not affect children 15 years of age or less.

Daily deaths: 73 deaths on 5th (15% rise), 66 on 4th, 64 on 3rd Feb.

Anticipation: One lac already infected.

Secondary cases: Thailand, Taiwan, Germany, Vietnam, Japan, France and the United States.

Deaths outside China: Philippines on February 2 (44-year-old Chinese man) and second death in Hong Kong (39 M, local) on February 4; both had comorbid conditions; both acquired infection from Wuhan.

ICU need: 20% needed ICU care; 15% of them died.

Fever: In all (no fever, no corona).

Cough: 75% cases.

Weakness or muscle ache: 50%.

Shortness of breath: 50%.

TLC: low.

Liver transaminase levels: raised.

Case fatality: 2% (Dr John Nicholls, University of Hong Kong) China is only reporting those who come for test, there are stricter guidelines for a case to be considered positive; actual mortality may be 0.8-1%, like outside China.

Case fatality in admitted cases: 15%.

Time to death: 14 days.

Time to pneumonia: 9 days.

Origin: Bats.

Mode of spread: Large droplets and predominately from people having lower respiratory infections.

Answer: Universal droplet precautions.

Incubation period: Up to 2 weeks, according to WHO, with mean being 5.5 days.

Transmission: Predominantly a large droplet and contact and less frequently by means of aerosols and fomites.

Once it was disclosed that SARS also spread through the fecal-oral route, there was reduced emphasis on the masks and greater emphasis on disinfection and washing hands. Hong Kong has far more cleanliness as compared to China and they are very aware of social hygiene. And other countries will be more aware of the social hygiene (than China). So in those countries, you may see less outbreaks and spread (Dr John Nicholls).

Healthcare workers: In Hong Kong, with SARS, there was a lot of infection of healthcare workers since they were close to patients and did invasive procedures. But now, there is not much evidence of healthcare workers getting sick or dying (unless China is not reporting it). This may suggest that it is not being spread by close aerosol contact but more likely by the fecal-oral route or with droplets. So, it may not be as contagious within hospitals. Makeshift hospitals will help.

Lab precautions: BSL-2 or -3.

Human-to-human contact period: Requires contact of 10 minutes within 6 feet.

Travel preferable seat: Choosing a window seat and staying there lowers the risk.

Travel advisory: Level 1 in all countries (Exercise normal safety precautions), Level 2 in all affected countries and states including Kerala (Exercise a high degree of caution), Level 3 in all countries with secondary cases (Reconsider your need to travel) and Level 4 in China (Do not travel). Hong Kong has imposed 14 days quarantine on people arriving from China. The Karnataka government has ordered that anybody arriving from the 23 coronavirus-affected countries must stay in isolation at home for 28 days. The home isolation requirement is regardless of the virus symptoms.

To date, 72 countries have implemented travel restrictions.

Indian Government: Foreigners who went to China on or after January 15 will not be allowed to enter India. All visas issued to Chinese nationals before February 5 have been suspended. These visa restrictions will not apply to aircrew, who may be Chinese nationals or belonging to other foreign nationalities coming from China via air, land or seaport, including Indo-Nepal, Indo-Bhutan, Indo-Bangladesh or Indo-Myanmar land borders.

IndiGo and Air India have suspended all flights between the two countries. SpiceJet continues to fly on Delhi-Hong Kong route.

High viral load: Detection of 2019-nCoV RNA in specimens from the upper respiratory tract with low Ct values on day 4 and day 7 of illness suggests high viral loads and potential for transmissibility. (*NEJM*)

Risk to other Asian countries, including India: Currently, people at risk are healthcare workers caring for 2019-nCoV patients and other close contacts of 2019-nCoV patients. For the general public, unlikely to be exposed to this virus, the immediate health risk from 2019-nCoV is considered low currently.

It is less likely to have serious illness in other countries. As patients with breathlessness are unlikely to board and patients will mild illness or asymptomatic illness are less likely to transmit infections.

Zoonotic but unlikely to spread through seafood: This new coronavirus is closely related to bat coronaviruses. Bats seem to be the likely primary reservoir for the virus. While SARS-CoV was transmitted to humans from exotic animals in wet markets, MERS-CoV transmitted from camels. The ancestral hosts were probably bats; however.

The virus has been traced to snakes in China. Snakes often hunt for bats. According to reports, snakes were sold in the local seafood market in Wuhan, thus raising the likelihood that the 2019-nCoV might have moved from the host species, i.e., bats, to snakes and then to humans. It is still not understood as to how the virus could adapt to both the cold-blooded and warm-blooded hosts.

Infectiousness to humans: This new virus seems to thrive better in primary human airway epithelial cells as compared to standard tissue-culture cells, unlike SARS-CoV or MERS-CoV. The 2019-nCoV will likely behave more like the SARS-CoV.

SARS-CoV and MERS-CoV affect the intrapulmonary epithelial cells more than the upper airway cells. Transmission thus occurs primarily from patients with recognized illness and not from patients with mild, nonspecific signs. However, *NEJM* has reported a case of 2019-nCoV infection acquired outside of Asia wherein transmission seems to have taken place during the incubation period in the index patient but the same has been challenged now.

2019-nCoV seems to employ the same cellular receptor as SARS-CoV (human angiotensin-converting enzyme 2 [hACE2]). Transmission is expected to occur only after signs of lower respiratory tract disease develop.

SARS is high (unintelligible) kind of inducer: This means that when it infects the lower part of the lung,

the body develops a very severe reaction against it and leads to lots of inflammation and scarring. In SARS, after the first 10-15 days, it wasn't the virus killing the patients; it was the body's reaction. Is this virus in the MERS or SARS kind picture or is this the other type of virus which is a milder coronavirus like the NL63 or the 229? It may be the mild (unintelligible) kind of inducer. [Dr John Nicholls, University of Hong Kong]

No sore throat: This new virus attacks the lungs as well, and not just the throat. Patients so far have not presented with a sore throat, because the 2019-nCoV attacks the intraepithelial cells of lung tissue.

Asymptomatic transmission: A report of a small cluster of five cases indicated transmission from asymptomatic individuals during the incubation period; all patients in this cluster had mild illness. Another person got infected while using gown, but the eyes were not covered. *NEJM* reported a transmission from asymptomatic case but the same has been challenged.

Mass Quarantine May Spark Irrational Fear, Anxiety, Stigma.

Evacuation: US, Japan, India have evacuated their citizens trapped in China's affected areas. All 645 evacuees from Wuhan tested negative for the deadly infection in India. Close to 80 Indian students are still stuck in Wuhan. Seventy of the 80 chose to stay behind at the time of the evacuation operation. Ten had expressed willingness to return to India but could not board as they failed the screening process at the airport.

Bangladesh scrapped plans to bring back its 171 nationals stuck. In China as the crew members refused to fly. State-run Biman Airlines' Boeing 777-300 ER aircraft on February 1 brought back 312 Bangladesh nationals.

Legal implications in India: Section 270 in The Indian Penal Code – 270. Malignant act likely to spread infection of disease dangerous to life.—Whoever malignantly does any act which is, and which he knows or has reason to believe to be, likely to spread the infection of any disease dangerous to life, shall be punished with imprisonment of either description for a term which may extend to 2 years, or with fine, or with both.

Asymptomatic: Unlike SARS, patients were symptomatic at about day 5. Some of the cases may be asymptomatic until about day 7. The first 5 days are probably asymptomatic.

Case fatality of coronavirus: 2%.

Case fatality of MERS: 34% (2012, killed 858 people out of the 2,494 infected).

Case fatality of SARS: 10% (Nov. 2002 - Jul. 2003, originated from Beijing, spread to 29 countries, with 8,096 people infected and 774 deaths).

Case fatality of Ebola: 50%.

Case fatality of Smallpox: 30-40%.

Case fatality of Measles: 10-15% developing countries.

Case fatality of Polio: 2-5% children and 15-30% adults.

Case fatality of Diphtheria: 5-10%.

Case fatality of Whooping cough: 4% infants < 1year, 1% children <4 years.

Case fatality of Swine flu: <0.1-4%.

Case fatality of seasonal flu: 0.01%.

Case fatality of current virus in Wuhan: 4.9%.

Case fatality of current virus in Hubei province: 3.1%.

Case fatality of current virus in Nationwide: 2.1%.

Case fatality of current virus in other provinces: 0.16%.

Number of flu deaths every year: 2,90,000-6,50,000 (795 to 1,781 deaths per day).

Lab tests: There are two ways to detect a virus: through the genetic material DNA or RNA and to detect the protein of the virus. The rapid tests look at the protein. It takes 8-12 weeks to make commercial antibodies. Currently, for the diagnostics tests, PCR is being used which gives a turnaround in 1-2 hours.

Treatment: No proven antiviral treatment.

With SARS, in 6 months the virus was gone and it never came back. Pharmaceutical companies may not spend millions to develop a vaccine for something, which may never come back.

Evidence of *E. coli*: Secondary infection is most likely the cause of deaths in the Philippines and Hong Kong.

SARS experience: A combination of lopinavir and ritonavir showed promise in lab.

MERS experience: Combination of lopinavir, ritonavir and recombinant interferon beta-1b has been tried.

Recreation of virus: Scientists in Australia have reportedly developed a lab-grown version of coronavirus.

Chloroquine had potent antiviral activity against the SARS-CoV, has been shown to have similar activity against HCoV-229E in cultured cells and against HCoV-OC43 both in cultured cells and in a mouse model.

Thai experience: Oseltamivir along with lopinavir and ritonavir, both HIV drugs.

Experimental drug: From Gilead Sciences Inc., called remdesevir (started on 6th Feb as a trial).

Russia and China drug: Arbidol, an antiviral drug used in Russia and China for treating influenza, could be combined with Darunavir, the anti-HIV drug, for treating patients with the coronavirus. (The coronavirus shares some similarity to HIV virus also).

PVP-I mouthwashes and gargles are known to reduce viral load in the oral cavity and the oropharynx. PVP-I has high potency for viricidal activity against hepatitis A and influenza, MERS and SARS.

DCGI approval: The Drug Controller General of India has approved the "restricted use" of a combination of drugs (lopinavir and ritonavir) used widely for controlling HIV infection in public health emergency for treating those affected by novel coronavirus.

Steroids: In SARS, people were put on long-term steroids ending with immunosuppression and late complications and death. The current protocol is short-term treatment.

UNIVERSAL RESPIRATORY DROPLETS PRECAUTIONS

Self-quarantining: 2 weeks.

Adherence: Strict.

Soap and water: Wash your hands often and for at least 20 seconds.

Alcohol-based hand sanitizer: If soap and water is not available.

Avoid touching: Your eyes, nose and mouth with unwashed hands.

Avoid close contact: (3-6 feet) with people who are sick with cough or breathlessness.

Stay home: When you are sick.

Cover your cough or sneeze with a tissue, then throw the tissue in the trash.

Clean and disinfect frequently touched objects and surfaces.

Surgical Masks: For patients.

N95 Masks: For healthcare providers and close contacts.

The world is facing a chronic shortage of gowns, masks, gloves and other protective equipment in the fight against coronavirus.

TEN COMMON MYTHS

1. People receiving packages from China are not at risk of contracting the new coronavirus as the virus does not survive long on objects, such as letters or packages.
2. There is no evidence that animals/pets such as dogs or cats can get infected with the new coronavirus. However, it is always in your best interests to wash your hands with soap and water after contact with petsto prevent transmission of common bacteria such as *E. coli* and *Salmonella*.
3. Pneumococcal vaccine and *Haemophilus influenzae* type B (Hib) vaccine, provide no protection against the new coronavirus.
4. Regularly rinsing the nose with saline does not protect people from infection with the new coronavirus or respiratory infections although it can hasten recovery from the common cold.
5. There is no evidence that using mouthwash protects you from infection with the new coronavirus although some brands of mouthwash can eliminate certain microbes for a few minutes in the saliva in your mouth.
6. Garlic may have some antimicrobial properties; however, there is no evidence that eating garlic protects people from the new coronavirus.
7. Sesame oil does not kill the new coronavirus. Chemical disinfectants that can kill the 2019-nCoV on surfaces are bleach/chlorine-based disinfectants, either solvents, 75% ethanol, peracetic acid and chloroform. However, they have little to no impact on the virus if you put them on the skin or under your nose. It is dangerous to put these chemicals on your skin.
8. People of all ages can be infected by the new coronavirus (2019-nCoV). Older people, and people with pre-existing medical conditions (such as asthma, diabetes, heart disease) have increased odds of becoming severely ill with the virus. People of all ages are advised to take steps to protect themselves from the virus, for example by following good hand hygiene and good respiratory hygiene.
9. Antibiotics do not work against viruses. Hence, antibiotics should not be used to prevent or treat the new coronavirus unless you suspect bacterial co-infection.
10. To date, there is no specific medicine recommended to prevent or treat the new coronavirus (2019-nCoV).

ROLE OF CMAAO AND OTHER MEDICAL ASSOCIATIONS

- All countries should be prepared for containment, including active surveillance, early detection, isolation and case management, tracking contacts and prevention of spread of the virus and to share full data with WHO.
- It is a legal requirement that all countries share information with WHO under the IHR.
- If 2019-nCoV is detected in an animal (information about the species, tests and epidemiological data), it must be reported to the World Organization for Animal Health (OIE) as an emerging disease.
- All countries should emphasize on reducing human infection, prevention of secondary transmission and international spread.

PMO SUGGESTIONS SENT

7th Jan: CMAAO Alert – WHO to monitor China's mysterious pneumonia of unknown virus outbreak.

8th Jan: CMAAO warns Asian citizens traveling to China over mystery pneumonia outbreak.

10th Jan: I wrote an editorial – Corona virus strain causing pneumonia in Wuhan, China, It's a new strain of coronavirus in the China pneumonia.

13th Jan: China virus outbreak linked to seafood market.

15th Jan: First case of China pneumonia virus found outside China in Thailand.

17th Jan: WHO issues warning after 'mysterious' Chinese coronavirus spreads to Japan.

17th Jan: India at threat of Coronavirus. CMAAO urges travel advisory on coronavirus: http://www.drugtodayonline.com/medical-news/nation/10379-cmaao-urges-travel-advisory-on-coronavirus.html

18th Jan: Indian government issues travel advisory as China's mysterious 'Coronavirus' spread in other countries.

18th Jan: WHO issues warning after mysterious Chinese Coronavirus spreads to Japan (http://blogs.kkaggarwal.com/tag/who/).

18th-20th Jan: Three countries meet, also discussed Coronavirus.

22nd Jan: Still not being declared to be a notifiable disease; N95 to be included in the list of essential drugs and price-capped; Oseltamivir should also be price-capped; flights should have masks available for all passengers; not declaring flu-like symptoms while boarding or landing should be a punishable offence (23rd Jan: India issues advisory to airports).

24th Jan: Inter Ministerial Committee needs to be formed on Coronavirus (PMO took a meeting on 24th evening).

25th Jan: Indian government should pay for Indians affected with the virus in China.

26th Jan: Need of National Droplet Infection Control Program; Policy to ban export of face masks; policy to evacuate Indians and people of neighboring countries from China's affected areas; Time to collaborate on Nosode therapy (Exports of masks banned on 31st January by Indian Government).

Action: Feb 1st: Ibrahim Mohamed Solih thanked India for the evacuation of seven Maldivian nationals from the coronavirus-hit Chinese city of Wuhan. India evacuated 647 people.

(On 30th Jan, India banned gloves, PEP and masks but on 8th lifted the ban on surgical masks/disposable masks and all gloves except NBR gloves. All other personal protection equipment, including N95 and equipment accompanying masks and gloves, shall remain banned.)

27th Jan: History of anti-fever drugs at airports should be taken.

28th Jan: Do research on Nosodes.

29th Jan: Closure of live markets all over the world, India should take lead.

30th Jan: Paid flu leave, surgical mask at public places, N95 for healthcare providers.

31st Jan: Respiratory hygiene advisory to schools, Pan-India task force to be made.

1st Feb: Disaster Budget is the need of the hour.

3rd Feb: 100 crore budget for Coronavirus; Private labs to be recognized; one dedicated coronavirus National help line; MTNL BSNL to have a line of advisory in their bills; isolation wards to be single rooms or two beds separated with 6 feet distance; national insurance to cover cost of treatment; Sea ports to have same precautions; price caps for masks and gloves; National Droplet Control Program; clarification that import of goods is not risky; and suspend AI flights to China and Hong Kong.

(Feb 4 - Air India suspended flight services to Hong Kong from Friday until March 28. Earlier, Air India had cancelled its flight to Shanghai from January 31 to February 14; and 5th Feb - The Ministry of Defence is setting up 10 new laboratories across the country, primarily to conduct research on viruses).

4th Feb: Kerala travel advisory needed (The Union Ministry of Health and Family Welfare issued a fresh travel advisory on Monday urging people to refrain from visiting China).

5th Feb: PM should talk about Coronavirus in Man Ki Baat or a special address.

6th Feb: Time to have makeshift bed policy to tackle deaths in Kota, Muzaffarpur and Coronavirus cases [Uttarakhand to set up two dedicated hospitals to tackle coronavirus: https://www.hindustantimes.com/india-news/uttarakhand-to-set-up-two-dedicated-hospitals-to-tackle-coronavirus/story-NYxBOw6XHTbugznTWa3CXK.html]

7th Feb: IPC 269 should be applicable to coronavirus.

8th Feb: Teleconsultation should be allowed for flu and coronavirus consultation.

Confirmed Cases and Deaths by Country and Territory

Country	Cases	Deaths	Region
China	40,171	908	Asia
Japan	96	0	Asia
Singapore	43	0	Asia
Hong Kong	36	1	Asia
Thailand	32	0	Asia
South Korea	27	0	Asia
Taiwan	18	0	Asia
Malaysia	17	0	Asia
Australia	15	0	Australia/Oceania
Vietnam	14	0	Asia
Germany	14	0	Europe
United States	12	0	North America
France	11	0	Europe
Macao	10	0	Asia
Canada	7	0	North America
United Arab Emirates	7	0	Asia
United Kingdom	4	0	Europe
Philippines	3	1	Asia
Italy	3	0	Europe
India	3	0	Asia
Russia	2	0	Europe
Spain	2	0	Europe
Cambodia	1	0	Asia
Nepal	1	0	Asia
Finland	1	0	Europe
Sweden	1	0	Europe
Sri Lanka	1	0	Asia
Belgium	1	0	Europe

Total Deaths of Novel Coronavirus (2019-nCoV)

Date	Total Deaths	Change in Total	Change in Total (%)
Feb 9	910	97	12
Feb 8	813	89	12
Feb 7	724	86	13
Feb 6	638	73	13
Feb 5	565	73	15
Feb 4	492	66	15
Feb 3	426	64	18
Feb 2	362	58	19
Feb 1	304	45	17
Jan 31	259	46	22
Jan 30	213	43	25
Jan 29	170	38	29
Jan 28	132	26	25
Jan 27	106	26	33
Jan 26	80	24	43
Jan 25	56	15	37
Jan 24	41	16	64
Jan 23	25	8	47

Daily Deaths of Novel Coronavirus (2019-nCoV)

Date	Daily Deaths	Change in Daily	Change in Daily (%)
Feb 9	97	8	9
Feb 8	89	3	3
Feb 7	86	13	18
Feb 6	73	0	0
Feb 5	73	7	11
Feb 4	66	2	3
Feb 3	64	6	10
Feb 2	58	13	29
Feb 1	45	-1	-2
Jan 31	46	3	7
Jan 30	43	5	13
Jan 29	38	12	46
Jan 28	26	0	0
Jan 27	26	2	8
Jan 26	24	9	60
Jan 25	15	-1	-6
Jan 24	16	8	100
Jan 23	8	0	0

(Source: https://www.worldometers.info/coronavirus/coronavirus-death-toll/)

IJCP SUTRA: *"Don't eat your snack while doing something else like surfing the Web, watching TV or working at your desk."*

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Sudden Blindness in Children Passing Roundworm Per Oral

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

ABSTRACT

Background: *Ascaris lumbricoides* infestation is the most prevalent parasitic infection among the children in tropical and developing countries but the incidence of sudden blindness after passing the worm per oral is undocumented. The lag period depends on the prodromes. Investigations reveal mere raised eosinophilic count and decreased hemoglobin with normal CT scan and CSF examination. **Materials:** Ten cases of sudden blindness investigated and treated at various centers without any positive response attending our center after 30-45 days of incidence from January 2018 to March 2019, were selected. **Methods:** Selected patients' parents were interrogated for the course of disease, treatment taken and their response. Patients were clinically examined, investigated for basic bioparameters, vision and were treated with the prescribed regime-containing pyridoxine, methylcobalamin, nicotinamide, pantothenic acid and herbal neurovitalizer composite. **Results:** All patients had progressive vision gain and attained complete vision after 6 months therapy without any adversity and residual effect or any alteration in hepatorenal profile. **Conclusion:** Sudden blindness in children after passing roundworm or with history of roundworm must be suspected for photoreceptor blockade by roundworm toxin and be treated with pyridoxine and herbal neurovitalizer to assure complete recovery.

Keywords: *Ascaris lumbricoides*, CT scan, cerebrospinal fluid, photoreceptor, neurovitalizer, recovery

Prevalence of intestinal worm infection has been found to be nearly 49.35% and *Ascaris lumbricoides* as the most common parasitic infection (46.85%) in an Indian study. Soil-transmitted helminth infections form the most important group of intestinal worms affecting 2 billion people worldwide causing considerable morbidity.

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A. lumbricoides remain the most prevalent parasitic infection despite therapeutic response to albendazole and mebendazole, but eradication is difficult due to recurrent infection.

Considering the changing effect of worm infestation, the Government of India (GoI) has launched a program to combat worm infestation, i.e., National deworming day for children of age group 1-19 years biannually.

As per the World Health Organization (WHO), >836 million children are at risk of parasitic manifestation worldwide and 214 million children are of age group 1-14 years. In addition, evidence of disproportionate worm infestation and self-drug use resulting in resistance to available deworming agent and presently a combination of parasitocide i.e., albendazole and ivermectin, is in consideration. As these agents only act on adult worm, not on cyst or ova, its recurrent dose must be prescribed as on 45th day every ovum develops to active adult roundworm.

MATERIALS AND METHODS

Materials

Ten children attending the Center for Critical Care with complaints of sudden blindness after passing

roundworm per oral having treated at various hospitals without any positive response and advised brain surgery were included in the study. Ophthalmological examination and CT brain showed no evident pathology except blood showing high eosinophilic count. Table 1 summarizes the clinical presentation of the study patients.

Methods

All the patients presenting with sudden blindness and associated history of passing roundworm per oral and treated at various hospitals without any vision improvement in spite of medication and no pathology detected on various investigations like CT brain, retinal examination and various hematological examinations, were interrogated, examined thoroughly and investigated for basic hematological, hepatic and renal profile.

All the selected patients were administered the following irrespective of age and presentation:

- Intravenous (IV) mannitol 10% with glycerine and 10% in therapeutic dose.
- Injection methylcobalamin, nicotinamide, pyridoxine and pantothenic acid with betamethasone, 1 mL IV every 4th day very slow.
- Syrup Herbal neuroenergizer 2.5-5 mL every 8 hours.
- Susp albendazole 400 mg *plus* ivermectin 3 mg at bedtime for 5 days.
- Bland and simple high carbohydrate diet.

Herbal neurovitalizer constitutes:

Each 5 mL–

- *Acorus calamus* 100 mg
- *Herpestis monnieria* 100 mg
- *Convolvulus pluricaulis* 100 mg
- *Nardostachys jatamansi* 100 mg
- *Cassia angustifolia* 100 mg

Patients' parents were instructed to daily ascertain visual response by finger counting or light reflex, and were also suggested to mark any adversity or new emerging manifestation and report immediately.

Patients were routinely examined every week to ascertain response to the therapy and safety profile. At the end of therapy, patients were examined by ophthalmologist for vision and visual acuity.

OBSERVATION AND RESULTS

Selected patients were in the age group 6-14 years (Table 2) and among them, 4 were male and 6 female (Fig. 1). They approached for medical care within the lag

Table 1. Clinical Presentation of Study Patients

Patient	Age/Sex	Clinical presentation	Lag period
A	10/F	History of passing roundworm per oral, loose motions, vomiting, fever, loss of vision both sides	3 days
B	9/M	Loose motions, vomiting, pain in abdomen, itching over the body, loss of vision both sides, passage of roundworm per oral	2 days
C	12/M	Vomiting, pain in abdomen, fever urticarial rash over the extremity, passage of roundworm per oral, loss of vision both sides	4 days
D	6/M	Vomiting, loose motions, involuntary body movement, urticarial rash, passing roundworm per oral, sudden blindness	2 days
E	13/F	Loose motions, urticarial rash, fever, shivering, nausea, pain in abdomen, passage of roundworm per oral, sudden blindness	3 days
F	12/F	Loose motions of white color, dark urine, intense itching with rash, fever, vomit of roundworm, abdominal pain, loss of vision	5 days
G	8/F	Agonizing pain in abdomen, loose motion, vomiting, urticarial rash, passage of roundworm per oral, loss of vision	4 days
H	8/M	Nausea, vomiting, urticarial rash, passage of roundworm per oral, loss of vision	5 days
I	6/F	Vomiting, loss of appetite, urticarial rash, passage of roundworm, loss of vision	4 days
J	14/F	Fever, pain in abdomen, vomiting, headache, urticarial rash, passage of roundworm both from mouth and stool	1 day

period of 3-5 days at appropriate center. Investigations included CT scan, ophthalmological examination to assess vision and retina status, which were within normal limits in all cases, except for raised eosinophilic count. Common presentation of the patients included sudden loss of vision, passage of roundworm per oral and lag period of blindness and passage of worm was 24-72 hours (Table 3).

Patients were treated with many neurotropics and topical eye drops without any positive response.

Majority of the patients attended our center after 30-45 days of the onset of blindness. Patients presenting with associated central nervous system (CNS) manifestation like involuntary movement and headache had very short lag period of 1 or 2 days.

At our center, hematological examination show raised eosinophil count with other normal parameters, i.e., hepatic and renal.

All patients showed visual improvement by 8th day of therapy and complete visual recovery by 6th month of therapy without any visual debility. Optometry confirmed the vision in all patients as 6/6 in both eyes (Tables 4 & 5 and Fig. 2)

Table 2. Distribution of Patients

Age group (years)	Number of patients		
	Male	Female	Total
6-8	2	2	4
8-10	1	1	2
10-12	-	-	-
12-14	1	3	4

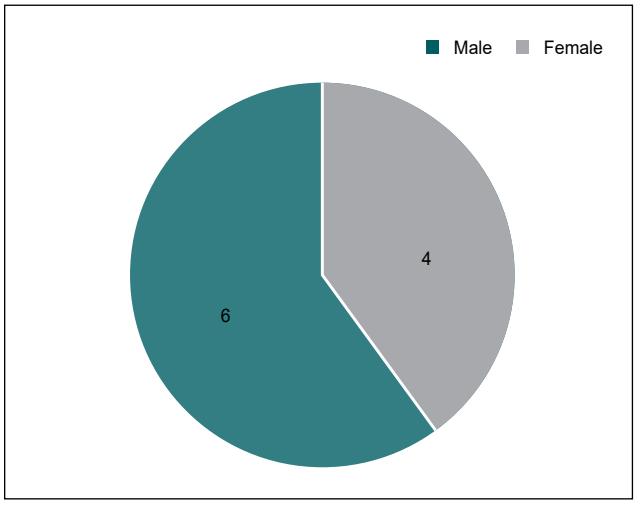

Figure 1. Pie diagram showing sex-wise composition of the patients.

Table 3. Presentation of the Patients

Sudden blindness
Passing worm per oral
Nausea and vomiting
Fever
Lag period of onset of blindness and passing the worm per oral: 24-72 hours
Blurring of vision
Sign of avitaminosis/xerosis/Bitot's spot

Table 4. Bioparameter Status at Various Stages

Basic bioparameters	Number of patients		
	A	B	C
Hematological			
Absolute eosinophil count			
<200/cc	-	-	8
200-300/cc	3	4	2
300-400/cc	6	6	0
400-500/cc	1	0	0
TLC			
<6000/cc	1	0	0
6000-7000/cc	8	10	10
>7000/cc	1	0	0
Hemoglobin percent			
<10 gm%	5	3	0
>10 gm%	5	7	10
Diabetic profile			
Blood sugar			
Fasting			
<100 mg%	9	10	10
>100 mg%	1	0	0
Postprandial			
<150 mg%	10	10	10
>150 mg%	0	0	0
Hepatic profile			
SGOT			
<30 IU	7	8	10
>30 IU	3	2	0
SGPT			
<30 IU	7	8	10
>30 IU	3	2	0

Table 4. Bioparameter Status at Various Stages

Basic bioparameters	Number of patients		
	A	B	C
Alkaline phosphatase			
<140 mg%	10	10	10
>140 mg%	0	0	0
Renal profile			
Blood urea			
<26 mg%	10	10	10
>26 mg%	0	0	0
Serum creatinine			
<1.5 mg%	10	10	10
>1.5 mg%	0	0	0
CT scan			
Altered	None	None	None
Unaltered	10	10	10
Vision			
Status of eye	Normal	Normal	Normal
PL			
Absent	10	10	0
Present	0	0	10
PR			
Absent	2	0	0
Present	8	10	10
Vision	Absent	Absent	Normal

A = At first center of treatment; B = At our center on admission; C = On completion of treatment.

Table 5. Outcome of the Study

Particulars	Number of patients
Perception of light	10
Finger counting	10
Blurred vision	None
Clear near vision	10
Clear distant vision	10
Completely normal vision	10
Safety profile	
Hematological	Improved in all
Hepatic profile	Normal in all
Renal profile	Normal in all

No adversity or sequel was noted in any case or any evidence of post-therapy withdrawal effect, i.e., decline in vision or visual acuity or any CNS manifestation.

DISCUSSION

Roundworm infestation is very common but manifestations like blindness after passing the worm per oral is very uncommon or remains unmarked. In addition, variable lag period of onset of blindness and worm passage, suggests its dependence on prodromes. Those who had CNS prodromes like headache and involuntary movement had earlier onset.

Patients' presentation on passing worm per oral suggests worm irritation leading to release of a polypeptide ASCARON which stimulates the intestinal mucosal nerve endings, resulting in nausea, vomiting and loose motions.

Absorption of toxin in blood causes anaphylactic reaction resulting in fever and urticarial rash while access to CSF results in neurosuppression due to inhibition of neurotransmitter GABA as a result of inhibition of co-enzyme pyridoxal phosphatase by the toxin.

Sudden blindness occurs as neuroconduction suppression results in blockade of neurotransmission from photoreceptors of retinal fovea (Fig. 3).

Figure 4 depicts the pattern of vision improvement in the patients. No change in bioparameters was observed in any case and eosinophil count came to normal.

All patients recovered of blindness having progressive vision gain from perception of light to normal vision in 6 months' duration with the treatment. It is attributed to:

- IV mannitol 10% with glycerine and 10% relieved neural edema.
- Supplementation of pyridoxine as injection of methylcobalamin, pyridoxine, nicotinamide and pantothenic acid competitively inhibits polypeptide and activates pyridoxal phosphatase and ensures increased neurotransmitter GABA. Methylcobalamin and pantothenic acid promote neuroconduction.
- Herbal composite constituents ensure neurovitalization and photoreceptor activation.
- Administration of albendazole *plus* ivermectin ensures worm eradication.
- Nutritious diet supports recovery.

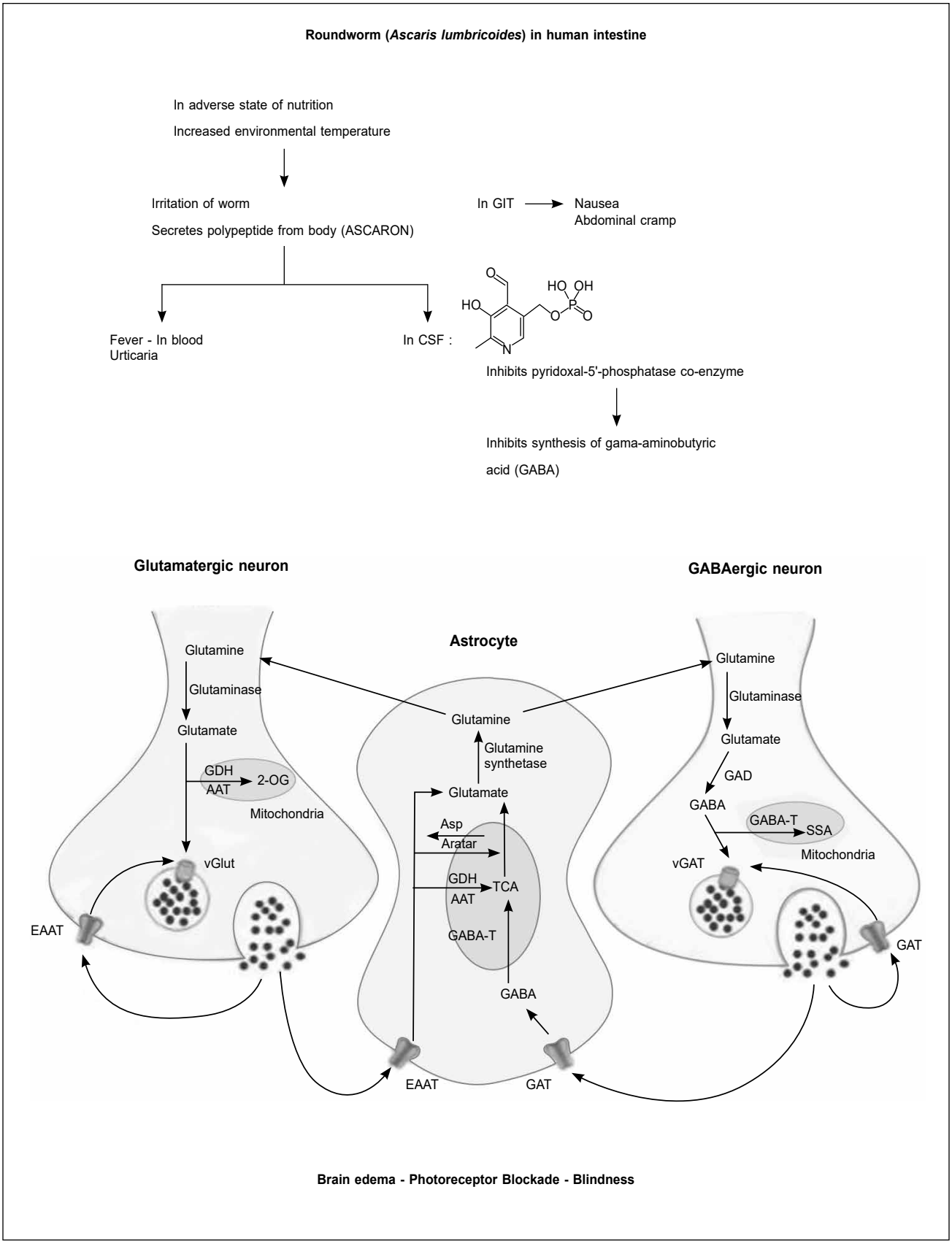

Figure 2. Roundworm kinetics in intestine.

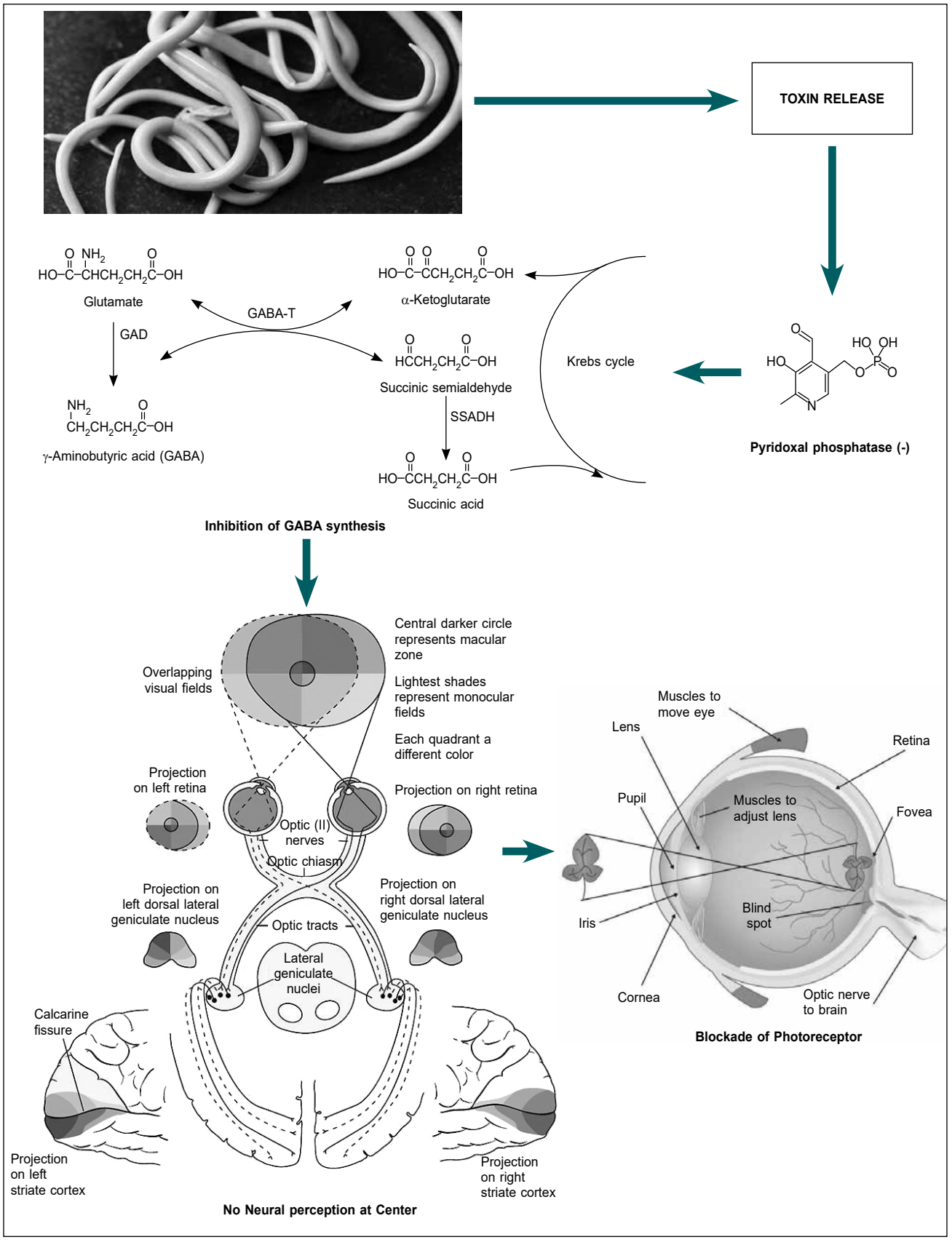

Figure 3. Schematic presentation of pathogenesis of sudden blindness.

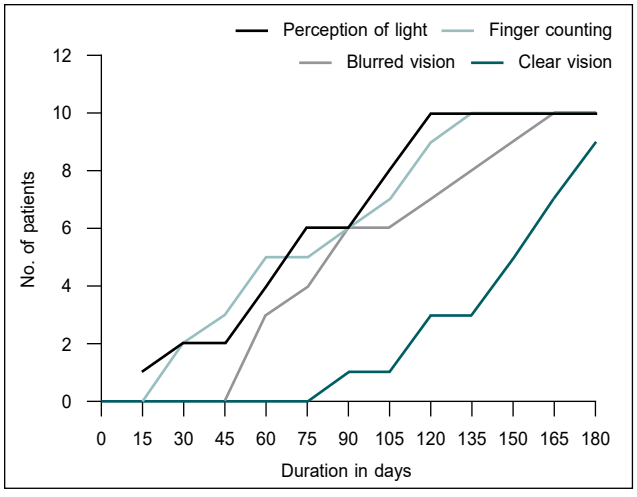

Figure 4. Pattern of vision improvement.

CONCLUSION

Sudden blindness after passing roundworm must be duly taken care of, suspecting Ascaris toxin as a factor. Treatment will ensure cure and safety from undue expenses, especially in tropical countries where roundworm infestation is very common. Herbal composite and pyridoxine supplementation proves a boon for cure.

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■■■■

Mom's Stress Tied to Brain Development in Fetuses with CHD

Larger portions of women pregnant with fetuses with congenital heart disease (CHD) tested positive for stress, anxiety and depression and this was linked to impairments in fetal brain development, a small case-control study found.

Almost two-thirds of pregnant women with fetuses with CHD tested positive for stress, 44% tested positive for anxiety and about 30% tested positive for depression compared to around a quarter of pregnant women with healthy fetuses testing positive for stress and depression, reported researchers. Stress and depression in mothers was linked with impairments in fetal cerebellar and hippocampal development, the authors wrote in *JAMA Pediatrics*.

Prenatal Air Pollution Exposure Tied to Childhood Blood Sugar

Kids who are exposed to air pollution in the womb may have higher blood sugar levels during childhood than kids without this exposure, according to a study that suggests particle pollution could be an environmental risk factor for diabetes.

The current study included 365 children in Mexico City who were exposed to average daily PM 2.5 levels of 22.4 micrograms per cubic meter of air ($\mu g/m^3$) while they were in the womb, far above the 12 μg limit set by Mexican regulators. From about age 5 till about age 7, kids' average levels of exposure to PM 2.5 in the womb were associated with 0.25% larger annual increases in HbA1c levels than would be expected with fine particulate matter exposure within Mexican regulatory limits, researchers calculated… (*Reuters*)

Drinking Green Tea, Rather Than Black, may Help You Live Longer, New Study Suggests

Drinking tea at least three times a week could reduce the risk of dying from cardiovascular disease and is linked with a longer and healthier life, at least in China, a new study suggests.

Chinese researchers found the health benefits associated with tea were more marked for drinkers of green, rather than black tea, and for those who had been drinking tea regularly over a longer period of time. The benefits were also clearer among men, the study indicated… (*CNN*)

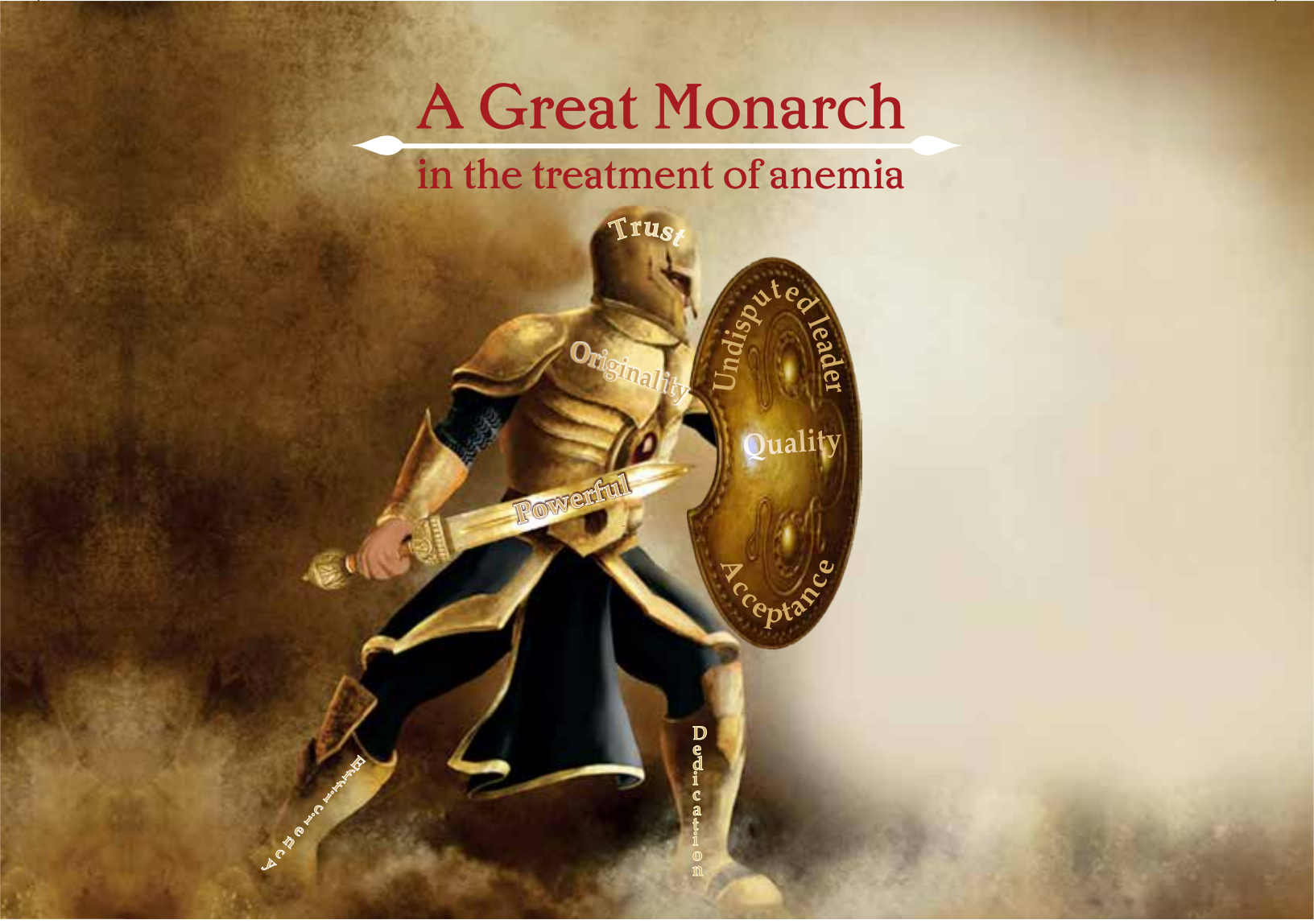
Diabetes Drug Class may Hold Promise for Gout Prevention

Sodium-glucose cotransporter-2 (SGLT2) inhibitors may reduce the risk for gout among adults with type 2 diabetes, new research suggests.

The study, involving more than 2,00,000 individuals from a US commercial insurance database, was published online in *Annals of Internal Medicine*. In this new study, there was a nearly 40% relative risk reduction in gout among adults prescribed SGLT2 inhibitors compared with those prescribed GLP-1 receptor agonists, which do not decrease uric acid levels. The absolute risk reduction was about three fewer adults with gout per 1000 person-years.

A Great Monarch

in the treatment of anemia



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

REKHA NH*, MOHAN KUMAR C†

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.

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 female. 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 with MELD score above 20%. There was significant rise in MELD score with fall in hemoglobin. Mean platelet count

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 (%)
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**

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

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.

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 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.

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Countries Gathered for the Global Forum on Childhood Pneumonia

Pneumonia claimed the lives of 8,00,000 children under the age of five in 2018, or one child every 39 seconds. That was more than any other disease. Yet pneumonia remains largely forgotten.

On January 29-31, nine leading health and children's organizations – ISGlobal, Save the Children, UNICEF, Every Breath Counts, the Bill & Melinda Gates Foundation, "la Caixa" Foundation, USAID, Unitaid and Gavi, the Vaccine Alliance – joined forces in Barcelona to host the world's first conference on childhood pneumonia. Participants at the Global Forum on Childhood Pneumonia agreed on concrete steps governments and their partners can take to dramatically reduce child pneumonia deaths. (*UNICEF*)

Burnout Linked to Potentially Deadly Irregular Heartbeat, Study Says

If you're feeling bone-deep mental and physical exhaustion, or what is otherwise known as burnout, new research suggests you could be at a higher risk for a potentially fatal heart flutter.

The study published in the *European Journal of Preventative Cardiology* suggests chronic stress and exhaustion could be a key factor in developing the disease. Investigators followed nearly 12,000 men and women who did not have AFib over a 25-year period. No association was found between levels of anger, social support or antidepressant use once the analysis was complete. Only people who scored highest in "vital exhaustion," a medical term for irritability, extreme fatigue and a feeling of demoralization, were more likely to develop atrial fibrillation… (*CNN*)

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Respiratory Functions During Various Phases of Menstrual Cycle

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ABSTRACT

The present study was conducted in 30 Indian healthy females. Peak expiratory flow rate (PEFR) was measured by Wright's peak flow meter in standing position during various phases of two menstrual cycles. The mean of PEFR of two menstrual cycles was considered. On comparison of luteal and menstrual phases, the PEFR difference was found highly significant ($p < 0.001$). Similarly on comparing proliferative and luteal phases, the PEFR difference was found highly significant ($p < 0.001$). But on comparing menstrual and proliferative phases, the PEFR difference was not found significant ($p > 0.05$).

Keywords: Peak expiratory flow rate, menstrual cycle, menstrual phase, proliferative phase, luteal phase

Peak expiratory flow rate (PEFR) is a highly sensitive and accurate index of airway obstruction and is very useful in the diagnosis, management, follow-up of bronchial asthma and predicts the status of ventilatory lung function. PEFR can also be used to guide the treatment of asthma.[1]

The variations in functional parameters of respiratory system may be related to fluctuations in the hormonal levels during various phases of menstrual cycle. PEFR is usually measured for the assessment of pulmonary functions. PEFR is maximal expiratory flow rate sustained by a subject for at least 10 msec expressed in liter per minute. PEFR has been used as measurement of ventilatory functions since long, as it is much simpler and less tiring procedure than maximum voluntary ventilation (MVV).[2]

MATERIAL AND METHODS

A written informed consent for PEFR was taken after explaining the method of study. Subjects were instructed to come to the laboratory on 2nd-4th day, 9th-12th day and 19th-21st day of menstrual cycles. Recordings were carried out during two menstrual cycles. When recording during any phase of a cycle was missed due to holiday or some other reason, then all the phases of next menstrual cycle were considered. Wright's peak flow meter is widely used to measure PEFR values.[1] PEFR was recorded by Wright's peak flow meter by connecting subject with the help of mouthpiece. The recording scale is up to 1,000 L/min. The subject performed the test in standing position by holding peak flow meter properly. They were asked to take a deep breath and then to exhale by forceful expiration as fast as possible after maintaining air tight seal between lips and mouthpiece of instrument. Maximum of three readings of PEFR was considered. PEFR was recorded in all phases of two menstrual cycles.

OBSERVATIONS AND RESULTS

The mean values of PEFR in Cycle 1 were 335.0 ± 32.88, 342.2 ± 32.53 and 381.2 ± 26.51 in menstrual, proliferative and luteal phases, respectively, while mean values of PEFR in Cycle 2 were 336.7 ± 29.63, 338.7 ± 28.74 and 387.0 ± 26.80 in menstrual, proliferative and luteal phases, respectively. When both cycles were considered, the mean PEFR values were 335.8 ± 30.85, 340.4 ± 29.73 and 384.1 ± 26.41 in menstrual, proliferative and luteal phases, respectively (Table 1). PEFR was found significantly increased in luteal phase as compared to menstrual and proliferative phases in the two individual menstrual cycles as well as the mean of two cycles.

On comparison of luteal and menstrual phases, the PEFR difference was found highly significant

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Table 1. PEFR in Liters/min in Different Phases of Menstrual Cycles

Cycles	Menstrual phase (2nd-4th day)	Proliferative phase (9th-12th day)	Luteal phase (19th-21st day)
Cycle 1	335.0 ± 32.88	342.2 ± 32.53	381.2 ± 26.51
Cycle 2	336.7 ± 29.63	338.7 ± 28.74	387.0 ± 26.80
Both cycles	335.8 ± 30.85	340.4 ± 29.73	384.1 ± 26.41

Table 2. Comparison of PEFR Among Different Phases of Menstrual Cycles

Cycles	Menstrual vs. Proliferative	Proliferative vs. Luteal	Luteal vs. Menstrual
Cycle 1	P > 0.05	P < 0.001	P < 0.001
Cycle 2	P > 0.05	P < 0.001	P < 0.001
Both cycles	P > 0.05	P < 0.001	P < 0.001

P < 0.001 = Highly significant; P > 0.05 = Not significant.

($p < 0.001$) in the two individual menstrual cycles as well as the mean of two cycles. Similarly, on comparing proliferative and luteal phases, the PEFR difference was found highly significant ($p < 0.001$) in the two individual menstrual cycles as well as the mean of two cycles. But on comparing menstrual and proliferative phases, the PEFR difference was not found significant ($p > 0.05$) in the two individual menstrual cycles as well as the mean of two cycles (Table 2).

DISCUSSION

Changes in lung function have been reported in different phases of menstrual cycle owing to action of the hormone progesterone. Some studies showed that phases of menstrual cycle and individual cycles had no significant effect on spirometry variables except for peak expiratory flow and respiratory static pressures. The correlations noted between sex hormones and respiratory control variables point towards a positive effect of female sex hormones controlling the thoracic pump muscles in luteal phase.[3] The pulmonary functions qualified as lung volumes and capacities seem to be better during luteal phase of menstrual cycle, indicative of a possible beneficial role of progesterone in the management of premenstrual asthma.[4]

Changes in lung function have been reported in different phases of menstrual cycle owing to the action of the hormone progesterone. PEFR and forced expiratory volume in 1 second (FEV_1) increased in luteal phase ($p < 0.05$) and this increase in PEFR and FEV_1 is suggestive of decreased airway resistance. Lower percentage of PEFR and slow vital capacity (SVC) in postmenopausal women compared to premenopausal women during follicular and luteal phase are likely due to decreased level of progesterone and estrogen. Reduced levels of estrogen and progesterone result in increased compression of thoracic spine, decreased relaxation of bronchial smooth muscle and decreased muscular strength, resulting in decreased level of forced expiratory flow between 25% and 75% of vital capacity (FEF_{25-75}), PEFR and SVC.[5]

Another study showed significantly higher serum progesterone and forced vital capacity (FVC), FEV_1 and PEFR during secretory phase and a strong positive correlation of serum progesterone in secretory phase with FVC and negative correlation with FEV_1%. The improvement of pulmonary function during secretory phase was related with increase in serum progesterone levels, which have a dual effect of overall smooth muscle relaxation and hyperventilation.[6]

Some other studies showed that although there was increase in FEV_1 and FVC in secretory phase which may be due to domination of estrogen in follicular phase which in turn increases the resting minute volume in secretory phase, but, there was no significant difference when PEFR was compared in different phases of menstrual cycle.[7]

A study was conducted to assess the normal physiological fluctuation of serum progesterone on PEFR%. PEFR% was higher in luteal phase as compared to follicular phase in premenopausal women; the relationship was significant ($p < 0.01$, $r = 0.995$). Thus, it was suggested that the normal cyclical progesterone hormone level should be considered while interpreting PEFR%.[8] Similarly, in our study also, PEFR was significantly higher in luteal phase than proliferative phase.

Both exogenous progesterone and estradiol administration have been reported to improve asthma in women. In a few patients, intramuscular supplementary progesterone eliminated the premenstrual fall in PEFR and allowed better control of asthma as lower concentration of progesterone in premenopausal phase may be a possible mechanism for premenstrual asthma.[9]

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Sports Medicine Group Issues Guidance on Athletes' Mental Health

Although participating in sports provides multiple benefits, it also exposes athletes to factors that can endanger their mental health. A new evidence-based, best practices document from the American Medical Society for Sports Medicine (AMSSM) is intended to help team physicians and other healthcare personnel prevent, detect, and treat psychological issues and mental health disorders in athletes.

The AMSSM Position Statement on Mental Health Issues and Psychological Factors in Athletes, published online in the *British Journal of Sports Medicine*, focuses on competitive athletes from youth up through collegiate, Olympic and professional athletes. In comparison to position or consensus statements on athletes and mental health released since 2017 by other professional organizations, the AMSSM document claims to break new ground.

"No Shortcuts to a Healthier World": WHO Chief Sets Out Health Priorities for the Decade

The head of the UN Health Agency, WHO, has set out his urgent global health challenges for the next 10 years – designated the "Decade of Action" by the UN General Assembly" – and underscored the importance of investing in public health, in a statement.

Tedros Adhanom Ghebreyesus wrote that the list of challenges is a response to concern that leaders are not committing sufficient resources to health, and are putting "lives, livelihoods and economies in jeopardy". The WHO identified 13 priorities for the decade, covering a wide range of issues affecting people across the planet… (*UN*)

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Symptom Correlation in Patients Undergoing Ambulatory 24-hour pH Study

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ABSTRACT

Background: There is scarce data from India on symptom correlation in patients undergoing ambulatory 24-hour pH monitoring. **Aim:** Retrospective analysis of symptom correlation in patients undergoing ambulatory 24-hour pH study at our center. **Material and methods:** The study included patients who had 24-hour pH testing from 2015 to 2017 for typical or extra-esophageal symptoms of gastroesophageal reflux disease (GERD). Patient information included age, gender and indications for the pH study. Collected data included reflux details in upright and recumbent position, correlation with meals, duration and number of reflux events, Johnson/DeMeester score, symptom index (SI) and symptom sensitivity index (SSI). Descriptive analysis was carried out by median and range for quantitative variables, and frequency and proportion for categorical variables. Chi-square tests and Mann-Whitney *U* test were used. P value <0.05 was considered statistically significant. **Results:** Thirty-six of the 66 patients had Johnson/DeMeester score >14.7 (Group 1). Heartburn, regurgitation and extra-esophageal symptoms were significantly more common in Group 1. These patients also had significantly more reflux in both upright and supine position, with significant reflux episodes in both positions. They also had more reflux episodes lasting for more than 5 minutes. Post meal reflux episodes were common. SI was significantly high in Group 1. The positive symptom correlation, as assessed by SI >50% and SSI >10%, was higher for heartburn, regurgitation compared to chest pain and extra-esophageal symptoms, although not statistically significant. **Conclusion:** About 45% of patients undergoing pH study had no pathological reflux. 24-hour pH study is useful to identify pathological acid exposure with good symptom correlation for typical as well as extra-esophageal symptoms.

Keywords: Reflux, symptom, severity, esophagus

Newer techniques for esophageal functional testing, such as impedance testing and wireless pH capsule monitoring, are currently available in most centers in the West. With impedance testing, movements of liquid and air within the esophageal lumen, either in an antegrade or retrograde direction, can be monitored and reflux can be detected independently of the acid in the refluxate.[1] Combined pH impedance monitoring can identify the causative agent for extra-esophageal symptoms of reflux.[2] Wireless pH capsule is well-tolerated by most patients and improves symptom assessment in those with atypical reflux symptoms in comparison to 24-hour pH monitoring.[3,4]

In India, ambulatory 24-hour esophageal pH monitoring is most popular and widely used. It provides quantitative information on esophageal acid exposure and symptom correlation with acid exposure events. Indications for 24-hour pH testing in our setting include testing prior to fundoplication, evaluation of nonerosive reflux disease, extra-esophageal symptoms of gastroesophageal reflux disease (GERD) and poor response to medical management. Symptom correlation in these patients may guide us to appropriate management.

The present study is a retrospective analysis of symptom correlation in patients undergoing ambulatory 24-hour pH study at GI Motility Unit, Institute of GI and HPB Sciences, Gleneagles Global Health City, Chennai, Tamil Nadu, India. A Johnson/DeMeester score of >14.7 pH was considered as significant for acid reflux in patients with typical and extra-esophageal symptoms of GERD.[5]

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MATERIAL AND METHODS

The study was retrospective and included patients who had 24-hour pH testing from 2015 to 2017 for typical or extra-esophageal symptoms of GERD. Patient information included age, gender and indications for the pH study. Gastroesophageal reflux (GER) symptoms were categorized as: typical GER symptoms (heartburn, regurgitation, dysphagia or combination), noncardiac chest pain and extra-esophageal symptoms that included hoarseness of voice, chronic cough, otalgia, wheeze and constant throat clearance.

The procedure was done using single sensor pH probe using standard protocol. The localization of the lower esophageal sphincter (LES) was determined by high resolution esophageal manometry (HREM). The pH probe was then passed into the stomach and using pull-through technique was placed 5 cm above the LES. Patients were asked to note a symptom directed documentation in relation to meal and posture (upright or supine). In addition, they were asked to identify three predominant symptoms that they associated with GERD and accordingly to tap the code on the pH recorder when these occurred. The data was stored via an interface on a compatible computer. Analysis was performed using computerized software and was also reviewed manually.

Data obtained included reflux details in upright and recumbent position, correlation with meals, duration and number of reflux events. Johnson/DeMeester score was available in the final computerized analysis.

Correlation of symptoms with pH was done by calculating symptom index (SI) for all the symptoms mentioned by the patient using the computerized software and values >50% were taken as positive. Symptom sensitivity index (SSI) was calculated for all the cases manually and values >10% were considered positive.[6,7] Both SI and SSI provide data on the strength of the association between symptoms and severity of reflux. The SI does not incorporate the total number of reflux episodes into account. Likewise, SSI does not take into account the total number of symptom episodes.

The flow chart of the study is shown in Figure 1.

STATISTICAL ANALYSIS

The data was entered in Microsoft Excel sheet. Descriptive analysis was carried out by median and range for quantitative variables, and frequency and proportion for categorical variables. Chi-square tests and Mann-Whitney *U* test were used to assess statistical significance. A p value <0.05 was considered statistically significant.

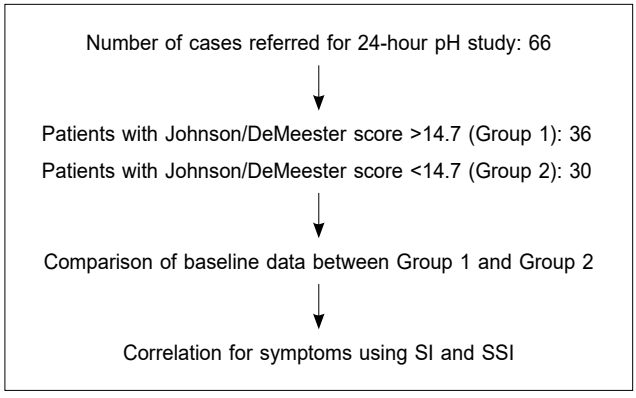

Figure 1. Flowchart of the study.

RESULTS

Sixty-six patients underwent upper endoscopy and ambulatory 24-hour pH monitoring during the study period. Endoscopy was normal in 52 (78.8%) and 13 of the remaining 14 had Los Angeles (LA) Grade A esophagitis. One patient had LA Grade B esophagitis. Thirty-six of the 66 patients had Johnson/DeMeester score >14.7 (Group 1).

Between Group 1 and Group 2, there was no difference in age and gender distribution (Table 1). Heartburn, regurgitation and extra-esophageal symptoms were significantly more common in Group 1. These patients also had significantly more reflux in both upright and supine position, with significant higher number of reflux episodes in both positions. They also had more reflux episodes lasting for more than 5 minutes. Post meal reflux episodes were common. SI was significantly high in Group 1.

Symptom Correlation as Noted by SI and SSI in Group 1

The positive symptom correlation, as assessed by SI >50%, was highest in patients with typical symptoms and least for those with extra-esophageal symptoms, but not statistically significant (p = 0.483) (Table 2). Similarly, the SSI was greater for heartburn, regurgitation compared to chest pain and extra-esophageal symptoms, although not statistically significant (Table 2).

DISCUSSION

The study highlights that 45% of patients undergoing pH study had no pathological reflux. Patients with pathological reflux presented with heartburn, regurgitation and extra-esophageal symptoms in both

Table 1. Comparison of Group 1 and Group 2

Parameter	Group 1 DM score >14.7 (n = 36)	Group 2 DM score <14.7 (n = 30)	P value
Age in years (median)	48 (25-72)	45 (24-69)	0.34
Sex (M:F)	22:14	24:6	0.09
Symptoms present in one or more combinations			
Heartburn	32 (88.8%)	14 (46.7%)	<0.0001
Regurgitation	28 (77.7%)	14 (46.7%)	0.002
Chest pain	7 (19.4%)	02 (6.6%)	0.08
Extra-esophageal symptoms	19 (52.7%)	06 (20%)	0.001
Upright pH <4 for >6.3% of time	18 (50%)	0 (0%)	<0.0001
Recumbent pH <4 for >1.2% of time	26 (72.2%)	6 (16.6%)	<0.0001
Median no. of reflux episodes in upright posture	63 (1-268)	23 (0-74)	<0.0001
Median no. of reflux episodes in recumbent position	18 (0-260)	3 (0-34)	0.002
Median no. of episodes >5 minutes	3 (0-23)	0 (0-1)	<0.0001
Median duration of longest episode of reflux in minutes	9 (0-781)	3 (0-17)	<0.0001
Median symptom index with meals	55.07% (0-100%)	21.2% (0-100%)	<0.0001
SI >50% (for all symptoms)	73/86 (84.8%)	18/36 (50%)	0.0001

DM: Johnson/DeMeester score.

Table 2. Correlation of SI and SSI with Symptoms

	Heartburn (n = 32)	Regurgitation (n = 28)	Chest pain (n = 7)	Atypical features (n = 19)	P value
Correlation of symptoms with SI					
Positive (>50%)	28 (87.5%)	25 (89.3%)	6 (85.7%)	14 (73.7%)	0.483
Negative (<50%)	4 (12.5%)	3 (10.7%)	1 (14.3%)	5 (26.3%)	
Correlation of symptoms with SSI					
Positive (>10%)	24 (67%)	22 (61%)	3 (43%)	9 (47.3%)	0.43
Negative (<10%)	12 (33%)	14 (39%)	4 (57%)	10 (52.7%)	

upright and supine position, with more frequent reflux episodes in either position lasting more than 5 minutes compared to those with a normal pH, with longer duration of reflux episodes with symptoms after a meal. Symptom correlation in those with pathological reflux was higher for typical GERD symptoms like regurgitation and heartburn.

Functional heartburn is characterized by the presence of symptoms of heartburn with physiological acid exposure while hypersensitive esophagus is characterized by normal acid exposure but positive correlation between symptoms and acid reflux events.[8] In our cohort of patients, 15 patients in Group 2 had normal acid exposure but an SI >50% and represent the hypersensitive esophagus subset. Addition of impedance monitoring to pH monitoring is likely to yield higher symptom correlation using various scoring systems.[9,10]

Ambulatory 24-hour esophageal pH monitoring has the ability to correlate symptoms with acid exposure events. SI and SSI are simple indices that assist in predicting response to proton pump inhibitors.[11] Despite these advantages, ambulatory pH monitoring has a few shortcomings too. It does not take into account the day-to-day variation in acid exposure[12] and the recommended

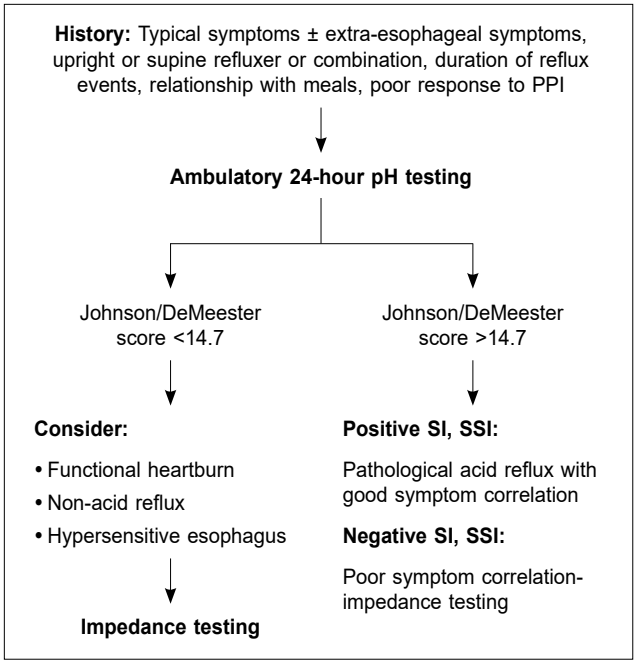

Figure 2. Interpretation of 24-hour ambulatory pH study.

cut-offs to distinguish pathological from physiological reflux differ considerably in various studies.[5,13,14] Furthermore, the available symptom indices rely on patient's recording of events. For example, frequent tappings or inappropriate pressing of position/symptom codes may lead to errors in analysis.

Earlier studies have highlighted a good correlation between pathological acid exposure time and symptoms like heartburn and regurgitation.[15] However, temporal relation of symptoms like globus sensation, hoarseness, chronic cough[9] and chest pain[10,16] with acid reflux is less clear. Furthermore, functional heartburn and hypersensitive esophagus can also coexist and interfere with symptom correlation.

Based on our preliminary observations and review of literature, we recommend an algorithmic approach for Indian patients undergoing ambulatory pH testing (Fig. 2).

To conclude, 24-hour pH study is useful to identify pathological acid exposure with good symptom correlation for typical as well as extra-esophageal symptoms. However, in those with physiological acid exposure with persistent symptoms and poor symptom correlation, impedance testing has an important role.

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Cervical Angina: An Unnoticed Cause of Noncardiac Chest Pain

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ABSTRACT

Introduction: Cervical angina is one of the commonly unnoticed causes of chest pain with frequent presentation in cardiology outpatient department (OPD). **Objectives:** This is a retrospective study with the objective to analyze the symptoms and study the clinical, neurophysiological and radiological profile of patients with cervical angina. **Study design:** A retrospective study was carried out in the Dept. of Neurology, SMS Medical College and Hospital, Jaipur, from September 2015 to July 2018. In this study, records of 25 patients were analyzed who were admitted and diagnosed with noncardiac chest pain after normal cardiac investigations who underwent neurological work-up. **Results:** Out of 25 patients, 8 (32%) were found to have cervical radiculopathy and 2 (8%) had carpal tunnel syndrome. Chest pain accompanied with neck pain was the most common presentation (24%) followed by left arm pain (16%) and shoulder pain (8%). **Conclusion:** A good history taking by physicians and cardiologists should be the basis to reach at the diagnosis of cervical angina. Thus, a high index of suspicion is required in order to save the patient from the burden of unnecessary invasive investigations and stress.

Keywords: Cervical angina, cervical radiculopathy, chest pain, neck pain

"Cervical angina is defined as a paroxysmal precordialgia that resembles true cardiac angina resulting from cervical pathology and nerve root compression," also known as pseudoangina.[1,2]

Cervical angina mostly occurs due to cervical spine disorders mimicking true angina pectoris, i.e., manifesting as pain in upper chest and scapular areas.[3,4] Pathologies like cervical intervertebral disk diseases, ossified posterior longitudinal ligament (OPLL) or other spinal disorders frequently present with atypical chest pain and are misdiagnosed as cardiac pain, thus, are subjected to an exhaustive list of costly investigations.[5] These patients are sometimes started on antianginal medications with no relief of symptoms subsequently. Thus, to decrease the financial burden and to reach the appropriate diagnosis, other mimickers of anginal pain should be thought of, one of them being cervical angina. Physicians and cardiologists should be well-versed with the symptomatology of cervical angina and keep a high index of suspicion while referring any patient with atypical chest pain for further evaluation. In this study, the importance of clinical symptomatology of cervical angina has been emphasized in order to save the patient from unnecessary expenditure of investigations and medications.

It is difficult to determine the cause of chest pain as cervical angina. Cervical angina may present with dull aching to moderately severe type of anterior chest pain with radiation to back, scapular region and arms. Neurological examination is mostly normal except for cases with prominent disk displacement. Thus, it strongly mimics angina pectoris and such patients usually present directly, or are referred, to a cardiologist for ruling out ischemic heart disease.

MATERIAL AND METHODS

A retrospective study was performed in the Dept. of Neurology, SMS Medical College and Hospital, Jaipur, from September 2015 to July 2018. In this study, records of 25 patients who were admitted and diagnosed with noncardiac chest pain after normal cardiac investigations and found unresponsive to antianginal medications who underwent neurological work-up were included.

The patients with true cardiac chest pain, or with any abnormality in cardiac work-up and those with past history of cervical spine surgery were excluded.

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RESULTS

The age of the patients ranged from 40 to 84 years (mean age 57.24 years; Table 1). Out of 25 patients, 10 (40%) patients had neurological cause of chest pain, in which 8 (32%) patients (5 males, 3 females) had cervical nerve root compression and 2 (8%) female patients had carpal tunnel syndrome. One female patient had bilateral carpal tunnel syndrome and 1 female patient had left-sided carpal tunnel syndrome (Table 2). The mean duration of symptoms was 4.36 months. Chest pain accompanied with neck pain was the most common presentation (24%) followed by left arm pain (16%) and shoulder pain (8%) (Table 3). Out of 25 patients, 16 (64%) patients had dull aching type of pain, 8 (32%) patients had radiating type of pain and 1 (8%) patient had burning type of pain (Table 4).

Table 1. Age Group-wise Presentation of Noncardiac Chest Pain

Age group	Number of cases	Percentage (%)
40-50	7	28
51-60	8	32
61-70	9	36
71-80	0	0
81-90	1	4

Table 2. Cause of Noncardiac Chest Pain

Cause	Number of cases	Percentage (%)
Radiculopathy	8	32
Carpal tunnel syndrome	2	8
Non-neurological	15	60

Table 3. Presentation of Noncardiac Chest Pain as Neurological Cause

Presentations	Number of cases	Percentage (%)
Chest pain with neck pain	6	24
Left arm pain	4	16
Chest pain with shoulder pain	2	8

Table 4. Nature of Noncardiac Chest Pain

Nature	Number of cases	Percentage (%)
Dull aching	16	64
Radiating	8	32
Burning	1	8

DISCUSSION

In this study, the patients of chest pain with normal cardiac investigations, i.e., electrocardiography (ECG), 2D echocardiography and coronary angiography who underwent neurological evaluation in the form of electrophysiology and cervical magnetic resonance imaging (MRI) were included. In addition to normalcy of investigations, nonresponse to antianginal medications was a strong criteria to defer the diagnosis of angina pectoris and evaluate the patients for noncardiac causes like cervical angina. In this study, electrophysiology and spinal MRI proved to be useful tools to verify the cause of chest pain as cervical angina.

Our study revealed that cervical angina can have diverse presentations such as cervical radiculopathy and carpal tunnel syndrome. The clinical symptomatology

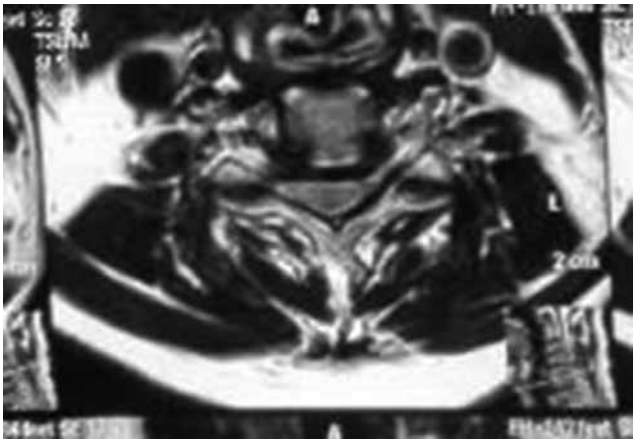

Figure 1. MRI T2W image axial section shows right C5 nerve root compression.

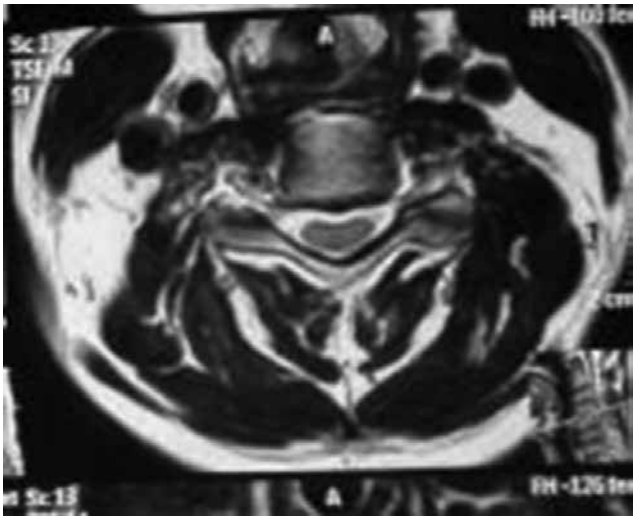

Figure 2. MRI T2W image axial section shows left C6 nerve root compression.

served as a guide to reach to a diagnosis. Patients had associated neck pain, left arm with shoulder pain in addition to chest pain. In many such cases, the clinician gets biased after hearing the symptomatology and suspect a diagnosis of coronary artery disease. Thus, one should keep all symptoms as well as neurological signs in mind before labeling the patient with a particular disease. Radicular pain occurs due to compression of the C5-C8 nerve roots, which carry sensorimotor supply to chest through medial and lateral pectoral nerves. C5-C6 and C6-C7 were the most common sites of pathological nerve root compression in our study (Figs. 1 and 2). MRI cervical spine may show disk desiccation, osteophytes formation, neuroforaminal compression and other age-related degenerative changes. This study demonstrates that cervical angina is an underdiagnosed and unnoticed entity which requires a high index of suspicion for diagnosis to prevent unnecessary financial and psychosocial burden.

CONCLUSION

Cervical angina is a strong mimicker of angina pectoris which requires a careful history taking by the physician and cardiologist. Unnecessary invasive investigations like coronary angiography can be prevented if a high index of suspicion is observed for cervical angina. This will lead to an early diagnosis thus saving the time and expenditure of patient, avoidance of transportation to higher center with catheterization laboratory facility and the most important of all, unnecessary stress to patient and family members.

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Single-Dose Anticoagulant Promising in Knee Replacement

A monoclonal antibody against coagulation factor XI is being studied to prevent venous thromboembolism (VTE) after knee arthroplasty, with a phase II study suggesting that a single, modest dose could be on par with standard therapy.

Factor XI inhibitor osocimab was associated with VTE rates from 15.7% to 29.9% at 10-13 days postoperatively, varying by dose (0.3-1.8 mg/kg) and whether the single IV infusion was given before or after knee replacement surgery, researchers showed in a paper published online in *JAMA*. The three highest postoperative doses showed noninferiority in efficacy against enoxaparin (26.3%) with a noninferiority margin of 5%.

Fractional Flow Reserve Helps CAD Management in Diabetes

Fractional flow reserve (FFR) makes a different impact on treatment decisions if diabetes is involved, registry data showed.

The proportion for which FFR would reclassify the treatment strategy was similar between those with and without diabetes (41.2% vs. 37.5%, p = 0.13) in two merged registries. Compared with controls; however, diabetic patients were more likely to be reclassified from medical therapy to revascularization than the other way around. Among diabetic patients, FFR-based deferral of stenting or surgery resulted in an 8.4% 1-year rate of major adverse cardiovascular events (MACE: all-cause death, MI or unplanned revascularization) compared to 13.1% for those who proceeded with revascularization (p = 0.04). The findings were published in *JAMA Cardiology*.

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Study of Prevalence of Hypothyroidism and Effect of Treatment with L-thyroxine in Patients of Chronic Kidney Disease

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ABSTRACT

Background: There is considerable overlap in the symptoms related to hypothyroidism and advanced chronic kidney disease (CKD), but little is known about the prevalence or severity of thyroid abnormalities in CKD. This study estimated the prevalence of hypothyroidism in CKD patients and investigated the effect of thyroid hormone replacement therapy (THRT) on changes in estimated glomerular filtration rates (eGFR) in the patient population studied. **Objectives:** 1). To estimate the prevalence of hypothyroidism in CKD patients. 2). Effect on progression of chronic renal failure after treatment of hypothyroidism in CKD patients. **Material and methods:** Ours was a descriptive longitudinal study conducted in MLB Medical College, Jhansi, Uttar Pradesh over a period of 1 year, on patients with CKD. A total of 120 CKD patients with serum creatinine levels available at least two times in previous 6 months were enrolled, screened for thyroid function and those detected with hypothyroidism were treated with L-thyroxine. Before and after treatment, comparisons were made and for statistical analysis, paired *t*-test was used for association. **Results:** Out of 120 study subjects, maximum patients were in the age group of 51-60 years (36.67%) with 65% being males and 35% females; 21 (17.5%) were found to have hypothyroidism, 18 (15%) had subclinical hypothyroidism and 3 (2.5%) had overt hypothyroidism. The stage-wise distribution of hypothyroidism in CKD patients was - 15.6% in Stage III, 16.67% in Stage IV and 20% in Stage V. The rate of decline in eGFR over 6 months was significantly reduced from 3.05 ± 2.02 mL/min/1.73 m^2 before the THRT to 1.02 ± 2.5 mL/min/1.73 m^2 after giving thyroid hormone replacement ($p < 0.001$). Among the patients given thyroid hormone replacement for 6 months, 61.9% showed slower decline in eGFR, 19% showed unchanged decline, 9.5% patients showed a faster decline in eGFR and 9.5% patients showed an improvement in eGFR after THRT. **Conclusion:** Hypothyroidism (15% subclinical and 2.5% overt) is a relatively common condition in CKD patients. Prevalence of hypothyroidism increased with progressively lower levels of GFR i.e., declining renal function. THRT attenuated the rate of decline in renal function in CKD patients with hypothyroidism, suggesting that THRT may delay reaching end-stage renal disease in these patients.

Keywords: Hypothyroidism, advanced chronic kidney disease, L-thyroxine, eGFR, THRT

Thyroid hormones are important in cellular growth and differentiation, and modulation of physiological functions in all human tissues including the kidney. They also play a role in maintenance of water and electrolyte homeostasis. Therefore, thyroid dysfunction, either hypothyroidism or hyperthyroidism is accompanied by alterations in the metabolism of water and electrolytes, as well as cardiovascular function. On the other hand, the kidney is an important target organ for thyroid hormone actions and for the metabolism and elimination of the thyroid hormones. Derangement in kidney function is associated with abnormalities in the thyroid hormone physiology.[1] Chronic kidney disease (CKD) affects both hypothalamus-pituitary-thyroid axis and thyroid hormone peripheral metabolism. The effects of impaired kidney function may lead to hypothyroidism, hyperthyroidism and nonthyroidal illness which are associated with deranged cardiovascular function, which will adversely affect the prognosis of CKD.[2]

Replacement of thyroid hormone is fundamental to the treatment of primary hypothyroidism. It relieves the symptoms of hypothyroidism and also alleviates the deleterious effects of overt hypothyroidism on the kidney.[3] Even though previous studies have

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demonstrated that L-thyroxine improves cardiac function and dyslipidemia in patients with subclinical hypothyroidism (SCH),[4,5] there is still a lack of consensus in current guidelines on whether to treat SCH patients with thyroid hormone or not.[6] In particular, little is known about the effect of thyroid hormone replacement on the changes in glomerular filtration rate (GFR) in CKD patients with SCH. The direct impact of thyroid hormone treatment on the changes in GFR in the same individuals with SCH could not be evaluated.[7]

In the present study, we compared the changes in GFR before and after thyroid hormone replacement in the same population of adult CKD patients with hypothyroidism. This study was done to simplify the importance of interactions between thyroid functions and kidney disease. This information is essential as it shows a link between two separate conditions. Information obtained from this study will help to increase clinical knowledge and enable clinicians to provide better management for their patients who have thyroid or kidney dysfunction.

AIMS AND OBJECTIVES

- To estimate the prevalence of hypothyroidism in CKD patients.
- Effect on progression of chronic renal failure after treatment of hypothyroidism in CKD patients.

MATERIAL AND METHODS

Study Design

This was a descriptive longitudinal study and patients detected with hypothyroidism were subjected to before and after comparison studies.

Study Site and Population

This study was conducted on 120 patients of CKD, selected randomly; attending the Nephrology Clinic and admitted in wards of Dept. of Medicine, MLB Medical College, Jhansi, Uttar Pradesh between March 2014 to April 2015. There were no drop outs or deaths during the study.

Methodology

Inclusion Criteria

- Patients with CKD, between 20-75 years of age with serum creatinine levels available at least two times in previous 6 months before the start of study.
- Informed consent.

Case Definition

Kidney damage for more than 3 months, as defined by structural or functional abnormalities of the kidney, with or without decreased GFR that can lead to decreased GFR, manifest by either:

Pathologic abnormalities, *or*

Markers of kidney damage, including abnormalities in the composition of the blood or urine,

Abnormalities in imaging tests.

eGFR <60 mL/min/1.73 m^2 for more than 3 months, with or without kidney damage.[8]

Estimation of eGFR done using the 4 variable MDRD formula:

GFR (mL/min/1.73 m^2) = 175 × [standardized S_{Cr} (micromol/L)]$^{-1.154}$ × [age (years)]$^{-0.203}$ × 1.212 (if black) × 0.742 (if female).

Exclusion Criteria

- Decline consent.
- Patients less than 20 or more than 75 years of age.
- Patients with heavy proteinuria including nephrotic syndrome or terminal malignancy.
- Patients who experienced acute exacerbation of underlying renal insufficiency due to dehydration, radio contrast dye, urinary tract obstruction, etc.
- Patients previously being treated for thyroid disease.

Thyroid function test and definition: In all patients, serum free triiodothyronine (FT3), free thyroxine (FT4) and thyroid-stimulating hormone (TSH) concentrations were measured. These levels were determined by chemiluminescence microparticle immunoassay. The diagnosis of SCH was solely based upon the results of a thyroid function test and was defined as a normal serum FT4 but elevated TSH levels, irrespective of clinical symptoms of hypothyroidism. Normal reference changes FT3 = 2.30-4.20 pg/mL, FT4 = 0.89-1.75 ng/dL and fTSH = 0.55-4.780 IU/mL.

Treatment of hypothyroidism and CKD: All the patients with SCH took L-thyroxine, initially administered at lowest doses necessary to normalize serum TSH levels, which was 25 µg daily. Patients with overt hypothyroidism were prescribed L-thyroxine at 50 µg daily dose. The dose of L-thyroxine was adjusted every 3 months according to the follow-up levels of TSH. The treatment of CKD was continued as before the start of study: the patients on conservative management

were prescribed oral hematinics, calcium supplements and antihypertensives and oral hypoglycemic agents (OHAs) if required, and the patients who were earlier on hemodialysis were continued with the same.

STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS trial version. The data was entered into Microsoft Excel Software. Continuous variables were expressed as mean ± standard deviation (SD) and categorical variables as number (percentage). We compared patients' clinical and biochemical parameters at following time points: 6 and 3 months before L-thyroxine, time of initiation of thyroid hormone supplement and at 3 and 6 months after L-thyroxine treatment. For association, paired *t*-test was applied and p value <0.001 was considered statistically significant.

OBSERVATIONS AND RESULTS

The distribution of study subjects was done according to the age (20-75 years) with maximum study subjects in the age group of 51-60 years (36.67%), with 65% being males and 35% females, stage-wise distribution of study subjects showed majority of participants in Stage IV (40%) followed by Stages III and V (36.67% and 33.33%, respectively). None of the study subjects included were in Stage I or II. Among the study subjects, 75% were on conservative management and 25% were on hemodialysis.

The primary disease process, leading to CKD was DM II (36.67%), followed by hypertension (25%), obstructive uropathy (15%), glomerulonephritis (11.67%), cystic diseases (3.33%) and other causes (8.33%).

Twenty-one subjects, out of 120 study subjects were found to have hypothyroidism (17.5%) out of which 3 were overt hypothyroid (2.5%) and 18 were subclinical hypothyroid (15%) (Table 1).

The distribution of hypothyroidism stage-wise in CKD showed an increasing prevalence of hypothyroidism with decline in eGFR - 15.6% in Stage III, 16.67% in Stage IV and 20% in Stage V (Table 2).

Hypothyroidism was found to be more common in females (19.04%) as compared to males (16.66%) (Table 3). The prevalence of hypothyroidism was 18.88% in patients with conservative management and 13.33% in study subjects on hemodialysis.

The rate of decline in eGFR over 6 months was significantly reduced from 3.05 ± 0.02 mL/min/1.73 m^2

Table 1. Thyroid Profile in CKD Patients

	Euthyroid	Overt hypothyroid	Subclinical hypothyroid
No. of subjects	99	3	18
Percentage (%)	82.50	2.50	15.0

Table 2. Stage-wise Distribution of Hypothyroidism in CKD Patients

	Stage I	Stage II	Stage III	Stage IV	Stage V
Total No. of subjects	0	0	32	48	40
No. of hypothyroid subjects	0	0	5	8	8
Percentage of hypothyroidism	0	0	15.6	16.67	20

Table 3. Gender Distribution of Hypothyroidism in CKD Patients

Gender	Total No. of subjects	No. of hypothyroid subjects	Hypothyroidism (%)
Male	78	12	16.66
Female	42	8	19.04

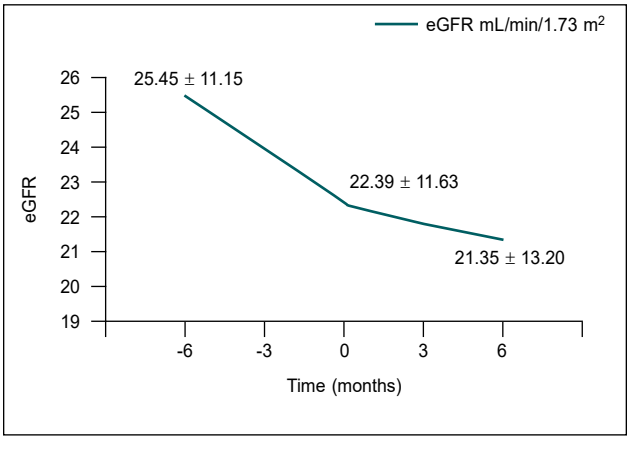

Figure 1. Comparison of rate of decline in eGFR before and after THRT.

Table 4. Changes in eGFR Overtime in CKD Patients

	-6	-3	0 (Baseline)	+3	+6
eGFR mL/min/1.73 m^2	25.45 ± 11.15	23.92 ± 11.56	22.39 ± 11.63	21.76 ± 12.14	21.35 ± 13.2

Table 5. Comparison of Rate of Decline in eGFR Before and After THRT

	6 months before THRT (-6 to 0 months)	6 months after THRT (0 to 6 months)	P value
Rate of decline of eGFR in mL/min/1.73 m^2 in 6 months	3.05 ± 0.02	1.02 ± 2.5	<0.001

before the thyroid hormone replacement therapy (THRT) to 1.02 ± 2.5 mL/min/1.73 m^2 after giving thyroid hormone replacement ($p < 0.001$) (Fig. 1 and Tables 4 & 5).

DISCUSSION

The presented study was conducted in Dept. of Medicine, MLB Medical College, Jhansi, Uttar Pradesh in 120 subjects from March 2014 to April 2015. The subjects were of CKD, distributed according to the age groups starting from 20 years of age, up to 75 years of age, with maximum study subjects in the group of 51-60 years (36.67%).

Of these, 78 (65%) were males and 42 (35%) were females. Classification of CKD into different stages in this study was done as per the National Kidney Foundation guidelines, with eGFR using the 4 variable Modification of Diet in Renal Disease (MDRD) formula.[8] Majority of the participants were CKD Stage IV (40%). Number of participants in CKD Stages III and V were 26.67% and 33.33%, respectively. None of the participants sampled were in CKD Stage I or II. This could be attributed to delay in seeking medical treatment; hence, patients were seen when the disease had progressed to more severe stages. According to the 2003-2006 National Health and Nutrition Examination Survey (NHANES) data of US adults more than 20 years of age, 15.32% is the most recent CKD prevalence with estimated stage-wise prevalence - Stage I (4.1%), Stage II (3.2%), Stage III (6.5%) and Stage IV+V (0.6%).[9]

Among the 120 patients of CKD included in the study, 90 subjects (75%) were on conservative management and 30 subjects (25%) were on hemodialysis.

Among the primary disease processes leading to CKD, the most common cause was found to be DM II (36.67%), followed by hypertensive nephrosclerosis (25%), glomerulonephritis (11.67%), obstructive uropathy (15%), cystic disease (3.33%) and other causes including human immunodeficiency virus (HIV) infection, pyelonephritis and cardiomyopathies (8.33%). These results were in concordance with NHANES 2003-2006 data of US, except the percentage prevalence of obstructive uropathy, which was found to be higher in our study subjects of Bundelkhand region.

In our study, the prevalence of hypothyroidism was found to be 17.5% i.e., 21 subjects including 18 subjects of SCH (i.e., 15%) and 3 subjects of overt hypothyroidism (i.e., 2.5%). The stage-wise distribution of hypothyroidism in CKD patients showed the prevalence of hypothyroidism to be 15.6% in Stage III, 16.67% in Stage IV and 20% in Stage V. We concluded that the prevalence of hypothyroidism increased with lower levels of eGFR. This was in concordance with previous study done by Lo et al,[10] who used data from NHANES III and revealed the prevalence of hypothyroidism, occurring in 10.9% of patients with Stage II CKD, 21% with Stage III CKD and 23.1% with Stage IV or V CKD. Among these hypothyroidism patients, 56% were considered subclinical. Moreover, Chonchol et al[11] showed that the prevalence of SCH increased from 7% at an eGFR >90 mL/min/1.73 m^2 to 17.9% at an eGFR <60 mL/min/1.73 m^2 in 3,089 outpatient adults.

In our study, the prevalence of hypothyroidism was found to be more in females (19.04%) as compared to males (16.66%). This was not in concordance with previous studies. Study among 137 subjects concluded at Kenyatta National Hospital, Kenya concluded that there was no statistically significant difference between prevalence of hypothyroidism in males and females. A study conducted by Allawi et al[12] on prevalence of hypothyroidism concluded it to be more in males (20%) as compared to females (6%). In relation to the type of treatment in CKD, the prevalence of hypothyroidism was found to be 18.88% on patients with conservative management and 13.33% in patients on hemodialysis.

At the time of commencement of thyroid hormone therapy in 21 hypothyroid subjects, the baseline characteristics are shown in Table 6.

The overall rate of decline in eGFR over 6 months was significantly blunted from 3.05 ± 2.02 to 1.02 ± 2.5 (mL/min/1.73 m^2) ($p < 0.001$) by THRT. The numbers of patients who had a slower fast or unchanged eGFR decline after THRT were determined, 61.9% patients had a slower decline in eGFR, 19% had unchanged decline, 9.5% had a faster decline and 9.5%

Table 6. Baseline Characteristics of Patients at the Time of Commencement of THRT

	Total (n = 21) (mean ± SD)
Age	44.1 ± 8.41
Men	13
Women	8
DM II	4
HTN	11
Obstructive uropathy	2
Others	4
SBP	136.57 ± 19.15
DBP	82.19 ± 9.44
Thyroid function test	
FT3	2.33 ± 0.49
FT4	0.89 ± 0.32
Serum TSH	9.32 ± 3.52
Kidney function test	
Serum creatinine	3.56 ± 1.39
eGFR	22.39 ± 11.63
Serum albumin	3.34 ± 0.42

DM II = Diabetes mellitus II; HTN = Hypertension; SBP = Systolic blood pressure; DBP = Diastolic blood pressure; FT3 = Free triiodothyronine; FT4 = Free thyroxine; TSH = Thyroid-stimulating hormone; eGFR = Estimated glomerular filtration rate.

patients showed an improvement in eGFR after thyroid replacement.

Among the patients who had a slower decline and improvement in eGFR, 20% (i.e., 3 patients) were of DM II, 53.3% (i.e., 8 patients) had systemic hypertension and 26.7% patients had other etiologies. These results were in concordance with the previous studies conducted.

A study conducted by Shin et al[13] on 113 CKD patients with SCH showed similar results with rates of decline in eGFR significantly attenuated by THRT (−4.31 ± 0.5 vs. −1.08 ± 0.36) ($p < 0.001$), but there was no significant change in serum FT3 and FT4 levels. Slower decline in eGFR was seen in 63.7% patients in this study. A similar study by Shin et al[7] conducted previous to the above mentioned study also demonstrated that thyroid hormone replacement preserved renal function, but in that study, the changes in eGFR were just compared between two different study populations, SCH patients with and without THRT. A study by Hataya et al[14] showed that eGFR increased rapidly over first 6 months after THRT in CKD patients, followed by a plateau. The improvement in eGFR was up to 30% overall.

CONCLUSION

The present study concluded that thyroid impairment in the form of hypothyroidism is common in CKD patients with SCH being more common and the prevalence of hypothyroidism increases with decline in eGFR levels. Since, thyroid dysfunction can cause significant changes in renal and cardiovascular functions, there is an increasing need to detect hypothyroidism earlier in CKD patients and to initiate early treatment to prevent morbidity and mortality associated. This study emphasized the role of THRT in patients of CKD with subclinical and overt hypothyroidism, as this alleviates the rate of decline in eGFR in these patients and may delay reaching end-stage renal disease in these patients.

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Sleep Problems in Older Adults Linked to Cognitive Decline and Dementia

People who have trouble falling asleep may be at increased risk of developing cognitive problems or dementia than their counterparts who sleep well, a research review suggests.

Researchers examined data on 51 previously published studies that followed middle-aged and older people in North America, Europe and East Asia for at least several years to see if sleep issues were associated with cognitive health over time. Individuals with insomnia were 27% more likely to develop cognitive problems, the study found. People who had sleep inadequacy, or an insufficient amount of quality rest, were 25% more likely to develop dementia, the researchers found… (*Reuters*)

Prostate Cancer: Adverse Effects Favor Less Invasive Tx Over Surgery

Men undergoing radical prostatectomy for localized prostate cancer had persistently worse adverse effects from treatment compared to those managed with surveillance or radiation, a large prospective cohort study found.

Among the more than 2,000 men in the study, few functional differences were seen at 5 years between the different treatment options, but sexual function and urinary incontinence remained worse for the group treated with prostatectomy compared to those on either active surveillance or external beam radiation therapy (EBRT) *plus* androgen deprivation therapy (ADT), reported Karen E Hoffman, MD, MHSc, MPH, of MD Anderson Cancer Center in Houston, and colleagues. The findings were published in *JAMA*.

Bad News on Anti-HER2 Heart Effects

Cardiotoxicity related to trastuzumab appeared to persist over a median follow-up of 7 years, a small cross-sectional, case-control study indicated.

In 22 patients who developed cardiotoxicity in the form of long-term impairment in cardiorespiratory fitness (CRF) (TOX group) during trastuzumab treatment, the resting mean left ventricular ejection fraction (LVEF) was significantly lower, at 56.9% compared with 62.4% in the 20 patients who had no evidence of cardiotoxicity during trastuzumab treatment (NOTOX group) and 65.3% among 15 healthy controls ($p < 0.001$ for both endpoints), reported Anthony Yu, MD, of Memorial Sloan Kettering Cancer Center (MSKCC) in New York City, and colleagues in *JAMA Cardiology*.

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Fasting Serum Magnesium Levels in Patients with Uncontrolled and Controlled T2DM in Relation to Its Complications

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ABSTRACT

Background: Magnesium deficiency is proposed factor in pathogenesis of diabetic complications. Hypomagnesemia can be both a cause and consequence of diabetic complications. **Objective:** The aim of our study was to know the relationships between magnesium levels and diabetes its association with level of control of diabetes. **Study design:** This study was done in MVJ Medical College and Research Hospital, Hoskote, Bangalore. A total of 75 cases of type 2 diabetes mellitus (T2DM) were taken for study after satisfying the inclusion and exclusion criteria and also 35 nondiabetic patients admitted during this period were also included in this study under control group. All the patients were evaluated in detail including fasting blood sugar (FBS), postprandial blood sugar (PPBS), glycated hemoglobin (HbA1c) and fasting serum magnesium levels were estimated by using Calmagite method. **Results:** The serum magnesium among cases and controls are 1.88 ± 0.28 mg/dL and 2.10 ± 0.29 mg/dL, respectively. The mean serum magnesium levels in patients with controlled diabetes were 2.04 mg/dL, while they were 1.73 mg/dL in uncontrolled T2DM. Significant association was found between hypomagnesemia and diabetic retinopathy and nephropathy. **Conclusion:** There was significant reduction in serum magnesium levels in diabetics compared to controls. There was significant correlation between magnesium levels and levels of control in diabetics. Uncontrolled diabetics had low levels of serum magnesium. Duration of diabetes and high levels FBS also had an association with low magnesium levels. Low magnesium levels were mainly associated with diabetic retinopathy and nephropathy.

Keywords: Type 2 diabetes mellitus, magnesium, diabetic nephropathy, diabetic retinopathy

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Several distinct type of DM are caused by a complex interaction of genetics and environmental factors. Depending upon etiology of DM, factors contributing to hyperglycemia include reduced insulin secretion, decreased glucose utilization and increased glucose production. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems such as microvascular (retinopathy, nephropathy, neuropathy) and macrovascular (coronary heart disease, peripheral arterial disease, cerebrovascular disease).[1]

Low magnesium status has repeatedly been demonstrated in patients with type 2 diabetes. Magnesium deficiency appears to have a negative impact on glucose homeostasis and insulin sensitivity in patients with type 2 diabetes.[2]

Magnesium deficiency has been found to be associated with microvascular disease in diabetes. Hypomagnesemia has been demonstrated in patients with diabetic retinopathy, lower levels of magnesium more is the risk for diabetic retinopathy. Magnesium depletion has also been associated with arrhythmogenesis, vasospasm, platelet activity and hypertension.[3]

The reason why magnesium deficiency occurs in diabetes are not clear but may include increased urinary loss, lower dietary intake or impaired absorption of magnesium compared to nondiabetic individuals.[4]

Low dietary intake can also contribute to hypomagnesemia in diabetics. Patients with type 2 diabetes

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are often overweight and may consume a diet higher in fat and lower in magnesium than nondiabetics.[5,6]

The present study was undertaken to know the relationships between magnesium levels and diabetes and association with level of control of diabetes.

MATERIAL AND METHODS

Patients with type 2 diabetes admitted in MVJ Medical College and Research Hospital, Hoskote, Bangalore for a period of 1 year were included in the study. A total of 75 cases of type 2 diabetes mellitus (T2DM) were taken for study and also 35 nondiabetic patients admitted during this period were also included in this study under control group. All the patients were evaluated in detail including fasting blood sugar (FBS), postprandial blood sugar (PPBS), glycated hemoglobin (HbA1c) and fasting serum magnesium levels were estimated by using Calmagite method.

Inclusion Criteria

All cases of T2DM and age- and sex-matched nondiabetic patients admitted to MVJ Medical College and Research Hospital, Hoskote, Bangalore.

Exclusion Criteria

Patients with:

- Chronic renal failure
- Acute myocardial infarction in last 6 months
- Malabsorption or chronic diarrhea
- History of alcohol abuse
- Hypertension, proteinuria, eclampsia
- History of epilepsy
- Patients on diuretics and receiving magnesium supplements or magnesium containing antacids.

STATISTICAL METHOD

T-test was used to find the significance of mean pattern of serum magnesium between cases/controls, controlled/uncontrolled. Analysis of variance (ANOVA) was used to find the mean pattern of serum magnesium in different complications in different range of FBS.

RESULTS

A comparative study consisting of 75 diabetics and 35 controls was conducted to find serum magnesium in DM cases when compared to controls and magnesium levels in relation to complications.

The mean age of diabetics was 59.56 ± 9.70 and 58.66 ± 10.26 was that of controls (Table 1). The mean serum magnesium levels in cases and controls was 1.88 mg/dL and 2.1 mg/dL, respectively with p value of <0.003, which was statistically significant (Table 1). Hypomagnesemia was seen in 38.6% of the cases, whereas only 2.9% of controls had hypomagnesemia (Table 1).

Mean serum magnesium levels among uncontrolled DM were lower as compared to patients with controlled DM (Table 2).

Mean serum magnesium levels in patients with and without diabetic retinopathy was 1.77 mg/dL and 2.01 mg/dL, respectively, showing that patient with diabetic retinopathy had significantly lower levels of serum magnesium compared to those without retinopathy ($p < 0.0006$) (Table 3). The mean serum magnesium levels in patients with and without diabetic neuropathy were 1.80 mg/dL and 2.09 mg/dL, respectively, which were statistically significant ($p < 0.0002$) (Table 3).

The mean serum magnesium levels in patients with and without diabetic neuropathy were 1.92 mg/dL and 1.83 mg/dL, respectively, which were not statistically significant ($p < 0.2120$) (Table 3). The mean serum magnesium levels in patients with and without ischemic heart disease (IHD) were 1.81 mg/dL and 1.92 mg/dL, respectively, which were not statistically significant ($p < 0.139$) (Table 3).

Table 1. Age, Sex, Mean FBS, Mean Serum Magnesium Among Cases and Controls

	Cases (n = 75)	Controls (n = 35)	P value
Mean age	59.56 ± 9.70	58.66 ± 10.26	
Sex			
Male	57.33%	57.14%	
Female	42.67%	42.86%	
Mean FBS (mg/dL)	206.33 ± 14.89	94.86 ± 11.78	0.0001
Mean serum magnesium (mg/dL)	1.88 ± 0.28	2.1 ± 0.29	<0.003
Serum magnesium			
<1.8	29 (38.6%)	1 (2.9%)	
1.8-2.5	45 (60.0%)	32 (91.4%)	
>2.5	1 (1.4%)	2 (5.7%)	

Table 2. Effect of Level of Control of DM on Serum Magnesium

Serum magnesium (mg/dL)	Controlled diabetes (n = 37)	Uncontrolled diabetes (n = 38)
Range (min-max)	1.5-2.7	1.1-2.1
Mean ± SD	2.04 ± 0.29	1.73 ± 0.23

P < 0.001

Table 3. Serum Magnesium Levels in Patients With and Without Retinopathy, Nephropathy, Neuropathy and IHD

Serum magnesium (mg/dL)	Mean ± SD	P value
Retinopathy	1.77 ± 0.22	<0.0006
NPDR (n = 23)	1.86 ± 0.25	
PDR (n = 16)	1.63 ± 0.20	
No retinopathy	2.01 ± 0.31	
Proteinuria (n = 53)	1.80 ± 0.28	<0.0002
Microalbuminuria (n = 35)	1.86 ± 0.29	
Macroalbuminuria (n = 18)	1.67 ± 0.20	
No proteinuria (n = 22)	2.09 ± 0.27	
Neuropathy	1.92 ± 0.32	<0.212
No neuropathy	1.83 ± 0.27	
IHD (n = 51)	1.81 ± 0.28	<0.139
No IHD (n = 24)	1.92 ± 0.32	

NPDR = Nonproliferative diabetic retinopathy; PDR = Proliferative diabetic retinopathy; IHD = Ischemic heart disease.

Mean serum magnesium levels in patients with one complication, two complications and three complications was 2.07 mg/dL, 1.79 mg/dL and 1.74 mg/dL, respectively, which means that as the number of complications increase mean serum magnesium levels decrease (Table 4).

Mean serum magnesium levels in higher FBS range was low as compared to low FBS range i.e.: in range 130-180 mg/dL, 181-230 mg/dL, 231-280 mg/dL, 281-330 mg/dL, they were 2.2 mg/dL, 1.76 mg/dL, 1.80 mg/dL, 1.73 mg/dL, respectively (Fig. 1).

Serum magnesium levels were low when HbA1c was on higher side i.e.: When HbA1c was >9.80 then serum magnesium level was <1.7 mg/dL and when HbA1c was <7.20 then serum magnesium level was >1.7 mg/dL (Table 5).

Table 4. Comparison of Serum Magnesium Levels According to the Number of Complications

Serum magnesium (mg/dL)	One complication (n = 25)	Two complications (n = 35)	All three (n = 13)
Mean ± SD	2.07 ± 0.30	1.79 ± 0.25	1.74 ± 0.29

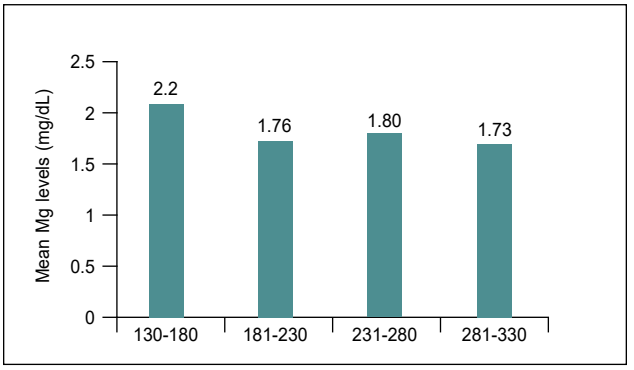

Figure 1. Comparison of serum magnesium levels according to different ranges of FBS.

Table 5. Comparison of Serum Magnesium Levels in Relation to HBA1c Levels

Serum magnesium (mg/dL)	<1.7	≥1.7
HbA1c	9.80 ± 1.75	7.20 ± 0.70

P < 0.001

Table 6. Comparison of Serum Magnesium Levels in Relation to Duration of Diabetes

Serum magnesium (mg/dL)	0-5 years (n = 17)	6-10 years (n = 39)	11-15 years (n = 12)	16-20 years (n = 7)
Mean ± SD	2.00 ± 0.36	1.90 ± 0.27	1.71 ± 0.29	1.78 ± 0.20

Mean serum magnesium levels according to the duration of diabetes i.e.: 0-5, 6-10, 11-15 and 16-20 years were 2.00, 1.90, 1.52 and 1.78 mg/dL, respectively (Table 6).

DISCUSSION

The present study included 75 diabetics and 35 nondiabetics. Serum magnesium levels were determined in all the subjects.

The present study had diabetic patients whose ages ranged for 41-80 years, which was consistent with study done by Biradar et al.[7]

Mean age	Cases	Controls
Biradar et al	55.42 ± 12.65	55.58 ± 12.84
Present study	59.56 ± 9.70	58.66 ± 10.26

Male patients in cases and controls were 57.3% and 57.14%, respectively and females were 42.6% and 42.8%, respectively.

Mean serum magnesium	Cases	Controls	P value
Mean ± SD	1.88 ± 0.28	2.10 ± 0.29	<0.003

In this study, serum magnesium levels were more in controlled group as compared to uncontrolled group, which was consistent with the study done by Jain et al.[8]

Mean serum magnesium levels (Mean ± SD)	Controlled diabetes	Uncontrolled diabetes
Jain et al	1.85 ± 0.08	1.68 ± 0.12
Present study	2.04 ± 0.29	1.73 ± 0.23

In present study, there was no any significant association between age and sex but duration of diabetes had a relation with serum magnesium levels; patients with duration of diabetes more than 5 years had a lower serum magnesium levels as compared to those with a duration less than 5 years.

In our study also significantly lower levels of serum magnesium were observed in diabetics with microvascular complications.

Hypomagnesemia has been reported in patients with diabetic retinopathy. Lower the level of serum magnesium greater is the risk of severe diabetic retinopathy, which was consistent with study done by Kauser et al and Mirza Shariff et al.[9,10]

Mean serum magnesium levels (mg/dL)	Retinopathy	No retinopathy
Kauser et al	1.79 ± 0.15	2.25 ± 0.16
Mirza Shariff et al	1.28 ± 0.30	1.60 ± 0.40
Present study	1.76 ± 0.23	2.01 ± 0.31

The mechanism by which hypomagnesemia predisposes to retinopathy is unclear. Grfton et al[11] have proposed the inositol transport theory to explain this association. But exact reason remains obscure.

Mean serum magnesium (mg/dL)	Microalbuminuria	Macroalbuminuria
Rao et al	2.0 ± 0.24	1.80 ± 0.20
Present study	1.86 ± 0.29	1.67 ± 0.20

Above Box shows that patients with macroalbuminuria had a lower serum magnesium level as compared to patients with microalbuminuria.[12]

There was no association seen with magnesium levels in patients with neuropathy. There was a correlation between serum magnesium levels and number of complications.

Patients with only one complication had mean serum magnesium level of 2.07 ± 0.03 mg/dL and patient with two complications had a mean of 1.79 ± 0.25 mg/dL and those with three complications had a mean of 1.74 ± 0.29 mg/dL.

Patient with more than one complication had much lower serum magnesium levels, indicating more the complications, lesser the magnesium levels.

CONCLUSION

- Serum magnesium levels were low in type 2 diabetics when compared to controls.
- Levels of serum magnesium were further lowered in uncontrolled type 2 diabetics than those in whom diabetes was controlled.
- Hypomagnesemia was associated with diabetic retinopathy and diabetic nephropathy.
- No correlation was found in respect to neuropathy and IHD.
- More the duration of diabetes and the levels of FBS, lower was the serum magnesium levels.
- Hypomagnesemia is a factor in type 2 diabetes and associated with various complications and duration of diabetes leading to various complications. Hence, it is worth measuring serum magnesium levels in patients with T2DM and probably correlate their relationship with various complications.

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■■■■

Dasatinib Superior to Imatinib in Pediatric ALL

In a head-to-head phase III trial out of China, dasatinib outperformed imatinib for survival in kids with Philadelphia chromosome-positive acute lymphoblastic leukemia (ALL), and proved superior in other oncologic outcomes.

Among 189 eligible patients undergoing intensive chemotherapy for their newly diagnosed disease, 71% of those randomized to dasatinib were alive and relapse free at 4 years, as compared to 49% of those assigned to imatinib mesylate (p = 0.005), Ching-Hon Pui, MD, of St. Jude Children's Research Hospital in Memphis, Tennessee and colleagues reported in *JAMA Oncology*.

2019 Second Hottest Year on Record, UN Confirms

Last year was the second warmest year on record, the World Meteorological Organization (WMO) confirmed.

"The average global temperature has risen by about 1.1°C since the pre-industrial era and ocean heat content is at a record level," said WMO Secretary-General Petteri Taalas. "On the current path of carbon dioxide emissions, we are heading towards a temperature increase of 3-5°C by the end of century." WMO added that 2019 and the past decade were characterized by retreating ice, record sea levels, increasing ocean heat and acidification and extreme weather, all of which have "major impacts" on human health and the natural environment… (*UN*)

Weight Loss Drug Lorcaserin Tied to "Possible Increased Risk of Cancer," FDA Says

The US FDA warns that prescription weight loss medicine lorcaserin might be associated with an increased risk of cancer.

The findings were the result of a clinical trial assessing the safety of the drugs lorcaserin, the FDA announced recently. "At this time, the cause of the cancer is uncertain, and we cannot conclude that lorcaserin contributes to the cancer risk. However, we wanted to make the public aware of this potential risk. We are continuing to evaluate the clinical trial results and will communicate our final conclusions and recommendations when we have completed our review," the FDA said in its announcement… (*CNN*)

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Indian Journal of Clinical Practice, Vol. 30, No. 9, February 2020

Foreign Body Metal Safety Pin in Nasopharynx

HIMANSHU THAKKAR

ABSTRACT

Cases of foreign body in nasopharynx are rarely encountered as they present with vague set of symptoms. We encountered a 1½-year-old female child with a history of putting safety pin in her right nostril. On X-ray skull lateral view, it was found in nasopharynx and was endoscopically removed immediately.

Keywords: Safety pin, nasopharynx, unique foreign body, X-ray nasopharynx

Foreign body ingestion and inhalation is a very common problem in children but foreign body in nasopharynx via nasal route in such a young age (1-1½ years) is very uncommon as diameter of nostril is very narrow at the age of 1½ year and when a child puts something in the nose, it remains stuck to the nose only. However, we present a case wherein a child lodged a safety pin in her nose and when her mother tried to catch it, the child immediately took a deep breath and the big safety pin went back in the nose and got stuck in a very deep part. Its one end was below posterior part of inferior turbinate and other end was in nasopharynx. Here we are going to discuss the case of foreign body in the nasopharynx of a 1 ½-year-old girl, how it presented to us and how we managed the case in emergency.

CASE REPORT

A 1½-year-old female child was admitted to our hospital with the history of foreign body in right nose. Parents gave history of accidental lodgement of foreign body (safety pin) in her right nostril by the child herself while playing at home.

On examination, there was no stridor or chest retraction. The oral cavity and oropharynx were normal and no foreign body was found. On anterior rhinoscopy, no foreign body was seen but there was minimal mucoid discharge in the nose. X-ray skull lateral view with neck was ordered to confirm the presence and position of the foreign body. The X-ray showed the presence of the metal safety pin that was lodged in nasopharynx (Fig. 1). What is unique about this case is the very young

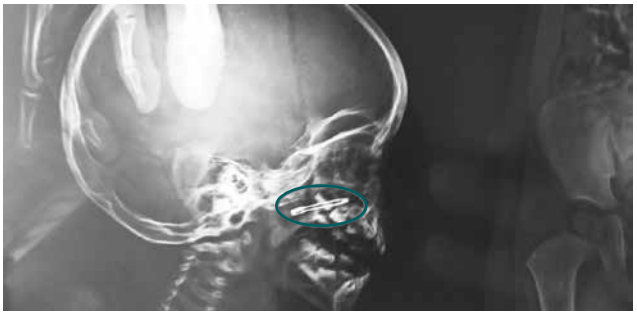

Figure 1. X-ray skull lateral view with neck showing metallic foreign body in the nasopharynx just above the soft palate. X-ray showed a radio-opaque foreign body (likely to be a safety pin) in the nasopharynx along the floor.

Figure 2. Foreign body safety pin removed from nasopharynx (Size approx. 3 cm).

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age of child (1½ year old); nature of foreign body, i.e., metal safety pin; site of lodgement of foreign body, that is nasopharynx; route of entry of foreign body, that is right nostril - a very narrow passage for such a big foreign body; and size of the foreign body - approximately 3 cm. We took the patient in operation theater and under general anesthesia, with the help on nasal endoscope, we removed metal safety pin from nasopharynx through nasal route (Fig. 2). The nasal endoscope was introduced through right nostril. One end of the pin that lied below posterior part of inferior turbinate was grasped with forceps and the safety pin, approximately 3 cm in size, was removed.

Postoperatively, there were no complications and the patient was discharged on the same day.

DISCUSSION

The presence of the foreign body in nasopharynx is a rare entity. In our case, the foreign body (safety pin) was present in nasopharynx. But the mode of entry of foreign body was through very narrow passage of right nostril. The size of foreign body was approximately 3 cm. We removed such a big foreign body endoscopically through nose. The child was very young - only 1½ year old. During procedure the pin might slip, it might open, and then it might slip down and get stuck to the larynx. However, despite all such possibilities and difficulties, we removed the pin endoscopically through nose without any complications. In addition to X-ray of the chest, X-ray skull lateral view including nasopharynx with neck is an important radiological investigation as X-rays are usually diagnostic for radio-opaque foreign bodies.

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Fourteen Percent of India's Under-Five Deaths Due to Pneumonia, Says Report

Fourteen percent of under-five deaths in India, approximately 1,27,000 deaths per year, occur due to pneumonia. In 2013, this figure was about 1,78,000.

Half of these deaths are estimated to occur in the northern belt of the country. The current pneumonia mortality rate is five per 1,000 live births and the target is to reduce this to less than three by 2025, says a new report… (*The Indian Express*)

Diuretic a Promising Treatment for Autism

Loop diuretic bumetanide seems to improve some of the core behavioral symptoms of autism by decreasing levels of the neurotransmitters gamma-aminobutyric acid (GABA), suggests new research published online January 27 in *Translational Psychiatry*.

Investigators noted that young children with autism spectrum disorder (ASD) treated with the diuretic for 3 months scored better on a behavior scale measuring emotional response as well as verbal and nonverbal communication compared with children taking a placebo.

Quick, No-Shock Cardioversion for Afib Feasible in EDs

Pharmacological- and electrical-first cardioversion seem to work similarly well for treating acute atrial fibrillation (Afib) in the emergency department, suggests the Canadian RAFF2 trial.

Investigators noted that the 204 people randomized to IV procainamide (*plus* electrical cardioversion if necessary, with up to three shocks) showed a 96% rate of conversion to sinus rhythm that was maintained for at least 30 minutes. Likewise, the shock-only arm (192 people; electrical conversion alone) had sinus rhythm restored in 92% (p = 0.07). The findings are published in the February 1 issue of *The Lancet*.

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

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"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

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Shalin Kataria
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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.

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Post-Dengue Guillain-Barre Syndrome: A Rare Association

MAHESH DAVE*, SHUBHAM KUMAR SHARMA†, JITENDRA SINGH CHAUDHARY‡

ABSTRACT

Dengue fever is a vector-borne disease, transmitted by female mosquito *Aedes aegypti*. The common symptoms may be in the form of high-grade fever, headache, periorbital pain, myalgia, arthralgia, fatigue, nausea, vomiting and skin rashes in mild cases to renal, hepatic, hemorrhagic tendencies, shock and neurological involvement in severe cases. Incidences of neurological symptoms varied from 0.5% to 21% in recent years. Guillain-Barre syndrome (GBS) may be one of the rare presentations following dengue viral infection with only 20 cases of GBS reported worldwide and most of the cases being in pediatric age group, whereas very few cases have been reported in adults. Hence, we are reporting a case of a 24-year-old male presenting with GBS, which occurred during recovery phase of dengue fever.

Keywords: Dengue fever, *Aedes aegypti*, Guillain-Barre syndrome

Dengue fever is a common vector-borne disease, transmitted by female mosquito *Aedes aegypti*. It is also called break-bone fever, caused by dengue virus which is an RNA virus, and belongs to Flaviviridae family, genus Flavivirus. There are 5 serotypes of dengue virus (DEN1, DEN2, DEN3, DEN4 and DEN5). Fifth serotype was announced in 2013.[1] Dengue fever has worldwide distribution but is predominantly seen in tropical and subtropical countries, like India. The World Health Organization (WHO) estimates an annual incidence of approximately 50 million infections, with approximately 5,00,000 people with dengue hemorrhagic fever. For the past 10 years, incidences of dengue fever are constantly increasing in India and from 1998 to 2009, 82,320 cases (6.32 per million population) were reported, which increased to 2,13,601 cases (34.8 per million population) from 2010 to 2017.

Dengue fever may present with variable symptoms which usually begin 4-6 days after infection and last for up to 10 days. These symptoms may be in the form of high-grade fever, headache, periorbital pain, myalgia, arthralgia, fatigue, nausea, vomiting and skin rashes (3-5 days after onset of fever) in mild cases to renal, hepatic, hemorrhagic tendencies, shock and neurological involvement in severe cases.

Incidences of neurological symptoms varied from 0.5% to 21% in recent years.[2,3] These may be in the form of encephalitis, meningoencephalitis, stroke, cerebellar syndromes, transverse myelitis and Guillain-Barre syndrome (GBS).

GBS may be one of the rare presentations following dengue viral infection and only 20 cases of GBS have been reported worldwide with most of the cases being in pediatric age group, and very few cases reported in adults.[4,5] Hence, we are reporting a case of GBS which occurred during recovery phase of dengue fever.

CASE REPORT

A 24-year-old male patient was admitted in medical ward with history of fever, headache, body ache, nausea, vomiting and retro-orbital pain for last 2 days. He was examined and found to have mild throat congestion without hepatosplenomegaly, chest was clear and there were no signs of meningeal irritation. For above febrile illness, patient was investigated and was found to have mild leukopenia (3,200/mm^3) with thrombocytopenia (48,000/mm^3). Malaria Parasite Quantitative Buffy Coat Test (MPQBC) and Scrub typhus serology was negative but Dengue serology (NS1 antigen) was found positive.

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Patient responded well with symptomatic therapy and hence was discharged after 5 days of admission. He remained asymptomatic for 2 days after discharge and then suddenly developed weakness of both the lower limbs, which progressed rapidly to involve both upper limbs over a period of 6-10 hours to the extent that he was not able to move the limbs and get up from lying down posture. He was readmitted in our ward and was further investigated, which revealed that he had history of paresthesia and numbness in both extremities without cranial nerve and bladder-bowel involvement. Patient was examined thoroughly and was found to have normal vital signs. Neurological examination revealed normal mental function and cranial nerves. Motor system examination revealed hypotonia in all 4 limbs, power 1/5 in both lower limbs, whereas 2/5 in both upper limbs. Deep tendon reflexes (DTR) were absent in both upper and lower limbs, plantars were found flexor bilaterally. Sensory system and other neurological examination including signs of meningeal irritation were found normal.

On the basis of history and clinical examination, we made our provisional diagnosis of post-Dengue GBS.

For confirmation of the above diagnosis, patient was investigated extensively which revealed that complete blood count (platelet 1.5 lacs/mm^3), renal function test, human immunodeficiency virus (HIV), hepatitis B and hepatitis C, immunological profile, chest X-ray, ECG, USG abdomen were normal, whereas liver function tests were slightly deranged (AST-60 IU/L and ALT-194 IU/L) and Dengue NS1 was negative, whereas IgM Dengue was found positive.

Patient underwent lumbar puncture and cerebrospinal fluid (CSF) was examined, which revealed albuminocytological dissociation (protein-82 mg/dL, cell count-2 cells/mm^3 only lymphocytes). Nerve conduction study was done in median, ulnar, peroneal and sural nerves and revealed reduced compound muscle action potential (CMAP) amplitude with delayed F wave latency and prolonged R median suggestive of both demyelinating and axonal neuropathy.

Patient was treated with intravenous immunoglobulin (IVIg) for 5 days and started improving in form of power in both upper and lower limbs significantly (4/5 in both upper limbs and 3/5 in both lower limbs), hence was discharged and advised to follow-up in the outpatient clinic.

DISCUSSION

Dengue fever is one of the leading causes of mortality and morbidity in tropical and subtropical regions of the world. Dengue fever may present with variable clinical presentation which may be in the form of mild febrile illness to dengue shock syndrome, dengue hemorrhagic fever and neurological complications.

Neurological manifestations in dengue fever are rare. Verma et al described neurological complications in dengue patients and noted that they have been categorized into three groups on the basis of possible pathological mechanisms:[6]

- Neurotropic complications such as encephalitis, myelitis and myositis
- Systemic complications such as hypokalemic periodic paralysis
- Post-infectious immune-mediated complications such as GBS, opsoclonus-myoclonus syndrome.

GBS is one of the rarest neurological presentations following dengue fever seen in adults. It is an acute fulminating polyradiculoneuropathy possibly autoimmune, post-infectious or post-vaccination in nature; males are predominantly involved. It is characterized by rapidly progressive areflexic motor paralysis with or without sensory involvement and without bowel-bladder involvement. Common variants of GBS are acute inflammatory demyelinating polyneuropathy, acute motor axonal neuropathy and acute motor sensory axonal neuropathy and Miller-Fisher syndrome.

Approximately 70% of cases of GBS occur 1-3 weeks after an acute infectious process. The common infectious agents which can cause GBS are *Campylobacter jejuni*, cytomegalovirus (CMV), Epstein-Barr virus, HIV, influenza and mycoplasma. The rare causes may be Zika and dengue viral infection.

The exact mechanism is unknown but possibly it may be due to cell-mediated immunological response to non-self antigen that misdirects to host nerve tissue through a resemblance of epitope mechanism (molecular mimicry).[7,8] Dengue virus would initiate this immunological event, leading to the disease. Myelin or axons could be the target of this immune response.

Diagnosis of GBS is mainly based on clinical and laboratory findings.

The following is the criteria for diagnosis of GBS (Asbury criteria):[9]

Required

- Progressive weakness
- Areflexia
- Duration <4weeks
- Exclude other causes (vasculitis, toxins, porphyria).

Supportive

- Symmetrical weakness
- Mild sensory involvement
- Cranial nerve involvement
- Absence of fever
- Typical CSF finding (albumin-cytological dissociation)
- Nerve conduction study suggestive of demyelination.

GBS can be treated by IVIg (2 g/kg body weight divided in 5 daily doses) or plasmapheresis, as they are equally effective for typical GBS. Glucocorticoids have not been found to be effective in the treatment of GBS.

CONCLUSION

GBS is a rare neurological complication of dengue infection which is generally underestimated. It should always be considered if a patient of dengue fever during the infection or in recovery phase develops progressive areflexic paralysis. The patient should be diagnosed and treated as early as possible to reduce morbidity and mortality. Thus, our case report calls attention to physicians for the possibility of GBS in association with dengue fever.

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Pan-resistant *C. auris* Found in New York City

Three patients in New York had "pan-resistant" *Candida auris* unresponsive to three or more classes of antifungal drugs, researchers found.

These individuals had no history of recent travel. Resistance apparently developed after exposure to antifungal medications, including echinocandins, during prolonged healthcare facility stays, reported Belinda Ostrowsky, MD, of the CDC and colleagues, writing in the *Morbidity and Mortality Weekly Report*. While the authors noted that there was no transmission of any pan-resistant isolates to other patients or the healthcare environment, they characterized this emerging pan-resistance as "concerning".

Four Months of Rifampicin may be Best Option for Latent TB

Four months of daily rifampicin is "short, safe and effective" and is likely the best way to achieve the ambitious goal set forth by the World Health Organization (WHO) to treat 30 million patients for latent tuberculosis (TB) infection by 2022, TB experts say in *Lancet Infectious Diseases*.

Across randomized trials and observational studies, compared with isoniazid, 4 months of daily rifampicin has "consistently" shown better completion rates, lower toxicity and similar effectiveness, they point out.

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Postural 2:1 Heart Block in an Elderly Male

ANKESH GUPTA*, AJIT GUPTA†

ABSTRACT

Syncope or dizziness is defined as a transient, self-limited loss of consciousness with an inability to maintain postural tone that is followed by spontaneous recovery. Syncopal episodes are typically triggered by a sudden, temporary drop in blood flow to the brain, which leads to loss of consciousness and muscle control. Commonest cause is reflex (vasovagal syncope); this is neurally-mediated during emotional stress, orthostatic stress, situational or carotid sinus hypersensitivity. Syncope due to cardiac causes increases with age and is found in 2-3% population over the age of 80 years. Cardiac causes like sick sinus, AV block, PSVT, VT, long QT syndrome, malfunctioning pacemakers or ICD, drugs may lead to syncope/dizziness. But AV block occurring due to change in posture from supine to sitting/erect posture without any of the above-mentioned cause is very rare. We encountered such a case in an elderly male and hence this case report.

Keywords: Syncope, vasovagal, posture, cardiac causes, atrioventricular block

Dizziness or syncope may occur in any human being due to inadequate perfusion of brain due to various reasons; commonest among it is reflex (vasovagal syncope). This is neurally-mediated during emotional stress, orthostatic stress, situational or carotid sinus hypersensitivity.[1] Other causes are numerous and approximately 40% population is affected once during lifetime (more common in young female), but only few need medical intervention. Syncope/dizziness due to cardiac causes increases with age and is found in 2-3% population over age of 80 years.

A careful history about posture, situation, recent medication or history of comorbidity may help in arriving at diagnosis and further management. Cardiac causes like sick sinus, atrioventricular (AV) block, paroxysmal supraventricular tachycardia (PSVT), ventricular tachycardia (VT), long QT syndrome, malfunctioning pacemakers or implantable cardioverter-defibrillator (ICD), drugs may lead to syncope/dizziness. But AV block with change in posture from supine to sitting/erect posture without any of the above-mentioned cause is very uncommon.[2] We encountered such a case in an elderly male and hence this case report.

CASE REPORT

An elderly male aged about 60 years suddenly felt dizziness and sense of palpitation (missing heart beats) during normal activity. Patient had no history of any comorbid conditions like diabetes, hypertension, coronary artery disease (CAD), drug intake or any other major illness in recent past but had a history of occasional episodes of palpitation for few seconds for past 30 years.

Holter monitoring had shown only few ventricular premature contractions in 2-3 reports, which was insignificant. Due to giddiness and inability to do normal activity, he was taken to tertiary care hospital. On examination, in supine posture, heart rate was 78/min regular, blood pressure was 140/86 mmHg, respiratory rate was 18/min. He was kept for observation in cardiac care unit.

All other investigations like complete blood count (CBC), liver function tests (LFT), renal function tests (RFT), chest X-ray, blood sugar level, electrolyte, troponin test and cardiac markers were within normal limits. ECG was normal in supine position but whenever patient assumed sitting position, he felt giddiness and irregular heart beat. So, ECG was recorded on 3 (Three) occasions at time intervals in supine as well as sitting posture, which showed 2:1 heart block (Figs. 1 and 2); on each occasion with assuming sitting posture. As the patient was symptomatic on assuming sitting posture,

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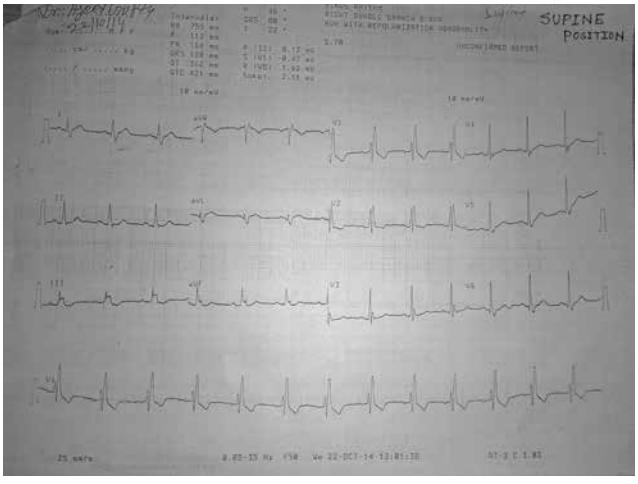

Figure 1. ECG in supine position.

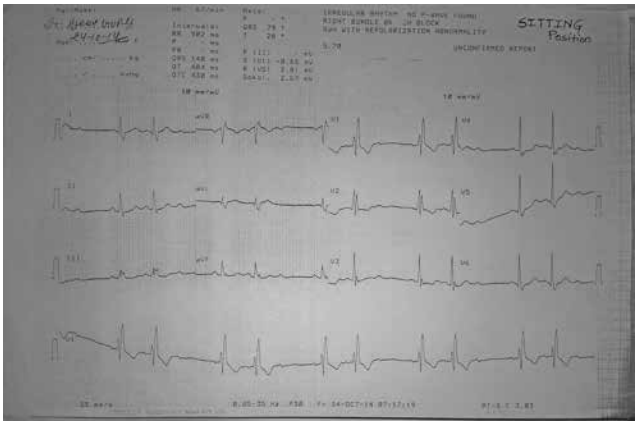

Figure 2. ECG in sitting position showing 2:1 heart block.

a permanent pacemaker device was implanted, that solved the problem.

DISCUSSION

Transient loss of consciousness or dizziness is a common symptom in humans due to transient fall in cerebral perfusion. Hypotension, i.e., a fall in blood pressure of 20 mmHg systolic and 10 mmHg diastolic, is acceptable with change in posture from supine to upright position but any fall more than that may be due to medications or failure of autonomic reflex with resulting pooling of blood in dependent part.

Most of the syncope is reflex mediated (depressor reflex) arising in heart, first described by Bezold, is compensated through activation of autonomic nervous system by vasoconstriction and increase in heart rate. Studies suggest that cardiac *C*-fibers are responsible for slowing heart rate and vasodilatation leading to pooling of blood in dependent part, carotid sinus hyperactivity, parasympathetic activation, organic heart disorders, rhythm abnormality are other leading causes of syncope.[3]

Paroxysmal heart block by act of sitting up in bed or assuming upright posture with severe symptoms like syncope and fainting without change in blood pressure has been reported by Klein et al in two of their cases, relieved by permanent pacemaker implant.[4] In a similar case report, Kartikeyan et al[5] reported reflex syncope in a 52-year-old lady with normal AV conduction in supine position but advanced AV block in upright posture, necessitating permanent pacemaker implant.

Such cases are encountered infrequently and literature reports only few cases of heart block with change of posture, as with this case. Because of rare occurrence we are reporting this case.

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FDA Approves First Targeted Therapy to Treat a Rare Mutation in Patients with Gastrointestinal Stromal Tumors

The US FDA has approved avapritinib for the treatment of adults with unresectable or metastatic gastrointestinal stromal tumor (GIST) – a type of tumor that occurs in the gastrointestinal tract, most commonly in the stomach or small intestine – harboring a platelet-derived growth factor receptor alpha (PDGFRA) exon 18 mutation. This approval includes GIST that harbors a PDGFRA D842V mutation, which is the most common exon 18 mutation. Avapritinib is a kinase inhibitor, meaning it blocks a type of enzyme called a kinase and helps keep the cancer cells from growing… (*FDA*)

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Omental Torsion: A Review of Literature and Case Report

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ABSTRACT

Eitel first described omental torsion in 1899. Omental torsion is rarely diagnosed preoperatively. Knowledge of this pathology is important to the surgeon as it mimics common acute surgical abdomen. For this reason, in the absence of diagnosed pre-existing abdominal pathology, including cyst, tumors, foci of intra-abdominal inflammation, postsurgical wounds or scarring and hernia sacs, omental torsion can present a surprise. Exploratory laparotomy represents the diagnostic and definitive therapeutic procedure; presently laparoscopy is the first choice procedure.

Keywords: Omental torsion, exploratory laparotomy, acute surgical abdomen

Omental torsion is a condition in which a pedicle of the omental apron twists on its longer axis to such an extent that its vascularity is compromised. Eitel, in 1899, first reported a case of omental torsion unassociated with hernia. Since that time many reports have appeared in the literature, notably by Morris, in which 164 cases of torsion of the omentum were gathered from 1905 to 1930. Primary omental torsion occurs when a mobile, thickened segment of omentum rotates around a proximal fixed point in the absence of any associated or secondary intra-abdominal pathology. Morris reported that, though omental torsion can occur at any age, it is mainly seen in the age group of 30 and 50 years with male predominance. Secondary omental torsion occurs due to underlying pathology. Morris, Adams, and Barcia & Nelson emphasized that hernias of the right inguinal variety were scrotal type, of long duration, easily reducible and that they almost invariably contained omentum. In this condition, patients suffering from recurring pain may have temporary twists of the omentum. The omental ball and the omental fibrotic thickenings occasionally found, result from these recurring attacks of incomplete omental torsion. A certain number of omental torsion are caused by inflammatory foci within the abdominal cavity, which produces an inflammation by contiguity in the neighboring omentum. This may be true in cases of mild or subsiding appendicitis or cholecystitis in which the original focus subsides but the changes induced in the omentum remain. Primary omental torsion is unipolar when the proximal omentum remains fixed and the rest is free. Secondary omental torsion is bipolar due to fixation of omentum both proximally to the colon and distally, subsequently to adhesions for pathological conditions.

CASE REPORT

A 37-year-old gentleman presented with pain in the right iliac region for the last 3 days with worsening of pain 2 hours prior to presentation. There was history of associated nausea and vomiting, with no history of obstipation or constipation. On examination, he was conscious, oriented to time, place and person with a pulse rate of 110/min and blood pressure of 110/90 mmHg. On abdominal examination, he had tenderness in the right iliac fossa with guarding and rigidity and rebound tenderness. Rovsing's sign and Blumberg sign were positive and a working diagnosis of appendicitis was made. During ultrasound, probe tenderness was present, appendix was not visualized but fat was seen to be extending to the abdominal wall. Routine investigations showed a normal hemogram with a total leukocyte count of 9,000 and polys 70%; rest of the investigations were within normal range. A differential diagnosis of acute appendicitis, Meckel's diverticulitis was made and the patient was shifted to omental torsion. Under general anesthesia, a laparoscopic examination was carried out which revealed a normal appendix;

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the small and the large bowels and the pelvic organs were healthy; the omentum was found to be twisted on itself and fixed to the posterior abdominal wall. The omental ball was suspended on its pedicle, which was twisted on its axis. The part of the omentum which was attached to the abdominal wall was separated and the twisted part of the omentum was resected. Our patient had uneventful recovery and was discharged on the 3rd post-op day. Histology showed omental pedicle of 10 × 10 × 6 cm with cyanotic look. Microscopy showed hemorrhagic infarction and fat necrosis.

DISCUSSION

Omental torsion is a rare pathological condition, which presents with generic symptoms and mimics acute abdominal conditions such as appendicitis, acute diverticulitis and Meckel's diverticulum. The predisposing factors for this condition are recognized anatomical anomalies like presence of tongue like projections in the omentum, bifid and accessory omentum, anomalous vascular blood supply and other vascular anomalies that modify the weight of omentum, vascular kinking and irregular omental pad seen mostly in obese patients. Secondary omental torsion is more common as compared to primary omental torsion and is associated with pre-existing abdominal pathologies including cysts, tumors, foci of intra-abdominal inflammations and surgical wounds or scarring and hernial sacs. The omentum twists in a clockwise direction, with engorgement of the tortuous veins that are easily compressed. This compromises the venous return and the distal omentum becomes congested and edematous. Recovery may follow or the process may go on. Resultant hemorrhagic extravasation creates a characteristic serosanguineous fluid inside the great omentum and abdominal cavity. As the torsion progresses, arterial occlusion leads to acute hemorrhagic infarction and eventual necrosis of the omentum. Furthermore, omental infarction can occur without torsion due to hypercoaguable state or vascular abnormalities predisposing to thrombosis. The diagnosis of omental torsion is a difficult one and is seldom made before surgery. Ultrasound and CT scan are helpful in clinching the diagnosis; usual ultrasound findings are evaluated as normal. Sometimes, ultrasound may show complex mass or a mixture of solid material and hypoechoic zones. CT scan is an effective procedure in diagnosis of acute abdominal torsion. Omental torsion is usually diagnosed on exploratory laparotomy that represents both diagnostic and therapeutic modality. Thus, laparoscopy is the first choice of procedure for diagnosis and treatment.

CONCLUSION

Omental torsion is a rare pathological condition, which mimics many acute abdominal conditions. The pathogenesis of omental torsion has not been established. The symptoms and laboratory findings are not specific and they mimic other pathological conditions. The differentiation helpful between primary torsion and secondary torsion is difficult to make and is seldom made before surgical operations. Both ultrasound and CT scan are helpful. Laparoscopy, nowadays, is the first choice procedure for diagnosis and treatment of acute abdominal torsion.

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A Frog in the Well's Score – Shortcomings of the Well's Score for Diagnosis of Acute Pulmonary Embolism

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ABSTRACT

Pulmonary embolism (PE) is one of the leading causes of undiagnosed deaths in patients worldwide due to its unpredictable clinical course and mimicry of various other diseases. The often over-used simplified Well's score and D-dimer test must be utilized with prudence to stratify the probability of PE. Astute interpretation of electrocardiography (ECG) signs and bedside echocardiography findings has helped Emergency Physicians narrow down a diagnosis of PE. PE remains a diagnostic challenge; nevertheless, with high index of suspicion, appropriate understanding of clinical probability scores and use of bedside screening tests like ECG and bedside echocardiography, PE can be rapidly diagnosed and managed in the Emergency Department.

Keywords: Emergency Department, pulmonary embolism, Well's score, bedside echocardiography, empirical heparin, CT pulmonary angiogram, McConnell's sign

Pulmonary embolism (PE) is one of the leading causes of undiagnosed deaths in patients worldwide due to its unpredictable clinical course, highly variable symptomatology, mimicry of various other diseases and difficulty in obtaining reliable diagnostic tests. The triad of cough, dyspnea and hemoptysis is found in abysmally low number of patients with PE. The often over-used simplified Well's score and D-dimer test must be utilized with prudence to stratify the probability of PE prior to confirmation with a computed tomography pulmonary angiography (CTPA), which is the gold standard diagnostic test for PE. However, high cost, unavailability in all medical centers, reliance on a normal renal function and high radiation output often make it unfeasible for all patients. Astute interpretation of pathognomonic electrocardiography (ECG) signs and characteristic bedside echocardiography findings have shown promise in helping Emergency Physicians narrow down a diagnosis of PE, as well as rapidly confirming the presence or absence of other conditions, which present in similar fashion. Studies have also shown that initiation of 'empirical heparin' in the Emergency Department (ED) greatly reduced morbidity and mortality in such patients for whom PE is suspected, but a CTPA is either delayed or not feasible. We present the case of a 76-year-old male with a different presentation from the usual described triad of PE. This shows how a broad suspicion and bedside echocardiography help in rapid diagnosis and treatment.

CASE REPORT

Mr KV, a 76-year-old man was brought to the ED, with a laceration measuring 7 cm, over the right parietal area of his scalp, associated with history of collapse in the bathroom early that morning. There were no witnessed seizures and he regained consciousness while in the ambulance towards the hospital, but vomited 4 times in quick succession. Over the last 1 month, he had suffered from recurrent fainting spells, which resolved spontaneously over half an hour and with no associated seizures or vomiting. He was not a smoker or consumer of alcohol, neither had he ever had any previous surgeries. There was no prior history of diabetes, hypertension, chronic kidney disease, ischemic heart disease, asthma or chronic obstructive pulmonary disease. On arrival, he was conscious and oriented (Glasgow Coma Scale [GCS]

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15/15), with bilateral equally reactive pupils. He was afebrile with regular pulse rate of 116/min and blood pressure of 140/90 mmHg. Although he had no respiratory discomfort, his respiratory rate was 26/min with pulse oximetry of 88% on room air. There was a 7 cm horizontal laceration over his right parietal region and the rest of systemic examination was unremarkable.

Arterial blood gas analysis demonstrated hypoxia (PaO_2 = 68% with an SaO_2 of 86%), but no other significant findings. His chest X-ray was unremarkable. Plain computed tomography (CT) brain was undertaken on account of sudden collapse in the toilet with multiple episodes of vomiting as well as similar episodes of collapse, in the past. However, it was a normal study. Baseline blood investigations indicated leukocytosis of 16,100/mm^3, with serum creatinine of 1.7 mg/dL. Due to his "comfortable hypoxia", the absence of clinical chest findings and persistent tachycardia, a diagnosis of PE was considered. Well's score was calculated to be 4.5 and bedside D-dimer assessment was found to be 4,910 ng/mL.

The ECG showed sinus tachycardia (Fig. 1). Bedside echocardiography showed dilated right ventricle and right atrium with positive McConnell's sign, i.e., regional right ventricular (RV) dysfunction, akinesia of the mid free wall, but normal motion at the apex. CTPA was deferred due to elevated creatinine. Unfractionated heparin therapy was empirically initiated with bolus dose of 5,000 units IV, and continued thereafter. The patient was admitted for further care and 3 days later, after normalizing the serum creatinine, CTPA was performed, confirming the diagnosis of PE - multiple filling defects involving the right pulmonary artery extending into the segmental branches. A representative image from the scan series is enclosed (Fig. 2). The patient was treated with 5 days of IV unfractionated heparin, after which he was discharged in a stable condition, on warfarin.

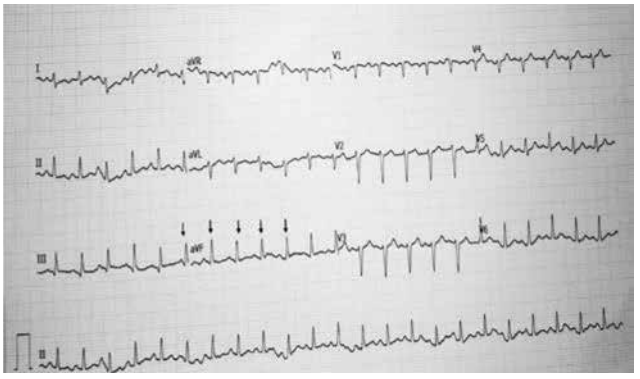

Figure 1. ECG of patient. Black arrows indicate sinus tachycardia.

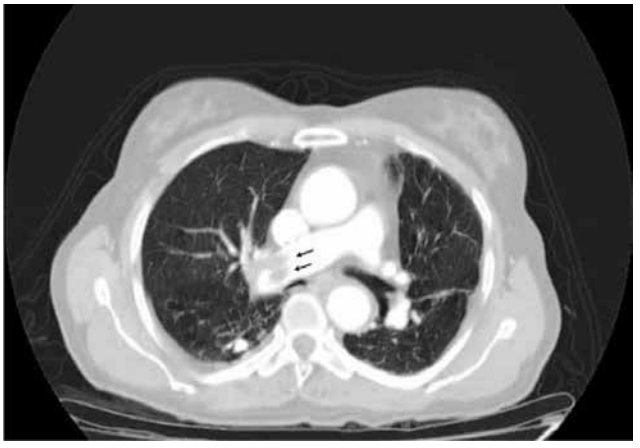

Figure 2. CTPA (*black arrows*) indicating multiple filling defects involving the right pulmonary artery extending into the segmental branches.

DISCUSSION

Acute PE is a major harbinger of death, a major cause of undiagnosed mortality worldwide. The diagnosis of PE has always been challenging, as it is the second leading cause of sudden death without a discernible cause, due to wide variety of presenting symptoms, quick progression and paucity of rapid diagnostic modalities with high sensitivity and specificity. The typical triad of "Chest Pain, Dyspnea and Hemoptysis" is found in absurdly few number of patients, and presentation of PE can vary greatly. The presentation could be extremely subtle with rare occurrences such as seizures, as part of the symptom complex. In fact, PE was identified in nearly 1 of every 6 patients hospitalized for a first episode of syncope. The commonly employed Well's score, though a useful clinical screening tool, has limited diagnostic capacity in PE. Conditions such as pneumonia, pneumothorax, sepsis or even panic attacks would sufficiently satisfy the Well's score criteria and lead to over-investigation for PE. Further, the challenge for diagnosis is frequently compounded by significant delay in organizing CTPA, due to multiple factors including unstable hemodynamic status of patient, deranged renal function and delay in obtaining CT in centers, which do not have the privilege of 24 × 7 imaging services.

Role of ECG

The role of ECG in prognosticating PE is increasingly recognized. The ECG in addition to clinical acumen, steers the Emergency Physician towards the diagnosis. McGinn and White described the first association between acute PE and specific ECG changes when they noted the

familiar 'S1Q3T3' pattern in 7 patients with acute cor pulmonale. However, it is reported that patients with normal ECGs at admission revealed diagnostic features of embolism in serial ECGs carried out subsequently. ECG findings in PE range from sinus tachycardia (44% of patients), right axis deviation (16% of patients), right bundle branch block (18% of patients), inverted T waves in leads V1-V4 (right ventricular strain pattern - 18% of patients), and the "S1Q3T3" pattern (20% of patients), and any one of these findings doubles the probability of PE. The most common ECG changes when compared with previous ECG in the setting of PE are T-wave inversion and flattening, most commonly in the inferior leads, and occurring in approximately one-third of cases. It has been observed that approximately one-quarter of patients will have new-onset sinus tachycardia.

The fact that ECG provides invaluable information for PE prognostication was reaffirmed by a meta-analysis of 39 studies (9,198 patients). ECG signs that were good predictors of a negative outcome included S1Q3T3, complete right bundle branch block, T-wave inversion, right axis deviation and atrial fibrillation for in-hospital mortality. It was concluded that ECG is potentially valuable in prognostication of acute PE. Moreover, changes in right-sided chest leads occur frequently in PE. Routinely recorded right-sided ECG appears to possess the greatest potential for diagnosing acute PE in patients who have not manifested typical changes in their standard 12-lead ECGs. However, it needs to be emphasized that approximately one-quarter of patients with PE may have no changes in their ECG.

Fragmented QRS (fQRS) is a convenient marker of myocardial scar evaluated by 12-lead ECG and is defined as additional spikes within the QRS complex. The presence of fragmented QRS complex (fQRS), as a simple and feasible ECG marker, seems to be a novel predictor of in-hospital adverse events and long-term all-cause mortality in PE patient population. There is scarcity of data on the prognostic importance of fQRS on short- and long-term outcomes in patients with PE.

Bedside Echocardiography

Bedside echocardiography demonstrates right ventricular dilation, reduced contractility with apical sparing, which is known as McConnell's sign and is very specific in acute PE.

Both these tests are useful for patients who are too unstable to be shifted out of the ED for CTPA, or who have deranged renal parameters, which make the use of IV contrast risky. Thrombolytic therapy, based on bedside echocardiography, has also been shown to produce successful outcome in low-resource settings.

D-dimer

D-dimer is a fibrin breakdown product which is elevated whenever the fibrinolytic system of the body is activated. The usage of D-dimer as a diagnostic marker for PE is to be discouraged, since the differential diagnoses for elevated D-dimer values in the setting of dyspnea are numerous, including sepsis, hemothorax, myocardial infarction, congestive cardiac failure, etc. D-dimer has very high sensitivity (up to 95%), but low specificity (approximately 45%) for PE, and must only be used as a 'rule out' rather than diagnostic test for patients with a low pre-test probability of PE. In a recent study on 614 patients, it has been reported that ECG signs of right ventricular strain are strongly related to elevated cardiac biomarkers and echocardiographic signs of right ventricular overload.

However, rapid point-of-care testing for D-dimer in patients who have simplified Well's score of <4, would be beneficial to indicate the clinical pathway to investigate for PE. A triad of circulatory collapse, right ventricular dilatation and large alveolar dead space is proposed for the rapid diagnosis and treatment of massive PE.

Thrombolytic Therapy

The role of thrombolytic therapy in acute PE patients is still controversial and early-onset thrombolytic therapy in the ED for high-risk and hemodynamically worsening patients appears safe and life-saving. Short-term effects of thrombolytics are well-known, whereas long-term effects on cardiac electrophysiology have not been reported before. In the absence of contraindications, it is reasonable to administer a patient with suspected PE 'empirical heparin' before confirmatory imaging, as early anticoagulation therapy is vital for management of acute PE and delay of which increases mortality significantly. Low-molecular weight heparin (LMWH) has several advantages over unfractionated heparin; however, in cases of deranged renal function, as seen in this case, unfractionated heparin is preferred.

CONCLUSION

Rapid diagnosis of PE in the ED greatly improves survival rates, but requires a systematic, multivariate approach involving high clinical suspicion, good understanding of pre-test probability with appropriate use of D-dimer, use of easily available bedside modalities such as ECG and bedside echocardiography and ideally, CTPA. Treatment can be started in the

ED on an empirical basis with unfractionated heparin, which can be continued or stopped depending on the angiography report. High Well's score is not diagnostic of PE in itself, neither is elevated D-dimer level. Appropriate clinical judgment must be used along with pre-test probability scoring and appropriate testing of D-dimer levels for all low-risk patients only. ECG and bedside echocardiography can be used for patients with elevated D-dimer levels to assess the right ventricular function and guide the Emergency Physician to start empirical heparin before shifting the patient for a CTPA.

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DCGI Approves 'Restricted Use' of Anti-HIV Drugs for nCoV Patients

New Delhi: The Drug Controller General of India (DCGI) has approved the "restricted use" of a combination of drugs used commonly for controlling HIV infection in public health emergency for treating those affected by novel coronavirus (nCoV), official sources said.

As per government sources, the Indian Council of Medical Research (ICMR) sought an emergency approval from the DCGI for the "restricted use" of the combination of two medications - lopinavir and ritonavir - for treatment of this respiratory ailment. "The DCGI has given a no objection for restricted use of this drug combination - lopinavir and ritonavir - in case of a public health emergency on patients affected by nCoV as per the treatment protocol designed by the ICMR," a government source said… (*ET Healthworld – PTI*)

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Waveforms and Deflections in Toxicology

SUNTHARI RAJKUMAR*, VIJAYAKUMAR N†, NANJILKUMARAN A†, UMARANI R‡

ABSTRACT

Introduced as pieces of wires in the early 18th century, the electrocardiograph (ECG) machine has become an important clinical bedside tool. This easily available, user friendly, noninvasive, inexpensive investigation has spread its wings not only in the field of cardiology, but in almost all other medical fields. Herewith we present a synopsis of few case reports of drug overdose (digoxin, β blockers, diazepam and tricyclic antidepressants) either accidental or by deliberate harmful intention who presented to our hospital, to highlight the importance of electrocardiogram (ECG) in toxicology field. One of the leading causes of mortality and morbidity is drug overdose and poisoning, more commonly in rural areas where sophisticated investigations like serum levels of toxins and treatment modalities may not be available. The cardiotoxic poisons bring changes in the ECG wave forms due to multiple effects, the most common being effects on ion channels. In such situations, ECG will help in early detection of life-threatening events, paving way for targeted and timely intervention.

Keywords: Waveforms, ion channels, cardiotoxic poisons, drug overdose

Electrocardiogram (ECG) is an important diagnostic tool in the field of cardiology as a patient with drug overdose and drug poisoning can present with typical ECG changes. Serial ECG is mandatory in patients with suspected exposure to cardiotoxic overdose.

Ionic current flow from cell to cell through the heart as a result of the activity of selectively permeable ion channels which, when activated transiently, open, allowing the movement of charged ions (Na^+, K^+, Cl^- and Ca^{2+}) across a muscle membrane that is otherwise impermeable. A sound knowledge of ECG interpretation and specific characteristics of cardiotoxic drugs is very much necessary to establish a good foundation for an early diagnosis and prompt management. Few case reports are presented here to highlight this fact.

CASE REPORT 1: BENZODIAZEPINE AND POTASSIUM CHANNEL

A 59-year-old female was brought to the emergency room (ER) with history of consumption of 10 mg diazepam tablets (unknown quantity). The patient was not a known case of hypertension, diabetes mellitus or coronary artery disease, had no other significant comorbid conditions and was not on any medications. There was no preceding history suggestive of any gastrointestinal disorders or underlying psychiatric disorders, trauma or similar weakness in the past. There was no significant family history.

At the time of presentation, the patient was slightly drowsy but was responding to oral commands. On examination, patient was afebrile, not anemic and not cyanosed and had no clubbing or pedal edema. She had a pulse rate of 90/min and blood pressure of 90/60 mmHg. Examination of cardiovascular system was normal. Bilateral air entry was present with no added sounds. Abdomen was not distended. Bowel sounds were present. Neurological examination revealed weakness of all four limbs with muscle power of Grade 3 with diminished deep tendon reflexes. There was no neck muscle weakness or ptosis. Pupils were equal and reacting to light. Fundus was normal. Bilateral plantars were flexors. Other modalities of neurological examination could not be elicited. Investigations revealed normal hemogram and renal parameters. Electrolyte analysis revealed sodium of 134 mEq/L, potassium of 2.5 mEq/L and chloride of 109 mEq/L. Arterial blood gas (ABG) analyses showed no evidence of acidosis or alkalosis.

ECG showed heart rate of 68 bpm, with normal sinus rhythm and no evidence of atrial enlargement or

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ventricular hypertrophy. There were no ST changes. However, prominent "U" waves were present in the precordial leads (V1-V3) (Fig. 1).

Following gastric decontamination, correction of potassium was done with potassium chloride. Figure 2 shows ECG after potassium chloride correction. Patient improved and was discharged on 7th day post-admission.

Diazepam

Diazepam, a prototype benzodiazepine, is the most commonly used drug for various effects acts on gamma-aminobutyric acid type A ($GABA_A$) receptor, as a positive allosteric modulator. It amplifies the inhibitory signal by opening the chloride ion channel, and thereby inhibits the neurons. With no risk of addiction and milder withdrawal symptoms, overdose is common and essentially never fatal. However, in a retrospective analysis of 53,931 people of diazepam poisoning, among the various side effects reported like hypotension, drowsiness, etc., 0.64% were found to have hypokalemia. Hypokalemia is more common in elderly females in the age group of 50-60 years. Several studies have found that the incidence of hypokalemia with diazepam overdose is maximum during the first few weeks and it steadily decreases with increasing duration of drug intake. The mechanism attributed to this includes the exhaustion of the $GABA_A$ receptors and resistance to diazepam on repeated exposures. If left unnoticed or untreated, diazepam can lead to major fatal outcomes such as impaired vision, ataxia, apnea, hypotension, respiratory depression, AV blocks and coma. Hypokalemia induced by diazepam is a rare yet a serious adverse effect, which is a completely reversible condition. Diazepam is the only benzodiazepine that does not cause QRS widening and oxazepam is the only one not causing prolongation of PR interval.

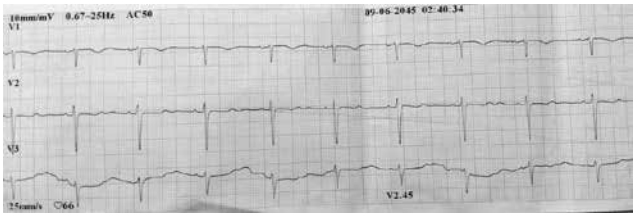

Figure 1. "U" waves.

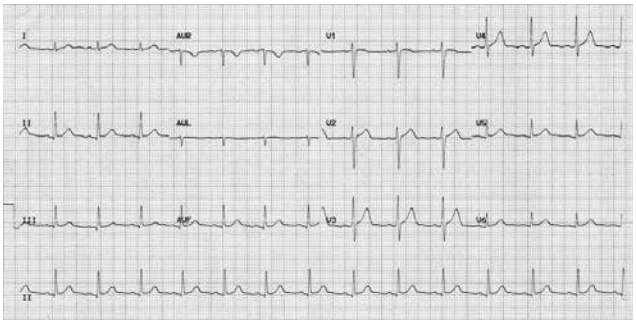

Figure 2. ECG taken after potassium chloride correction.

The use of flumazenil as an antidote for benzodiazepine poisoning is very less as the risks outweigh the benefits as it also acts as an inverse agonist. Hence, in the absence of a safe antidote, identifying the electrolyte imbalance by ECG and correcting them will be more relevant in diazepam poisoning.

CASE REPORT 2: TRICYCLIC ANTIDEPRESSANT AND SODIUM CHANNEL

A 32-year-old female patient presented to ER after 3 hours of history of consumption of 10 tablets of amitriptyline (10 mg) and 10 tablets of clonazepam (0.5 mg). There was no preceding history of chest pain, palpitation, breathlessness, convulsions and loss of sensorium. She was a known case of psychogenic nonepileptic seizure for the past 1 year and was on regular treatment with amitriptyline 10 mg, clonazepam 0.5 mg and sodium valproate 600 mg. On examination, patient was drowsy, responding to deep painful stimuli and febrile. She had a pulse rate of 140/min and blood pressure of 100/60 mmHg. Pupils were equal and reacting to light. Fundus was normal. Plantar reflexes were flexors. Other modalities of neurological examination could not be elicited. Examination of cardiovascular system/respiratory system/abdomen was normal.

Investigations revealed a normal hemogram, renal parameters and metabolic acidosis (pH - 7.24, HCO_3^- - 11 mEq/L, pCO_2 - 35 mmHg). ECG was taken at the time of admission (Fig. 3 a-c).

Patient was treated with activated charcoal 1 g/kg and acidosis was corrected by sodium bicarbonate infusion.

Tricyclic Antidepressant Poisoning

Poisoning with tricyclic antidepressants (TCAs) is an important cause of drug-related poisoning with mortality of 1.3%. Neurological and cardiovascular toxicity, resulting in reduced levels of consciousness, reduced blood pressure and arrhythmias, are mainly responsible for mortality attributed to TCA overdose. It causes mild symptoms such as agitation, due to slow absorption in overdose, reduced by the cholinergic antagonist effects of TCA, which may worsen over time, leading to convulsions, coma and death.

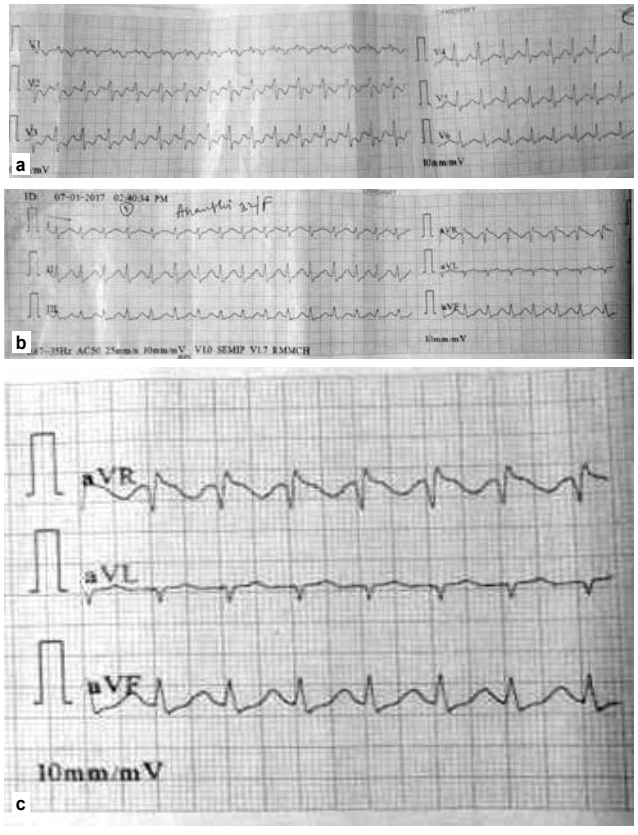

Figure 3 a-c. ECG figures reveal sinus tachycardia, right axis deviation, prolonged PR interval, QRS width prolongation with QTc interval of 0.506 sec, aVR was positive with deep S-wave.

Cholinergic antagonist effects of TCAs include delirium, widened pupils, reduced gut motility and retention of urine. Cardiovascular effects include α receptor blockage in vasodilatation, blockage of sodium channel resulting in increased depolarization time and the inhibition of potassium channels causing increased repolarization time and dysrhythmias. Neurological symptoms can include lowered levels of consciousness, due to antihistaminic effects and seizures due to TCA antagonist effects on the $GABA_A$ receptor.

ECG findings are used for:

- Risk stratification
- To guide subsequent therapy.

The typical ECG changes that can be found in a TCA overdose are QRS width >100 ms, QTc prolongation >430 ms and R/S ratio 0.7 in lead aVR, R in aVR of >3 mm and right axis deviation of 130-270° in the terminal 40 ms of the QRS. These ECG findings are identified as the most important risk stratification, more important than serum drug levels for the prediction of complications (seizure, dysrhythmias such as torsade de pointes) following a TCA overdose and thereby resolve by the administration of 1-2 units/kg of sodium bicarbonate. Sodium bicarbonate acts at three levels. It raises the sodium gradient across the affected sodium channel counteracting the drug-induced side effect of sodium channel blocking action, increases the pH, which promotes dissociation of TCA from cardiac sodium channels and finally TCAs bind more easily to protein in the higher pH range resulting in a lower pharmacologically active TCA concentration. Alkalinization to a pH of 7.45-7.55 is advised until normalization of the QRS interval, even in the absence of initial acidosis. When the PH becomes >7.6, the risk of dysrhythmias increases.

Similar ECG changes can occur in cocaine toxicity and class IA, IC antiarrhythmic drugs. Hence, these drugs should be avoided because of their ability to block cardiac sodium channels.

CASE REPORT 3: DIGITALIS AND CALCIUM CHANNEL

A 28-year-old male patient presented to ER with complaints of palpitation and giddiness of 2 hours duration. There was no history of chest pain, breathlessness, convulsions and loss of sensorium. He was a known case of rheumatic heart disease with atrial fibrillation for the past 2 years and was on regular treatment with digoxin 0.25. Inadvertently, he took 4 tablets of digoxin.

ECG was taken at ER which showed an irregular RR interval with controlled ventricular rate, absent P waves and inverse tick sign (Fig. 4).

Digoxin

A positive inotropic drug, digoxin inhibits the Na^+ K^+ ATPase, increases calcium concentration in the cell and thus, the effects of digoxin act through all 3 ions. Digoxin toxicity is most common in elderly patients with kidney injury and electrolyte imbalance like hypokalemia, hyperkalemia, hypercalcemia, calcium channel blockers and diuretics. Digoxin has very narrow therapeutic index (0.5-2 ng/mL).

Thus ECG helps us:

- *To find out toxicity versus effect*: Classical digoxin effect (Fig. 5): It appears as a down sloping of ST segment, also known as "Reverse tick"/"Reverse check sign."
- Digoxin toxicity (Fig. 6): The most common dysrhythmia associated with toxicity induced by

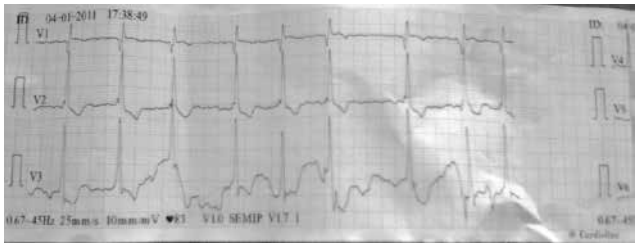

Figure 4. ECG showing irregular RR interval with controlled ventricular rate, absent P waves and inverse tick sign.

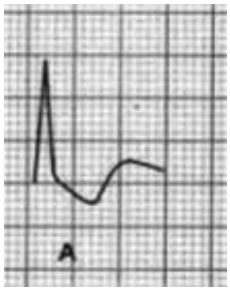

Figure 5. Digoxin effect - T wave rises above the baseline.

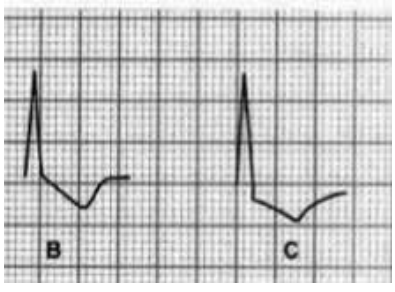

Figure 6. Digoxin toxicity - T wave does not rise above the baseline.

these agents is frequent premature ventricular beats, paroxysmal atrial tachycardia with variable block or accelerated junctional rhythm is highly suggestive of digitalis toxicity.

- *Help us to identify electrolyte disturbances*: Hyperkalemia is one of the indicator for Fab fragment treatment in digoxin toxicity, when estimation of serum digoxin level is not available or amount of ingested digoxin not known.

CASE REPORT 4: β BLOCKERS AND SODIUM, POTASSIUM CHANNELS

A 60-year-old female, known hypertensive, diabetic and dyslipidemic, on regular treatment, was brought to ER with history of giddiness since 2 hours duration. She had a dispute with her family members and consumed 10 tablets of antihypertensive drugs (bisoprolol). On examination, patient was conscious, responding to oral commands. She had a pulse rate of 45/min and blood pressure of 90/60 mmHg. Pupils were equal and reacting to light. Fundus was normal. Plantar reflexes were flexors. Other modalities of neurological examination could not be elicited. Examination of cardiovascular system/respiratory system/abdomen was normal.

ECG taken at ER showed heart rate of 42/min, NSR, no ST, T-wave changes (Fig. 7).

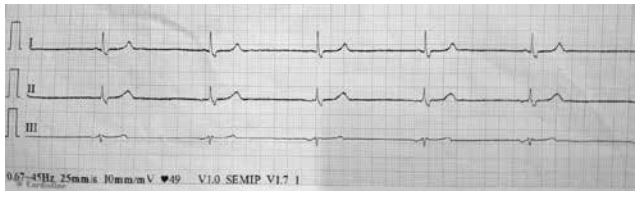

Figure 7. ECG showing no ST, T-wave changes.

β-blocker Toxicity

β blockers act mainly on cardiac β_1 receptors and produce decreased automaticity, negative chronotropic and inotropic effect. Hence, these drugs not only have a direct effect on the myocardium, but also exert an indirect effect by blocking the sodium and the potassium channels, thereby depressing sinoatrial and atrioventricular nodal activity.

The hallmark of β-blocker poisoning is myocardial depression and decreased contractility leading to bradycardia, hypotension and in large dose, cardiogenic shock. Highly lipophilic β blockers like propranolol readily cross the blood-brain barrier and can produce central nervous system (CNS) effects such as seizures and coma. β blockers with membrane stabilizing property, such as propranolol or acebutolol, may prolong the QRS interval (>0.10 sec) and predispose to dysrhythmias. These inhibitory effects of propranolol on the fast inward sodium current producing prolongation of QRS may be used as predictors of propranolol-induced seizures. Prolonged PR can be an early sign of β-blocker overdose. Propranolol overdose has been associated with a higher mortality rate compared with other β blockers. Sotalol is a unique β-blocker in that it possesses the ability to block delayed rectifier potassium channels in a dose-dependent fashion.

General goals of therapy are aimed at improving the inotropic and chronotropic effect. Potential intervention utilized to manage severe toxicity includes intravenous fluid, atropine, glucagon, calcium and vasopressors.

CONCLUSION

To summarize, the myocardial resting and action potential depends mainly on sodium, potassium and calcium ion channels. Many cardiotoxic poisons have well-known effect on these channels producing varied ECG findings. Hence, toxidrome approach, in the management of poisoning, should also include ECG interpretation for guided, targeted, interventions.

Toxidrome approach: In patients with normal sinus rhythm (like TCA toxicity), subtle changes like prolonged QTC, etc. should be looked for. Bradycardia

in poisoned patients can be assessed with the toxidrome approach to search for signs of toxicity of drugs like digoxin overdose (PVC), β-blocker poisoning (AV block). ECG of tachycardia patients should be assessed for wide complexes (TCA poisoning, Na^+ channel blockade drugs) - R-wave in aVR, S in lead 1, aVL; QTc prolongation and ischemia.

Reasonable period of observation in patients with normal ECG without other signs of cardiotoxicity is usually 6-8 hours, but in patients exposed to sustained release preparations or drugs (like citalopram) with delayed toxicity may be beyond 24 hours. Serial ECGs should be performed in patients with suspected cardiotoxicity.

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Brittle Baby Bones When Moms Smoke in Pregnancy

Smoking in pregnancy is linked to abnormal bone development in offspring, suggested a population-based study from Sweden.

Mothers who smoked during pregnancy had children with a higher risk of fracture during their first year of life, compared with children not exposed to smoking (HR 1.27, 95% CI 1.12-1.45), reported researchers in the *BMJ*.

H. pylori Treatment Cuts Stomach Cancer in High-risk Patients

People with *Helicobacter pylori* infection and a first-degree family history of gastric cancer – two key risk factors for the cancer – had a significantly reduced risk of this malignancy when the infection was eradicated, revealed a randomized placebo-controlled trial.

During a median follow-up of 9.2 years, gastric cancer developed in 10 participants (1.2%) in the treatment group and 23 (2.7%) in the placebo group, for a HR of 0.45 (95% CI 0.21-0.94, p = 0.03), reported researchers in *The New England Journal of Medicine*.

Indian Journal of Clinical Practice, Vol. 30, No. 9, February 2020

Coronavirus Update: All Questions Answered

KK AGGARWAL

It's Not New

Every decade, a zoonotic coronavirus crosses species that infect humans and in this decade, we have a virus, called 2019-nCoV, first identified in Wuhan, China, in persons exposed to a seafood market.

Name

The name 'coronavirus' is derived from its shape, resembling a crown or solar corona when seen under an electron microscope.

The three deadly human respiratory coronaviruses so far:

1. Severe acute respiratory syndrome coronavirus (SARS-CoV)
2. Middle East respiratory syndrome coronavirus (MERS-CoV)
3. 2019-nCoV: The virus is 75-80% identical to SARS-CoV.

Pathogenesis

Infection with these coronaviruses is associated with a severe inflammatory response.

It has High Mortality

In the current situation, the mortality rate is 2%. The severity of illness is a cause for concern.

Its Zoonotic

It is closely related to several bat coronaviruses. It seems that bats are the primary reservoir for the virus. SARS-CoV was transmitted to humans from exotic animals in wet markets, and MERS-CoV transmitted to humans from camels. The ancestral hosts were probably bats in both the situations.

It is More Infectious to Humans

The 2019-nCoV seems to thrive better in primary human airway epithelial cells than in standard tissue-culture cells, unlike SARS-CoV or MERS-CoV. The 2019-nCoV seems likely to behave more like SARS-CoV.

Human-to-human Infection is Weak

SARS-CoV and MERS-CoV affect intrapulmonary epithelial cells more than upper airway cells. **Transmission thus occurs from patients with recognized illness and not from patients with mild, nonspecific signs.**

2019-nCoV seems to use the same cellular receptor as SARS-CoV (human angiotensin-converting enzyme 2 [hACE2]). **Transmission thus seems to occur only after signs of lower respiratory tract disease develop.**

The median time from onset of symptoms to first hospital admission was 7.0 days (4.0-8.0), to shortness of breath was 8.0 days (5.0-13.0), to ARDS was 9.0 days (8.0-14.0), to mechanical ventilation was 10.5 days (7.0-14.0), and to ICU admission was 10.5 days.

Its Unlikely to Spread by Eating Sea Food in India

The infection has been traced to snakes in China, so, it is unlikely to spread in India by eating sea food. Snakes hunt for bats. Reports suggest that snakes were sold in the local seafood market in Wuhan. It is quite possible that the 2019-nCoV jumped from the host species, i.e., bats, to snakes and then to humans at the beginning of the outbreak. It is not yet known how the virus could adapt to both the cold-blooded and warm-blooded hosts.

Flight Transmission

There have been reports of transmission of foodborne diseases on aircraft, including cholera, shigellosis, salmonellosis and staphylococcal food poisoning. Transmission of smallpox on aircraft was reported in 1965. An influenza outbreak was reported in 1979 among passengers on a flight that had a 3 hours' ground delay before takeoff. The influenza attack rate very high (72%) among passengers. It was attributed to the failure of operation of ventilation system during the ground delay. Measles may also have been transmitted aboard international flights. No case of active TB has been identified due to exposure on a commercial aircraft.

President, CMAAO and HCFI
Past National President, IMA

However, transmission of *Mycobacterium tuberculosis* may occur during long (>8 hours) flights, from an infectious passenger or crew member to other passengers or crew members.

It's a Large Droplet Infection

Transmission of 2019-nCoV probably occurs through large droplets and contact and less frequently through aerosols and fomites.

Universal Droplets Precautions is the Answer

1. Quarantining for 2 weeks of the lower respiratory tract infection (LRTI) patient
2. Timely diagnosis
3. Strict adherence to universal precautions.

Its All Over

Australia, Macau, Hong Kong, France, Japan, Malaysia, Nepal, Singapore, Taiwan, South Korea, Thailand, United states and Vietnam.

Is it a Public Health Emergency?

It is a Public Health Emergency of International Concern (It is mandatory to report to WHO human and animal cases).

■■■■

Dramatic Health Benefits Following Air Pollution Reduction

- Starting at Week 1 of a ban on smoking in Ireland, there was a 13% drop in all-cause mortality, a 26% reduction in ischemic heart disease, a 32% reduction in stroke and a 38% reduction in chronic obstructive pulmonary disease. The greatest benefits in that case occurred among nonsmokers.
- In the United States, a 13-month closure of a steel mill in Utah resulted in reducing hospitalizations for pneumonia, pleurisy, bronchitis and asthma by half. School absenteeism decreased by 40%, and daily mortality fell by 16% for every 100 $\mu g/m^3$ PM 10 decrease. Women who were pregnant during the mill closing were less likely to have premature births.
- A 17-day "transportation strategy", in Atlanta, Georgia during the 1996 Olympic Games involved closing parts of the city to help athletes make it to their events on time, but also greatly decreased air pollution. In the following 4 weeks, children's visits for asthma to clinics dropped by more than 40% and trips to emergency departments by 11%. Hospitalizations for asthma decreased by 19%. Similarly, when China imposed factory and travel restrictions for the Beijing Olympics, lung function improved within 2 months, with fewer asthma-related physician visits and less cardiovascular mortality.
- In Nigeria, families who had clean cook stoves that reduced indoor air pollution during a 9-month pregnancy term saw higher birthweights, greater gestational age at delivery and less perinatal mortality.
- Twenty-five years after enactment of the Clean Air Act, the US EPA estimated that the health benefits exceeded the cost by 32:1, saving 2 trillion dollars, and has been heralded as one of the most effective public health policies of all time in the United States. Emissions of the major pollutants (PM, sulfur oxides, nitrogen oxides, carbon monoxide, volatile organic compounds and lead) were reduced by 73% between 1990 and 2015 while the US gross domestic product grew by more than 250%.

(Source: Abstracts from American Thoracic Society's journal, Annals of the American Thoracic Society)

FDA Approves First Drug for Treatment of Peanut Allergy for Children

The US FDA has approved Palforzia [Peanut (*Arachis hypogaea*) Allergen Powder-dnfp] to check allergic reactions, including anaphylaxis, that can occur with accidental exposure to peanuts. Treatment with Palforzia may be started in individuals ages 4-17 years with a confirmed diagnosis of peanut allergy and may be continued in individuals 4 years of age and older. Those taking Palforzia must avoid peanuts in their diets… (*FDA*)

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Time for Homoeopaths to Join Fight Against Coronavirus to Show That Nosodes Work

KK AGGARWAL

It's the time for the Homoeopaths all over the world to join the fight against coronavirus and show that the concept of nosodes works.

Modern medicine uses vaccines for prevention and it has none for the current coronavirus. A "Vaccine" is any substance used in active immunization. "Active immunization" is the inoculation, usually by injection, of a special antigen to promote antibody production. These may be dead bacteria (e.g., Typhoid), dead viruses (e.g., Salk polio), live viruses (e.g., Sabin's polio), or toxoids (e.g., Tetanus or Diphtheria).

Homoeopathy has its own theory regarding vaccination. It never introduces pathogenic microorganisms into the body, so its medicine cannot strictly be called vaccines. **The equivalent are Nosodes**, which have a prophylactic or preventative effect. They are always taken orally. These nosodes are prepared by a process of diluting and succession, called potentization, so that there is no trace of the original pathogen remaining.

A nosode (from nosos, the Greek word meaning 'disease') is a homoeopathic preparation made from matter from a sick animal or person. Substances such as respiratory discharges or diseased tissues are used. The preparation, using alcohol, as well as the repeated dilution and succession, essentially renders the substances harmless, while producing a powerful remedy.

Homoeopathy is a science where the matter is converted into nonmatter before it is used in the clinical practice. **During the 200-year history of Homoeopathy, this form of medicine has proved to be extraordinarily effective in preventing and curing epidemic diseases.** Dr Samuel Hahnemann had great success in treating epidemics of scarlet fever. Villages treated with his prophylactics entirely escaped dreaded epidemics, including the Plague.

President, Heart Care Foundation of India

The Journal of the American Institute for Homeopathy, May 1921, had a long article about the use of homoeopathy in the flu epidemic. Dr TA McCann, from Dayton, Ohio reported that 24,000 cases of flu treated allopathically had a mortality rate of 28.2% while 26,000 cases of flu treated homoeopathically had a mortality rate of 1.05%.

This last figure was supported by Dean WA Pearson of Philadelphia (Hahnemann College) who collected 26,795 cases of flu treated with homoeopathy with the above result. Dr Herbert A Roberts from Derby, CT, said that 30 physicians in Connecticut responded to his request for data. They reported 6,602 cases with 55 deaths, which is less than 1%. Dr Roberts was working as a physician on a troop ship during WWI. He had 81 cases of flu on the way over to Europe. He reported, *"All recovered and were landed. Every man received homoeopathic treatment. One ship lost 31 on the way."*—Julian Winston

Nosodes have been used in prophylaxis. Examples would be the use of *Influenzinum* in flu prophylaxis or *Morbillinum* in a measles epidemic. Closely related to this would be the use of the sarcode *Anas barbare hepatis et cardus extractum* (liver and heart of the Barbary duck) for 'flu'. Derived from tissues of the native host of influenza, this remedy is prepared from tissue containing and reacting to the influenza virus.

For preparing Nosodes, specific preparations are used in the prevention of corresponding diseases. e.g. - Morbillinum - Measles, Variolinum - Smallpox, Influenzinum - Influenza, Diphtherinum - Diphtheria.

Dr HC Allen notes about the use of Diphtherinum, "The author has used it for 25 years as a prophylactic and has never known a second case of diphtheria to occur in a family after it had been administered".

Homoeopathic preparations have not been shown to raise antibody levels. Smits tested the titer of antibodies to diphtheria, polio and tetanus in 10 children before and 1 month after giving homoeopathic preparations of these three vaccines (DTPol 30K and 200K). He found no rise in antibody levels (Smits, 1995). He speculates that protection afforded by a homoeopathic remedy acts on a "deeper" level than that of antibodies.

Homoeopathic remedies reduce the patient's sensitivity to the dynamic stimulus of the virus or bacteria, thus lessening the patient's predisposition to being overcome by this stimulus (Golden, 1994).

If homoeopathic remedies do not produce an increase in antibody levels, then the only way to measure the effectiveness of homoeopathic prophylaxis is through clinical results. In modern medicine, a similar concept has been used in making a lung cancer nosode equivalent by repeatedly radiating the lung cancer tissue. I personally have seen many anecdote cases that nosodes work.

■■■■

First Approval for Fast-Acting Lispro for Diabetes; EU OKs Oral Semaglutide

The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has issued a positive opinion for the oral glucagon-like peptide (GLP-1) receptor agonist semaglutide for adults with insufficiently controlled type 2 diabetes who seek to improve glycemic control as an adjunct to diet and exercise.

CHMP has also recommended approval of a fast-acting, or mealtime, version of insulin lispro for the treatment of adults with diabetes, which seems to be the first approval worldwide of this form of insulin lispro… (*Medscape*)

Warming Temperatures could Mean More Heat-related Illnesses and New Diseases, Experts Warn

Rising temperatures triggering extreme weather events around the world could lead to an increase in heat-related illnesses and deaths, as well as the threat of new infectious diseases, suggest experts.

A new paper published in the *Journal of Clinical Investigation* says that with climate change, cases of heat cramps, heat exhaustion and potentially fatal heat strokes are expected to increase… (*CNN*)

Ultrasensitive Test Better Predicts Final Menstrual Period

A new way of more precisely measuring anti-Müllerian hormone (AMH) in women's blood may predict menopause and final menstrual period to within a window of 1-2 years, much better than current methods, suggests a new study published online in the *Journal of Clinical Endocrinology and Metabolism*.

The study revealed that the ultrasensitive AMH test had significantly better accuracy for predicting final menstrual period within the next 2 years compared to follicle-stimulating hormone (FSH), as well as the next 3 years. About the same degree of accuracy was noted with AMH and FSH at 12 months. For women with an AMH <10 pg/mL, the likelihood of having a final menstrual period in the next 12 months ranged from 51% for those younger than 48 years to 79% for those aged 51 years or older.

VTE Risk Persists After IBD Discharge, Particularly in Nonsurgical Patients

Post-discharge VTE was noted to be more than twice as likely to occur in nonsurgical patients with inflammatory bowel disease (IBD) than controls, revealed a Canadian population-based study. Surgical patients with ulcerative colitis but not Crohn's disease were also found to have a higher risk of post-discharge VTE.

Investigators found a cumulative incidence of VTE at 12 months after hospital discharge of 2.29% for nonsurgical IBD patients and 1.57% for surgical IBD patients. The incidence rose in the nonsurgical IBD cohort by 4% per year for an incidence rate ratio of 1.04 (95% CI 1.02-1.05). The findings were published online in *Inflammatory Bowel Diseases*.

Indian Journal of Clinical Practice, Vol. 30, No. 9, February 2020

What will Happen if an Employee doesn't Furnish PAN or Aadhaar to the Employer for Tax Deduction at Source on Salary Paid to the Former?

KK AGGARWAL

PAN/Aadhaar rules for AY 2020: As per Section 139A(5B), it is obligatory for employers (who are responsible for deducting tax at source) to quote PAN or Aadhaar number as the case may be, of the persons from whose income tax has been deducted.

Employees may end up paying a lot in tax if they don't furnish PAN or Aadhaar before the employee (who is responsible for deducting TDS on salary). Such employees may end up paying over 20% of their income in tax to the government.

Section 206AA in the Act makes furnishing of PAN or Aadhaar number as the case may be, by the employee compulsory in case of receipt of any sum or income or amount, on which tax is deductible.

Taxpayers are also liable to furnish their correct PAN or Aadhaar number as the case may be, to their deductors. Non-furnishing of PAN or Aadhaar number as the case may be, by the deductee (employee) to the deductor (employer) will result in deduction of TDS at higher rates u/s 206AA of the Act.

If an employee (deductee) fails to furnish his/her PAN or Aadhaar number, as the case may be, to the deductor (employer), the latter will be responsible to collect TDS at higher of the following rates:

i) at the rate specified in the relevant provision of this Act; or

ii) at the rate or rates in force; or

iii) at the rate of 20%.

The employer will determine the tax amount in all the three conditions and apply the higher rate of TDS.

However, where the income of the employee computed for TDS u/s 192 is below taxable limit, no tax will be deducted. But where the income of the employee computed for TDS u/s 192 is above the taxable limit, the deductor will calculate the average rate of income- tax based on rates in force as provided in Section 192.

If the tax so calculated is below 20%, deduction of tax will be made at the rate of 20% and in case the average rate exceeds 20%, tax is to be deducted at the average rate.

Health and Education cess at 4% will not be deducted, in case the tax is deducted at 20% u/s 206AA of the Act.

As per Section 139A(5B), it is obligatory for employers (who are responsible for deducting tax at source) to quote PAN or Aadhaar number as the case may be, of the persons from whose income tax has been deducted in the statement furnished u/s 192(2C), certificates furnished u/s 203 and all statements prepared and delivered as per the provisions of Section 200(3) of the Income Tax Act. (*Informal News*)

President, CMAAO and HCFI
Past National President, IMA

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Medtalks with Dr KK Aggarwal

New Study Claims to have Found Root of Fatal Malaria Infection

The common fact about the disease is that the parasites carried and spread by Anopheles mosquito bites are behind the infectious disease.

Washington DC: The origin of Malaria infection has finally been revealed. A new study has come up with the data that can aggravate the treatment of the complex infection.

According to Professor Ian Cheeseman from Texas Biomedical Research Institute, "We don't know what is inside malaria infections, or how many different genetically distinct strains of parasites there are. We don't know how related they are to each other. We don't know how many mosquitoes they came from."

Borna Disease Virus can be the Cause of Unidentified Encephalitis

A virus that jumps from shrews (chachundar) to humans seems to have been causing encephalitis unnoticed for decades in regions where the host shrew lives in the wild.

Eight newly-identified fatal cases of Borna disease virus 1 (BoDV-1) suggest that where the virus occurs in the wild, it could be responsible for high proportion of severe and deadly cases of encephalitis, according to results from 56 patients who had developed signs of encephalitis over the past 20 years, published in *The Lancet Infectious Diseases* journal.

TB Treatment Made Easy with 'Zero Tuberculosis' Initiative

There are many tuberculosis (TB) patients who have received help from Zero Tuberculosis started by Amit Verma, Assistant Professor at the Pharmacy Department of Mahatma Jyotiba Phule Rohilkhand University, in October. Verma launched Zero Tuberculosis, a unique digital platform, on Facebook to help poor TB patients.

Bareilly: A 24-year-old woman suffering from tuberculosis (TB) was not getting free medicines regularly due to "carelessness" of accredited social health activists (ASHA) of her village in Bhamora area of Bareilly district. The woman, an illiterate, was too sceptical to lodge a complaint with senior officials. Last month, however, she received a call from a volunteer of 'Zero Tuberculosis', who asked her several questions about her disease and the treatment. The woman told the volunteer that she was not getting medicines regularly. The volunteer shared her problem with district tuberculosis officials, who immediately ensured that ASHA workers provide her with the monthly medicines on time.

New Machine can Keep Livers Alive Outside Body for 1 Week

London: Researchers have developed a novel machine which can repair injured human livers, and keep them alive outside the body for 1 week. This may increase the number of available organs for transplantation.

According to the researchers, including those from ETH Zurich in Switzerland, injured livers can regain full function with the help of the new technology for several days, with the potential to save the lives of patients suffering from liver disease, or a variety of cancers.

Pathways That Extend Lifespan by 500% Identified

Science Daily: Scientists at the MDI Biological Laboratory, in collaboration with scientists from the Buck Institute for Research on Aging in Novato, Calif., and Nanjing University in China, have identified synergistic cellular pathways for longevity that increase the lifespan about 5 times in *Caenorhabditis elegans*, a nematode worm used as a model in aging research. The increase in lifespan would be the equivalent of a human living for 400 or 500 years.

C. elegans is a popular model in aging research because it shares many of its genes with humans and because its short lifespan of only 3-4 weeks allows scientists to rapidly assess the effects of genetic and environmental interventions to extend healthy lifespan.

Several drugs that increase healthy lifespan by altering these pathways are in the pipeline. The discovery of the synergistic effect opens the door to even more effective anti-aging therapies.

The new research uses a double mutant in which the insulin signaling (IIS) and target of rapamycin (TOR) pathways have been genetically altered. Because alteration of the IIS pathways yields a 100% increase in lifespan and alteration of the TOR pathway yields a 30% increase, the double mutant would be expected to

live 130% longer. But instead, its lifespan was amplified by 500%.

The paper focuses on how longevity is regulated in the mitochondria.

Draft Policy on Rare Diseases and the Role Played by IMA and HCFI

The Indian government has come up with a new draft National Policy for Rare Diseases, 2020, which highlights "scarce resources" to provide financial support for treatment of rare diseases. The draft policy proposes to set up a registry under Indian Council of Medical Research (ICMR) to create a database and provide financial assistance of up to Rs. 15 lakh to Ayushman Bharat beneficiaries for rare diseases that require a one-time treatment in tertiary hospitals only.

The government plans to notify certain medical institutes as Centers of Excellence for Rare Diseases. To begin with, these will include Delhi's All India Institute of Medical Sciences and Maulana Azad Medical College, Chandigarh's Post Graduate Institute of Medical Education and Research, Mumbai's King Edward Medical Hospital, Lucknow's Sanjay Gandhi Post Graduate Institute of Medical Sciences and three others.

The draft policy also categorizes rare diseases under three categories based on clinical experiences and treatment availability.

Category 1: Disorders amenable to one time treatment (curative) – Prioritize funding for this category as one time treatment cost ranges from 5 to 20 lakhs, which is much less compared to long-term therapy, treatment outcome is good, facilities for treatment are available in both private and public sector with good expertise and outcome. Funding should also include support for follow-up therapy and ceiling on existing funding limit should be made flexible. Examples are certain immune deficiency disorders that can be cured with treatment, and certain diseases such as Tyrosinemia, Fabry disease and Maple Syrup Urine Disease, which require kidney or liver transplants.

Category 2: Disorders requiring long-term/life-long therapy – Cost of therapy for most disorders in this category is prohibitive and families cannot afford it without some support.

Category 3: Disorders for which no known therapy is currently available but requires supportive care (Supportive therapy is the only available option, Need to provide care and support services).

Role of IMA and HCFI

- From 2014 to 2017, during my tenure as HSG and later National President, IMA; we had been fighting about this issue.
- 2015: hhttps://ordindia.org/uncategorized/indian-needs-extra-health-budget-for-rare-diseases/27th Feb 2015. IMA stand that more budget is required.
- 2016: http://blogs.kkaggarwal.com/2016/12/rare-diseases-and-rare-drugs/as HSG IMA, I wrote this to all the government agencies. Should CRS, insurance companies and government subsidy under one roof be the answer for such diseases and drugs?
- 2018: July 17, Policies for management of rare diseases and their treatment a must in India: http://blogs.kkaggarwal.com/2018/07/policies-for/
- Based on our and many other NGOs' efforts, the Health Ministry had formulated a national policy on treatment of rare diseases in 2017, which envisaged the setting up of a corpus fund with an initial amount of ₹100 crore towards funding treatment of rare genetic diseases, but this never picked up due to budget constraints.
- The draft policy does not provide financial assistance to rare diseases that require lifelong treatment like Gaucher's Disease, Hurler Syndrome, Wolman disease. Treatment for some of these diseases may vary from Rs. 10 lakhs to more than Rs. 1 crore per year. For these diseases, the government has sought alternate funding mechanism like setting up a digital platform for voluntary and corporate donations.
- This policy is also based on our persistent efforts at Heart Care Foundation of India (HCFI). HCFI filed a representation with Hon'ble Delhi High Court requesting the Hon'ble Court to direct the Central Government as well as the State Government to follow the suggestions/directions as given by this Hon'ble Court judgment dated 17.04.2014 in the matter titled as "Mohd. Ahmed (minor) versus Union of India & Others, Writ petition (Civil) No. 7279/2013. The said representation converted into PIL was duly accepted and disposed off vide order dated 15th July, 2019 whereby the government has been asked to consider the same. As per the high court directions "*All government hospitals could have a separate CSR/Charitable entity/account wherein donations can be received. The donations could be subject to an audit.*"

- In the US, the Orphan Drugs Act provides incentives to drug manufacturers to encourage them to manufacture drugs for rare diseases, and similar incentives are also provided in the UK and certain other developed countries.

HCFI recommendations

A petition in the Delhi High Court regarding directions that government provide free treatment for rare diseases - the Delhi High Court in W.P. (C) No. 4444/2016, W.P. (C) No. 7730/2016, and W.P. (C) No. 7729/2013 directed the Ministry of Health to frame a national policy on treatment of rare diseases. The government has issued draft guidelines.

Here are HCFI suggestions

- Various countries have used different approaches for funding treatment for rare diseases. European countries cover the cost through their National Health Services. In USA, once a drug is approved by the Food and Drug Administration (FDA), the insurance company will need to cover the cost. In other countries, the government pays for the cost of the treatment, for instance in Egypt, Thailand, Argentina, Chile, Peru, Serbia, Malaysia and Philippines.
- According to the proposed draft policy, Ayushman Bharat scheme will cover up to 15 lakhs as one time cost for the treatment of curable diseases under category 1 and a crowd funding mechanism will be created for diseases requiring long-term treatment under categories 2 and 3.
- Up to 15 lakhs as one time treatment cost should be considered even for category B and category C patients. The cost of maintenance in them may be covered through a crowd funding mechanism.
- The Department of Financial Services and Insurance Regulatory and Development Authority (IRDA) should amend the acts to consider that once a treatment of a rare/genetic disease has been approved by the Drug Controller General of India (DCGI), the same should be covered under the available insurance cover.
- Once a treatment is approved by DCGI, the same should also be covered by CGHS, PSU, ESI, etc.
- Based on this, the Ayushman Bharat should also consider up to 15 lakhs grant for all organ donations apart from sanctioning for rare diseases curable transplants.

Practice-Changing Studies from American College of Gastroenterology

- Oral budesonide suspension 2 mg for 12 weeks shows striking efficacy for eosinophilic esophagitis.
- Avoidant/restrictive food intake disorder (ARFID) is increasingly being emphasized in adult gastroenterology. This is a diagnosis that's established by restriction or avoidance of food intake that is associated with weight loss, nutritional deficiencies, dependence on tube feedings or oral supplements, or significant psychosocial impairment.
- Vedolizumab for ulcerative colitis: Shift from IV to SC now. It is a monoclonal antibody targeting the alpha-4 beta-7 integrin.
- Obeticholic acid, a selective farnesoid X receptor agonist, which regulates bile acid homeostasis, is effective in nonalcoholic steatohepatitis (NASH).
- There is no apparent increased risk for metachronous lesions in young adults with adenomas.
- Hyperbaric oxygen is a new intervention for refractory pouchitis.

Belgian Doctors Face Trial in Country's First Euthanasia Case

Three Belgian doctors went on trial for murder for helping a woman end her life.

The doctors, are accused of unlawfully poisoning 38-year-old Tine Nys on April 27, 2010.

They are the first doctors to go on trial for euthanasia in Belgium since the country legalized the practice in 2002.

Nys's parents and sisters, who were present at her death, complained that the euthanasia was carried out in an amateurish manner and that Nys did not have an incurable mental disorder, a key condition for granting euthanasia.

Belgian law allows adults to request the right to die on condition that they are facing unbearable physical or mental suffering resulting from a serious and incurable disorder. It was extended to terminally ill children in 2014.

Most patients choosing medically assisted death have terminal cancer, but mental suffering has extended, for example, to twins born deaf and becoming blind who are unable to bear not being able to see or hear each other.

In neighboring the Netherlands, where euthanasia is also legal, a doctor was acquitted in a trial in September after being accused of failing to secure proper consent from a woman who had Alzheimer's.

1,700 Doctors with PG Diploma from IGNOU can't Practice Cardiology, MCI Refuses to Recognize their Degrees

The 2-year course was started in 2006 to train doctors as Cardiologists in 70 hospitals all over the country. From 2006 to 2012, nearly 1,700 doctors opted for the course. The university stopped fresh enrollment in the year 2013 after the Medical Council of India (MCI) refused to grant a license to students pursuing it. Some doctors who had earlier taken the course approached the Delhi High Court. In September, the court asked the Union Health Ministry to opine in the matter.

The MCI-Board of Governors also concluded that these doctors cannot be allowed to work as Cardiologists.

Reason given: Evaluation of the training program was not done within 1 year of starting it according to the Indian Medical Act, 1956 rules.

My Comments

MCI Ethics Regulation: 1.4.2 Physicians shall display as suffix to their names only recognized medical degrees or such certificates/diplomas and memberships/honors which confer professional knowledge or recognizes any exemplary qualification/achievements.

Under clause 1.4.2, there should be no reason not to write about their diploma on their letterhead along with the name of IGNOU. It will still be IGNOU-certified and not MCI-certified.

The clause 1.4.2 does not stop people from doing non-MCI diploma or take certificates. It gives options of only recognized medical degrees or such certificates/diplomas. MCI itself has no Diploma or a certificate course in Cardiology, so other certificate and diplomas courses will invariably be started by institutions. The MCI clause 7.20 should not be read in isolation but read with 1.4.2.

7.20 A Physician shall not claim to be specialist unless he has a special qualification in that branch.

Also, the reason given by MCI is technical and not on merit.

Important 2019 Take Home Heart Messages

- Icosapent ethyl, a prescription omega-3 fatty acid, reduced the risk for cardiovascular (CV) events by 25% in people with elevated triglyceride levels who were taking statins. REDUCE-IT led the US FDA to approve icosapent ethyl for CV risk reduction in December.
- COMPLETE trial: STEMI heart attack with multivessel disease benefits from complete revascularization of any other angiographically significant lesions, rather than a strategy of intervention only in the culprit lesion.
- DAPA-HF trial showed that the glucose-lowering drug dapagliflozin is beneficial in patients with heart failure, both with and without type 2 diabetes.
- In a large-scale study of over 4,19,000 Apple Watch users, the device accurately detected atrial fibrillation in more than one-third of the participants who received notifications of an irregular pulse.
- EXTEND trial: It's possible to extend the window for thrombolysis out to 9 hours after ischemic stroke onset in some patients.
- PARTNER 3 trial: Patients with severe aortic stenosis at low surgical risk who had transcatheter aortic valve replacement using the SAPIEN 3 system had lower odds of stroke, rehospitalization and death compared with those who had traditional surgery.
- Five-year findings from the NOBLE trial demonstrate that percutaneous coronary intervention is not as effective as coronary artery bypass grafting in reducing the risk of death, myocardial infarction (MI), repeat revascularization, and stroke in patients with left main disease.
- In children with familial hypercholesterolemia (FH), statin therapy beginning at a young age reduced incidence of CV events from 26% to 1% at age 39, and reduced death from CV causes from 7% to 1% at age 39.
- In older women, reducing sedentary time by just 1 hour each day equated to a 26% lower risk of heart disease and a 12% lower risk of CVD overall. The physical activity didn't have to happen all at once — it could be accumulated throughout the day.
- Older women who engaged in light physical activity, such as gardening or walking, had a 42% lower risk of MI or coronary death than the least-active women.
- Taking anti-BP drug at bedtime led to a 45% reduction of CV events.
- SPRINT MIND study: Intensive BP-lowering cuts the risk for mild cognitive impairment in adults aged 50 years and older.
- Children exposed to second-hand smoke from their parents were at a higher risk for atrial fibrillation. For every pack per day increase in parental smoking, their children were 18% more likely to develop atrial fibrillation.

Source: Medscape

World Health Assembly has Designated 2020 the 'International Year of the Nurse and the Midwife'

The World Health Organization (WHO) has designated 2020 as the "Year of the Nurse and Midwife", in honor of the 200th birth anniversary of Florence Nightingale.

The year 2020 is significant for WHO in the context of nursing and midwifery strengthening for Universal Health Coverage. WHO is leading the development of the first-ever State of the World's Nursing report which will be launched in 2020, prior to the 73rd World Health Assembly.

The year 2020 will be a major global effort to highlight an acute shortage of these crucial health workers.

The world needs 9 million more nurses and midwives if it is to achieve Universal Health Coverage by 2030.

Nurses are often the first, and only, point of care in their communities.

Nurses and midwives devote their lives to caring for mothers and children; giving lifesaving immunizations and health advice; looking after older people and generally meeting everyday essential health needs.

18 Important Medical Research Outcomes of 2019

1. New neurons proliferate in the hippocampus as we age, even into the ninth decade of life (*Nature Medicine*).
2. Novel protein-coding genes evolve on a *de novo* basis far more commonly than previously thought (*Nature Ecology and Evolution*).
3. Children's long bones grow with the help of a stem cell niche with a radical clonality switch that develops in the epiphyseal growth plate (*Nature*).
4. 10,000 steps or less: Researchers who ran a study of nearly 17,000 women found that cut-off for mortality benefit was just 4,400 (*JAMA Internal Medicine*).
5. Comparing the DNA of primary colorectal cancer tumors and metastases in the liver or brain revealed that for 80% of the 21 patients in the study, metastases took root early (*Nature Genetics*).
6. Typhoid toxin may not be required for people infected with Salmonella Typhi to develop typhoid fever (*Nature Medicine*).
7. Assessing myocardial viability is not a helpful marker to predict the long-term outcome of coronary artery bypass grafting surgery (*NEJM*).
8. Rising BMI among people living in rural areas — not cities — is the main driver of the global obesity epidemic (*Nature*).
9. The brain microbiome: It might actually exist, and herpes virus might play a role in Alzheimer's disease (*Neuron*).
10. Cardiac stem-cell therapy appears to work by stimulating the immunologic wound-healing process rather than generating new cells (*Nature*).
11. Even if patients with severe aortic stenosis have no symptoms, early surgery to replace the aortic valve lowers their risk for death (*NEJM*).
12. Could we inherit mitochondrial DNA from our fathers as well as our mothers? The answer is Yes (*Proc Natl Acad Sci*).
13. Screen time: not so bad for kids' well-being after all? (*Nature Human Behaviour*).
14. The morning meal may not help people lose weight, according to a meta-analysis published in the *BMJ*.
15. Applying evolutionary game theory to cancer therapy, as researchers did in a paper in *Nature Ecology and Evolution*, challenges the traditional approach of blasting tumors with the maximum tolerable dose of chemotherapy.
16. Type 2 diabetes and high lipoprotein(a) [Lp(a)] levels were associated with a 3.5-fold higher risk for a CV event compared to having no diabetes or a low Lp(a) level (<24 nmol/L or approximately 10 mg/dL) (*Diabetes Care*).
17. In an observational registry study of Swedish outpatients with type 1 diabetes, those who had high plasma Lp(a) levels — defined as >120 nmol/L or approximately 50 mg/dL — were more likely to have albuminuria, calcified aortic valve disease, or a composite measure of CVD. And patients whose blood glucose level (A1c <6.9%) was well-controlled had lower Lp(a) levels (*Diabetes Care*).
18. Caloric restriction can reduce insulin resistance, weight, hepatic fat and CV risk factors, regardless of carbohydrate content. To achieve caloric restriction one can go for fasting regimens as time-restricted eating (meals consumed within a limited number of hours), alternate-day fasting, and the 5:2 eating pattern (unrestricted eating for 5 days, followed by 2 days of restricted intake).

Source: Medsacpe

FDA Makes Legal Smoking Age Raised to 21: All Countries should Raise it and Make it Uniform

The smoking age is the minimum legal age required to purchase or smoke tobacco products. Most countries have laws that restrict those below a minimum age from legally purchasing tobacco products.

The US FDA has raised the legal smoking age from 18 to 21. As per FDA "On December 20, 2019, the President signed legislation to amend the Federal Food, Drug and Cosmetic Act and raised the federal minimum age of sale of tobacco products from 18 to 21 years. It is now illegal for a retailer to sell any tobacco product to anyone under 21."

CMAAO welcomes this decision and urges all National Medical Associations to urge their respective governments to follow the same.

In India, in 2014, the Health Ministry set up a committee to recommend amendments to the Tobacco Regulation Act, which may suggest raising minimum age for smoking from 18 years to 25; however, the same was never implemented.

The legal smoking age in different countries are given below:

- Singapore 19
- Thailand 20
- India 18
- Pakistan 18
- Sri Lanka 21
- Bangladesh 16
- Nepal 18
- Malaysia 19
- Korea 19 (purchasing age 20)
- New Zealand 18
- Australia 18
- Hong Kong 18
- Philippines 18
- Taiwan 18
- Japan 20
- Indonesia 18

Mission Delhi Now will Cover 78 sq. kms Area: Call 14430

Easy way to remember the number: do not gather around (Section 144 of IPC) any victim of more than 30 years with suspected heart attack (call 14430).

Mission Delhi is a successful ICMR-AIIMS pilot to provide care to acute STEMI Heart Attack patients. It was launched on 25th April, 2019 and now covers 78 sq. kms area around AIIMS covering a population of 20-25 lakhs in the National capital.

Under 'Mission DELHI' (Delhi Emergency Life Heart-Attack Initiative), an emergency medical service, a motorbike-borne assistance unit can be quickly summoned for a person suffering heart attack or chest pain.

On getting a call, the pair would rush to the spot, gather basic information on the patient's medical history, conduct a quick medical examination, take the ECG, and establish a virtual connect with the cardiologists at AIIMS and deliver expert medical advice and treatment. While the emergency treatment is being provided, a CATS ambulance will arrive and take the patient for further treatment.

Even as the patient is on way to the hospital, doctors at AIIMS control center will evaluate the data received from the nurses to establish further course of treatment.

Motorcycle ambulances can reach people in narrow lanes in congested areas. The attempt is to reach patients within 10 minutes.

It is important to remove the clot that is stopping the blood flow. If the heart walls are damaged, they cannot be repaired. Clot busters are almost equal to angioplasty. In this project, the clot buster will be given very soon even at home.

Toll Free Emergency Helpline numbers are 1800111044 and 14430.

The project must be started all over India and even in Asian countries. It so far has helped only 44 cases, which means its still not in the mind of local doctors and the other healthcare providers. It needs to be advertised widely and extensively. Also, the project must cover the cases of cardiac arrest also.

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Annual Conference of Endocrine Society of India (ESICON 2019)

21-24TH NOVEMBER, 2019 | HOTEL LE MERIDIEN, NAGPUR

ARTIFICIAL INTELLIGENCE IN DIABETES MELLITUS

Dr KM Prasanna Kumar, Bengaluru, Karnataka

- Diabetology needs an adaptation process to incorporate new tools for diabetes management.
- Technology and particularly sensors and computer applications have become a key instrument in diabetes management for healthcare providers and patients.
- Modern diabetes care units should include a diabetes technologist for dealing with technology.
- Artificial intelligence (AI) methods, in combination with the latest technologies, including medical devices, mobile computing and sensor technologies, have the potential to enable the creation and delivery of better management services to deal with chronic diseases like diabetes mellitus.
- Knowledge on insulin pumps and glucose sensors has been increasing, but comprehension about AI and smart applications performance remains largely inadequate.
- Benefits of AI tool – Highly useful in large scale screening and hospitals; Portable and very simple to use: the user merely needs to enter the values in the computer interface and instant diagnosis is available; Such methods of early diabetes detection may be beneficial in reducing the number of diabetes patients in the future.

ADULT TURNER MANAGEMENT

Dr Arpandev Bhattacharyya, Bengaluru, Karnataka

- Turner syndrome (TS) is the commonest chromosomal abnormality in females.
- It is an important cause of short stature and primary ovarian insufficiency in females. It is never too late to diagnose TS. It is associated with a risk of atherosclerosis and congenital heart disease.
- Cardiovascular disease is the most serious health issue. Hence, active surveillance is the key. Detection at diagnosis and sequential follow-up by specialist at regular intervals are needed. Aggressive BP control is important.
- Spontaneous pregnancy is rare due to follicular depletion. Solution is *in vitro* fertilization (IVF) with donor oocyte. It is important to keep an eye on possible comorbidities.
- Yearly check for thyroid disease, glucose intolerance, dyslipidemia, liver abnormalities and celiac disease should be conducted.
- Screening for hearing loss is needed. Neuropsychiatric evaluation may be done, as and when needed.
- Special touch with the patient with TS is needed for long-term follow-up.

Hormone replacement therapy (HRT) is a must unless proved otherwise.

OSTEOPOROSIS AND CKD – WHAT IS NEW?

Prof (Dr) Peter R Ebeling, Australia

- Fracture risk and fracture-related complications and costs are higher in type 2 diabetes mellitus and chronic kidney disease (CKD) patients.
- DXA T score does classify fracture risk in type 2 diabetes mellitus and CKD patients. More information is needed about novel imaging methods.
- PTH and bone turnover markers, particularly bone-specific alkaline phosphatase (BSAP), predict bone loss and can help guide treatment in CKD. Bone biopsies are only needed when turnover and/or osteomalacia cannot be determined noninvasively.

An individual and tailored approach to managing bone disease is critical in type 2 diabetes mellitus and CKD patients.

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News and Views

Stepped-up Efforts Needed to Fight Pneumonia

Scaling up pneumonia-related interventions could save the lives of nearly 9 million children over the next decade, the United Nations Children's Fund said.

According to a new scientific model produced by Johns Hopkins University, in the United States, improving pneumonia treatment and prevention services could prevent up to 3.2 million children below five from dying. It would create 'a ripple effect' that would help prevent the deaths of an additional 5.7 million children from other major childhood diseases, underscoring the need for integrated health services… (*UN*)

Cabinet Approves Raising Upper Limit for Permitting Abortions to 24 Weeks

The Union Cabinet has approved extending the upper limit for permitting abortions from the present 20 weeks to 24 weeks. The Cabinet approved the Medical Termination of Pregnancy (Amendment) Bill, 2020 to amend the Medical Termination of Pregnancy Act, 1971. Union Minister Prakash Javadekar said that the upper limit for permitting abortions has been extended from 20 weeks to 24 weeks. He also stated that this will ensure safe termination of pregnancies and also provide women with reproductive rights over their bodies… (*ET Healthworld – PTI*)

Fruits, Vegetables, Tea Consumption Linked with Lower Alzheimer's Risk

Elderly people consuming diets rich in flavonols, antioxidants found in fruits, vegetables and tea, may be less likely to develop Alzheimer's disease, suggests a new study.

Researchers followed 921 people without dementia for about 6 years. During the study, 220 people were diagnosed with probable Alzheimer's disease. Researchers noted that people who had the most flavonols in their diet were about half as likely to develop Alzheimer's as those who consumed the least. The findings were published in the journal *Neurology*… (*Reuters*)

Gut Microbiome Less Diverse in Teens with Obesity and PCOS

Teens with obesity and polycystic ovary syndrome (PCOS) have decreased bacterial diversity and a more unhealthy gut microbiome in comparison with similar-sized teens without PCOS, suggests a new study published online in the *Journal of Clinical Endocrinology & Metabolism*.

Researchers also noted that higher testosterone levels, often found in women with PCOS, were associated with decreased bacterial diversity in the gut.

Heavy Traffic Pollution may Affect Kids' Brain Development

High levels of exposure to traffic-related air pollution at a very young age may result in structural changes in the brain, suggests an imaging study.

Brain scans of 12-year-old children showed reduced thickness of the cortex and decreased gray matter volume in those who lived less than a quarter of a mile (400 meters) from a major highway at age 1, according to a report published in *PLoS ONE*… (*Reuters*)

Respiratory Changes After Weight Loss Surgery: Study

Within 6 months of undergoing weight loss surgery, obese patients exhibited structural changes on airway imaging that correlated with respiratory symptom improvements, reported researchers in a study published online in *Radiology*.

Investigators used inspiratory and expiratory chest computerized tomography (CT) imaging to assess changes in the respiratory systems of patients before undergoing bariatric surgery and 6 months after having the surgery, when significant weight loss had occurred. There were significant reductions in air trapping and less tracheal collapse at 6 months, which correlated with improvements in symptoms as measured by dyspnea scores.

Beer, Wine, Spirit Makers Pledge Age-restriction Labels on Drinks

Brussels: Twelve leading beer, wine and spirits companies have pledged to put clear age-restriction labels on their drinks and set tighter controls on access to their online content in a bid to reduce underage drinking.

The International Alliance for Responsible Drinking (IARD), which includes Anheuser-Busch InBev (ABI BR),

Diageo (DGE.L) and Pernod Ricard (PERP.PA), say age-restriction symbols or wording would be in place in all markets by 2024. The labels would also extend to alcohol-free versions of established brands… (*Reuters*)

Two Biologics on Par for Controlling Arthralgias in IBD

Vedolizumab was just as effective as infliximab in controlling arthralgias among patients with inflammatory bowel disease (IBD), according to a head-to-head comparison presented at the annual Crohn's & Colitis Congress (CCC).

Among 154 biologic-naive adults with Crohn's disease or ulcerative colitis, no difference in the rate of new-onset arthralgias could be seen between the two therapies at 1 year (25% vs. 26%, p = 1.0), reported Samantha Mehta, PharmD, of Healix Infusion therapy in Sugar Land, Texas.

'Micro-Strategies' may Help Maintain Weight Loss Long-term

Behavioral and psychological strategies such as setting daily goals, maintaining a positive mindset, and thinking about past successes may be the key to maintaining weight loss long-term among participants of commercial weight management programs, suggests a new US study.

Investigators studied over 4,500 successful weight loss maintainers who had used WW International (formerly Weight Watchers). The study, published online in *Obesity* showed that, compared with over 500 obese individuals with stable weight, weight loss maintainers were more likely to use a variety of self-monitoring and psychological coping strategies. They were also more willing to ignore food cravings and had stronger habits towards healthy eating and weight loss maintainers had better quality of life.

End Discrimination Against Women and Children Affected by Leprosy

Governments must put an end to the informal segregation and institutionalized neglect of hundreds of thousands of women and children affected by leprosy, an independent UN human rights expert said on World Leprosy Day.

"Too many women and children affected by leprosy – also known as Hansen's disease – are victims of stereotypes, physical and verbal abuse, delays of diagnosis and lack of adequate care", declared Alice Cruz, UN Special Rapporteur on the elimination of discrimination against persons affected by leprosy and their family members. The UN expert expressed concern over the "complete lack of specific plans by States to address the particular needs of women and children affected by leprosy and to end discrimination and violence against them"… (*UN*)

Blue-Light Therapy Helps Heal the Brain

Early morning exposure to blue wavelength light can help heal the brain following mild traumatic brain injury (mTBI), new research suggests.

Results of a small, randomized controlled trial suggested that blue-light therapy improved brain structure and function, cognition and sleep in these patients. Investigators enrolled 32 adults into the randomized, double-blind, placebo-controlled trial. Participants who underwent blue-light therapy experienced improvement in a number of sleep-related assessments and demonstrated significantly reduced daytime sleepiness (p = 0.027) than their counterparts in the sham light therapy group. Executive function also improved after the intervention. Blue-light therapy was associated with increased volume of the posterior thalamus, greater thalamo-cortical functional connectivity, and increased axonal integrity of these pathways. The study was published in the February issue of *Neurobiology of Disease*.

Human and Analogue Insulins Equivalent for Major Outcomes

There was no difference between human and analogue insulin in terms of cardiovascular and mortality outcomes, but cost is another matter, said authors of a large retrospective study.

Data on 1,27,000 adults with type 2 diabetes who initiated insulin during 2000-2013 and median 2.5 years of follow-up, revealed that users of human versus analogue insulin products had similar rates of major cardiovascular events, cardiovascular mortality, and overall mortality, reported Patrick O'Connor, MD, of the HealthPartners Institute in Minneapolis, and colleagues in *JAMA Network Open*.

Guided Self-help Intervention Reduces Refugees' Psychological Distress and Improves Well-being in Humanitarian Crises

A guided self-help approach that provides strategies for managing distress and coping with adversity is safe, and resulted in meaningful improvements in psychological distress and functioning compared to enhanced usual care over 3 months in female refugees living in a settlement in Uganda, according to a randomized trial

involving nearly 700 South Sudanese refugee women, published in *The Lancet Global Health*.

This is the first randomized trial of a guided self-help group intervention in a low-resource humanitarian setting. Although longer follow-up is needed to determine the long-term effects of the intervention, guided self-help could be a promising first-line strategy to address the vast gap in mental health support in areas where humanitarian access is difficult, such as South Sudan and Syria… (*WHO*)

New Survey Reveals Secret to Longevity; Healthiest and Unhealthiest Cities in India

Chandigarh has been found to be the healthiest city in India, while Kolkata scored the lowest, as per GOQii India Fit Report 2020. A year-long study of about 5 million people was conducted to get an overview of the health and lifestyle of India. The study found only 38% of Indians to be healthy. Women were found to be unhealthier than men, with about 71% of them falling in the unhealthy category in "High Risk Assessment spectrum". 90-year olds and centenarians were also surveyed in India to find out the secret to longevity. Turns out, eating nutritious food, staying active, socializing and sound sleep are key… (*The Indian Express*)

Coconut Oil Consumption Linked to Increased LDL

Combining the findings from 16 published studies, investigators found that use of coconut oil was associated with increases in low-density lipoprotein (LDL) and total cholesterol levels, potentially putting people at higher risk for cardiovascular disease (CVD).

Compared to nontropical olive, soybean or canola oil, high consumption of coconut oil substantially increased LDL cholesterol. Consuming 3 to 4 tablespoons of coconut oil daily was associated with an estimated 10 mg/dL increase—about a 9% jump—in LDL levels. The systematic review and meta-analysis was published online in *Circulation*.

Latent CMV Protects Bone in RA

Fewer patients with early rheumatoid arthritis (RA) who were seropositive for cytomegalovirus (CMV) had bone erosion progression at 1 year, French researchers reported.

In a large cohort of RA patients, a change from baseline of at least 1 unit on the erosion Sharp score after 1 year of follow-up was observed in 16.1% of those who were CMV positive compared with 25.2% of those who were seronegative (p = 0.0128), reported researchers. This could occur as a result of the effects of CMV infection on osteoclastogenesis, they explained in *Arthritis Research & Therapy*.

Healthcare's a Human Right, not "a Privilege for the Rich" UNAIDS Argues

The UN agency devoted to ending AIDS as a public health threat called on top politicians and governments across the world to ensure the right to quality health care is upheld, and not just a privilege to be enjoyed by the wealthy.

In a press release, UNAIDS Executive Director Winnie Byanyima said that the right to health "is eluding the poor and people trying to lift themselves out of poverty are being crushed by the unacceptably high costs of health care", with at least half the world's population unable to access essential health services… (*UN*)

FDA Approves First Treatment for Thyroid Eye Disease

The US FDA has approved teprotumumab-trbw for the treatment of adults with thyroid eye disease, a rare condition where the muscles and fatty tissues behind the eye become inflamed, causing the eyes to be pushed forward and bulge outwards (proptosis). The approval represents the first drug approved for the treatment of thyroid eye disease… (*FDA*)

A 'Healthy' Diet: More Complex Than Just Low Fat or Low Carbs

A low-carbohydrate and low-fat diet was not linked with total mortality, researchers reported.

Evaluating nearly 40,000 US adults, those who consumed a diet comprising of low-carbs, but high total protein and fat, didn't see any reduced all-cause mortality risk (hazard ratio [HR] of 0.97, per 20-percentile increase in diet score, 95% confidence interval [CI] 0.93-1.00, p = 0.06 for trend). This lack of association, as described in *JAMA Internal Medicine*, was seen with a low-fat diet as well (HR of 0.97 per 20-percentile increase in diet score, 95% CI 0.93-1.02, p = 0.34 for trend). However, specific types and quality of macronutrients consumed had a significant association with total mortality risk.

New Use for Methotrexate in Spondyloarthritis?

Adding methotrexate to adalimumab in axial spondyloarthritis was associated with reduced immunogenicity, as shown by a lower rate of developing antidrug antibodies, French researchers reported.

Among 107 patients with spondyloarthritis, 25% of those given methotrexate along with adalimumab developed antidrug antibodies by week 26 compared with 47.3% of those who received adalimumab as monotherapy, for a relative risk of 0.53 (95% CI 0.31-0.91), reported Denis Mulleman, MD, PhD, of the University of Tours, and colleagues in *RMD Open: Rheumatic & Musculoskeletal Diseases*.

Smoking Greatly Increases Risk of Complications After Surgery

Tobacco smokers are at significantly higher risk than nonsmokers for post-surgical complications including impaired heart and lung functions, infections and delayed or impaired wound healing.

New evidence reveals that smokers who quit approximately 4 weeks or more before surgery have a lower risk of complication and better results 6 months afterwards. Patients who quit smoking tobacco have lower odds of experiencing complications with anesthesia when compared to regular smokers.

A new joint study by the World Health Organization (WHO), the University of Newcastle, Australia and the World Federation of Societies of Anaesthesiologists (WFSA), shows that every tobacco-free week after 4 weeks improves health outcomes by 19%, due to improved blood flow throughout the body to essential organs… (*WHO*)

Waist Size may be More Important Than Weight for Multiple Heart Attack Risk

Heart attack survivors who carry extra weight around their belly are at greater risk of another heart attack, new research has found. The latest study, published in the *European Journal of Preventative Cardiology*, is the first time researchers have found a link between belly fat and the risk of a subsequent heart attack or stroke. The link was particularly strong in men, researchers said… (*CNN*)

Novel Approach Shows Early Promise in Boosting Memory in Alzheimer's

Very early research suggests a novel, noninvasive brain stimulation technique guided by ultrasound may improve memory in Alzheimer's disease (AD).

Investigators found that ultrasound-guided transcranial pulse stimulation (TPS) administered to a small number of patients with probable AD improved memory for up to 3 months and that these improvements correlated with improvements in brain networks observed on functional magnetic resonance imaging (fMRI). The study was published online in *Advanced Science*.

Elevated Testosterone may Lower Asthma Risk in Women

Elevated levels of serum testosterone appeared to be significantly associated with a reduced risk for asthma in women, and obesity modifies this risk, researchers reported.

Findings from the first population-based study of its kind suggest that sex hormones play a key role in the widely recognized gender differences in asthma presentation among adults. Very elevated levels of free testosterone in women (fourth quartile vs. first quartile) were associated with a lower risk of asthma (OR 0.56, 95% CI 0.39-0.80). Among obese women, both elevated free testosterone (OR 0.59, 95% CI 0.37-0.91) and elevated estradiol (OR 0.43, 95% CI 0.23-0.78) were linked to lower asthma risk. The findings were published in the *American Journal of Respiratory and Critical Care Medicine*.

Lack of New Antibiotics Threatens Global Efforts to Contain Drug-resistant Infections

Declining private investment and lack of innovation in the development of new antibiotics are undermining efforts to combat drug-resistant infections, says the WHO.

Two new reports reveal a weak pipeline for antibiotic agents. The 60 products in development (50 antibiotics and 10 biologics) bring little benefit over existing treatments and very few target the most critical resistant bacteria (Gram-negative bacteria). While pre-clinical candidates are more innovative, it will take years before they reach patients… (*WHO*)

FDA Approves CVD Benefit for Once-Weekly Semaglutide

The US FDA has approved an additional indication—reduction of CVD risk—for the injectable formulation of the glucagon-like peptide 1 (GLP-1) agonist semaglutide in the treatment of type 2 diabetes and has added new trial data information to the label of the oral version pertaining to CV safety.

On January 16, the FDA expanded the once-weekly injectable semaglutide's label to include an indication for reducing the risk for major adverse cardiovascular events (MACE), including CV death, nonfatal myocardial infarction (MI) or nonfatal stroke, in adults with type 2 diabetes who have established CVD… (*Medscape*)

Bezlotoxumab Reduces Rates of Recurrent *C. difficile* Infection

The monoclonal antibody bezlotoxumab reduces the rate of recurrent *Clostridioides difficile* infection (CDI), suggest findings from the MODIFY II trial.

Investigators evaluated results from 295 MODIFY II participants who were followed for 12 months to assess the long-term rates of recurrent CDI and *C. difficile* colonization following antitoxin infusion. The recurrent CDI incidence rates during the core study for these patients were 25.3% with actoxumab *plus* bezlotoxumab, 18.8% with bezlotoxumab alone and 50.0% with placebo. The 12-month incidence rates of recurrent CDI among the 168 patients with a sustained clinical cure during the core study were 27.6% with actoxumab *plus* bezlotoxumab, 18.8% with bezlotoxumab alone, and 51.5% with placebo, the researchers report in *Clinical Infectious Diseases*.

Climate Crisis, Epidemics and Drug Resistance Among Next Decade's Urgent Health Challenges, WHO Says

Climate change, infectious diseases, anti-vaxxers and antimicrobial resistance all made their way onto the World Health Organization's list of health challenges facing the next decade.

The list was developed with input from experts around the world and presented "urgent, global health challenges," according to WHO. "The list reflects a deep concern that leaders are not investing enough resources in core health priorities and systems, putting lives and economies in jeopardy," WHO Director-General Dr Tedros Adhanom Ghebreyesus wrote in a Tweet… (*CNN*)

High BP Begins at Early Age in Women Than Men

Blood pressure (BP) begins to increase at younger ages in women than in men, and it goes up at a faster rate, a study revealed.

On average, women who develop heart disease are about 10 years older than men who develop it. But this report suggests that high BP begins at a younger age in women than men, and rises faster. Investigators found that by the time women are in their 20s, they show faster rates of increases in BP than men, and the difference persists throughout life. The variation was significant for all BP measures—systolic and diastolic, as well as for pulse pressure and for mean arterial pressure… (*ET Healthworld*)

What We Thought to be the Normal Body Temperature has Changed, Claims Study

We know the normal body temperature to be 98.6°F (37°C). The number was determined by German doctor Carl Reinhold August Wunderlich in 1851, following millions of readings from 25,000 German patients.

Researchers at Stanford University; however, have recently recorded a drop in the normal body temperature. The study found the average temperature to have dropped by 0.03°C and 0.29°C per decade, for men and women respectively, over the past 150 years. Julie Parsonnet, Professor of Medicine at the University, attributes the drop in the normal body temperature to several factors, including change in height and weight, which impacts body temperature, besides better nutrition, better medical care and better public health… (*The Indian Express*)

New Head Injury Data Reinforce Restricted Antipsychotic Use in Dementia

Antipsychotic medications increase the risk of head injury and traumatic brain injury (TBI) in people with Alzheimer's disease (AD), new research shows.

These new data support long-standing evidence-based clinical guidance to limit the use of antipsychotics in dementia patients to those with the most severe neuropsychiatric symptoms and for as short a time as possible.

The study published online in the *Journal of the American Geriatrics Society*, noted that in multivariable-adjusted analyses, antipsychotic use was associated with a 29% higher risk of head injury (adjusted HR, 1.29; 95% CI, 1.14-1.47). The head injury event rate per 100 person-years was 1.65 in antipsychotic users vs. 1.26 in nonusers. Antipsychotic use was also tied to a 22% higher risk of TBI (adjusted HR, 1.23; 95% CI, 1.03-1.46), with 0.90 events per 100 person-years in users compared with 0.72 per 100 person-years in nonusers.

CDC Maps America's High Levels of Inactivity

All states and territories had more than 15% of adults who were physically inactive and this estimate ranged from 17.3% to 47.7%, according to new state maps of adult physical inactivity prevalence released by the Centers for Disease Control and Prevention (CDC).

"Too many adults are inactive, and they may not know how much it affects their health," said Ruth Petersen, MD, Director of CDC's Division of Nutrition, Physical Activity, and Obesity. "Being physically active helps

you sleep better, feel better and reduce your risk of obesity, heart disease, type 2 diabetes and some cancers." (*CDC*)

Alcohol Consumption Among Binge Drinkers on the Rise

Among adults classified as binge drinkers, their bingeing appears to have intensified over time, federal survey data indicated.

The number of drinks consumed each year by individuals whose self-reported drinking habits put them in the "binge drinker" category increased 12% from 2011 to 2017, said Dafna Kanny, PhD, of the CDC's National Center for Chronic Disease Prevention and Health Promotion in Atlanta, and colleagues. Overall, the annual number of drinks consumed by binge drinkers rose from 472 to 529 from 2011 through 2017, the researchers wrote in the *Morbidity and Mortality Weekly Report*. Total drinks consumed per year increased significantly for both women (from 256 to 290) and men (from 587 to 666).

Repair of Proximal Humerus Fracture Linked to Worse Outcomes in Elderly

Higher rates of surgery for proximal humerus fracture among Medicare beneficiaries are associated with increased costs, adverse events, and mortality, according to new findings in *JAMA Network Open*.

Risks seemed to be especially high for older, sicker or frailer patients. Higher rates of surgery were associated with higher costs in the year following surgery. Each 1% increase in surgery rate was associated with a 0.09 percentage point increase in adverse events and a 0.09 percentage point rise in mortality, while 1-year adverse event rates increased by 0.19 percentage points for each 1% increase in the surgery rate. Risks were more marked for patients with more comorbidities, higher frailty index scores, and those 80 and older.

Your Fitbit could Help Health Officials Predict Flu Outbreaks in Real-time

That Fitbit you've been wearing could help health officials stop the flu from spreading.

Researchers working at the Scripps Research Translational Institute reviewed de-identified data from users wearing Fitbits and found that they were able to do real-time flu prediction at the state level. This marks the first time heart rate trackers and sleep data have been used to predict the flu or any infectious disease in real time, according to the study authors… (*CNN*)

Sepsis Linked to 1-in-5 Deaths Worldwide, Says Study

Sepsis played a direct role in the deaths of 11 million people in 2017, almost twice as many as previously estimated, according to a study.

That represents one death for every 5 cases of the condition, and 1-in-5 deaths from all causes worldwide, researchers reported in *The Lancet*. Some 85% of cases in 2017 were in low- or middle-income countries, with the highest burden in sub-Saharan Africa, the South Pacific and Asia. Most affected were children under 5 years old, who accounted for more than 40% of all cases… (*ET Healthworld*)

Less Tongue Fat from Weight Loss may Help Sleep Apnea

Reduced tongue fat may be the reason that losing weight is linked to improved function among obese people with obstructive sleep apnea (OSA), new study indicates.

The researchers studied 67 obese patients with OSA who were undergoing intensive lifestyle modification or bariatric surgery. They noted that several upper airway measurements changed with weight loss in addition to tongue fat, including the shape of the retropalatal airway and pterygoid volume and the lateral walls. However, other upper airway dimensions did not change. "New treatments that reduce tongue fat should be considered for patients with OSA," write researchers in the *American Journal of Respiratory and Critical Care Medicine*.

ACIP Updates Recommendations for Adult Vaccines

The CDC has released an updated schedule for adult vaccines. The update includes changes regarding the administration of several vaccines, including influenza, human papillomavirus (HPV), hepatitis A and B and meningitis B, as well as the pneumococcal 13-valent conjugate (PCV13) vaccine.

The schedule, revised annually by the Advisory Committee on Immunization Practices (ACIP) of the CDC, was published online in the *Annals of Internal Medicine* and on the *CDC website*.

■■■■

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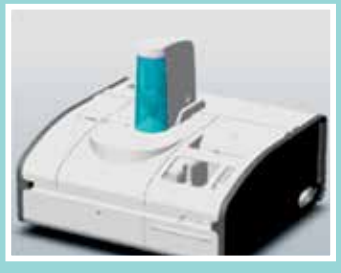

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How to Finish Your Pending Work?

KK AGGARWAL

- This involves principles of time management and some Vedic principles.
- The first thing to do is to make a checklist of all the pending work by writing it down and re-categorizing them depending upon the urgency and importance.
- Pending work can be classified under following four sections:
  - Urgent and important: Should be done immediately.
  - Important but not urgent: Should be scheduled as per the time available.
  - Not important and not urgent: Learn to say no and dump it.
  - Urgent but not important: This work should be delegated to others.
- Urgency of the work is decided by the deadlines available.
- The importance of the work is decided by directing the result of the work to the mind, body or the soul. One should see whether the result of the work gives pleasure to the body, mind or the soul. The one which is giving pleasure to the soul will be free of fear or guilt.
- When choosing between simple or difficult, choose the difficult jobs first so that you do not carry them back home in the mind. In terms of importance, difficult files are more important than simple files.
- When choosing right versus convenient action, give priority to the right action and not the convenient action.
- Delegation of work and team work is very important.
- When deadlines are available, it is always better not to keep the work just near the deadlines.
- Anticipate delay and keep time for unforeseen movements.
- Work is work and not something personal.
- Always remember the spiritual principle that you get what you deserve and not what you desire. So, never get attached to the results of your actions.
- Yoga, pranayama, afternoon naps and meditation help to prioritize your work.
- Follow the principles of creativity and learn to give breaks in between jobs so that the mind is relaxed and can take soul boosting decisions.
- Remember, Yudhishthir never kept anything pending for tomorrow. In this way you can have a fearless, undisturbed sleep.
- Organizing your pending list always helps.
- Do not waste time on learning material on which you are already an expert.
- Take advantage of down time. If you find free time in your routine, then convert it into a creative time so that you can plan strategies or do something new.
- Always get up at the same time and never disturb your sleep time.

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

Group Editor-in-Chief, IJCP Group

■■■■

New Form of Insulin may Improve Diabetes Treatment, Says Study

Scientists have developed a new form of insulin that could improve the clinical delivery of the drug for people living with diabetes. The researchers, including those from The Florey Institute of Neuroscience and Mental Health in Australia, synthesized an insulin analogue called glycoinsulin, and revealed that it can also lower blood glucose levels in preclinical studies. According to the study, published in the *Journal of the American Chemical Society*, glycoinsulin can achieve insulin-like effects without forming fibrils, which are clumps arising when insulin compounds aggregate together… (*The Indian Express*)

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Teamwork Lesson

When you see geese flying along in "V" formation, you might consider what science has discovered as to why they fly that way. As each bird flaps its wings, it creates uplift for the bird immediately. By flying in "V" formation, the whole flock adds at least 71% greater flying range than if each bird flew on its own. People who share a common direction and sense of community can get where they are going more quickly and easily because they are traveling on the thrust of one another.

When a goose falls out of formation, it suddenly feels the drag and resistance of trying to do it alone – and quickly gets back into formation to take advantage of the lifting power of the bird in front. If we have as much sense as a goose, we will stay in formation with those people who are headed the same way we are.

When the head goose gets tired, it rotates back in the wing and another goose flies point. It is sensible to take turns doing demanding jobs, whether with people or with geese flying south. Geese honk from behind to encourage those up front to keep up their speed.

What messages do we give when we honk from behind? Finally, and this is important, when a goose gets sick or is wounded by gunshot, and falls out of formation, two other geese fall out with that goose and follow it down to lend help and protection. They stay with the fallen goose until it is able to fly or until it dies, and only then do they launch out on their own, or with another formation to catch up with their group.

If we have the sense of a goose, we will stand by each other like that.

■■■■

Delaying Revascularization Based on Fractional Flow Reserve Seems Effective

Delaying revascularization for up to 2 years based on fractional flow reserve (FFR) seems both safe and appropriate in real-world practice, according to researchers in Japan.

The researchers assessed registry data from 28 Japanese centers. In all, 1,263 prospectively enrolled patients with 1,447 lesions in whom revascularization was deferred based on FFR were involved in the analysis. The cumulative 2-year incidence of target-vessel failure (TVF) was 5.5% in deferred lesions, primarily on account of a high rate (5.2%) of clinically driven target-vessel revascularization (CDTVR). The incidence significantly increased with decreasing FFR, particularly in the proximal location. During follow-up, the 2-year incidence of cardiac death was 0.41% and that of target-vessel related myocardial infarction was also 0.41%. The findings were published in *Circulation: Cardiovascular Interventions*.

Chinese Herbal may be Chemoprotective Against Colorectal Cancer

The herbal-based supplement berberine reduced the recurrence risk of colorectal adenomas and polypoid lesions after polypectomy versus placebo, a Chinese randomized trial found.

With median follow-up of 2 years, 36% of berberine recipients and 47% of placebo recipients had recurrent adenomas, for an unadjusted relative risk ratio for recurrence of 0.77 (95% CI 0.66-0.91, p = 0.001), reported Jing-Yuan Fang, MD, of Shanghai Jiao-Tong University School of Medicine in Shanghai, and colleagues in *The Lancet Gastroenterology & Hepatology*. Advanced adenomas were detected in 3% of the berberine group vs. 6% in the placebo group, while non-advanced adenomas were detected in 33% vs. 41% in these two arms.

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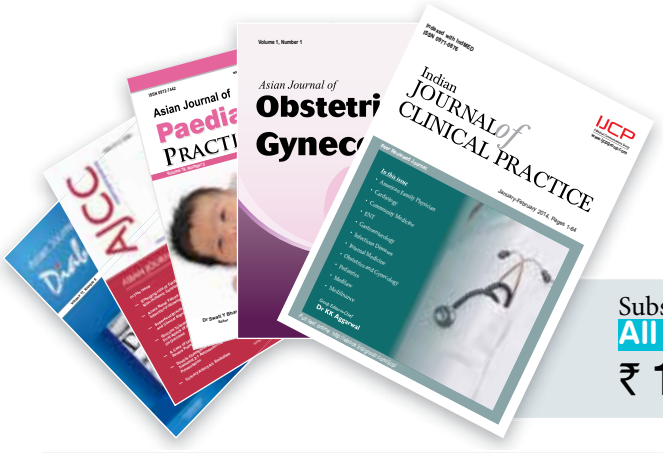

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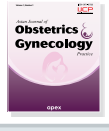
Asian Journal of Obs & Gynae Practice 	4	1,500/- ☐	550/- ☐
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Lighter Side of Medicine

HUMOR

How does Juliet maintain a constant body temperature?

Through "Romeostasis!"

What did one cell say to his sister cell when she stepped on his toe?

Ouch, "mitosis!"

How do you eat DNA-spaghetti?

With a replication fork!

Where do they send the criminal neurons?

To the chain ganglion!

What's a pirate's favorite amino acid?

Arrrrrr-ginine!

What's the difference between a dog and a marine biologist?

One wags a tail and the other tags a whale!

Employer: Do you have trouble making decisions?

Interviewee: Well … yes and no!

What do a fudge cake and meditation have in common?

Both bring you a "piece" or "peace" of heaven!

What kind of music should you listen to while fishing?

Something "catchy!"

What goes up and never comes down?

Age!

What did the ice cream say to the unhappy cake?

Hey, what's eating you?

What did one candle ask the other?

Don't birthdays burn you up?

What do farmers use to make crop circles?

Pro-tractor!

Why do cows like being told farmer jokes?

Because they like being "amoosed."

Bill struggled to get up early in the morning, and as a result, he was always late for work. His boss got fed up of his constant lateness and so threatened to fire him if he didn't get his act together.

So, Bill went to see his doctor who gave him a pill and told him to take it just before going to bed.

Bill did as advised and slept very well and actually beat the alarm clock by 2 hours. He fixed himself a nice breakfast and drove happily to work, with plenty of time on hand.

When he reached office, he said, "Boss, that pill the doctor gave me actually worked!"

His boss said, "That's all very well, but where were you yesterday?"

Three old, retired men were playing golf. All 3 had hearing loss as they got older.

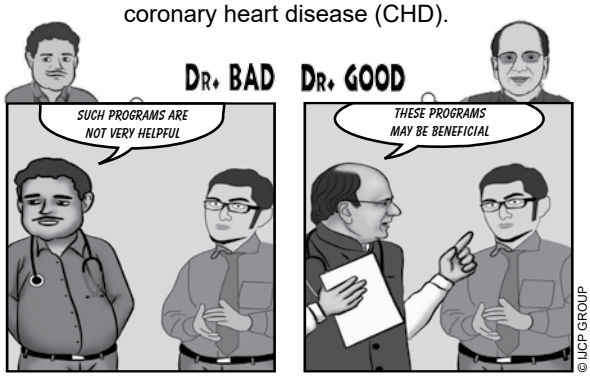
First man: Windy, isn't it?

Second man: No, it's Thursday.

Third man: So am I. Let's have a juice!

Dr. Good and Dr. Bad

SITUATION: A man with type 2 diabetes was suggested to attend a program on the risk of developing coronary heart disease (CHD).



LESSON: Educating individuals with type 2 diabetes about the risk of developing CHD is necessary. It may help in motivating them to perform healthy behaviors, which may, in turn, be beneficial for controlling and reducing CHD.

Int J Nurs Pract. 2018;24(1).

IJCP SUTRA: *"It is best to refrain from consuming alcohol. For those who still wish to drink, they should restrict it to not more than 80 mL of alcohol in a day or 80 g in a week."*

Indian JOURNAL of CLINICAL PRACTICE

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

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University Grants Commission (20737/15554).

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The Medical Council of India (UGC, ICI)

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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.

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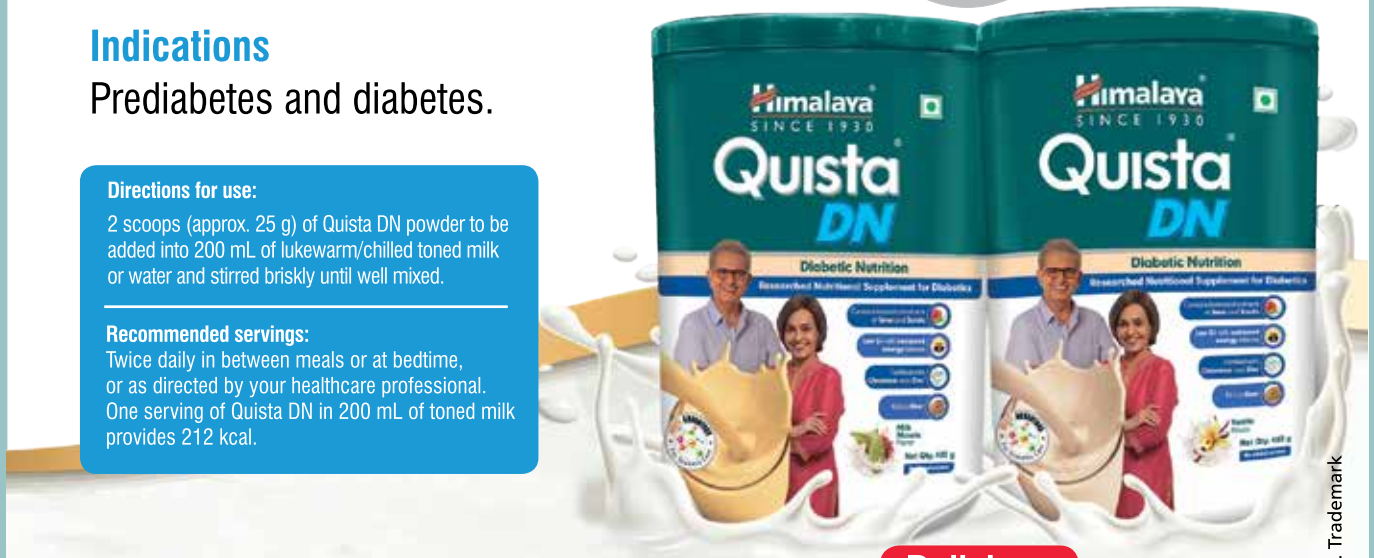

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