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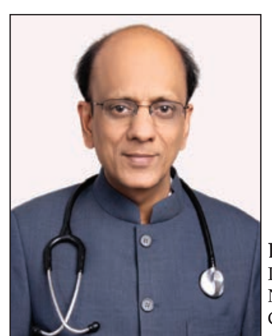

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Not Just the Government, Citizens Too Share the Responsibility to Control Pollution

Air pollution has been in the news, especially since the last few years. Evidence of the harmful effects of air pollution on public health is accumulating. And, each time the Air Quality Index (AQI) crosses the red zone indicting 'very poor' or 'severe' air quality, much is written about or talked about to ascribe blame for this rise in pollution to dangerous levels. This year too, the pollution levels increased to 'severe' levels in the National Capital Region (NCR) post-Diwali. This despite the ban on the sale of firecrackers in NCR by the Supreme Court of India.

Such high levels of pollution are not only harmful to people with existing disease, but also for healthy individuals.

This situation should give us all pause to think. It is easy and very convenient to be on the sidelines and fault-find the government in its apathy or lack of stringent measures to bring down the pollution levels. It's not just air pollution, noise pollution and water pollution are also a serious cause for concern.

"*Ask not what your country can do for you, ask what you can do for your country*". These historic words from President John F Kennedy challenge us to act for the betterment of the society we live in.

Instead of always pointing a finger at the government, we should introspect and ask ourselves "Am I really a responsible citizen?"

Preventing and controlling pollution is not the sole responsibility of the government. Most of existing pollution levels are man-made, so we also must contribute in the efforts to control pollution. It is the moral duty of each one of as an active member of the society to take steps to help control pollution. As responsible citizens, we must respect laws of the state in place and abide by them. We must make individual efforts to control pollution.

Here are some simple steps that each one of us can take can help reduce pollution. More can be added to this list. Of importance here is that 90% of these are a matter of personal choice. Only about 10% factors are beyond one's control.

1. I will not burn agarbatti, incense sticks and dhoop batti at my home or workplace till pollution levels drop.
2. I will not burn flame producing candles.
3. I will not use kerosene oil for any purpose.
4. I will avoid using polythene bags, or plastic.
5. I will use products, which can be recycled, as much as possible.
6. I will not use wood and coal for any purpose, be it cooking or heating.
7. If any unfortunate death occurs in my family, I will bravely opt for electric cremation.
8. I will not smoke cigarettes/beedis nor allow anyone else to do so.
9. I will resort to wet mopping the floors in my house and workplace.

10. Wherever possible, I will practice carpooling.
11. I will opt for public transportation as much as possible.
12. I will regularly get my vehicle/s checked for pollution standards and serviced so that it is in good condition.
13. I will walk or cycle for short distance commutes.
14. I will make sure that the ACs at my home/vehicle/ workplace do not have a choked filter. If yes, I will regularly get the AC checked and serviced as scheduled.
15. I will check air purifiers at my home and workplace for choked filters and replace them if necessary.
16. I will not burn leaves/garbage/ paper waste.
17. I will raise my voice against air pollution.
18. If at a petrol pump, I see no mechanism for absorbing toxic vapors, I will speak up.
19. I will object to any unsafe construction in my vicinity.
20. I will not allow construction material to linger on roads after the work is finished.
21. I will insist that the roads in my vicinity are cleaned only mechanically between 12 pm to 5 am.
22. I will talk to my RWA to plant more trees and make sure that pavements have no exposed soil.
23. I will sell my diesel car and buy a CNG one.
24. I will avidly vote for heavy taxes on crackers and tobacco.
25. I will educate people every day to avoid contributing to air pollution, and how to avoid pollutant exposure.

Answer yes to most of the above, if not all, to do your bit and make your significant contribution.

Not just the government, each one of us has a civic responsibility and the contribution from each of us, no matter however small, has an impact. Every little step taken at the individual level will only work towards the well-being of the society as a whole.

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

■■■■

Aseptic and Bacterial Meningitis: Evaluation, Treatment, and Prevention

HILLARY R MOUNT, SEAN D. BOYLE

ABSTRACT

The etiologies of meningitis range in severity from benign and self-limited to life-threatening with potentially severe morbidity. Bacterial meningitis is a medical emergency that requires prompt recognition and treatment. Mortality remains high despite the introduction of vaccinations for common pathogens that have reduced the incidence of meningitis worldwide. Aseptic meningitis is the most common form of meningitis with an annual incidence of 7.6 per 100,000 adults. Most cases of aseptic meningitis are viral and require supportive care. Viral meningitis is generally self-limited with a good prognosis. Examination maneuvers such as Kernig sign or Brudzinski sign may not be useful to differentiate bacterial from aseptic meningitis because of variable sensitivity and specificity. Because clinical findings are also unreliable, the diagnosis relies on the examination of cerebrospinal fluid obtained from lumbar puncture. Delayed initiation of antibiotics can worsen mortality. Treatment should be started promptly in cases where transfer, imaging, or lumbar puncture may slow a definitive diagnosis. Empiric antibiotics should be directed toward the most likely pathogens and should be adjusted by patient age and risk factors. Dexamethasone should be administered to children and adults with suspected bacterial meningitis before or at the time of initiation of antibiotics. Vaccination against the most common pathogens that cause bacterial meningitis is recommended. Chemoprophylaxis of close contacts is helpful in preventing additional infections.

Keywords: Bacterial meningitis, medical emergency, aseptic meningitis, viral meningitis, empiric antibiotics, dexamethasone, vaccination, chemoprophylaxis

Patients with meningitis present a particular challenge for physicians. Etiologies range in severity from benign and self-limited to life-threatening with potentially severe morbidity. To further complicate the diagnostic process, physical examination and testing are limited in sensitivity and specificity. Advances in vaccination have reduced the incidence of bacterial meningitis; however, it remains a significant disease with high rates of morbidity and mortality, making its timely diagnosis and treatment an important concern.[1]

ETIOLOGY

Meningitis is an inflammatory process involving the meninges. The differential diagnosis is broad (Table 1). Aseptic meningitis is the most common form. The annual incidence is unknown because of underreporting, but European studies have shown 70 cases per 100,000 children younger than one year, 5.2 cases per 100,000 children one to 14 years of age, and 7.6 per 100,000 adults.[2,3] Aseptic is differentiated from bacterial meningitis if there is meningeal inflammation without signs of bacterial growth in cultures. These cases are often viral, and enterovirus is the most common pathogen in immunocompetent individuals.[2,4] The most common etiology in U.S. adults hospitalized for meningitis is enterovirus (50.9%), followed by unknown etiology (18.7%), bacterial (13.9%), herpes simplex virus (HSV; 8.3%), noninfectious (3.5%), fungal (2.7%), arboviruses (1.1%), and other viruses (0.8%).[5] Enterovirus and mosquito-borne viruses, such as St. Louis encephalitis and West Nile virus, often present in the summer and early fall.[4,6] HSV and varicella zoster virus can cause meningitis and encephalitis.[2]

Causative bacteria in community-acquired bacterial meningitis vary depending on age, vaccination status, and recent trauma or instrumentation[7,8] (Table 2[9]). Vaccination has nearly eliminated the risk of *Haemophilus influenzae* and substantially reduced the rates of

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Source: Adapted from Am Fam Physician. 2017;96(5):314-322.

Neisseria meningitidis and *Streptococcus pneumoniae* as causes of meningitis in the developed world.[10] Between 1998 and 2007, the overall annual incidence of bacterial meningitis in the United States decreased from 1 to 0.69 per 100,000 persons.[1] This decrease has been most dramatic in children two months to 10 years of age, shifting the burden of disease to an older population.[1] Annual incidence is still highest in neonates at 40 per 100,000, and has remained largely unchanged.[1] Older patients are at highest risk of *S. pneumoniae* meningitis, whereas children and young adults have a higher risk of *N. meningitidis* meningitis.[1,11] Patients older than 60 years and patients who are immunocompromised are at higher risk of *Listeria monocytogenes* meningitis, although rates remain low.[11]

PRESENTATION

Presentation can be similar for aseptic and bacterial meningitis, but patients with bacterial meningitis are generally more ill-appearing. Fever, headache, neck stiffness, and altered mental status are classic symptoms of meningitis, and a combination of two of these occurs in 95% of adults presenting with bacterial meningitis.[12] However, less than one-half of patients present with all of these symptoms.[12,13]

Presentation varies with age. Older patients are less likely to have headache and neck stiffness, and more likely to have altered mental status and focal neurologic deficits[11,13] (Table 3[11-13]). Presentation also varies in young children, with vague symptoms such as irritability, lethargy, or poor feeding.[14] Arboviruses such as West Nile virus typically cause encephalitis but can present without altered mental status or focal neurologic findings.[6] Similarly, HSV can cause a spectrum of disease from meningitis to life-threatening encephalitis. HSV meningitis can present with or without cutaneous lesions and should be considered as an etiology in persons presenting with altered mental status, focal neurologic deficits, or seizure.[15]

The time from symptom onset to presentation for medical care tends to be shorter in bacterial meningitis, with 47% of patients presenting after less than 24 hours of symptoms.[16] Patients with viral meningitis have a median presentation of two days after symptom onset.[17]

Examination findings that may indicate meningeal irritation include a positive Kernig sign, positive Brudzinski sign, neck stiffness, and jolt accentuation of headache (i.e., worsening of headache by horizontal rotation of the head two to three times per second). Physical examination findings have shown wide variability in their sensitivity and specificity, and are not

Table 1. Differential Diagnosis of Meningitis

Common
Bacterial meningitis
Viral meningitis
Uncommon
Behçet syndrome
Benign recurrent lymphocytic meningitis (Mollaret meningitis)
Central nervous system abscess
Drug-induced meningitis (e.g., nonsteroidal anti-inflammatory drugs, trimethoprim/sulfamethoxazole)
Ehrlichiosis
Fungal meningitis
Human immunodeficiency virus
Leptomeningeal carcinomatosis
Lyme disease (neuroborreliosis)*
Neoplastic meningitis
Neurosarcoidosis
Neurosyphilis*
Parasitic meningitis*
Systemic lupus erythematosus
Tuberculous meningitis*
Vasculitis

*More common in geographic areas with higher incidence of these infections.

Table 3. Clinical and Laboratory Features of Meningitis in Adults and Older Adults

Clinical feature	Adults (%)*	Older adults† (%)*
Headache	87 to 92	60 to 77
Neck stiffness	83 to 86	31 to 78
Nausea	74	36
Fever	72 to 77	48 to 84
Positive blood culture	62 to 66	73
Altered mental status	60 to 69	84
Focal neurologic deficit	29 to 33	46
Rash	26	4 to 11
Seizure	5	5
Papilledema	3	4

*Percentage of patients with bacterial meningitis who exhibit these characteristics.

†Patients older than 60 to 65 years.

Information from references 11 through 13.

reliable to rule out bacterial meningitis.[18-20] Examples of Kernig and Brudzinski tests are available at https://www.youtube.com/watch?v=Evx48zcKFDA and https://www.youtube.com/watch?v=rN-R7-hh5x4.

DIAGNOSIS

Because of the poor performance of clinical signs to rule out meningitis, all patients who present with symptoms concerning for meningitis should undergo prompt lumbar puncture (LP) and evaluation of cerebrospinal fluid (CSF) for definitive diagnosis. Because of the risk of increased intracranial pressure with brain inflammation, the Infectious Diseases Society of America recommends performing computed tomography of the head before LP in specific high-risk patients to reduce the possibility of cerebral herniation during the procedure (Table 4).[7,21,22] However, recent retrospective data have shown that removing the restriction on LP in patients with altered mental status reduced mortality from 11.7% to 6.9%, suggesting it may be safe to proceed with LP in these patients.[22]

The CSF findings typical of aseptic meningitis are a relatively low and predominantly lymphocytic pleocytosis, normal glucose level, and a normal to slightly elevated protein level (Table 5[9]). Bacterial meningitis classically has a very high and predominantly neutrophilic pleocytosis, low glucose level, and high protein level. This is not the case for all patients and can vary in older patients and those with partially treated bacterial meningitis, immunosuppression, or meningitis caused by *L. monocytogenes*.[11] It is important to use age-adjusted values for white blood cell counts when interpreting CSF results in neonates and young infants.[23] In up to 57% of children with aseptic meningitis, neutrophils predominate the CSF; therefore, cell type alone cannot be used to differentiate between aseptic and bacterial meningitis in children between 30 days and 18 years of age.[24]

Table 4. Risk Factors for Cerebral Herniation in Patients Undergoing Lumbar Puncture

Altered mental status*
Focal neurologic deficit
History of central nervous system disease
Hypertension with bradycardia
Immunosuppression
Papilledema
Respiratory abnormalities
Seizure (in the previous 30 minutes to one week)

*Retrospective data showed that removing the restriction on lumbar puncture in patients with altered mental status reduced mortality from 11.7% to 6.9%.[22]

Information from references 7, 21, and 22.

CSF results can be variable, and decisions about treatment with antibiotics while awaiting culture results can be challenging. There are a number of clinical decision tools that have been developed for use in children to help differentiate between aseptic and bacterial meningitis in the setting of pleocytosis. The Bacterial Meningitis Score has a sensitivity of 99% to 100% and a specificity of 52% to 62%, and appears to be the most specific tool available currently, although it is not widely used.[25-27] The score can be calculated online at http://reference.medscape.com/calculator/bacterial-meningitis-score-child.

Serum procalcitonin, serum C-reactive protein, and CSF lactate levels can be useful in distinguishing between aseptic and bacterial meningitis.[28-33] C-reactive protein has a high negative predictive value but a much lower positive predictive value.[28] Procalcitonin is sensitive (96%) and specific (89% to 98%) for bacterial causes of meningitis.[29,30] CSF lactate also has a high sensitivity (93% to 97%) and specificity (92% to 96%).[31-33] CSF latex agglutination testing for common bacterial pathogens is rapid and, if positive, can be useful in patients with negative Gram stain if LP was performed after antibiotics were administered. This test cannot be used to rule out bacterial meningitis.[7]

Because CSF enterovirus polymerase chain reaction testing is more rapid than bacterial cultures, a positive test result can prompt discontinuation of antibiotic treatment, thus reducing antibiotic exposure and cost in patients admitted for suspected meningitis.[34] Similarly, polymerase chain reaction testing can be used to detect West Nile virus when seasonally appropriate in areas of higher incidence. HSV and varicella zoster viral polymerase chain reaction testing should be used in the setting of meningoencephalitis.

TREATMENT

Initial Management

Prompt recognition of a potential case of meningitis is essential so that empiric treatment may begin as soon as possible. The initial management strategy is outlined in Figure 1.[7,9] Stabilization of the patient's cardiopulmonary status takes priority. Intravenous fluids may be beneficial within the first 48 hours, but further study is needed to determine the appropriate intravenous fluid management.[35] A meta-analysis

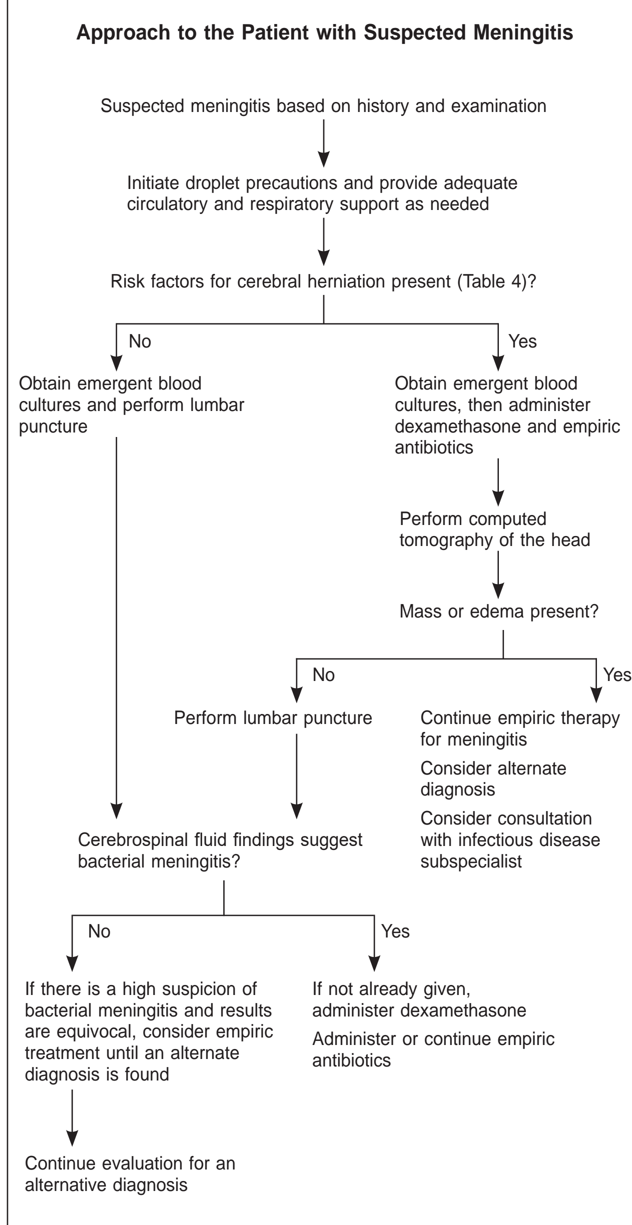

Figure 1. Algorithm for the initial management of suspected acute meningitis.

Information from references 7 and 9.

of studies with variable quality in children showed that fluids may decrease spasticity, seizures, and chronic severe neurologic sequelae.[35] The next urgent requirement is initiating empiric antibiotics as soon as possible after blood cultures are drawn and the LP is performed. Antibiotics should not be delayed if there is any lag time in performing the LP (e.g., transfer to clinical site that can perform the test, need for head computed tomography before LP).[7,8] Droplet isolation precautions should be instituted for the first 24 hours of treatment.[23]

Antimicrobials

Before CSF results are available, patients with suspected bacterial meningitis should be treated with antibiotics as quickly as possible.[8,22,36,37] Acyclovir should be added if there is concern for HSV meningitis or encephalitis. Door-to-antibiotic time lapse of more than six hours has an adjusted odds ratio for mortality of 8.4.[37] If CSF results are more consistent with aseptic meningitis, antibiotics can be discontinued, depending on the severity of the presentation and overall clinical picture. Selection of the appropriate empiric antibiotic regimen is primarily based on age (Table 2[9]). Specific pathogens are more prevalent in certain age groups, but empiric coverage should cover most possible culprits. Viral meningitis (non-HSV) management is focused on supportive care.

Treatment of tuberculous, cryptococcal, or other fungal meningitides is beyond the scope of this article, but should be considered if risk factors are present (e.g., travel to endemic areas, immunocompromised state, human immunodeficiency virus infection). These patients, as well as those coinfected with human immunodeficiency virus, should be managed in consultation with an infectious disease subspecialist when available.

Length of treatment varies based on the pathogen identified (Table 6[7]). Intravenous antibiotics should be used to complete the full treatment course, but outpatient management can be considered in persons who are clinically improving after at least six days of therapy with reliable outpatient arrangements (i.e., intravenous access, home health care, reliable follow-up, and a safe home environment).[7]

Corticosteroids

Corticosteroids are traditionally used as adjunctive treatment in meningitis to reduce the inflammatory response. The evidence for corticosteroids is heterogeneous and limited to specific bacterial pathogens,[38-44] but the organism is not usually known at the time of the initial presentation. A 2015 Cochrane review found a nonsignificant reduction in overall mortality (relative risk [RR] = 0.90), as well as a significant reduction in severe hearing loss (RR = 0.51), any hearing loss (RR = 0.58), and short-term neurologic sequelae (RR = 0.64) with the use of dexamethasone in high-income countries.[41] The number needed to treat to decrease mortality in the *S. pneumoniae* subgroup was 18 and the number needed to treat to prevent hearing loss was 21.38,[41] There was a small increase in recurrent fever in patients given corticosteroids (number needed to harm = 16) with no worse outcome.[38,41]

The best evidence supports the use of dexamethasone 10 to 20 minutes before or concomitantly with antibiotic administration in the following groups: infants and children with *H. influenzae* type B, adults with *S. pneumoniae*, or patients with *Mycobacterium tuberculosis* without concomitant human immunodeficiency virus infection.[7,8,42,45] Some evidence also shows a benefit with corticosteroids in children older than six weeks with pneumococcal meningitis.[45]

Because the etiology is not known at presentation, dexamethasone should be given before or at the time of initial antibiotics while awaiting the final culture results in all patients older than six weeks with suspected bacterial meningitis. Dexamethasone can be discontinued after four days or earlier if the pathogen is not *H. influenzae* or *S. pneumoniae*, or if CSF findings are more consistent with aseptic meningitis.[46]

Repeat Testing

Repeat LP is generally not needed but should be considered to evaluate CSF parameters in persons who are not clinically improving after 48 hours of appropriate treatment. Repeating the LP can identify resistant pathogens, confirm the diagnosis if initial results were negative, and determine the length of treatment for neonates with a gram-negative bacterial pathogen until CSF sterilization is documented.[7,47]

Prognosis

Prognosis varies by age and etiology of meningitis. In a large analysis of patients from 1998 to 2007, the overall mortality rate in those with bacterial meningitis was 14.8%.[1] Worse outcomes occurred in those with low Glasgow Coma Scale scores, systemic compromise (e.g., low CSF white blood cell count, tachycardia, positive blood cultures, abnormal neurologic examination, fever), alcoholism, and pneumococcal infection.[11-13,16] Mortality is generally higher in pneumococcal meningitis (30%) than other types, especially penicillin-resistant strains.[12,48,49] Viral meningitis outside the neonatal period has lower mortality and complication rates, but large studies or reviews are lacking. One large cohort study found a 4.5% mortality rate and a 30.9% rate of complications, such as developmental delay, seizure disorder, or hearing loss, for childhood encephalitis and meningitis combined.[50] Tuberculous meningitis also has a higher mortality rate (19.3%) with a higher risk of neurologic disease in survivors (53.9%).[51] A recent prospective cohort study also found that males had a higher risk of unfavorable outcomes (odds ratio = 1.34) and death (odds ratio = 1.47).[52]

Complications from bacterial meningitis also vary by age (Table 7[1,11,12,46,53-56]). Neurologic sequelae such as hearing loss occur in approximately 6% to 31% of children and can resolve within 48 hours, but may be permanent in 2% to 7% of children.[53-56] An audiology assessment should be considered in children before discharge.[8] Follow-up should assess for hearing loss (including referral for cochlear implants, if present), psychosocial problems, neurologic disease, or developmental delay.[57] Testing for complement deficiency should be considered if there is more than one episode of meningitis, one episode plus another serious infection, meningococcal disease other than serogroup B, or meningitis with a strong family history of the disease.[57]

PREVENTION

Vaccination

Vaccines that have decreased the incidence of meningitis include *H. influenzae* type B, *S. pneumoniae*, and *N. meningitidis*.[58-60] Administration of one of the meningococcal vaccines that covers serogroups A, C, W, and Y (MPSV4, Hib-MenCY, MenACWY-D, or MenACWY-CRM) is recommended for patients 11 to 12 years of age, with a booster at 16 years of age.

Table 7. Incidence of Complications from Bacterial Meningitis

Complication	Frequency (%)
Children	
No sequelae	83.6
Cognitive impairment or low IQ	45
Academic limitations	29.9
Reversible hearing loss	6.7 to 31
Spasticity or paresis	3.5
Deafness	2.4 to 7
Seizure disorder	1.8 to 4.2
Mortality	0.3 to 3.8
Adult (age > 16 years)	
Focal neurologic deficits	37 to 50
Cardiorespiratory failure	29 to 38
Seizures	15 to 24
Mortality	14.8 to 21
Hearing loss	14 to 69
Hemiparesis	4 to 6

Information from references 1, 11, 12, 46, and 53 through 56.

Table 8. Chemoprophylaxis for Bacterial Meningitis

Pathogen	Indication	Antimicrobial agent	Dosage	Comments
Haemophilus influenzae (postexposure prophylaxis)	Living in a household with one or more unvaccinated or incompletely vaccinated children younger than 48 months	Rifampin	20 mg per kg per day, up to 600 mg per day, for four days	—
Neisseria meningitidis (postexposure prophylaxis)	Close contact (for more than eight hours) with someone with *N. meningitidis* infection	Ceftriaxone	Single intramuscular dose of 250 mg (125 mg if younger than 15 years)	—
	Contact with oral secretions of someone with *N. meningitidis* infection	*or* Ciprofloxacin	Adults: single dose of 500 mg	Rare resistant isolates
		or Rifampin	Adults: 600 mg every 12 hours for two days	Not fully effective and rare resistant isolates
			Children one month or older: 10 mg per kg every 12 hours for two days	
			Children younger than one month: 5 mg per kg every 12 hours for two days	
Streptococcus agalactiae (group B streptococcus; women in the intrapartum period)	Previous birth to an infant with invasive *S. agalactiae* infection	Penicillin G	Initial dose of 5 million units intravenously, then 2.5 to 3 million units every four hours during the intrapartum period	—
	Colonization at 35 to 37 weeks' gestation	*or* If allergic to penicillin: Cefazolin	2 g followed by 1 g every eight hours	—
	Bacteriuria during pregnancy			
	High risk because of fever, amniotic fluid rupture for more than 18 hours, or delivery before 37 weeks' gestation	*or* Clindamycin	900 mg every eight hours	Clindamycin susceptibility must be confirmed by antimicrobial susceptibility test
		or Vancomycin	15 to 20 mg per kg every 12 hours	—

Information from references 9, 14, and 64 through 68.

However, the initial dose should be given earlier in the setting of a high-risk condition, such as functional asplenia or complement deficiencies, travel to endemic areas, or a community outbreak.[60] There are also two available vaccines for meningococcal type B strains (MenB-4C and MenB-FHbp) to be used in patients with complement disease or functional asplenia, or in healthy individuals at risk during a serogroup B outbreak as determined by the Centers for Disease Control and Prevention.[60]

The Advisory Committee on Immunization Practices recently added a category B recommendation (individual clinical decision making) for consideration of vaccination with serogroup B vaccines in healthy patients 16 to 23 years of age (preferred age of 16 to 18 years).[60,61] The serogroup B vaccines are not interchangeable, so care should be taken to ensure completion of the series with the same brand that was used for the initial dose.

Chemoprophylaxis

Treatment with chemoprophylactic antibiotics should be given to close contacts[7,62,63] (Table 8[9,14,64-68]). Appropriate antibiotics should be given to identified contacts within 24 hours of the patient's diagnosis and should not be given if contact occurred more than 14 days before the patient's onset of symptoms.[63] Options for chemoprophylaxis are rifampin, ceftriaxone, and ciprofloxacin, although rifampin has been associated with resistant isolates.[62,63]

Note: For complete article visit: www.aafp.org/afp.

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Practice Guidelines

LOW BACK PAIN: AMERICAN COLLEGE OF PHYSICIANS PRACTICE GUIDELINE ON NONINVASIVE TREATMENTS

Low back pain occurs in most persons living in the United States and has been shown to have high costs, health care–related and indirect (e.g., missed work days, reduced efficiency at work and home), totaling about $100 billion in 2006. Often, management is based on how long symptoms have persisted, possible etiologies, occurrence of radicular symptoms, and abnormalities found on physical examination or radiography. The American College of Physicians has released a guideline, which partially updates its 2007 guideline, to provide recommendations for noninvasive treatment of acute (duration less than four weeks), subacute (duration of four to 12 weeks), and chronic (duration longer than 12 weeks) low back pain. It does not address topical or epidural therapies.

Recommendations

It should be noted that any improvements in pain or function with medication or other nonpharmacologic options have been found to be minimal based on the literature, and did not show well-defined differences vs. control treatments; therefore, treatment decisions should be based on patient preference, availability, possible harms, and cost. Persons with any type of low back pain should be encouraged to remain as active as pain allows.

Acute and Subacute Pain

Because acute and subacute low back pain often resolve spontaneously with time, superficial heat, massage, acupuncture, and spinal manipulation are all appropriate treatment options to try initially. Harms that have been reported with these treatments are sparse and not severe. Based on evidence of moderate quality, heat wraps result in moderate improvement of pain and disability compared with placebo. Based on evidence of low quality, massage results in moderate improvement in pain and function in the short term compared with sham therapy in persons with subacute pain, and acupuncture results in minimal improvement in pain compared with sham acupuncture but does not appear to improve function. Also based on evidence of low quality, spinal manipulation results in minimal improvement in function compared with sham manipulation; data were insufficient to make conclusions about how it affects pain.

If the patient or physician chooses medication, a nonsteroidal anti-inflammatory drug (NSAID) or skeletal muscle relaxant can be considered; the decision between the two medication classes should be based on patient preference and the risks associated with each. Compared with placebo, NSAIDs result in a minor improvement in pain and function based on evidence of moderate and low quality, respectively. Based on evidence of moderate quality, muscle relaxants improve pain in the short term compared with placebo.

Physicians should discuss with patients the typically encouraging prognosis associated with acute low back pain, such as the high probability of the pain improving considerably within one month, so that they do not have to undergo tests or treatments that can be expensive and possibly harmful.

Chronic Pain

For chronic low back pain, exercise, multidisciplinary rehabilitation, acupuncture, mindfulness-based stress reduction, tai chi, yoga, motor control exercises, progressive relaxation, electromyography biofeedback training, low-level laser therapy, operant therapy, cognitive behavior therapy, and spinal manipulation are first-line options and have fewer harms compared with medication; therefore, they should be tried initially. Evidence of moderate quality indicates that exercise results in minimal improvement in pain and function compared with no exercise, and that mindfulness-based stress reduction successfully treats pain, with one trial indicating a minimal improvement in pain and function compared with standard treatment.

The evidence for the following interventions is of low quality. Multidisciplinary rehabilitation results in moderate improvement in pain in the short term and minimal improvement in disability compared with no rehabilitation, and Iyengar yoga results in moderate improvement in pain scores and improvement in function compared with standard treatment. Motor control exercises result in moderate improvement in

Source: Adapted from Am Fam Physician. 2017;96(6):407-408.

pain scores and minimal improvement in function compared with nominal treatment. Compared with sham therapies, acupuncture results in moderate improvement in pain for up to three months after it is performed, but it does not appear to improve function; low-level laser therapy results in minimal improvement in pain; and spinal manipulation does not result in a difference in pain. Compared with a wait-list control group, tai chi resulted in moderate improvement in pain; progressive relaxation therapy resulted in moderate improvement in pain and function; and operant therapy, cognitive behavior therapy, and electromyography biofeedback training resulted in minimal improvement in pain, but not a difference in function.

If these nonpharmacologic treatments are ineffective, an NSAID would be considered a first-line treatment option, with tramadol and duloxetine being second-line options. NSAIDs result in minimal to moderate improvement in pain compared with placebo and no to minimal improvement in function based on moderate- and low-quality evidence, respectively. Based on evidence of moderate quality and compared with placebo, tramadol results in moderate improvement in pain in the short term and a minimal improvement in function, and duloxetine results in a minimal improvement in pain and function. Traditional opioids should be considered for treatment only if these other treatments do not help and the benefits of their use outweigh the risks, which are discussed with the patient.

■■■■

Photo Quiz

A PERSISTENT RASH ON THE BACK, CHEST, AND ABDOMEN

A 62-year-old woman presented with an erythematous, pruritic, expanding rash on her back, chest, and left lower abdomen (Figures 1 and 2). It appeared two months earlier and did not improve with conservative home treatment, including application of skin lotion, petroleum jelly, and an over-the-counter topical steroid cream. There was no pain or drainage from the affected area. The patient was diagnosed with breast cancer three years earlier, for which she underwent right simple mastectomy and left modified radical mastectomy.

She was afebrile on physical examination. The rash was a large, erythematous plaque with discrete borders. There was some slight edema noted in the lower portion of the back. There was no tenderness or warmth. A punch biopsy was performed.

Question

Based on the patient's history and physical examination findings, which one of the following is the most likely diagnosis?

A. Inflammatory breast cancer.

B. Mycosis fungoides.

C. Radiation dermatitis.

D. Tinea corporis.

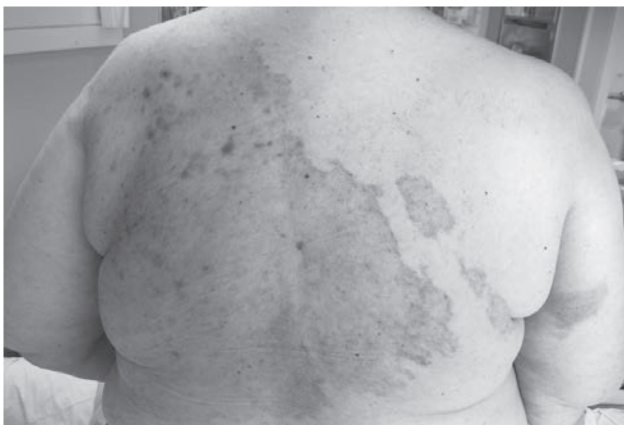

Figure 1.

Figure 2.

SEE THE FOLLOWING PAGE FOR DISCUSSION.

Source: Adapted from Am Fam Physician. 2017;96(6):391-392.

Discussion

The answer is A: inflammatory breast cancer. Inflammatory breast cancer is a rare subtype of locally advanced primary breast cancer, accounting for roughly 2.5% of breast cancers in the United States.[1] It is characterized by the disruption of dermal lymphatics with tumor emboli, leading to diffuse skin erythema, ulceration, and edema.[2] It is commonly high grade, estrogen receptor negative, and progesterone receptor negative, and it often affects younger patients.[3] Onset of symptoms can be rapid over days to weeks. Erythema and edema can appear overnight, and the breast may swell to two to three times its normal size within weeks. Recurrent inflammatory breast cancer appears with the same skin and microscopic characteristics as the original primary breast cancer biopsies.

Inflammatory breast cancer is an aggressive carcinoma with a five-year survival rate of roughly 50% even with multimodal therapy.[1] Poor prognostic factors include metastasis to lymph nodes, extensive erythema, estrogen receptor–negative disease, and the *TP53* gene mutation.[4] This highly malignant cancer is often misdiagnosed as a benign infectious or inflammatory process and can also mimic other tumors, such as sarcomas.[5]

Mycosis fungoides is the most common form of cutaneous T cell lymphoma. It has a variable presentation, including rash-like patches or lesions that may be pruritic. Diagnosis is based on clinical presentation and histopathology.

Radiation dermatitis can be acute or chronic but is always associated with recent radiation therapy. Blisters and erythema are typically observed in the acute phase. Chronic radiation dermatitis presents as atrophic indurated plaques that are typically white or yellow.

Tinea corporis is a fungal infection that causes red, scaly, pruritic rings that are raised and dry. It can appear anywhere on the body but is more common in warm, moist areas, such as under the breasts or in the groin.

Summary Table

Condition	Characteristics
Inflammatory breast cancer	Skin erythema, ulceration, and edema; punch biopsy shows breast tumor pathology
Mycosis fungoides	Rash-like patches or lesions that may be pruritic; biopsy shows cutaneous T cell lymphoma
Radiation dermatitis	Recent radiation exposure; acute: blisters, erythema; chronic: atrophic indurated plaques that are typically white or yellow
Tinea corporis	Red, scaly, pruritic rings that appear raised and dry

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Nasal Mucociliary Clearance in 500 Healthy Indians

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ABSTRACT

Nasal mucociliary transport serves as the first host defense against the inhalation of atmospheric particulate matter. Nasal mucociliary clearance (NMC) is determined to obtain an *in vivo* measurement of the effectiveness of the interaction between the cilia and mucus. Various techniques are employed for measuring NMC namely saccharin test and tests using dyes or radiolabeled particles. Saccharin test, an inexpensive, simple, reproducible and noninvasive method was used to establish normative data within healthy Indian subjects. The mean value of NMC obtained was 8.47 ± 0.41 minutes (range 5.3-18.9 minutes). It was 8.34 ± 0.58 in males and 8.21 ± 0.59 in females. There was no statistical difference between the two genders (p > 0.05).

Keywords: Nasal mucociliary clearance time, healthy subjects, saccharin test

Nose, apart from being the integral part of one`s personality, is regarded as sense of pride more so in males especially in India. Nose performs important physiological functions like respiration and olfaction. The inspired air is conducted through the nose and during this conduction, the air temperature and humidity is adjusted to normal body temperature and the particulate matter is removed by mucociliary action to render it safe for lower respiratory tract. On account of large surface i.e., 70 m^2 and continuous exposure to air (i.e., 10^4 Liters/day) the lungs are especially open to threats from environment.[1]

A normal person inhales approximately 10^{10} dust particles daily.[2] Many of these particles contain living organisms like bacteria, viruses, fungi and mycoplasma. The mucociliary system of the airways forms a highly efficient defense system that protects the lungs against these particles as well as inhaled chemical irritants. The nasal mucosa constitutes the first-line of defense having a high capacity to remove inhaled particulate matter including irritating substances.[3]

Nasal mucociliary clearance (NMC) is a primary innate defense mechanism of the nose and paranasal sinuses whereby mucus secreted into the upper airways (by the goblet cells of the respiratory epithelium) traps inhaled particulate matter, allergens and pathogens. This is then transported by the ciliated cells of the respiratory epithelium to the nasopharynx, oropharynx and finally hypopharynx, where it is swallowed.[4]

The factors affecting the ciliary action includes temperature (<10 and >45°C), drying, isotonicity of secretions, infection, pH (good function in slight alkaline medium) and drugs. Acetylcholine and adrenaline increase, whereas propranolol decreases the NMC. Various tests to measure mucociliary clearance time include: Quinian method, Andersen method and electron microscopy.[5]

Nasal secretions contains mainly glycoproteins like sialomucins and sulfomucins; however, it mainly contains water. There are also ions, enzymes like lysozymes and lactoferrin, circulatory proteins like macroglobulin, immunoglobulins and cells (surface epithelium, basophil, eosinophil, leukocytes). Cilia found on the surface of the cells in respiratory tract propel the mucus backward towards the nasopharynx by cilia beating in a metachronous fashion. Each cell contains around 200 cilia with approximate length of 5 µm and they beat with frequency of 10-20 Hz (Avg-14Hz), which is constant between 32-40°. There are two phases of ciliary movement (i.e.. rapid propulsive phase and slow recovery phase).[6,7]

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NMC is the mirror image of bronchial mucociliary clearance[8] and the ciliary beat frequency of nasal mucosa correlates with that of tracheal mucosa.[9,10] NMC is influenced by physiological factors such as the amount of mucus produced; the ciliary beat efficiency; anatomic factors such as nasal airflow, patency of the sinus ostia in the prechambers and biochemical factors such as mucus composition. Impairment of NMC results in the accumulation of respiratory secretions and reduced lung defences leading to infections and inflammation.[10] NMC, thus functions as a biomarker of nasal mucosal functions and can serve as an early warning system for susceptibility to respiratory diseases.[11]

NMC is generally determined to obtain an *in vivo* measurement of the effectiveness of interaction between cilia and mucus. Evidence states that mucociliary clearance in trachea and main bronchi are at a similar rate as in the nose. Thus, NMC is considered to be representative of pulmonary mucociliary clearance as well.[9]

The NMC can vary due to habit, habitat, humidity and temperature. Hence, the present study was undertaken to evaluate the NMC in 500 healthy subjects of Haryana (India) using Anderson`s saccharin method to establish normative data of NMC for Indian population.

MATERIAL AND METHODS

The present study was conducted in the Dept. of Otorhinolaryngology and Physiology, Pt. BD Sharma Postgraduate Institute of Medical Sciences, Rohtak, Haryana on a total of 500 healthy subjects of either sex between age group of 14-49 years in outpatient department by using Anderson's saccharin method.[12]

Smokers, passive smokers, tobacco chewers and snuff users were excluded from the study. Subjects who had local pathology such as deviated nasal septum, nasal polyps, nasal allergy, rhinosinusitis and upper respiratory infection in the preceding 2 weeks were also excluded. Similarly, subjects with self-reported diabetes, chronic systemic diseases, bronchiectasis, valvular heart disease, bleeding diatheses and intake of any medication(s) particularly antihistaminics were also excluded. All the above mentioned factors are known to affect NMC.

Saccharin test is a simple, noninvasive reproducible method while methods using radiolabeled particles are time consuming, cumbersome and expensive.[12]

In the present study, classical saccharin test was performed in sitting position. An approximately 1 mm diameter particle of saccharin was placed 1 cm behind the anterior end of the inferior nasal turbinate at the floor of nose. The subject was requested not to smoke, eat, drink, cough or sneeze during the test. The test was repeated in the other nostril and the average of two sides was taken to obviate any effect of nasal cycle on NMC.

Subjects were asked to report the change in taste as soon as it was perceived. The time from the placement of the saccharin particle to the initial perception of the sweet taste was taken as NMC time and was recorded in minutes. The test was terminated after 30 minutes, if the patient didn't appreciate the change of taste. These subjects were excluded from the study as it was presumed that there was some abnormality in taste perception, which was verified by directly placing the saccharin particle on the tongue.[12]

RESULT

A total of 500 healthy subjects comprising of 290 males and 210 females of 14-49 years of age group were included to establish NMC time (Fig. 1). The mean value of NMC obtained was 8.47 ± 0.41 minutes with a range of 5.3-18.9 minutes. It was 8.34 ± 0.58 in males and 8.21 ± 0.59 in females. There was no statistical difference between the two sexes ($p > 0.05$).

DISCUSSION

NMC is determined to obtain an *in vivo* measurement of the effectiveness of the interaction between the cilia and mucus. Various techniques are employed for measuring NMC namely: Anderson`s saccharin test, NMC time using color dye, NMC time using combination of color substance *plus* saccharin and using teflon disks. NMC is also measured by gamma-scintigraphy using ^{99m}Tc, which is a very accurate method. However, it is time consuming and a very expensive method.[13] Normal value of NMC time is up to 20 minutes. If it is 21-30

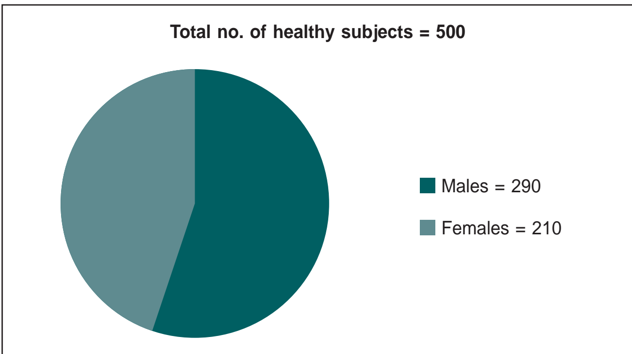

Figure 1. Distribution of normal subject with relation to gender.

minutes it is prolonged, 31-60 minutes is severely prolonged and over 60 minutes is grossly prolonged.[8]

Saccharin test is usually performed prior to referring patients for ciliary beat frequency estimation, as it is reported that all patients with primary ciliary dyskinesia have NMC >60 minutes, if correct precautions are observed. The only disadvantage of this method is that the determination of transit time may be influenced by the taste threshold of the patient.[13]

Increased NMC time signifying a decline in mucociliary clearance could be attributed to a variety of anatomical, physiological and biochemical changes which occur during the normal aging process, which may affect the response of the lung to inhaled agents.[14] Anatomical changes that occur with aging include nasal mucosal damage which has accumulated from infections over the years, ciliary ultrastructural defects such as the occurrence of increased central microtubular disorientation, altered proportions of elastic tissues and collagen. Physiological alterations that could impair mucociliary clearance include abnormally slow or uncoordinated ciliary beating where neighboring cilia do not beat in a coordinated fashion and in the same direction. This could be the result of abnormal ciliary ultrastructure or occur *de novo*.[15]

Passali et al (1985) reported the normal values of NMC in healthy children was 9.96 minutes.[16] Yadav et al (1999) studied NMC in 30 children of adenoiditis of either sex in the age group of 6-14 years and 30 healthy controls. They reported the mean value of NMC was 8.18 ± 1.81 minutes (5.08-13.02 minutes) in healthy children.[17] Ranga et al (2000) studied NMC in 50 children of either sex suffering from adenotonsillar hypertrophy and healthy controls in the age group of 6-14 years and they observed that the NMC time in healthy children was 8.55 ± 2.11 minutes (5.09-13.5 minutes).[18] Yadav et al (2001) studied NMC in 100 healthy school children in the age group 4-15 years and they observed the mean value of NMC time was 5.7 ± 2.59 minutes in males and 6.37 ± 2.59 in females. The difference between males and females was not statistically significant ($p > 0.10$).[19] The NMC time reported in normal Indian children is lower as compared to European (Italian) children. This may be due to racial factors like configuration of skull.

Singh et al (1994) studied nasal mucus clearance in chronic smokers and healthy controls. They observed the normal value of NMC time in healthy controls was 7.5 minutes (range 6.0-9.4 minutes).[20] Singh et al (1995) studied the effect of irradiation on mucociliary clearance in 25 subjects with the mean age of 52.2 ± 14.6 years and 25 controls with mean age of 43.8 ± 16.3 years. They observed the NMC time in control group was 6.6 ± 2.4 minutes.[21] Singh et al (1998) studied NMC in diseases of lower respiratory tract using Anderson`s saccharin method. They observed NMC time in 100 controls (44 females and 56 females) in the age group of 14-49 years was 8.4 ± 0.4 minutes (range 5.3-18.9).[22]

Yadav et al (2003) studied nasal mucus clearance in 30 adult patients of either sex suffering from perennial allergic rhinitis as well as 30 healthy controls. They reported NMC time in healthy controls was 8.21 ± 0.25 minutes.[23] Yadav et al (2005) studied mucociliary clearance in 50 cases of bronchial asthma with mean age of 28.6 years (23 males and 27 females) and 25 normal controls (12 males and 13 females) with the mean age of 25.5 years. They reported that the NMC time was 7.90 ± 0.32 minutes in healthy controls.[24]

Yadav et al (2011) studied the effects of aging on NMC in 240 normal subjects (120 males and 120 females) of age group 11-70 years and they observed the mean value of NMC time was in range between 7.34-14.48 minutes in males and 7.36-15.38 in females.[25] Yadav et al (2014) studied affects of passive smoking on NMC among 50 active and 50 passive smokers in the age group of 25-50 years and they observed NMC time in their control group of 50 healthy subjects was 8.57 ± 2.12.[26]

Garg et al (2016) studied NMC in various phases of menstrual cycle among 30 healthy female medical students of age group 18-24 years. They observed NMC time was 10.81 ± 2.14 (menstrual), 8.233 ± 1.94 (proliferative), 11.12 ± 2.11 (luteal) phases of cycle.[27]

Yadav et al (2016) studied mucociliary clearance in 75 patients of bronchiectasis of either sex in the age group 18-60 years and 25 normal persons (13 males and 12 females). They reported NMC time was 7.84 ± 0.92 minutes in control group.[28]

The mean value of NMC obtained in our study was 8.47 ± 0.41 minutes with a range of 5.3-18.9 minutes. It was 8.34 ± 0.58 in males and 8.21 ± 0.59 in females. The NMC time of the present study is comparable with most of the Indian studies including from our institution indicating that NMC time is constant irrespective of place of study.[20-27] However, reported NMC time in literature is lower in children.[16-19] This may be due to the fact that children are more prone to nasal catarrh and faster NMC time is the way of nature or body defense to wash out the offending organisms

usually the viruses. The reported increased NMC in adults as compared to children may be due to normal aging.[15] However, most of the studies reported world over have studied 25-100 healthy subjects, whereas we studied 500 normal healthy subjects. Hence, it is more authentic normative data for future reference on NMC time.

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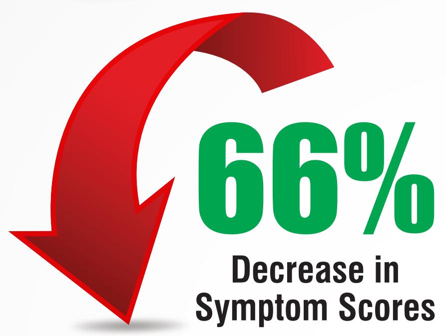
ReSync Mind & Body in GERD, IBS & Gastroparesis



66% Decrease in Symptom Scores

Tolerability 97%

Largest Surveillance of Wokride On
15000 Indian
patients suffering form GERD

* Visit in Every 15 days, with 1-2 Assessments
Ref:- Ther Clin Risk Manag. 2007 March; 3(1): 149–155. Published online 2007 March.

WOKRIDE/CAP/SPEC/SG/SS/VA-03/4041/Q2-17-18

Integrated Approach to Disorders of Gut-Brain Interaction: Place of Prokinetics and Combinations with Proton Pump Inhibitors

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RESYNC Panel of Gastroenterologists: Dr Gourdas Choudhuri (Gurgaon), Dr Manish Bhatnagar (Ahmedabad), Dr Sethu Babu (Hyderabad), Dr VG Mohan Prasad (Coimbatore), Dr Tarun Lahiri Mazumdar (Kolkata), Dr Atul Shende (Indore) and Dr Sanjeev Khanna (Mumbai)

ABSTRACT

It is being increasingly recognized that there is a considerable overlap between clinical presentation and symptoms of upper and lower gastrointestinal (GI) disorders. An integral connection of the gut receptors and the brain has also been shown now. Though the term 'functional' GI disorders has been in use for long, it is now understood and accepted that factors like visceral hypersensitivity, central sensory dysregulation, GI dysmotility, alteration of the gut flora, GI inflammation with changes in barrier function and gut immunity, as well as presence of psychosocial factors may all have a role to play. Therefore, the new term 'disorders of gut-brain interaction' (DGBI) has been suggested. In this context, it is important to understand the place and appropriate usage of prokinetics and their combinations as these are available and prescribed commonly in India. Recognizing overlap of GI symptoms, and understanding the gut-brain receptors with relevance to the action of prokinetics, can help make rational treatment decisions and selection of appropriate pharmacotherapy.

Keywords: Gut-brain, overlap, GERD, dyspepsia, constipation, dysmotility, prokinetic

In the wake of the recent Rome IV guidelines and repeated evidence of upper and lower gastrointestinal (GI) symptom overlap, the concept of approaching the same as disorders of gut-brain interaction (DGBI) has been recommended.[1]

A panel discussion called the 'Resync GI panel' of experts in the field of Gastroenterology was done for an integrated management of GI disorders by 'syncing' the brain, upper and lower GI as a unified system, and understand therapeutic options which are in sync with this concept with special reference to prokinetics and their combinations with proton pump inhibitors (PPIs). The detailed literature review and panel discussion is presented in two parts: understanding the upper GI-lower GI–brain connect and pharmacological management of GI disorders.

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UNDERSTANDING THE BRAIN-UPPER GI-LOWER GI CONNECT

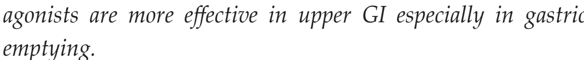
Gastrointestinal nerve supply comprises of myenteric and submucosal plexus, parasympathetic supply from vagus nerve (till proximal colon) and distally by sacral nerves and sympathetic nerve supply from T6 to T9 and L2 to L5.[2] The various GI receptors are summarized in Table 1.[3-6]

Summary Comments from the Panel

- *Due to the presence of 5-HT4 receptors throughout the GI tract, prokinetic drugs with 5-HT4 agonistic action can improve motility of both upper and lower GI tract.*
- *Drugs inhibiting D2 receptors or 5-HT3 receptors will additionally act on chemoreceptor trigger zone (CTZ) to prevent vomiting. Drugs with selective D2 receptor antagonistic action mainly improve upper GI motility.*
- *Cholinergic receptors are present throughout the GI tract but their density decreases as we move from proximal to distal colon. Prokinetic drugs acting on these receptors as*

Table 1. Summary of GI Receptors

Important GI receptors with location	Function
Cholinergic receptors[3] Mainly M3 and lesser extent M2 throughout GI tract (more in upper GI) - Density decreases as we move from proximal to distal colon	Increase LES tone Increase peristalsis and gastric emptying Increase intestinal motility Increase GI secretions Act centrally to decrease vomiting
Adrenergic receptors[4] Alpha1, beta1 and 2 - GI smooth muscles	Decrease peristalsis, gut motility and GI secretions
Dopaminergic receptors[5] Mainly D2 receptors in upper GI - esophagus, stomach, CTZ and brain	Inhibit acetylcholine release - decrease LES tone and esophageal peristalsis Cause of nausea and vomiting Decrease gastric emptying
Serotoninergic receptors[6] 5-HT4 (throughout GI tract) - acts on proximal GI through acetylcholine release (contracts longitudinal muscle) and on distal GI by directly relaxing circular muscle 5-HT3 (CTZ and vomiting center, enteric neurons)	Increase sphincter tone (LES) Increase peristalsis Increase gastric emptying Increase intestinal motility Increase GI secretions Induces vomiting and increases secretions and motility



agonists are more effective in upper GI especially in gastric emptying.

- *Knowledge of the GI receptors as well as the mechanism of action of various GI motility drugs on these receptors is very crucial in selecting the appropriate therapy for particular subsets of patients.*

As per Rome IV recent criteria, bowel disorders exist as a continuum rather than as independent disorders. The guidelines recommend doing away with the 'functional' word and have now given the term as 'disorders of gut-brain interaction' thereby establishing a hypothesis of upper GI-lower GI-brain connect.[1] Therefore, gastroesophageal reflux disease (GERD), functional dyspepsia (FD), chronic constipation and irritable bowel syndrome (IBS), etc. are different clinical manifestations of disordered functioning of the GI tract (Fig. 1).[7]

In both FD and IBS, the pathophysiology is likely to be mixed.[8] There is a significant overlap of the pathophysiological mechanism which forms the basis of functional bowel disorders by both FD and IBS.[9] Levels of evidence are maximum for intestinal dysmotility and visceral hypersensitivity for both IBS and FD, however, central sensory dysregulation, alteration in GI flora, GI inflammation and psychosocial factors may also play a role.

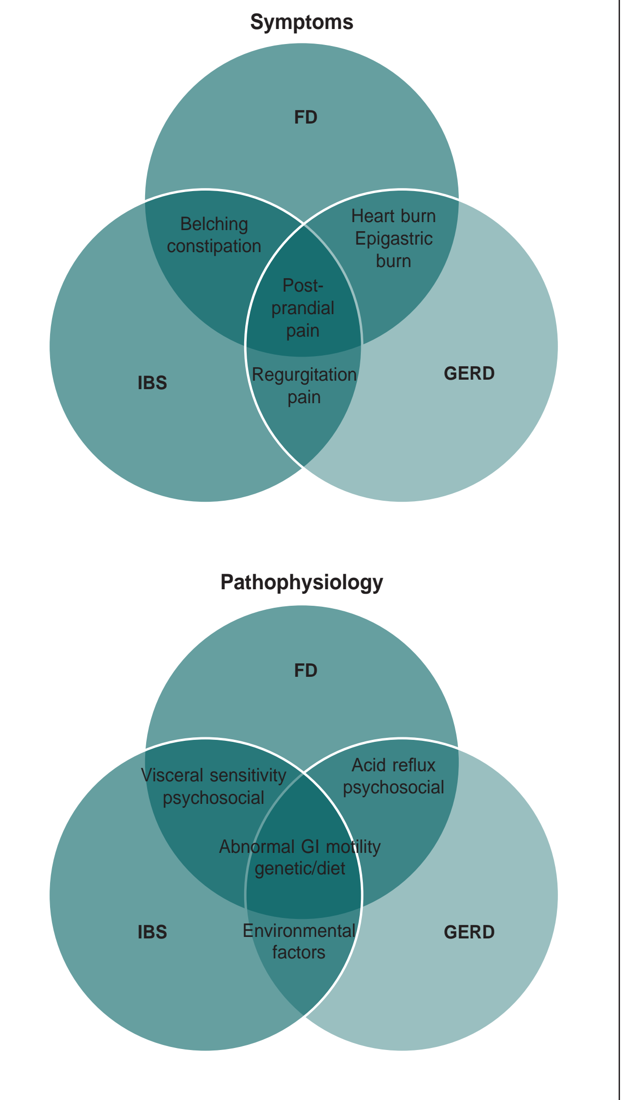


Figure 1. Different clinical manifestations and pathophysiology of disordered function of the GI tract.[7]

Summary Comments from the Panel

- *Based on clinical experience and patient presentation, upper GI and lower GI exist in continuum and not as separate entities.*
- *The recent Rome IV has given clear objectives and removed subjective components and terminologies (like 'functional' and 'discomfort').*
- *Investigating the patient thoroughly, (with special emphasis on GI allergies) as well as studying diet and nutrition, lifestyle*

- *factors and intake of drugs (nonsteroidal anti-inflammatory drugs [NSAIDs], etc.) was recommended before labeling GI disorders as 'functional'.*
- *Visceral hypersensitivity, gut microbiota, local immunity and inflammation, GI barrier function and a psychogenic component play an important role in these disorders.*

Prevalence of Overlap of GERD, IBS, FD: What does the Literature Say?

Overlap rate of FD-IBS is in the range of 11-27%.[8,10] In population-based studies, the estimated prevalence of IBS among dyspeptic subjects, ranges from 13% to 29%, while the prevalence of FD among IBS subjects ranges between 29% and 87%.

In-patient-based series, as opposed to community series, the prevalence of overlap was shown to be even higher with 26-46% of FD patients having concomitant IBS and as many as 87% of IBS patients having concomitant FD. In a population-based study from Mumbai, India, the prevalence of dyspepsia was 30%, while among subjects with IBS, the prevalence of dyspepsia was 58%. In another study from India by Goshal et al, about 50% patients showed an overlap of FD-IBS. GERD and IBS symptoms were both found in dyspeptic patients in 16-32% cases.[11]

The prevalence of IBS, among subjects with dyspepsia at 14% was greater than in the general population where it was 7.5%. The frequency of FD, IBS and FD-IBS overlap was found to be 53%, 21% and 1.6%, respectively.[12,13] In Asia, Shah et al found that 58% of subjects with IBS had dyspeptic symptoms, 14% of subjects with dyspeptic symptoms had IBS. It was seen that 41.4% had visited a physician for their complaints and 40% received treatment with antacids, acid suppressors or a prokinetic drug.[13]

Door-to-door survey in a rural Indian population revealed that 21.7% had GI symptoms (dyspepsia: 14.9%, IBS: 2.7% and dyspepsia-IBS overlap: 4.1%). Dyspepsia patients more often had overlap of epigastric pain and postprandial distress rather than any specific subtype. Chewing tobacco, intake of aerated soft drink, intake of coffee/tea, disturbed sleep, vegetarianism and anxiety parameters were associated features. It was seen that dyspepsia was a predictor of IBS and abdominal bloating was often associated with dyspepsia and dyspepsia-IBS overlap.[14]

Summary Comments from the Panel

- *In clinical practice, overlap between upper and lower GI symptoms in patient presentation is very high and underestimated in studies. In actual practice, the overlap is in up to 80-90% patients.*
- *There is a significant amount of data among Asian populations especially in Japan as well as in India which show overlap of GERD, IBS and dyspepsia showing their existence as a continuum and not distinct disorders.*

Mechanism Underlying GERD and Dyspepsia

The mechanisms underlying reflux in GERD include frequent TLESRs (transient lower esophageal sphincter relaxations) as seen in day burpers and reduced LES tone seen in night burners who have low LES pressure and therefore greater reflux of gastric contents on lying down. Night burners are known to have longer durations of continuous acid exposure or lowered pH contributing to a greater risk of erosive esophagitis. Increasing LES tone along and improving gastric emptying along with acid suppression are crucial in these patients to prevent development of erosive lesions.[15]

GERD can coexist with delayed gastric emptying wherein there is progressive dilatation of proximal stomach and shortened LES. Hence, greater amounts of solid and liquid materials remains in the stomach after meals and because of its defective emptying, reflux occurs. Not surprisingly, these patients complain more often than those with normal gastric emptying of dyspepsia symptoms like postprandial distension, generalized bloating and abdominal pain, in addition to the usual symptoms of gastroesophageal reflux.[16]

Many GERD patients also suffer from constipation, indicating that they may have reduced motility of the entire GI tract. Symptomatic constipation may be a risk factor not only for the occurrence of GERD, but also refractoriness to PPI monotherapy. In a study refractory factors for PPI therapy in GERD have seen to be high pre-treatment the frequency scale for the symptoms of GERD (FSSG) score, female gender, low body mass index (BMI), low alcohol consumption and symptomatic constipation, the odds ratio being highest in coexisting symptomatic constipation.[17]

PPIs are unstable at a low pH, so retention of PPIs in stomach for a long time may result in impaired acid suppressive effect, so improving transit of the PPI to the upper intestine will be of benefit, which can be aided by adding a prokinetic. Also as some GERD patients refractory to PPI monotherapy have dyspeptic (dysmotility) symptoms, most of them respond to the addition of a prokinetic agent. Adding a prokinetic

agent to the standard dose of PPI is considered more cost-effective than doubling the dose of the PPI in countries like Japan.

Summary Comments from the Panel

- *In past, peptic ulcer was seen more commonly in clinical practice but now GERD is on rise. Bloating and dyspepsia are common complaints along with reflux and regurgitation.*
- *Nocturnal refluxes can be very dangerous. Acid can stay in esophagus for up to 3 hours/180 minutes, which can have serious detrimental effects in supine position contributing to a greater risk of erosive esophagitis. Increasing LES tone, improving gastric emptying along with acid suppression will benefit these patients.*
- *When Psyllium husk (e.g., isabgol) is administered to patients with constipation in GERD, there is increased fecal bulk which further aggravates bloating and acidity symptoms, so use of polyethylene glycol or prokinetic agents to enhance gastric emptying will bring better symptomatic relief from both constipation, dyspeptic and acidic symptoms.*
- Helicobacter pylori *positivity is seen in more than 60% Indian population due to low sanitation and hygiene, but may not be associated with clinically active disease.* H. pylori *testing is recommended in intention to treat (for* H. pylori *eradication) population like patients of gastroduodenal ulcer or FD; however, is not routinely recommended in GERD.*

Gastroparesis: Delayed Gastric Emptying/Constipation

Gastroparesis is a condition of abnormal gastric motility characterized by delayed gastric emptying in the absence of mechanical outlet obstruction. The true prevalence of gastroparesis is unknown; however, it has been estimated that up to 4% of the adult population experiences symptomatic manifestations of this condition.

Constipation may also be associated with gastroparesis. Treatment of constipation with an osmotic laxative has shown to improve dyspeptic symptoms as well as gastric emptying delay. Routine motility testing or gastric scan to confirm gastroparesis by presence of food in stomach at the end of 4 hours are not recommended except if nausea and vomiting persist. Prokinetics may improve predominant symptoms of decreased gastric emptying viz. nausea, vomiting, bloating and constipation.[18]

Summary Comments from the Panel

- *Bristol's stool chart guidelines for IBS in Rome IV can improve diagnosing and categorization.*
- *Good history taking and eliciting patient symptomatology by understanding local and language factors helps in ascertaining right treatment approach and classifying the patient's condition.*
- *Physician's and patient's conception of constipation can differ. Frequency and consistency of stools is not enough alone to judge constipation. Several other factors like time taken for patient to evacuate, incomplete defecation and number of attempts taken to completely evacuate or feel complete evacuation are also determinants.*
- *In diabetic patients, if proper gastric emptying is achieved via prokinetics then even sugar levels (patients who are on oral hypoglycemics) are maintained better or vice versa.*

Depression in FGID

Psychological factors are now accepted to play an important role in many GI symptoms through "gut-brain interactions". In psychiatric tradition, these GI symptoms are often seen as functional symptoms caused by depression. Previous studies have found a high depression level in patients with GI symptoms, and depression is considered an important predictor of FD and IBS. GI symptoms were reported by over 90% major depressive disorder (MDD) patients in one study.

In an outpatient study with IBS and FD in comprehensive hospitals in big cities in China, the prevalence of depressive symptom in FD and IBS were 13.5% and 13.8%, respectively, while less than 12% of depressive subjects had been recognized and treated.[19] The American College of Gastroenterology (ACG) 2017 guidelines recommend use of tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitor (SSRIs) in management of DGBI when response to a PPI alone is not satisfactory.[20]

Summary Comments from the Panel

- *DGBIs may be associated with depression which is often underlying, mild and undiagnosed. Treating the same can improve therapy response of GI symptoms also.*
- *TCAs and SSRIs (SSRRIs like escitalopram) can be considered in lack of response to PPIs to address the psychosomatic component of GI problems by mood elevation as well as relaxing gastric fundus to prevent reflux.*
- *However, when seen in real world clinical practice, TCAs/SSRIs are given only to 20% of patients diagnosed with DGBIs while psychiatric referrals are rare, not preferred by either treating physician or patient.*
- *A drug which can address both upper and lower GI motility with an impact on depressive symptoms can be a worthwhile choice of therapy in DGBI.*

An integrated approach to manage DGBIs presenting with upper and lower GI symptomatology with

psychosocial components can involve targeting the appropriate GI receptors, which address the motility of the entire GI tract and syncing the gut-brain axis.

PHARMACOLOGICAL MANAGEMENT OF GI DISORDERS

Review and Comparison of Prokinetic Agents

The clinical data and literature for the 6 commonly prescribed prokinetics in Indian market was reviewed (viz. levosulpiride, acotiamide, itopride, domperidone, cinitapride and mosapride) along with their mechanism of action on upper/lower GI and safety profile and a comparative analysis between levosulpiride and some of these prokinetics (metoclopramide, domperidone, cisapride, itopride) (Table 2).[21-35]

Comparative clinical studies of levosulpiride showed better efficacy than other prokinetics in relieving upper GI symptoms viz. that of regurgitation, vomiting and dyspepsia.[32-35] A small study also showed improved abdominal pain and constipation in patients of IBS.[36]

Levosulpiride can act on multiple levels in DGBI. It acts as a D2 receptor antagonist and a 5-HT4 receptor agonist, therefore it is effective in upper and lower GI symptom relief as well as has action on CTZ. Therefore, levosulpiride can help reduce reflux, vomiting, dyspepsia, bloating and constipation symptoms. Levosulpiride is an atypical neuroleptic, crosses blood-brain barrier and preferentially blocks the presynaptic dopaminergic D2 receptors in brain thereby providing antidepressant effect in the lower doses itself of 50-100 mg. At higher doses, used in psychosis (300 mg or higher), levosulpiride shows antagonism at postsynaptic D2 receptors, which gives rise to neuroleptic action but may also contribute to extrapyramidal side effects.[21-23]

Metoclopramide, another D2 receptor antagonist also crosses blood-brain barrier but does not show atypical dose dependent D2 inhibition, therefore extrapyramidal side effects are present more commonly. Domperidone does not cross blood-brain barrier and being a selective D2 receptor antagonist without 5-HT4 action, it is mainly an upper GI prokinetic and useful in regurgitation, vomiting and dyspeptic symptoms. Domperidone is not recommended for long-term use due to Food and Drug Administration (FDA) cardiac alert.[37]

Itopride acts through cholinergic agonistic and D2 antagonistic pathway and is devoid of 5-HT4 agonism, therefore being effective mainly in upper GI dysmotility.[25-27]

All prokinetics with D2 receptor antagonism are also known to produce galactorrhea and therefore this should be kept in mind, while prescribing in fertile female population.[37]

Acotiamide acts through a cholinergic mechanism and is mainly helpful in postprandial bloating (postprandial distress syndrome [PDS] in patients with dyspepsia) and not in nocturnal reflux, vomiting or constipation.[24]

In three large pivotal randomized controlled trials, prucalopride has been effective in relieving symptoms of chronic constipation and has shown some limited evidence in reducing acid reflux symptoms in chronic constipation patients but larger studies are needed to prove its efficacy in reflux disorders.[38]

Cinitapride, a nonselective 5-HT4 agonist, has shown its efficacy in reflux, dyspepsia and constipation but is known to be associated with increased cardiovascular events in predisposed subjects.[30] Cisapride and tegaserod, both 5-HT4 agonists have been withdrawn for reasons of cardiac safety.[37] Mosapride is now available in Indian market which affects both dyspeptic symptoms and constipation but like other 5-HT4 agonists alone, is devoid of action on the CTZ to suppress nausea/vomiting.[31]

The possible reasons for superior efficacy of levosulpiride cited in literature include both dopaminergic + serotonergic mechanism affecting complete GI motility as well as effect on visceral sensitivity along with synergistic antidepressant activity.

Summary Comments from the Panel

- *In patients who are nonresponsive to initial PPI monotherapy and have symptoms of GI dysmotility, adding a prokinetic agent can be an effective option.*
- *Of all the prokinetic agents currently available in Indian market, levosulpiride outscores in terms of efficacy as seen in various studies, and is the only one which acts at multiple levels of upper and lower GI, the gut-brain axis and CTZ. Caution is advised to follow a strict dosing regimen with regular follow-up, to monitor for rare extrapyramidal side effects. If given in recommended dosage (75 mg/day) for appropriate duration (6-8 weeks), no serious adverse events have been reported in clinical studies.*
- *Metoclopramide crosses the blood-brain barrier causes extrapyramidal symptoms as an adverse effect to a much greater extent when compared with levosulpiride.*
- *Domperidone does not cross blood-brain barrier and is an effective upper GI prokinetic with antinausea/vomiting action also.*

Table 2. Literature Search: Levosulpiride versus Other Prokinetic Agents[32-35]

Drugs compared	Clinical condition	Study design	N	Results	Remarks
Metoclopramide (M) vs. Domperidone (D) vs. Levosulpiride (LS)[32]	Nonulcer FD	Open labeled, RCT - 3 parallel groups: LS 15 mg, D 10 mg and M 10 mg t.i.d. - FD assessed by SF-LFD questionnaire at baseline, 4 wks.	113/120 (38 M, 35 D, 40 LS)	All three therapeutic interventions i.e., LS, D and M effective in improving dyspeptic symptoms - Overall relief rates were significantly higher in the LS group ($p < 0.004$) as compared to D, M group at Week 4.	Dual (dopaminergic + serotonergic mechanism) of LS, effect on visceral sensitivity and synergistic anti-depressant activity was considered for better result.
Levosulpiride (LS) vs. Domperidone (D)[33]	FD	Prospective, double-blind, RCT-Group A: LS 25 mg t.i.d. - 4 weeks, Group B: D 10 mg t.i.d. - 4 weeks. Individual symptoms (abdominal pain, discomfort, nausea, vomiting, anorexia, postprandial bloating, belching, regurgitation, heart burn & abdominal fullness) and severity assessed by 3 point scale at baseline (0), 2, 4 & 8 weeks.	171/182 : 91 each in LS and D group	Highly significant ($p > 0.001$) improvement in symptoms: post-prandial bloating (82%), abdominal pain (81.63%) with LS as compared to D [postprandial bloating (57%), abdominal pain (45%)]. Both groups were comparable for other symptoms.	3 times more nonserious adverse effects observed with LS as compared to D, most common being sedation. Antidepressant activity of LS contributes to increasing gastric motility.
Levosulpiride (LS) vs. Cisapride (C)[34]	FD with delayed gastric emptying	Double-blind 4 weeks RCT - postprandial nausea, vomiting, bloating, belching, abdominal pain, early satiety, anorexia and drowsiness - assessed for severity (VAS), frequency and impact on daily life (4 point scale) - LS (25 mg t.d.s.) and C (10 mg t.d.s.)	30/group	Both C and LS significantly improved ($p < 0.001$) all dyspeptic symptoms. No statistically significant differences in improvement of duration, severity or frequency of overall symptoms. LS was superior to C ($p < 0.05$) in improving symptom impact on QoL. Nausea, vomiting and early satiety showed a significant improvement ($p < 0.01$) in LS, vs. C in severity and frequency.	Both C and LS induced significant ($p < 0.001$) increase in gastric emptying rate, from baseline. No statistically significant difference between the two groups seen. Among patients with no variations in gastric emptying times, symptom scores improved in 78% with LS and 44% with C.
Levosulpiride (LS) vs. Itopride (IT)[35]	GERD	RCT with 3 groups - The control group received rabeprazole and the two test groups received LS and IT. Symptom relief assessed at the end of 2 weeks.	210 - divided in 3 groups	Symptomatic relief and endoscopic recovery, improved QoL is early with LS than IT. LS has lesser side effects (37.2% vs. 73.4%) and better healing outcome (83.6% vs. 54.5%).	Dosage of LS and IT were not standardized.

- *Acotiamide is mainly useful for upper GI symptoms of delayed gastric emptying and bloating.*
- *Itopride mainly has action as an upper GI prokinetic while evidence with prucalopride is mainly for chronic constipation. Mosapride is effective in upper and lower GI symptoms, however, not when vomiting is associated.*
- *D2 receptor antagonists should be used cautiously in fertile female population due to possible occurrence of galactorrhea.*

Place of PPI-Prokinetic Combination in Integrated Management of GI Disorders

PPIs are regarded as first-line agents in management of upper GI disorders like GERD and dyspepsia. However, partial or nonresponse to PPIs has been seen commonly in DGBIs. Various studies on the effect of prokinetics with PPIs as combination therapy were reviewed.[17,39-42]

In a study, high pre-treatment FSSG, acidic and dyspeptic symptom score and presence of constipation suggesting an overall GI dysmotility and were seen to be primary reasons of PPI nonresponse in GERD patients. Such patients showed better symptom relief on adding a prokinetic.[40] Prokinetic addition is seen as a better strategy in countries like Japan than doubling PPI dose in these patients or switching PPIs. Improvement in both acidic and dyspeptic symptoms is seen with adding prokinetics to PPIs, suggesting that improved GI motility improves PPI pharmacokinetics in terms of reaching upper GI for effective absorption and effect. Delayed gastric emptying and slower GI transit increases PPI gastric acid exposure and decreases response. Nausea and vomiting symptoms also respond well with an appropriate prokinetic added to PPI.

Prokinetics increase LES tone, therefore act as a useful add on to PPIs in night burner GERDs to prevent development of erosive esophagitis. Nonacid reflux is also known to be a cause of reflux symptoms where adding a prokinetic would give more benefit than PPI alone in o.d. or b.i.d. dosing.[17] In patients with predominant night reflux symptoms and those who have associated constipation, evening dosing of PPI-prokinetic combination should be considered as an alternative to traditional pre-breakfast dosing. Timing the dose 30-45 minutes before dinner is critical and patient should be explained the same to maintain compliance.

Constipation is seen to worsen reflux, which is further aggravated by adding bulk forming laxatives to therapy, therefore adding a prokinetic to a PPI in such patients can help improve constipation and reflux symptoms. For the same reason adding prokinetic to PPI is also useful in patients of gastroparesis (diabetic or postoperative) who also often have co-existing constipation.

Duration of therapy should be 4-8 weeks for PPI-prokinetic combinations. Prolonged continuous therapy is not recommended. Patients have a tendency to repeat dosing through over-the-counter and repeat purchase so effective patient counseling on the long-term risks and effects of PPI should be imparted. The patient should also be educated on the importance of regular follow-up, strictly adhering to the dose prescribed and timing of taking the dose.

Summary Comments from the Panel

- *It is recommended to add prokinetics to PPIs in following patients:*
  - *Patients having no or partial response to PPI therapy.*
  - *Presence of symptoms of upper and lower GI dysmotility - nausea-vomiting, bloating, postprandial fullness and constipation. A prokinetic with action on all these symptoms acting at various levels of gut-brain axis, is the ideal choice as seen with levosulpiride.*
  - *In GERD patients with predominant nocturnal regurgitation, coexisting dysmotility symptoms, high acidic/dyspeptic symptom scores and coexisting constipation. Adding a prokinetic in these patients can be a more beneficial option than doubling PPI dose or switching PPI.*
  - *In patients with predominant night reflux symptoms and also those with coexisting constipation, pre-dinner dosing of PPI-prokinetic should be considered instead of morning.*
- *Dose and duration of PPI-prokinetic combination use should be well-monitored, and over-the-counter or long-term therapy strictly discouraged. Patient should be well followed up for adverse events.*
- *Prokinetic agents further augment the efficacy of PPIs as they promote faster gastric transit and intestinal absorption of PPIs thereby augmenting PPI response.*

CONCLUSION

It is now accepted and well-recognized that bowel disorders exist as a continuum rather than discreet entities. There is substantial evidence and data available to show that clinically, patients present commonly with significant overlap of upper and lower GI symptoms. There is also a psychosocial component to bowel disorders, which is often under recognized. Therefore, the integrated approach to manage DGBI is the need of the hour.

Appropriate use of prokinetics with PPIs, represents a promising approach to manage these gut-brain disorders. Prokinetics not only provide additional benefit to PPIs by reducing dysmotility or dyspeptic symptoms in the GI tract, but can also improve the gastric transit of PPIs and enhance their effect on relief of acidic symptoms. Prokinetics which exert action at multiple levels of the gut-brain axis through various GI and brain receptors, can give better overall symptomatic relief and thereby improve the quality-of-life of the patients.

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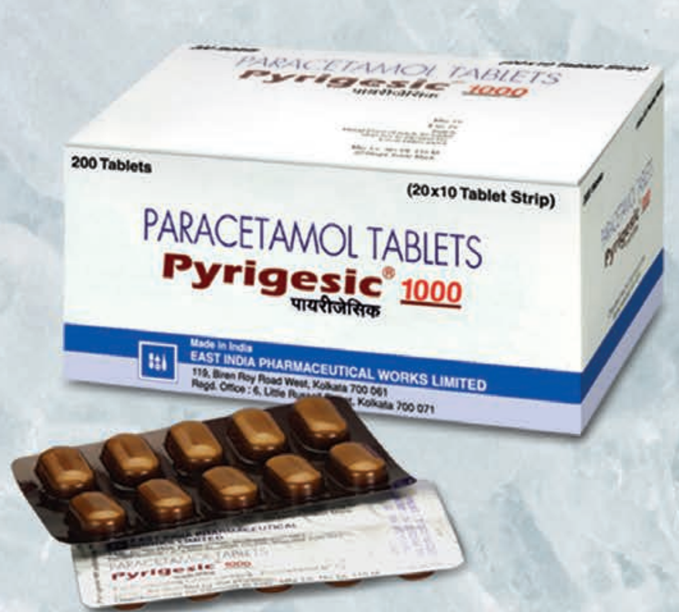

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Atypical Presentation of Tuberculous Pleural Effusion

V PADMA*, NN ANAND*, MADUMITHA†, SMA SYED MOHAMMED JAVID†, KARTHIKEYAN†

ABSTRACT

Tuberculosis is a major public health problem in developing countries. Pleural effusion is the second most common presentation of extrapulmonary tuberculosis. Diagnosis of pleural effusion can be established by demonstration of pleural fluid examination and pleural biopsy. Here we report a case who presented with hemorrhagic pleural effusion with lytic lesions in CT thorax suggesting malignancy, which on MRI spine turned out to be a tuberculous effusion.

Keywords: Extrapulmonary tuberculosis, pleural effusion, malignancy, tuberculous effusion

CASE REPORT

A middle-aged woman presented with complaints of dull lower back ache, which was aggravated on bending for past 3 months, breathlessness of Grade 1 to 2, relieved by lying on right side, cough with minimal expectoration which contained yellow-colored sputum for about a week and low-grade intermittent fever for 2 days. She is a known case of type 2 diabetes mellitus for about 10 years on oral hypoglycemic agents and insulin. She is a known hypertensive for 2 years well-controlled with antihypertensives.

On examination, her hemodynamic status was normal. She had tenderness over D11, D12 area of spine. Respiratory system examination revealed chest wall movements decreased on right hemithorax, vocal fremitus and vocal resonance decreased on right side, stony dullness on percussion present on right side below 3rd intercostal space up to liver margin, auscultation revealed absent breath sounds on right side below 3rd intercostal space. Other system examination was normal.

Blood investigations were all within normal limits except for moderate anemia with hemoglobin 7.6. Peripheral smear showed predominantly microcytic hypochromic RBC's with mild anisocytosis.

X-ray chest revealed right-sided pleural effusion (Fig. 1). CT thorax showed multiple destructive osteolytic lesions in D2, D10, D11, D12 vertebrae involving transverse process, pedicle, lamina with associated pre- and paravertebral soft tissue components, adjacent articular margins with associated soft tissue component of ribs involved (Fig. 2). Possibility of metastases needed to be considered.

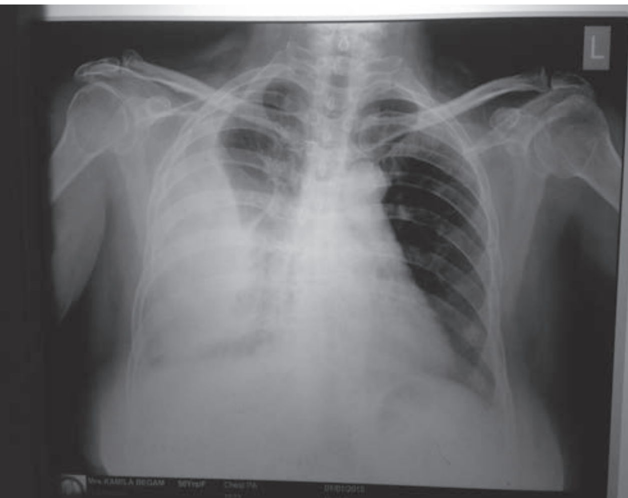

Figure 1. X-ray chest showing right-sided pleural effusion.

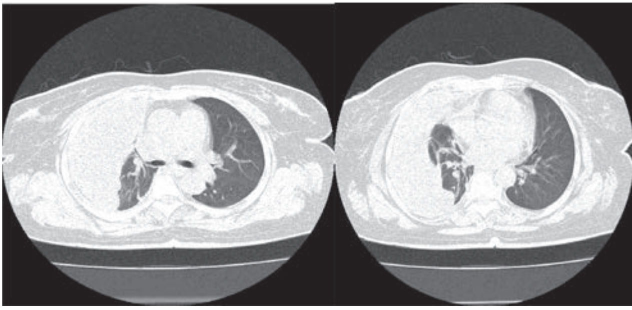

Figure 2. CT thorax.

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Figure 3. MRI thoracic vertebra.

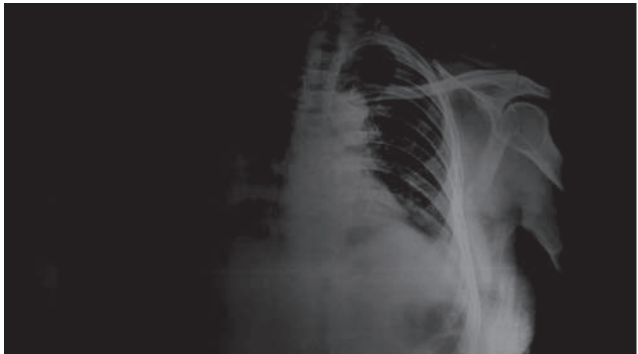

Figure 4. X-ray after 2 weeks of ATT showing resolution.

Magnetic resonance imaging (MRI) revealed lytic sclerotic destruction of D2, D11, D12 vertebrae with abnormal signal intensity D11-D12 disc and paravertebral soft tissue showing rim enhancement. Lytic destruction of posterior elements of D8, D9, D10 vertebrae and posterior aspect of 9th rib with associated left paraspinal soft tissue predominantly rim enhancement with possibilities of infective pathology; possibility of metastases was less likely (Fig. 3).

Pleural fluid was hemorrhagic with adenosine deaminase (ADA) levels of about 52.80. Cytology showed lymphocyte predominant serofibrinous background, s/o chronic inflammatory pathology. Since, pleural fluid was hemorrhagic and CT thorax reports were suggestive of bony metastasis, intense search for primary malignancy was made. Tumor markers turned out to be negative. Meanwhile patient's diabetes was brought under control. MRI spine was taken which was suggestive of tuberculosis spine. Patient was started on antituberculous treatment and is on regular follow-up. Patient is symptomatically better. The size of pleural effusion has decreased and her bony pain is also symptomatically better (Fig. 4).

DISCUSSION

Spinal involvement is usually a result of hematogenous spread of *Mycobacterium tuberculosis* into the dense vasculature of cancellous bone of the vertebral bodies.

The primary infection site is either a pulmonary lesion or an infection of the genitourinary system.[1-3]

Spread occurs either via the arterial or the venous route. An arterial arcade, in the subchondral region of each vertebra, is derived from anterior and posterior spinal arteries; this arcade form a rich vascular plexus. This vascular plexus facilitates hematogenous spread of the infection in the paradiskal regions. Batson's paravertebral venous plexus in the vertebra is a valve-less system that allows free flow of blood in both directions depending upon the pressure generated by the intra-abdominal and intrathoracic cavities following strenuous activities like coughing. Spread of the infection via the intraosseous venous system may be responsible for central vertebral body lesions.

In patients with noncontiguous vertebral tuberculosis, again it is the vertebral venous system that spreads the infection to multiple vertebrae. Spinal tuberculosis is initially apparent in the anterior inferior portion of the vertebral body. Later on it spreads into the central part of the body or disk. Paradiskal, anterior and central lesions are the common types of vertebral involvement. In the central lesion, the disk is not involved and collapse of the vertebral body produces vertebra plana. Vertebra plana indicates complete compression of the vertebral body. In younger patients, the disk is primarily involved because it is more vascularized.

In old age, the disk is not primarily involved because of its age-related avascularity. In spinal tuberculosis, there is involvement of more than one vertebra because its segmental arteries bifurcate to supply two adjacent vertebrae. Spread of the disease beneath the anterior or posterior longitudinal ligaments involves multiple contiguous vertebrae. A lack of proteolytic enzymes in mycobacterial infections (in comparison with pyogenic infections) has been suggested as the cause of the subligamentous spread of infection.

In spinal tuberculosis, characteristically, there is destruction of the intervertebral disk space and the adjacent vertebral bodies, collapse of the spinal elements and anterior wedging leading to the characteristic angulation and gibbus (palpable deformity because of involvement of multiple vertebrae) formation.[4-6]

The upper lumbar and lower thoracic spine are most frequently involved sites. More than one vertebra is typically affected, and the vertebral body is more frequently affected than the posterior arch.[7] Distortion of spinal column leads to spinal deformities.

Clinical Presentation

Back pain is the most frequent symptom of spinal tuberculosis. The intensity of pain varies from constant mild dull aching to severe disabling. Pain is typically localized to the site of involvement and is most common in the thoracic region. The pain may be aggravated by spinal motion, coughing and weight-bearing, because of advanced disk disruption and spinal instability, nerve root compression or pathological fracture. Chronic back pain as the only symptom was observed in 61% of cases of spinal tuberculosis. Neurologic deficits are common with involvement of thoracic and cervical regions. Left untreated, early neurologic involvement may progress to complete paraplegia or tetraplegia. Paraplegia may occur at any time and during any stage of the vertebral disease.[8,9]

The reported incidence of neurological deficit in spinal tuberculosis varies from 23% to 76%. The level of spinal cord involvement determines the extent of neurological manifestations. In cervical spinal tuberculosis, patients manifest with symptoms of cord or root compression. The earliest signs are pain, weakness and numbness of the upper and lower extremities, eventually progressing to tetraplegia.

If the thoracic or lumbar spine is involved, upper extremity function remains normal while lower-extremity symptoms progress over time eventually leading to paraplegia.

Patients with cauda-equina compression due to lumbar and sacral vertebral damage have weakness, numbness and pain, but have decreased or absent reflexes among the affected muscle groups. This is in contrast to the hyperreflexia seen with spinal cord compression along with bladder involvement (cauda-equina syndrome).

Pleural effusion due to tuberculosis and malignancy have certain distinctive features which are given in Table 1.

Exudative Effusions

- Neoplasms: Metastatic disease, mesothelium
- Infectious diseases: Bacterial, viral, fungal, parasitic, tuberculous
- Pulmonary embolism
- Gastrointestinal disease: Esophageal perforation, pancreatic disease, diaphragmatic hernia, abdominal abscess
- Uremia
- Meig's syndrome: Ovarian fibroma, ascites, right-sided pleural effusion

Table 1. Distinctive Features of Tuberculosis Pleural Effusion and that Due to Malignancy

	TB	Malignancy
Age	Can occur at any age.	Usually above 50 years age
Risk factor	Contact history	Exposure to smoking, fumes, asbestos, vinyl chloride, family history
Symptoms	Cough with expectoration	Symptoms related to primary site of the tumour
Pleural fluid gross	Mostly amber colored may be haemorrhagic	Mostly haemorrhagic
P.F Character	Moderate effusion	Recurrent (fills with in 1 month), rapid and massive
Cytology	Lymphocyte predominant	Malignant cytology
Bone Involvement	Potts spine, other bony structure including bones	Bone metastasis usually vertebra, and other long bones
Prognosis	Good	Worst

- Drug-induced: Bromocriptine, amiadarone, nitrofurantoin, dantrolene
- Chylothorax, hemothorax.

Malignancies Causing Pleural Effusion

- Bronchogenic carcinoma
- Mesothelioma
- Leukemia, lymphoma
- Secondaries from breast, ovarian malignancies.

Management

The management of exudative effusions depends on the underlying etiology of the effusion.

Indications for urgent drainage of parapneumonic effusions include:

- Frankly purulent fluid
- A pleural fluid pH of <7.0-7.1
- Loculated effusions
- Bacteria on Gram stain or culture.

Malignant pleural effusions signify incurable diseases with considerable morbidity and a dismal mean survival of less than 1 year.

For some patients, drainage of large, malignant effusions relieves dyspnea caused by distortion of the diaphragm and chest wall produced by the effusion.

For patients with lung entrapment from malignant effusions indwelling tunneled catheter drainage systems are the preferred treatment and provide good palliation of symptoms. In patients without lung entrapment, pleurodesis (also known as pleural sclerosis) is another option to prevent recurrence of symptomatic effusions.

Surgical intervention is most often required for parapneumonic effusions that cannot be drained adequately by needle or small-bore cannula. Pleurodesis by insufflating talc directly onto the pleural surface using video-assisted thoracoscopy. Decortication is usually required for trapped lungs to remove the thick, inelastic pleural peel that restricts ventilation and produces progressive or refractory dyspnea. It is also useful for treating trapped lung.

Surgically implanted pleuroperitoneal shunts are another treatment option for recurrent, symptomatic effusions, most often in the setting of malignancy.

CONCLUSION

The prognosis for spinal tuberculosis is improved by early diagnosis and rapid intervention. A high-degree of clinical suspicion is required if patients present with chronic back pain, even in the absence of neurological symptoms and signs. Medical treatment is generally effective. Surgical intervention is necessary in advanced cases with marked bony involvement, abscess formation or paraplegia. Spinal tuberculosis affects young people, so efforts should be made for its effective prevention. Controlling the spread of tuberculosis is only way available to prevent spinal tuberculosis.

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■■■■

Early Treatment of Undifferentiated Arthritis Delays Progression to RA

Findings from a systematic review and meta-analysis reported online in *Arthritis Care & Research* show that treating patients with early undifferentiated arthritis significantly delayed progression to rheumatoid arthritis (RA). Patients treated with methotrexate were particularly less likely to develop RA at 12 months than patients treated without methotrexate.

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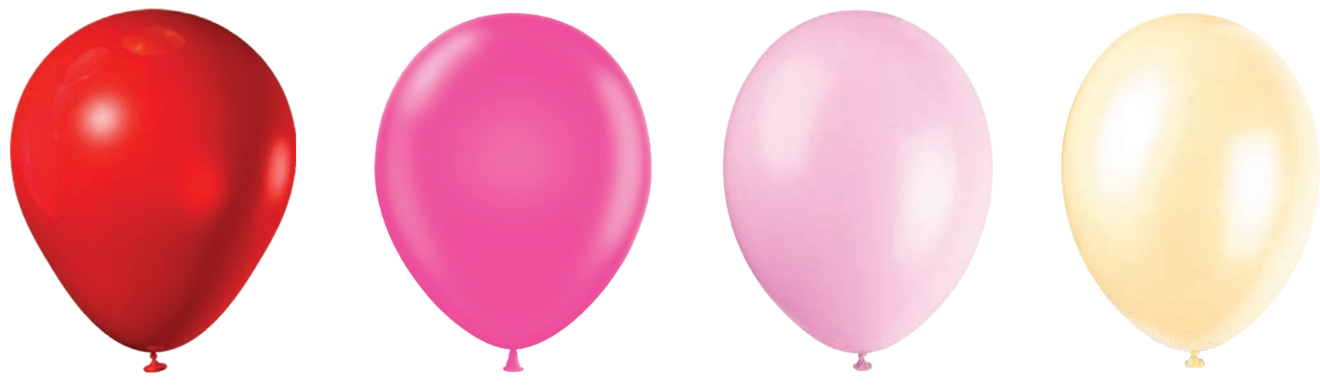

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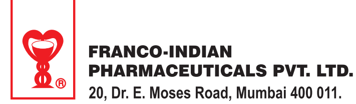

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Study of Prevalence of Hypothyroidism and Effect of Treatment with L-thyroxine in Patients of Chronic Kidney Disease

NS SENGAR*, NIPUN GUPTA†, NANDITA PRABHAT‡

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] 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 chronic kidney disease (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 ± .02 mL/min/1.73 m^2 before the THRT to 1.02 ± 2.5 mL/min/1.73 m^2 after

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

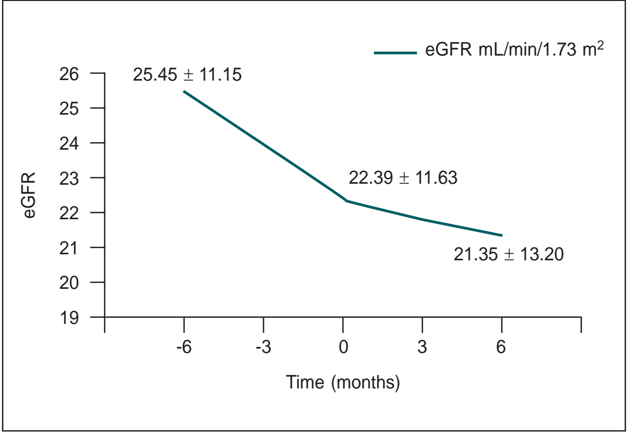

Figure 1. Comparison of rate of decline in eGFR before and after THRT.

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 ± 112.02	1.02 ± 2.5	<0.001

giving thyroid hormone replacement ($p < 0.001$) (Fig. 1 and Table 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% patients showed an improvement in eGFR after thyroid replacement.

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.

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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Updated Guidelines for Treatment for Patients with Ventricular Arrhythmias

The American College of Cardiology (ACC), American Heart Association (AHA) and the Heart Rhythm Society (HRS) have jointly published new guidelines for the management of adults who have ventricular arrhythmias or who are at risk for sudden cardiac death, including diseases and syndromes associated with a risk of sudden cardiac death from ventricular arrhythmias.

According to the guidelines, patients considering implantation of a new implantable cardioverter defibrillator (ICD) or replacement of an existing one should be informed of their individual risk of sudden cardiac death and nonsudden death from heart failure or noncardiac conditions, and the effectiveness and potential complications of the ICD. In patients nearing the end of life from other illness, clinicians should discuss ICD shock deactivation as they reassess their patients' goals and preferences.

Emphasizing on the role of shared decision making between patients and their doctors, the guidelines say that treatment decisions should also take into consideration, the health goals, preferences and values of the patients.

The "2017 AHA/ACC/HRS Guideline for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death" have been published online October 30, 2017 in the *Journal of the American College of Cardiology, Circulation and Heart Rhythm*.

(Source: ACC News Release, October 30, 2017)

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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.

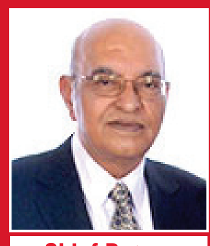
Objectives

- 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



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

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

http://heartcarefoundationfund.heartcarefoundation.org

Pulmonary Function Tests in Metabolic Syndrome

SHAKTHI KJS*, R MADHUMATHI*, VASANTHA KAMATH*

ABSTRACT

Background: The prevalence of metabolic syndrome varies around the world. It reflects the age and ethnicity of the populations involved in the study and the diagnostic criteria applied. Impaired pulmonary function has been reported to be associated with insulin resistance and metabolic abnormalities. There is increasing evidence that impaired lung function is more than a simple reflection of airflow limitation; it may also be a marker of premature death. This study has been conducted to find out the association between suspected pulmonary involvement, as assessed by pulmonary function tests and metabolic syndrome, as well as the correlation between metabolic abnormalities and lung compliance in an apparently healthy population. **Material and methods:** Patients evaluated/admitted for minor ailments to Victoria Hospital and Bowring and Lady Curzon Hospital attached to Bangalore Medical College and Research Institute who fulfilled the criteria for metabolic syndrome were treated and pulmonary function tests were carried out after taking consent from the patients. **Results:** Among 50 patients, normal pulmonary function tests was seen in 20 patients and remaining 30 patients showed deranged pulmonary function tests. Among them, 15 patients showed forced expiratory volume in 1 second (FEV1) less than lower limit of normal and FEV1/FVC (forced vital capacity) ratio less than lower limit of normal (obstructive pattern) and 15 patients showed FVC less than lower limit of normal and FEV1/FVC ratio more than lower limit of normal (restrictive pattern). **Conclusion:** There is a positive association between metabolic syndrome and lung function impairment. Both obstructive and restrictive pattern is seen with metabolic syndrome. However, there was no independent correlation between individual metabolic syndrome components and pulmonary function tests.

Keywords: Metabolic syndrome, impaired lung function, pulmonary function tests, obstructive pattern, restrictive pattern

The prevalence of metabolic syndrome varies around the world. It reflects the age and ethnicity of the populations involved in the study and the diagnostic criteria applied. Greater industrialization is associated with rising rates of obesity, diabetes, hypertension which is anticipated to increase prevalence of the metabolic syndrome dramatically, especially as the age of the population increases. The mechanisms underlying the relationship between impaired lung function and cardiovascular risk are unclear.[1]

Impaired pulmonary function has been reported to be associated with insulin resistance and metabolic abnormalities. There is increasing evidence that impaired lung function is more than a simple reflection of airflow limitation; it may also be a marker of premature death.[2] Several large prospective studies have shown that lung function impairment was predictive of increased cardiovascular morbidity and mortality, independent of smoking.[3,4] Positive associations with lung function impairment have been reported for major cardiovascular risk factors, such as hypertension,[5,6] type 2 diabetes mellitus,[7-9] dyslipidemia and overall obesity.[10,11]

This study has been conducted to find out the association between suspected pulmonary involvement, as assessed by pulmonary function tests and metabolic syndrome, as well as the correlation between metabolic abnormalities and lung compliance in an apparently healthy population.

MATERIAL AND METHODS

Patients evaluated/admitted for minor ailments like fever, common cold, bodyache, etc. attending the inpatient and outpatient clinics were included in the study. Patients were treated for their minor illness and pulmonary function tests were carried out after taking consent from the patient. Fifty patients who fulfilled the criteria for metabolic syndrome were included in the study. The study was conducted over a period of 2 years.

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Inclusion Criteria

According to the International Diabetes Federation (IDF) criteria, waist circumference >90 cm in males >80 cm in females, triglycerides >150 mg/dL or on specific medication, low high-density lipoprotein (HDL) cholesterol: <40 mg/dL and <50 mg/dL in men and women, respectively, or on specific medication, blood pressure >130 mm systolic or >85 mm diastolic or on specific medication, fasting plasma glucose: ≥100 mg/dL or specific medication or previously diagnosed type 2 diabetes mellitus/impaired fasting glucose/impaired glucose tolerance/diabetes mellitus.

Exclusion Criteria

Patients with cardiopulmonary diseases, neuromuscular disorders, musculoskeletal disorders, in postoperative state, any serious systemic illnesses, endocrine abnormalities (hypothyroidism, Cushing's syndrome, etc.), individuals below 18 years of age and smokers were excluded from the study.

Waist circumference (in cm) was measured at a point midway between the lower rib and iliac crest, in a horizontal plane, measured to the nearest 0.1 cm. Blood pressure was measured after patient resting for about 15 minutes.

All the maneuvers were performed in sitting position and at rest. A thorough instruction was given to each subject about the performance of the maneuvers, most of the times we demonstrated to them by doing the maneuvers ourselves on the machine. Every subject was given ample time to understand carefully, every part of the procedure and was asked to perform it number of times before we selected the best one. A soft nose chip was put over the nose to occlude the nostrils, disposable mouthpieces were used to minimize cross infection.

RESULTS

In our study, the total number of patients with metabolic syndrome were 50. Maximum number was in the age group of 51-60 (34%) followed by 61-70 (30%). The youngest patient was 30 years old and the oldest was 80 years old. Mean age group was 57.06 ± 12.40. Our study included 28 male patients (56.0%) and 22 female patients (44.0%). Mean height and weight of patients in our study were 1.59 ± 0.06 and 79.18 ± 6.52, respectively. The mean waist circumference and body mass index (BMI) were 97.34 ± 15.42 and 31.39 ± 1.86, respectively. The mean fasting blood sugar (FBS) and postprandial blood sugar (PPBS) in our study was 164.02 ± 28.02 and 251.82 ± 47.03, respectively. The mean level of triglycerides and HDL in our study were 205.58 ± 37.37 and 27.90 ± 6.55, respectively (Table 1). There was no significant differences between males and females among the investigations done and the pulmonary function tests performed.

Table 1. Comparison of Clinical and Study Variables According to Gender

Variables	Gender		P value
	Male	Female	
Age in years	59.57 ± 12.66	53.68 ± 11.57	0.107
WC (cm)	100.00 ± 20.05	93.95 ± 4.08	0.171
BMI (kg/m^2)	31.10 ± 1.44	31.77 ± 2.27	0.219
Pulse (bpm)	80.17 ± 5.81	78.45 ± 7.22	0.354
SBP (mmHg)	145.50 ± 5.03	145.45 ± 7.09	0.979
DBP (mmHg)	87.79 ± 5.79	89.82 ± 5.27	0.207
FBS (mg/dL)	168.61 ± 28.98	158.18 ± 26.25	0.195
PPBS (mg/dL)	255.25 ± 46.40	247.45 ± 48.55	0.566
Urea (mg/dL)	29.00 ± 7.86	21.36 ± 7.61	0.001
Creatinine (mg/dL)	0.89 ± 0.23	0.85 ± 0.28	0.518
TC (mg/dL)	248.82 ± 30.02	251.32 ± 29.14	0.769
HDL (mg/dL)	27.61 ± 7.02	28.27 ± 6.05	0.725
LDL (mg/dL)	176.5 ± 21.53	177.45 ± 19.6	0.872
TGs (mg/dL)	203.04 ± 35.18	208.82 ± 40.6	0.592
FVC	2.09 ± 1.00	2.35 ± 1.04	0.369
FEV1	1.67 ± 0.87	1.73 ± 0.92	0.821
FEV1/FVC (%)	78.66 ± 11.69	72.76 ± 13.46	0.108
PEF	3.43 ± 2.12	3.74 ± 2.42	0.635
MEF_{25}	0.99 ± 0.73	0.88 ± 0.56	0.576
MEF_{50}	2.01 ± 1.20	1.85 ± 1.23	0.651
MEF_{75}	2.89 ± 1.74	2.94 ± 1.94	0.916
PIF	2.91 ± 1.66	2.62 ± 1.71	0.559
T3	109.28 ± 26.93	122.27 ± 25.32	0.089
T4	7.84 ± 2.20	7.10 ± 1.23	0.165
TSH	3.37 ± 0.77	2.67 ± 0.92	0.005

WC = Waist circumference; BMI = Body mass index; SBP = Systolic blood pressure; DBP = Diastolic blood pressure; FBS = Fasting blood sugar; PPBS = Postprandial blood sugar; TC = Total cholesterol; HDL = High-density lipoprotein; LDL = Low-density lipoprotein; TG = Triglyceride; FVC = Forced vital capacity; FEV1 = Forced expiratory volume in 1 second; PEF = Peak expiratory flow; MEF = Maximal expiratory flow; PIF = Peak inspiratory flow; T3 = Triiodothyronine; T4 = Thyroxine; TSH = Thyroid-stimulating hormone.

Table 2. Distribution of Pulmonary Function Test of Patients Studied

Variables	Number of patients (n = 50)	Percentage (%)
FVC		
<2.09	19	38.0
>2.09	31	62.0
FEV1/FVC (%)		
<76	15	30.0
76-94	33	66.0
>94	2	4.0

In our study, 19 (38%) patients had forced vital capacity (FVC) less than lower limit of normal. And 31 (68%) patients had FVC more than lower limit of normal. Forced expiratory volume in 1 second (FEV1)/FVC ratio less than 76% was found in 15 (30%) patients and FEV1/FVC ratio between 76-94% was found in 33 (66%) patients and more than 94% was seen in 2 (4%) patients. Among 50 patients, normal pulmonary function test was seen in 20 patients and remaining 30 patients showed deranged pulmonary function tests. Among them, 15 patients showed FEV1 less than lower limit of normal and FEV1/FVC ratio less than lower limit of normal (obstructive pattern) and 15 patients showed FVC less than lower limit of normal and FEV1/FVC ratio more than lower limit of normal (restrictive pattern) (Table 2).

According to our study, there was no independent correlation between individual metabolic syndrome components and pulmonary function tests. Pearson's correlation co-efficient R value showed trivial correlation between individual component of metabolic syndrome and pulmonary function tests (Table 3).

Statistical Methods

Student *t*-test (two-tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Levene's test for homogeneity of variance has been performed to assess the homogeneity of variance.

DISCUSSION

The present study was done to determine pulmonary function tests in metabolic syndrome as well as to determine the relation between individual component of metabolic syndrome and pulmonary function tests.

Table 3. Pearson Correlation of Components of Metabolic Syndrome with Pulmonary Function Tests

Parameters	R value
WC vs. FEV1	-0.09696
WC vs. FVC	-0.08715
WC vs. FEV1/FVC	-0.0937
BMI vs. FEV1	-0.07883
BMI vs. FVC	-0.04362
BMI vs. FEV1/FVC	0.008287
HDL vs. FEV1	-0.03478
HDL vs. FVC	0.025457
HDL vs. FEV1/FVC	-0.19903
LDL vs. FEV1	-0.12261
LDL vs. FVC	-0.09532
LDL vs. FEV1/FVC	0.131155
TG vs. FEV1	0.100789
TG vs. FVC	0.14708
TG vs. FEV1/FVC	0.080905
FBS vs. FEV1	0.127207
FBS vs. FVC	0.091231
FBS vs. FEV1/FVC	0.264271

Many studies concluded that pulmonary function drops among obese people.[12,13] Previously, studies have used BMI, waist circumference, waist/hip circumference ratio, abdominal thickness (height) and skin thickness test as the markers that show obesity.[14,15] The study included 50 patients of metabolic syndrome. Patients were evaluated with detailed history, meticulous examination and laboratory investigations. Laboratory investigations included fasting lipid profile, FBS, PPBS level, thyroid function tests, ECG, chest X-ray and pulmonary function tests.

Study by Kim et al[16] showed that FVC values were significantly lower in the metabolic syndrome group compared with those of the nonmetabolic syndrome. The results of study suggested that decreased vital capacity in Korean adult male subjects are associated with metabolic syndrome. In our study, FVC <2.09 (lower limit of normal FVC) was found in 19 (38%) patients of which 4 patients had FEV1/FVC less than 76.0% (lower limit of normal FEV1/FVC) and remaining 15 patients had FEV1/FVC more than 76.0%.

In our study, the mean value of FEV1/FVC is 76.01 ± 12.73%. The mean FEV1/FVC in nonobese Indian is 85 ± 9%. In a study by Leone et al,[1] mean FEV1/FVC was 81.3 ± 7.8%. In a study by Nakajima et al,[17] the FEV1/FVC mean value was 81.7 ± 6.3%.

Among 50 patients, normal pulmonary function test was seen in only 20 patients, while the remaining 30 patients showed deranged pulmonary function tests. Among them, 15 patients showed FEV1 less than lower limit of normal and FEV1/FVC ratio less than lower limit of normal (obstructive pattern) and 15 patients showed FVC less than lower limit of normal and FEV1/FVC ratio more than lower limit of normal (restrictive pattern).

In a study by Leone et al[1] involving 1,21,965 patients; it was concluded that lung function impairment and metabolic syndrome had a positive independent relationship mainly due to abdominal obesity. All factors were inversely related to lung function but abdominal obesity was the strongest predictor of lung function impairment.

In population-based survey done by Lam et al,[18] 7,358 patients underwent spirometry, a structured interview and measurement of fasting metabolic marker levels. In this study also, it was concluded that airflow obstruction was associated with metabolic syndrome and in particular its central obesity component.

However, in a study by Kim et al[16] which included 1,951 male patients, it was seen that decreased vital capacity in Korean adult male subjects was associated with metabolic syndrome irrespective of obesity. In metabolic syndrome group, both FEV1 and FVC values, but not FEV1/FVC ratio were lower than the subjects in nonmetabolic syndrome.

In another study on 2,396 apparently healthy adults, Nakajima et al[17] came to the conclusion that impaired restrictive pulmonary function, but not obstructive pattern might be associated with metabolic disorders and metabolic syndrome in a severity dependent manner.

Bae et al,[19] in a study on 1,370 Korean patients, found that in men, all metabolic syndrome components were associated with pulmonary function impairment and the more metabolic syndrome components men had, the more severe was their pulmonary function decline. In women, no components of metabolic syndrome were associated with pulmonary function impairment.

In the Strong Heart Study (SHS), a multicenter, prospective study involving 2,396 patients, Yeh et al[20] concluded that reduced lung function was independently associated with metabolic syndrome and with diabetes mellitus, and impaired lung function presents before the development of metabolic syndrome or diabetes mellitus; these associations may have resulted from the effects of obesity and inflammation.

A study by Lin et al[21] involving 46,514 patients concluded that obesity and metabolic syndrome were associated with impaired lung function in adults in Taiwan. Results implied that obesity and insulin resistance may be the common pathways underlying lung function impairment and metabolic syndrome. Moreover, lung function test may be applied as an additional evaluation for metabolic syndrome in a clinical setting.

Costa et al,[22] conducted a study in 40 women, 20 obese and 20 nonobese, and concluded that the alterations evidenced in the components of the vital capacity (inspiratory reserve volume and expiratory reserve volume) suggest damage to the chest mechanics was caused by obesity and probably contributed to a reduction of the maximal voluntary ventilation.

In a study by Fimognari et al[23] on 159 consecutive nondiabetic elderly persons attending two social centers, it was concluded that, restrictive, but not obstructive respiratory pattern, is associated with metabolic syndrome and insulin resistance, and does not only reflect a limitation of ventilation due to visceral obesity. Metabolic abnormalities likely mediate cardiovascular risk in patients with restrictive respiratory impairment.

According to a study done on 50 patients with in type 1 diabetes mellitus by Makkar et al,[24] spirometric evaluation showed varying derangements in the different parameters of pulmonary function tests, suggestive of dominantly restrictive with some obstructive pattern as indicated by significant decline in FVC, peak expiratory flow rate (PEFR) and maximum expiratory flow at 75% (MEF_{75}).

We found a positive independent relationship between lung function impairment and metabolic syndrome. However, there was no independent correlation between individual metabolic syndrome components and pulmonary function tests according to our study. We observed that metabolic syndrome was associated with both obstructive and restrictive pattern of lung impairment. Metabolic syndrome remained independently associated with lung function impairment.

CONCLUSION

There is a positive association between metabolic syndrome and lung function impairment. Both obstructive and restrictive pattern is seen with metabolic syndrome. However, there was no independent correlation between individual metabolic syndrome components and pulmonary function tests.

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Analysis of Maternal Mortality in a Rural Referral Medical College Hospital in Hassan, Karnataka State, India

PREMALATHA HL*, ABHILASHA

ABSTRACT

Maternal mortality rate (MMR) is an indicator to measure the summary of information about mother and childbirth. It is estimated that about 350-450 maternal deaths occur per 1,00,000 live births each year in India.

Keywords: Retrospective study, maternal mortality, risk factors, causes of death

Though India has made an appreciable progress in improving the overall health status of its population, but it is far from satisfactory. Pregnancy is a normal health state that most women aspire to at some point in their lives. This physiological process carries with it serious risks of maternal morbidity and mortality.

Maternal mortality rate (MMR) is the measure of number of maternal deaths due to pregnancy or within 42 days of termination of pregnancy, irrespective of the duration or site of the pregnancy from any cause related to or aggravated by the pregnancy and its management but not from accidental or incidental causes.

Although various safe motherhood initiatives have been taken, yet the decline in MMR is far from the desired level of 100 by 2012 set by the National Rural Health Mission (NRHM) and 109 by 2015 as per millennium development goals.

Maternal death is a greater social tragedy than a perinatal loss. In spite of advances in obstetrics, anesthesia and blood product transfusion and in antibiotics, decline in MMR in India has been slow. Those who suffer generally live in remote places and are poor and helpless. It is not only useful to evaluate the performance but also is a measure of the social status of community and availability of Maternal and Child Health Services. The major causes of maternal mortality are hemorrhage, hypertension disorder, sepsis, obstructed labor, unsafe abortions.

UNICEF`s 2009 State of the World`s Children report, which was released in January said that India`s fight to lower MMR is failing due to growing social inequalities and shortages in primary healthcare facilities. In most developed nations MMR has been reduced to as low as 5-20/1,00,000 live births.

MMR in India stands at 230/1,00,000 live births against China`s 50/1,00,000 and Srilanka's 35/1,00,000; by comparison and China is the most populated country in the world.

Maternal audit is essential to make critical appraisal of standards and to continue to improve the methods of management pattern of maternal complications. In 1960, four major causes of death were hemorrhage, abortion, hypertensive disorders and pulmonary embolism. Even today hemorrhage stands first as the cause for death as reported in some studies.

The health problems of mother and newborn arise as a result of synergistic effects of malnutrition, poverty, illiteracy, unhygienic living conditions, infections and unregulated fertility, ignorance, apathy. At the same time, poor infrastructure and ineffective public health services, failure of transport facilities, failure to provide

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adequate man power, failure to empower the woman resources, failure to provide adequate functioning blood banks, is also responsible for low inadequate obstetric care and rise in maternal mortality, rather than a lack of technical knowledge (World Health Organization [WHO]).

The results of a large scale survey have however shown that there was no decline in the MMR in India over time indicating an urgent public health concern. WHO estimates show that out of the 5,29,000 maternal deaths globally each year, 1,36,000 (25.7%) are likely to experience some obstetrical and medical complications and die in India. Recent estimates (WHO and UNICEF) place the figure around 300-500/1,00,000 live births. In Karnataka, MMR is 217/1,00,000 live births. But in reality, it may be higher because of under registration of deaths in the country and absence of cause of death information.

AIMS AND OBJECTIVES

To analyze the causes of maternal death in a rural referral hospital like Hassan Institute of Medical Sciences, Hassan, Karnataka. Analysis of maternal death is an essential exercise with a view to understand the common complications leading to maternal deaths and is helpful to find the remedies. This knowledge may help to decrease maternal deaths, for the majority of causes are preventable with the current day knowledge and technology.

MATERIAL AND METHODS

Analysis of maternal deaths over 4 years were carried out from 2006 to 2009, which occurred at Hassan Institute of Medical Sciences, Hassan, Karnataka. Cases were scrutinized from various aspects likely to be related to maternal deaths like age, parity, locality, socioeconomic status, literacy, antenatal registration and check-ups, period of gestation, mode of delivery, admission to death interval, direct and indirect causes of death. All the data were collected from records and maternal mortality statistics of the year provided by the record section of the hospital. Maternal mortality was calculated by means of maternal deaths and total live births for that particular year.

RESULTS AND ANALYSIS

It was seen that the MMR/1,00,000 live births for the years 2006, 2007, 2008 and 2009 was 106.43, 160.58, 102.6, 146.1, respectively (Table 1 and Fig. 1).

Age- and parity-wise distribution of patients is shown in Table 2 and Figure 2 a and b.

It was observed that the maximum number of deaths occurred during postpartum period (80%). Distribution of subjects based on time of maternal death is shown in Table 3 and Figure 3.

Maximum number of deaths occurred during the hospital vaginal delivery (43.33%) closely followed by cesarean delivery (33.33%), while equal number of deaths occurred during home delivery, laparotomy for rupture uterus and undelivered (6.67%). The least number of deaths (3.33%) occurred during forceps delivery (Table 4 and Fig. 4).

Table 1. Year-wise Distribution of Maternal Deaths

Year	No. of maternal deaths	No. of live births	MMR/1,00,000 live births
2006	5	4,698	106.43
2007	8	4,982	160.58
2008	6	5,848	102.6
2009	11	7,529	146.1

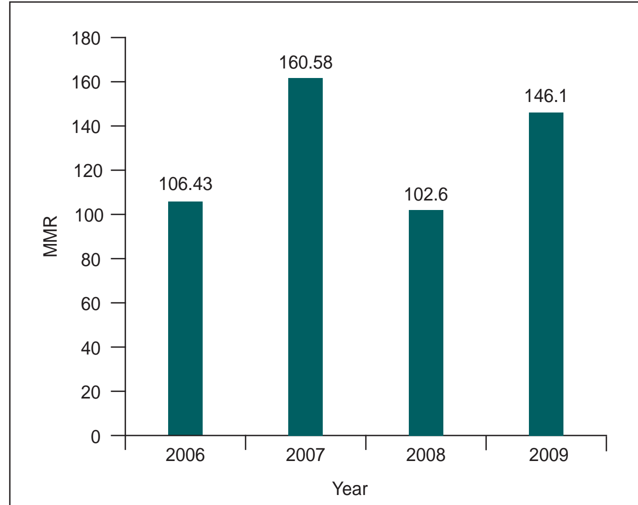
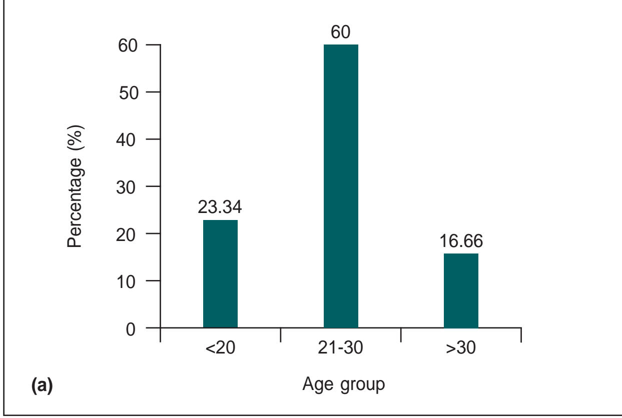


Figure 1. Year-wise distribution of maternal deaths.

Table 2. Age- and Parity-wise Distribution

Age (years)	Prime gravida	Second gravida	Multi gravida	Grand multi	Percentage (%)
<20	7	---	---	---	23.34
21-30	9	4	5	---	60
>30	---	1	4	---	16.66



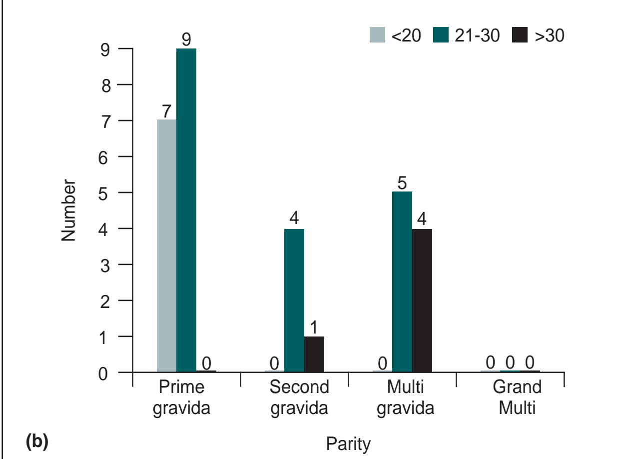


Figure 2 a and b. Age- and parity-wise distributions of subjects.

Table 3. Distribution of Subjects Based on Time of Maternal Death

Timing of maternal death	No. of maternal deaths	Maternal deaths (%)
Antepartum	5	16.67
Intrapartum	----	0
Postpartum	24	80
Post abortal	1	3.33

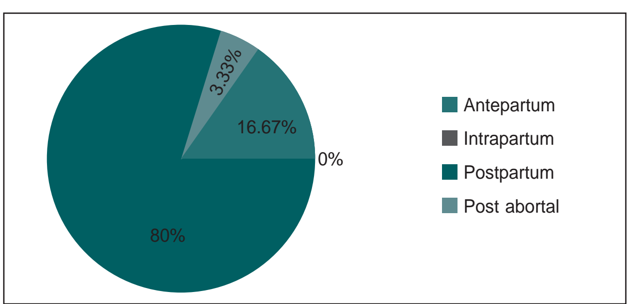


Figure 3. Distribution of subjects based on time of maternal death.

Table 4. Distribution of Subjects Based on Type of Delivery

Type of delivery	No. of maternal deaths	Maternal deaths (%)
Home delivery	2	6.67
Hospital vaginal delivery	13	43.33
Forceps delivery	1	3.33
Cesarean delivery	10	33.33
Laparotomy for rupture uterus	2	6.67
Undelivered	2	6.67

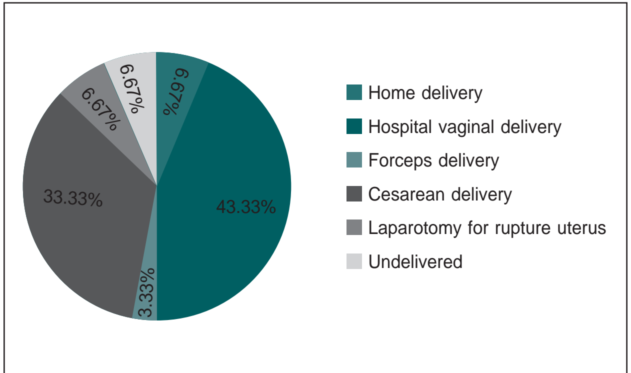


Figure 4. Distribution of subjects based on type of delivery.

Table 5. Distribution of Subjects Based on Admission to Death Interval

Admission (death interval)	No. of cases	Cases (%)
<24 hours	24	80
1-3 days	1	3.33
>3 days	5	16.67

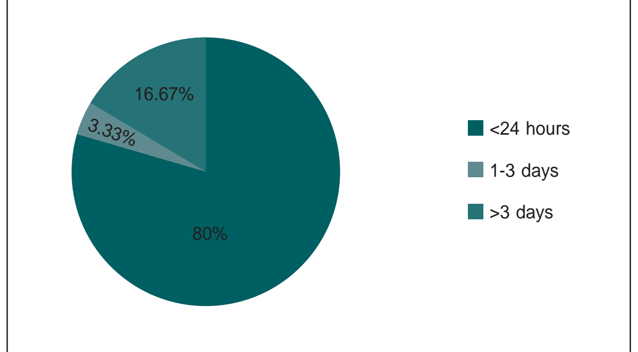


Figure 5. Distribution of subjects based on admission to death interval.

The distribution of subjects based on admission to death interval is shown in Table 5 and Figure 5. It was seen that the maximum number of deaths occurred within 24 hours of delivery.

Table 6. Analysis of Causes of Maternal Mortality

Causes of death	2006	2007	2008	2009	Percentage (%)
CHD with CCF		1	-	1	7.14
APH abruption	1	1	-	1	10.7
Eclampsia		2	-	1	10.7
Postpartum sepsis and CVT	1	1	1	-	10.7
PPH	2	2	1	5	35.7
Anemia	1	1	1	1	14.2
Septic abortion	-	-	1	-	3.57
Jaundice	-	-	1	1	7.14
Rupture uterus	-	-	2	-	7.14

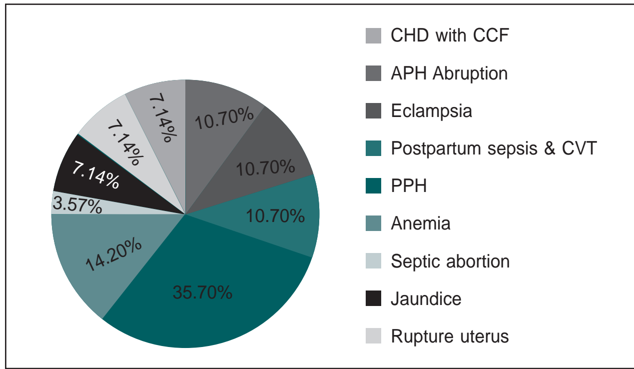


Figure 6. Analysis of causes of maternal mortality.

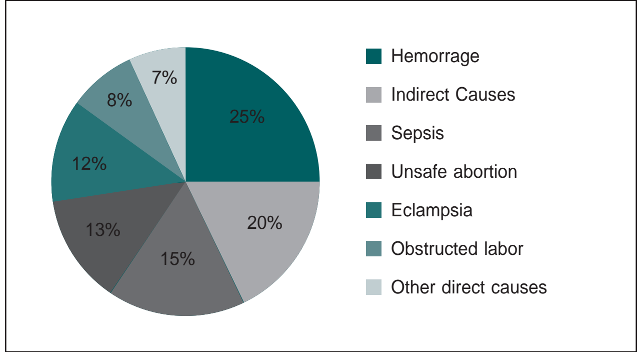


Figure 7. Causes of maternal deaths in standard books.

Analysis of causes of maternal mortality shows that maximum number of death occurred due to postpartum hemorrhage (PPH) in our study (Table 6 and Fig. 6). Analysis of causes of maternal deaths in standard books is given in Figure 7.

DISCUSSION

Estimates for MMR of India was 150 to 350 as reported by WHO in 2008. This study was conducted in a rural medical college to investigate the risk factors for maternal mortality. After going through the statistics, it was found that MMR was increased with increase in number of deliveries. Increased MMR was seen in woman aged between 21-30 years - 60%.

Eighty percent of deaths had occurred within 24 hours. Forty-three percent were hospital vaginal deliveries and 33% were delivered by cesarean operation. Approximately 35.7% deaths were due to PPH and 14.2% were due to anemia. About 10.7% deaths were due to antepartum hemorrhage (APH), eclampsia and postpartum sepsis. About 7.14% deaths were due to coronary heart disease (CHD) and congestive cardiac failure (CCF), ruptured uterus, jaundice; deaths due to abortion occurred in less than 3.57%; this may be due to safe abortion practices.

The causes of maternal deaths are multiple, complex but almost preventable. About 43% of deaths occurred following institutional delivery at Hassan Institute of Medical Sciences (HIMS), Karnataka. A study published in April 2010 in *The Lancet* shows that the number of annual maternal deaths worldwide declined from roughly 5,25,000 in 1980 to about 3,43,000 in 2008. The troubling news in these two studies is that progress has been unequal: while many countries are showing a downward trend, in some maternal deaths actually increased. A study has shown that MMR also increased in America from 7.1% in 1999 to 13.3% in 2008. The fact is that pregnancy always carries risk of unexpected complications, and 15% of pregnancies everywhere are life-threatening.

Mortality ratio measurements are difficult and complex. As a matter of fact under registration is frequent in both developing and developed countries. MMR measurement should be simple affordable, effective and evidence-based, particularly in poorer countries. The information collected should be used to help improve maternal health outcome and empower health professionals to examine their current practices or those of the facility in which they work. For correct estimation of maternal mortality, it requires

knowledge of death of pregnant women and cause of death, because the information obtained will be used as the basic for action. Health promoters and community health workers can be trained to report these events as part of their jobs, as can traditional birth attendants who provide antenatal care and attend deliveries. India's long-standing strategy has been promotion of facility based intrapartum care. One of the vowed goals of the National Population Policy (2000) is to attain an institutional delivery rate of 80% by 2010. Nationwide, the proportion of deliveries in institutions has increased from 34% in 1998-99 to 41% in 2002-2004.

Further acceleration in the direction is inevitable under NRHM launched in 2005. This scheme provides a conditional cash transfer to mothers for institutional deliveries and a cash incentive for health workers, who facilitate this process, with 24/7 delivery services and nearly 3,000 public facilities planned to be upgraded to provide comprehensive emergency obstetric care by 2012. In 1997-98, India's MMR stood at 398, this declined to 301 in 2001-2003. The prediction for 2015 is 160, although this misses India's 5th Millennium Development Goal (MDG 5), which is pegged at 109. A faster decline in MMR is a distinct possibility because of the extraordinary attention given to maternal health under the NRHM, increased resources are also flowing to education, women's empowerment and rural employment. One priority of the NRHM is to have a female health volunteer called ASHA (Accredited Social Health Activist). Other efforts are being made to provide quality reproductive health services including institutional delivery, safe abortions, treatment of reproductive tract infections (RTIs) and family planning services to meet unmet needs, while ensuring full reproductive choice to women.

Under NRHM, the main strategy to reduce MMR focuses on institutional deliveries and provision of mean emergency obstetric care (EmOC). The government has recently changed policy to allow staff nurse and auxiliary nurse midwives (ANMs) to initiate treatment of pregnancy related complications, including IV fluids, oxytocics, antibiotics and magnesium sulfate - all earlier restricted to administration by doctors. The government has also started the retraining of ANMs to improve their skills as skilled birth attendants (SBAs). The central government has encouraged a 16-week training of MBBS doctors in anesthesia and comprehensive EmOC.

CONCLUSION

Maternal health services and maternal and child health (MCH) focused on antenatal care and high-risk approach. It is thought that good antenatal care and identifying high-risk woman, institutional deliveries, Janani Suraksha Yojana and help of ASHA's will reduce the MMR. But after implementing several years of these Yojanas, the studies have shown that MMR is still high. After going through the statistics in our institution, it is not possible to predict which mother will develop complications and hence the high risk approach does not help much. Anemia should be eradicated in the society. The project development process should ensure that all the critical inputs such as staff, drugs, blood banks, equipments are provided which is woefully inadequate at present. Mass education about the importance of antenatal check-ups and registration, institutional deliveries and providing timely transportation facilities will reduce the MMR.

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Changes in Ultrasonography Indicators of Abnormally Invasive Placenta During Pregnancy

The aim of a new study published in the *International Journal of Gynecology and Obstetrics* was to determine whether the prevalence of ultrasonography signs of abnormally invasive placenta (AIP) change during pregnancy. This retrospective analysis recruited 105 women with a prenatal diagnosis of AIP, confirmed at delivery, between January 1, 2007, and April 30, 2017. Ultrasonography signs of AIP were recorded at four different phases of pregnancy: early first (6-9 weeks), first (11 to 14 weeks), second (15-24 weeks) and third trimesters (25-36 weeks). The findings revealed that low implantation of the gestational sac was present on all ultrasonography images from the early first trimester in comparison with, on 27.7% images, from 11-14 weeks of pregnancy. The identification of loss of the clear space, placental lacunae, bladder wall interruption, and uterovesical hypervascularity all increased from the early first trimester onwards; these could all be identified in a majority of patients at 11-14 weeks of pregnancy. Hence, it was inferred that the prevalence of ultrasonography signs suggestive of AIP varied throughout pregnancy. It was stated that during the early first trimester, indicators of AIP were similar to those of a cesarean scar pregnancy; while classical ultrasonography signs of AIP were already present at 11-14 weeks of pregnancy for most patients.

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Low-dose Spinal Anesthesia: A Safe Option in Molar Pregnancy with Thyrotoxicosis

BHAVNA SRIRAMKA*, RANJITA ACHARYA†

ABSTRACT

Hydatidiform mole often has an association with thyrotoxicosis. Molar pregnancy usually presents with severe vaginal bleeding requiring emergency suction evacuation and time for proper treatment of thyrotoxicosis may not be available making perioperative management of these patients difficult. We recently had an encounter of a 26-year-old female of hydatidiform mole associated with thyrotoxicosis presenting with vaginal bleeding, which was successfully managed with low-dose spinal anesthesia under cover of antithyroid medication, steroids and β blockers. Patient was then shifted to intensive care unit in the postoperative period and later to the ward after 2 days. Eventually, she was discharged on the fifth postoperative day with near normal thyroid profile and completely asymptomatic. Timely diagnosis with a high degree of suspicion of thyrotoxicosis association, proper anesthesia plan and vigilant postoperative management is essential in dealing such a dreadful situation. We recommend low-dose spinal anesthesia as a safe option in such situation.

Keywords: Hydatidiform mole, thyrotoxicosis, low-dose, spinal anesthesia, safety

Gestational trophoblastic disease is an abnormal proliferation of trophoblastic epithelium of which hydatidiform mole is a result of malformation of chorionic vilosities predisposing to malignant neoplasia. Curry et al described it as a pregnancy usually lacking an intact fetus, in which the placental villi are characterized by edema and loss of vasculature, and showing varying degrees of trophoblastic proliferation.[1] It may present with many complications, of which trophoblastic thyrotoxicosis is life-threatening.[2] Complete moles have prevalence of hyperthyroidism as high as 7%.[3] Thyrotoxicosis and hemorrhage have overlapping signs and many times can be missed. We hereby present a case where a molar pregnancy associated with hyperthyroidism presented with vaginal bleeding and was posted for emergency dilatation and curettage. It highlights the perioperative management and optimization of hyperthyroid state prior to surgical evacuation of the hydatidiform mole.

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CASE REPORT

A 26-year-old patient weighing 48 kg with body mass index (BMI) 26.2 was admitted to the Dept. of Obstetrics and Gynecology with complaints of amenorrhea of 12 weeks, abdominal pain and vaginal bleeding. She was febrile (101.6°F), tachypneic (respiratory rate [RR]-26), tachycardiac (127 bpm), hypertensive (160/92 mmHg), with pale mucous membranes and dehydrated. Urine pregnancy test was positive. Thyroid gland was palpable and of normal size. Cardiorespiratory examinations were normal.

Laboratory investigations upon admission were hemoglobin - 8.2 g/dL, hematocrit - 30.3%, leukocytes - 13,800, platelets - 3.04 lacs, with normal coagulation profile, decreased thyroid-stimulating hormone (TSH) - 0.08 (range 0.35-5.5) and raised total T3 - 388 ng/dL (range = 80-150 ng/dL). The levels of human chorionic gonadotropin (hCG) were 6,38,000 UI/L. Abdominal pelvic ultrasound showed uterine volume of 1,680 cm^3 with multiple anechoic cystic vesicles compatible with complete hydatidiform mole. She was shifted to the operating room on the same day of hospitalization to undergo an emergency uterine curettage due to severe vaginal bleeding.

A high risk informed and written consent for anesthesia and surgery was taken and availability of postoperative intensive care unit (ICU) care was ensured. A low-dose

spinal anesthesia was planned. The goals were to reduce temperature, tachycardia, hypertension and proper oxygenation with adequate anesthesia. One hour prior to the surgery - tablet propylthiouracil 150 mg was given followed by injection dexamethasone 2 mg IV, injection dexmedetomidine started @1 μg/kg for 10 minutes followed by 0.4 μg/kg/hr and along with it infusion of injection esmolol started @1 mg/kg IV over 30 seconds and then 0.2 mg/kg/min titrated according to heart rate and blood pressure. Injection acetaminophen 500 mg was given for temperature control. Hydration was maintained with Ringer lactate.

Spinal anesthesia was given with intrathecal 2 mL of bupivacaine (0.5% H) and 25 μg of fentanyl given after clear aspiration of cerebrospinal fluid (CSF) in L2-L3 space. After 8 minutes, the motor block was Grade 2 (Bromage scale) and sensory block was T8. Patient was lightly sedated and comfortable. Vitals were stable with heart rate reduced to 98/min, blood pressure reduced to 134/86 mmHg and RR 14/min, temperature dropped to 100^0F maintaining SpO_2 99%. She was allowed to breath in venturimask with FiO_2 of 0.5. Surgeons were then allowed to perform uterine curettage. One unit of whole blood was transfused. Surgery went uneventfully and then patient was shifted to the ICU, where she was continued on tablet propylthiouracil 100 mg 8-hourly for 1 day and dexamethasone was tapered over 4 days. Tablet propranolol 10 mg 8-hourly was given for 2 days. Patient was hemodynamically stable in the postoperative period, was shifted to the regular ward after 2 days and from the hospital after 5 days.

DISCUSSION

Complete hydatidiform mole, most commonly presents with vaginal bleeding occurring at 6-16 weeks of gestation in 80-90% of cases, followed by hyperemesis and hyperthyroidism.[2,4,5] Acute respiratory distress syndrome (27%) has also been reported as a result of trophoblastic embolization, sepsis, amniotic fluid embolism and transfusion related acute lung injury.[6] Consumption coagulopathy is yet another complication which may be due to factors released by the molar tissue that could trigger the coagulation cascade, resulting in disseminated intravascular coagulation (DIC) and multiorgan failure.[7]

Clinical hyperthyroidism in a patient with hydatidiform mole was first reported in 1955 by Tisne et al.[8] The glycoprotein hormone hCG has a structural analogy with TSH and so can cause cross-reactivity with their receptors.[9] For every 10,000 mU/mL increase in serum hCG, FT4 increases by 0.1 ng/dL and TSH decreases by 0.1 mIU/mL.[10] Hyperthyroidism may be a result of this significant rise in hCG levels in hydatidiform mole, which calls for a prompt treatment that is uterine evacuation thereby decreasing the hCG values. Hyperthyroidism can co-exist with anemia secondary to vaginal bleeding and their clinical presentations are often overlapping. Tachycardia, tachypnea with fever and hypertension calls for a suspicion of thyroid storm.

High output cardiac failure, thyroid storm, hypertension, embolization of pulmonary arteries, hypovolemia, DIC and pulmonary edema are the anesthetic challenges to be aware of when dealing with molar pregnancy.[11,12] Goals of anesthetic management are to ensure hemodynamic stability and maintain proper oxygenation thereby providing adequate anesthesia for surgery. Both regional and general anesthesia have been described in the literature for management of molar pregnancy.[13]

In hypotensive patients with bleeding, the choice is general anesthesia. Regional anesthesia is a safer option in stable patients with emergency surgeries with full stomach having the advantages of no tocolytic effect on the uterus and avoiding airway instrumentation but is contraindicated in DIC.[3,14] Our patient diagnosed with hyperthyroidism having hypertension, and severe bleeding was stabilized in the limited time available with antithyroids, steroids, sedatives, blood transfusion and IV fluids and planned for a low-dose spinal anesthesia to prevent hemodynamic instability.

CONCLUSION

Anesthesiologists need to be vigilant of the perioperative complications associated with a molar pregnancy. A detailed work-up, optimization of the patient, careful selection of anesthesia with postoperative intensive care management is of paramount importance when dealing any case of molar pregnancy.

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Long-term Reproductive Outcome of Adults Born at a Very Low Birth Weight

A new study published in the *Early Human Development* evaluated the reproductive outcome of very low birth weight (VLBW, <1,500 g) infants who survive to adulthood (next-generation). This retrospective study included infants born at a single tertiary center between 1982 and 1997, who survived till 18 years of age (first-generation). The results identified first-generation 67,183 births, including 618 VLBW; while 193 males and 184 female VLBW infants survived to adulthood. On the other hand, all first-generation patients from the VLBW group had half the reproductive rate when compared to the normal birth weight group. Moreover, male and female VLBW survivors had no significant risk for a VLBW neonate in the next-generation. Thus, it was inferred that VLBW infants who reach adulthood develop a significantly lower reproductive capacity.

Variation in Use of Prophylactic Antibiotics in Gynecologic Procedures

A new study published in the *Southern Medical Journal* examined variations in the use of prophylactic antibiotics in patients undergoing gynecologic surgery, and to determine whether an educational intervention to gynecologists was associated with a significant decrease in unindicated prophylactic antibiotics. This was a retrospective chart review for all women undergoing gynecologic surgery at a hospital in Texas. An educational intervention regarding prophylactic antibiotic usage was held for obstetricians and gynecologists in the middle of that year. Subjects were included if they had procedures with a Current Procedural Terminology code corresponding to a procedure that does not require prophylactic antibiotics. The findings showed that a significant decrease in unindicated prophylactic antibiotic use was demonstrated - from 45.7% pre-intervention to 24.9% post-intervention. Before the educational intervention, gynecology oncology, reproductive endocrinology, and infertility divisions had the highest rates of unindicated antibiotic use, vis 91.7% and 91.7%, respectively. Whereas, the generalist and urogynecology divisions had the lowest rates for specialists before the intervention, vis 20.6% and 30.8%, respectively. Post-intervention, all the divisions demonstrated an improvement in their rates of unindicated prophylactic antibiotic use. The urogynecology division demonstrated an improvement that was clinically significant although statistically significant. Moreover, the adverse event rates were not different between subjects who received preoperative prophylactic antibiotics and in those who did not. Thus, it was concluded that a simple educational intervention was associated with a considerable decrease in unindicated prophylactic antibiotics in gynecologic procedures.

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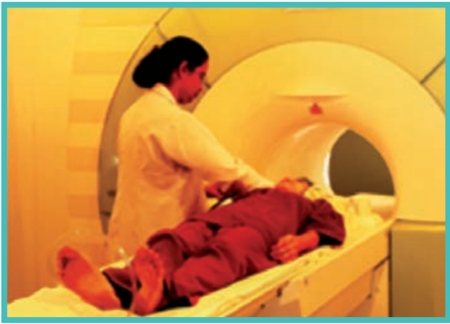

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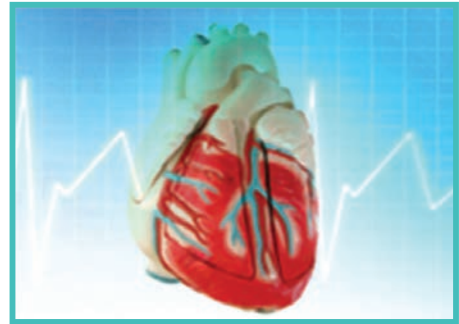

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Chondrosarcoma of Right Upper Limb: Largest of Its Kind Operated in Our Institute

VIJAY JAGAD*, MUNISH MAHAJAN*, AMITABH KUMAR UPADHYA†, SEEMA CHABBRA‡

ABSTRACT

Chondrosarcoma of extremities is the second most common site for this particular bone tumor. Neoadjuvant chemoradiotherapy is frequently used to down stage tumor for limb-sparing surgery in locally advanced tumor, but chondrosarcoma is relatively resistant to chemotherapy and radiotherapy, and hence sometimes mutilating surgery like forequarter amputation has to be performed. In this case also patient presented with locally advanced chondrosarcoma of right upper extremity and we had to perform forequarter amputation to achieve adequate clearance.

Keywords: Chondrosarcoma, forequarter amputation

CASE REPORT

A 56-year-old man, presented to our Surgical Oncology OPD with complaints of massive swelling of right upper limb for past 2 years. To begin with, patient had noticed the swelling just below the right shoulder joint that gradually progressed to attain the present size. Patient had visited many oncology centers and he was offered multiple treatments consisting of combination of chemotherapy and radiotherapy, but all were fruitless. He then approached our institute. On examination, the whole of the upper extremity and the right shoulder was engulfed by the tumor (Fig. 1). Confirmation of the type of tumor was done by core cut biopsy, which revealed chondrosarcoma intermediate grade. Computed tomography (CT) scan of chest with upper abdominal cuts was done that revealed large tumoral mass involving the right humerus and scapula with involvement of shoulder girdle muscles. Pectoral muscles were also involved by the tumor. There was no evidence of metastasis in chest as well as in abdomen. According to the Enneking staging, it was Stage IIB. As the patient had already received neoadjuvant chemotherapy and radiotherapy but the tumor size was still increasing, he was planned for forequarter amputation. Patient tolerated the procedure well and the final histopathology report revealed evenly placed anaplastic chondrocytes within lacuna in a chondroid background suggestive of intermediate grade chondrosarcoma with all resection margins free

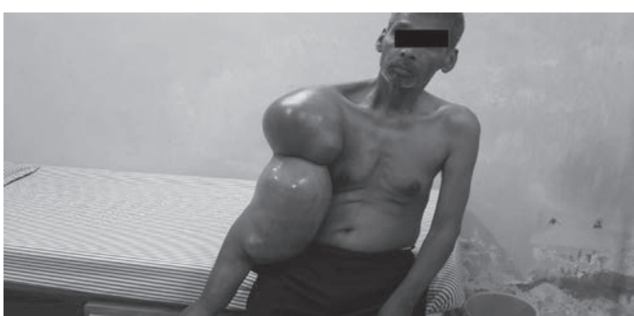

Figure 1. Preoperative figure of the tumor involving whole of the right upper limb and the right shoulder.

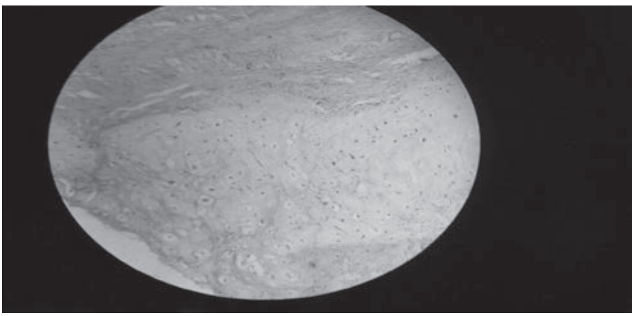

Figure 2. Hematoxylin and eosin-stained slide with 10X power showing - evenly placed anaplastic chondrocytes in lacuna within chondroid background.

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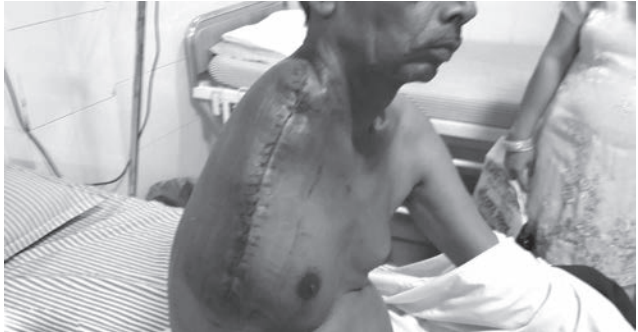

Figure 3. Postoperative photograph of the patient after stitch removal.

of tumor (Fig. 2). On follow-up after 14 days stitches were removed (Fig. 3), and he was kept on close follow-up to look for recurrence or metastasis. After 1½ years, the patient is still on follow-up and he is disease-free locally as well as in terms of distant metastasis.

DISCUSSION

Chondrosarcoma is a malignant cartilaginous matrix-producing tumor with diverse morphologic features. The peak age of occurrence is between 40 to 70 years.[1] The most common primary sites include the pelvis followed by femur and humerus.[2] Most common presenting symptoms are pain and swelling at the site of tumor. About 90% of chondrosarcomas are primary bone tumors, but around 10% develop from pre-existing osteochondromas, enchondromas or fibrous dysplasia.[3] Chondrosarcomas are graded on a scale from 1 to 3, based upon nuclear size, staining pattern (hyperchromasia), mitotic activity and degree of cellularity. Histological grade is one of the most important indicators of clinical behavior and prognosis.[4] Metastasis in chondrosarcoma depends upon the grade of the tumor. Patients with Grade II and III have higher chances of metastasis than compared to Grade I and that can range from 60% to 70%.[5]

Chondrosarcomas are relatively resistant to chemotherapy and radiotherapy and therefore treatment depends upon the completeness of surgical resection. En-bloc resection of the tumor has shown to improve the survival of the patient.[6] Surgical resection margin and the grade of the tumor has been found to be independent prognostic marker for survival of the patient.[7]

This patient who presented to our institute had already received neoadjuvant chemotherapy and radiotherapy to downstage the disease but there was no change. Complete right upper limb along with scapula and shoulder girdle muscle was involved. CT scan revealed no evidence of distant metastasis. Complete en-bloc removal of the tumor i.e., forequarter amputation was required. Pros and cons of the surgery was discussed and with due consent patient underwent surgery. Now the patient has been kept on follow-up, as the final histopathology revealed intermediate grade chondrosarcoma. Patient has been explained about the risk of distant metastasis. Patient is being followed according to the National Comprehensive Cancer Network (NCCN) guidelines with physical examination, complete blood count and chest as well as local imaging every 3 months for the first 2 years, every 4 months during year 3, every 6 months for years 4 and 5, then annually. It has also been explained that routine post-treatment surveillance has to be extended up to 10 years, as late recurrences can occur.[8]

CONCLUSION

Chondrosarcomas are usually low-grade tumors affecting mainly the pelvic region and the extremities. Complete surgical excision with negative margins is the best treatment to be offered to improve survival. As these tumors are relatively resistant to radiotherapy and chemotherapy, downstaging of the tumor for limb preservation surgery is not possible and patients in locally advanced stage disease have to undergo mutilating surgeries with functional compromise.

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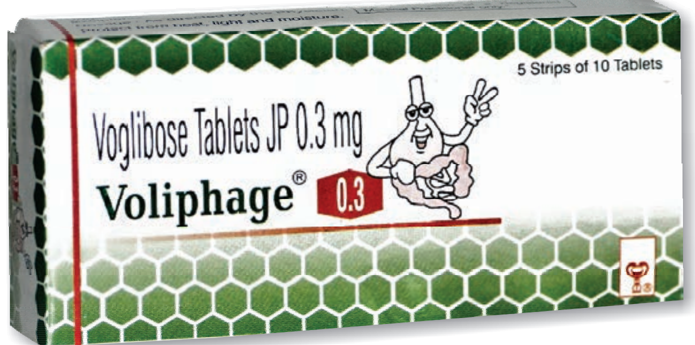

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Unicentric Castleman's Disease

MUNISH MAHAJAN*, VIJAY J JAGAD*

ABSTRACT

Castleman's disease (CD), a rare disease of lymph nodes and related tissues is an atypical lymphoproliferative disorder. It occurs in two forms unicentric and multicentric. Unicentric CD commonly occurs in the mediastinal region. Here we present a case of unicentric CD in a retroperitoneal lymph node.

Keywords: Castleman's disease, lymphoproliferative disorder, unicentric

Castleman's disease (CD) is a rare form of lymph node hyperplasia of unknown etiology.[1] It was first described in 1954, and subsequently better defined by Castleman in 1956.[2] CD is classified into two clinical subtypes: a localized and a multifocal subtype. CD may occur anywhere along the lymphatic system, although the most common location (70%) is the mediastinum. Extrathoracic sites have been reported in the neck, axilla, pelvis and retroperitoneum.[2]

Unicentric forms of CD have been reported as single, mediastinal masses with systemic symptoms that could be resolved after surgical excision. On the other hand, patients with multicentric CD, defined by the involvement of at least 2 noncontiguous, lymph node areas, were often refractory to treatment and show worse clinical outcomes.[3]

Surgery is the optimal therapeutic approach only in the localized form, while for unresectable or disseminated disease, partial surgical resection, steroids, chemotherapy and radiotherapy have been employed with some measurable success.[2] There are three major histological subtypes: hyaline-vascular CD (HV-CD), plasma cell CD (PC-CD) and a plasmablastic-variant associated with human herpesvirus 8 and human immunodeficiency virus. The first is much more frequent (91-96%). The majority (57-91%) of localized disease is hyaline-vascular.[2]

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CASE REPORT

A 31-year-old lady presented to outpatient department with 20 days history of pain upper abdomen radiating to back. Ultrasonography of abdomen and computed

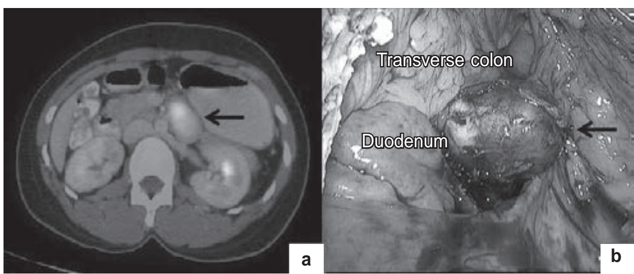

Figure 1. Hypermetabolic lesion of size 3.5 × 2.5 cm along lower border of pancreas (*arrow head*) **(a)**; well-circumscribed lymph node mass in retroperitoneum along lower border of pancreas *(arrow head)* **(b)**.

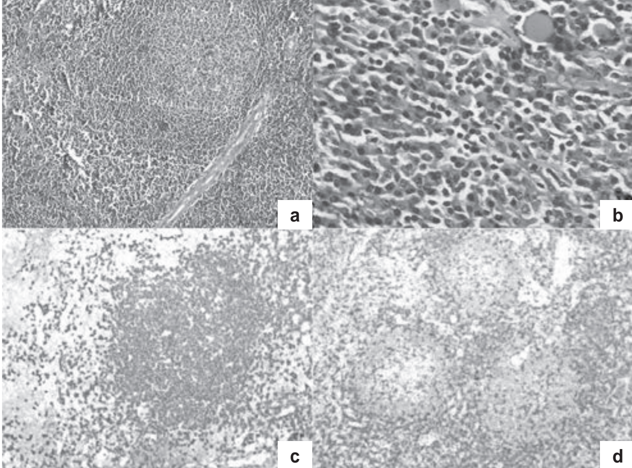

Figure 2. Atretic germinal center with prominent mantle zone and increased vascular proliferation **(a)**; interfollicular prominence of plasma cells **(b)**; CD20 diffuse positive in follicles **(c)**; CD3 highlighting interfollicular T cells **(d)**.

tomography (CT) of abdomen done elsewhere were suggestive of para-aortic lymph node mass along the lower border of pancreas. Guided fine needle aspiration cytology (FNAC) done from the lymph node mass was inconclusive. Positron emission tomography (PET) CT showed hypermetabolic lesion of size 3.5 × 2.5 cm in para-aortic region along inferior border of pancreas (Fig. 1a). Patient underwent laparoscopic excision of lymph node mass (Fig. 1b).

Histopathological examination (HPE) showed atretic germinal center with prominent mantle zone and increased vascular proliferation with interfollicular prominence of plasma cells (Fig. 2 a and b). Immunohistochemistry (IHC), showed CD20 diffuse positive in follicles and CD3 positivity highlighting interfollicular T cells (Fig. 2 c and d). Based upon aforementioned findings diagnosis of unicentric Castleman's disease (mixed variant) was made.

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■■■■

Long-term Use of PPIs Increase Risk of Stomach Cancer PPI

According to a study published online October 31, 2017 in the journal *Gut*, long-term use of proton pump inhibitors (PPIs) even after *Helicobacter pylori* eradication therapy double the risk of stomach cancer. The risk increased with duration of use of PPIs.

Pembrolizumab-trastuzumab Active in Resistant HER2 Breast Cancer

A pilot study presented at the San Antonio Breast Cancer Symposium suggested that immunotherapy proved active in at least a subgroup of patients with metastatic, trastuzumab-resistant HER2-positive breast cancer. The combination of pembrolizumab and trastuzumab resulted in an objective response rate of 15% in patients with detectable levels of PD-L1 expression. The response rate increased to about 40% in a smaller subgroup of patients with PD-L1 expression in at least 5% of tumor-infiltrating lymphocytes (TILs). The investigators found a significant association between baseline stromal TILs and both objective response rate and disease control rate.

Study Identifies New Biomarkers to Diagnose Pancreatic Cancer

A study published in the *British Journal of Cancer*, online November 9, 2017 has identified four new biomarkers which improved sensitivity (95%) and specificity (94.1%) for the diagnosis of pancreatic cancer when combined with CA19-9. The new biomarkers include apolipoprotein E (APOE), inter-alpha-trypsin inhibitor heavy chain H3 (ITIH3), apolipoprotein A-I (APOA1), apolipoprotein L1 (APOL1).

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Effect of Olmesartan on the Carotid Artery Atherosclerotic Plaque Progression in Hypertension

VINOD SHARMA

The beneficial effects of olmesartan on the prevention of vascular remodeling and carotid artery atherosclerotic plaque progression in subjects with hypertension are very well-documented. The Multicenter Olmesartan atherosclerosis Regression Evaluation (MORE) study, was a double-blind trial conducted in patients with hypertension who were at increased cardiovascular risk (presence of carotid wall thickening and a defined atherosclerotic plaque), using noninvasive two- and three-dimensional ultrasonography.

This double-blind trial compared the effects of a 2-year treatment based on either olmesartan medoxomil or atenolol on common carotid intima-media thickness and plaque volume (PV). It was observed that large PVs (>33 μL) were significantly reduced over the 104-week treatment period only in those subjects who were put on olmesartan-based therapy. Also, it has been seen that administration of olmesartan to subjects with diabetes was associated with reduced arterial stiffness while amlodipine had no effect.

The Vascular Improvement with Olmesartan Study (VIOS) was conducted to evaluate whether an olmesartan-based therapeutic regimen could reverse vascular hypertrophy independent of the magnitude of blood pressure (BP)-lowering. A total number of 100 subjects with stage 1 hypertension without diabetes were enrolled in this trial, which compared the effects of olmesartan-based therapy versus atenolol-based therapy on BP control and changes in wall/media lumen (W/L) ratio from small resistance arterioles obtained from these patients through the technique of gluteal biopsies. Samples were obtained from 22 atenolol recipients (100 mg/day), 27 olmesartan medoxomil recipients (40 mg/day) and 11 normal volunteer controls. Additional antihypertensive medications (hydrochlorothiazide 12.5-25 mg/day, amlodipine 5-10 mg/day or hydralazine 50-100 mg twice-daily) were given to achieve BP control below 140/90 mmHg. It was seen that patients in the atenolol-based regimen group required more medications versus patients randomized to the olmesartan-based group. Moreover, a greater percentage of patients having olmesartan-based therapy achieved and maintained an ideal BP of ≤120/80 mmHg at 4 weeks (24% in the olmesartan-based therapy vs. 8% in the atenolol-based therapy [$p < 0.05$]).

At the completion of the 52-week period, comparable decreases in arterial pressure resulting in the physiological levels of BP (≤120/80 mmHg) were observed in patients assigned to each of the two regimens. Normalization of BP, however, was associated with the regression of vascular hypertrophy only in those subjects assigned to the olmesartan-based therapy. In these subjects, the reduction in W/L ratio of small resistance vessels (from 14.9% to 11.1%; $p < 0.01$) was numerically equivalent to the W/L ratio determined in the subset of normotensive volunteers from whom subcutaneous small arteriole resistance vessels were obtained. Since, the addition of hydrochlorothiazide and amlodipine were required in >59% of the subjects and no differences existed in the dosing and time periods in which these agents were incorporated to the treatment regimen for both arms of the study, the data demonstrated that the selective effect of AT1 receptor blockade in the reversal of vascular hypertrophy in small resistance vessels was directly responsible for the reduction of peripheral vascular resistance.

Also, noninvasive measurements of central aortic pressure and determination of the augmentation index by applanation tonometry revealed that decreases in the indices of vascular compliance occurred only in those subjects receiving the olmesartan-based therapy.

SUGGESTED READING

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National Heart Institute, New Delhi

Principles of Practice and Duties of Physicians

WHAT SHOULD BE THE CHARACTER ATTRIBUTES OF A DOCTOR AS DEFINED BY THE MCI?

The Medical Council of India (MCI) Code of Ethics Regulations 2002 has defined the character of doctors in

Regulation 1.1.

"1.1.1 A physician shall uphold the dignity and honour of his profession.

1.1.2 The prime object of the medical profession is to render service to humanity; reward or financial gain is a subordinate consideration. Who-so-ever chooses his profession, assumes the obligation to conduct himself in accordance with its ideals. A physician should be an upright man, instructed in the art of healings. He shall keep himself pure in character and be diligent in caring for the sick; he should be modest, sober, patient, prompt in discharging his duty without anxiety; conducting himself with propriety in his profession and in all the actions of his life."

CAN A PERSON WHO HAS OBTAINED QUALIFICATION IN ANY OTHER INDIAN SYSTEMS OF MEDICINE PRACTICE THE MODERN SYSTEM OF MEDICINE?

No, a person who holds a degree in other systems of medicine cannot practice modern system of medicine or Allopathy. Regulation 1.1.3 of the Indian Medical Council Act is very clear on this issue.

"1.1.3 No person other than a doctor having qualification recognised by Medical Council of India and registered with MCI/State Medical Council (SMC) is allowed to practice Modern System of Medicine or Surgery. A person obtaining qualification in any other system of Medicine is not allowed to practice Modern System of Medicine in any form."

IS MEMBERSHIP IN A MEDICAL SOCIETY/ASSOCIATION MANDATORY FOR A DOCTOR?

The MCI has issued guidelines in this regard as below.

"1.2.2 Membership in Medical Society: For the advancement of his profession, a physician should affiliate with associations and societies of allopathic medical professions and involve actively in the functioning of such bodies.

1.2.3 A physician should participate in professional meetings as part of Continuing Medical Education programmes, for at least 30 hours every 5 years, organised by reputed professional academic bodies or any other authorised organisations. The compliance of this requirement shall be informed regularly to MCI or the SMC as the case may be."

THE FAMILY OF THE PATIENT HAS ASKED FOR THE MEDICAL RECORDS OF THE PATIENT. CAN THE DOCTOR REFUSE?

The MCI has laid down strict guidelines on this issue in Regulation 1.3.2: "If any request is made for medical records either by the patients/authorised attendant or legal authorities involved, the same may be duly acknowledged and documents shall be issued within the period of 72 hours."

Failure to adhere to these guidelines is regarded as professional misconduct and renders a doctor liable for disciplinary action as per Chapter 7, Regulation 7.2: "If he/she does not maintain the medical records of his/her indoor patients for a period of 3 years as per Regulation 1.3 and refuses to provide the same within 72 hours when the patient or his/her authorised representative makes a request for it as per the Regulation 1.3.2."

IS IT MANDATORY FOR A DOCTOR TO DISPLAY HIS/HER REGISTRATION NUMBER ACCORDED TO HIM/HER BY THE SMC OR MCI ON THE PRESCRIPTIONS PADS?

Regulation 1.4 of MCI Act outlines directions for doctors regarding display of registration numbers.

As per Regulation 1.4.1, "Every physician shall display the registration number accorded to him by the SMC/MCI in his clinic and in all his prescriptions, certificates, money receipts given to his patients."

Regulation 7.3 states that "If he/she does not display the registration number accorded to him/her by the SMC or the MCI in his clinic, prescriptions and certificates, etc. issued by him…", it is considered as professional misconduct rendering him/her liable for disciplinary action.

CAN A DOCTOR WHO IS PREPARING FOR 'MCH' SUFFIX 'MCH' DEGREE AFTER HIS NAME?

Regulation 1.4.2 of the Indian Medical Council Act clarifies that no doctor should suffix any degree after

their name unless they have cleared the exam for the said degree. Preparing for a degree e.g., MCh does not mean that one can add MCh to your qualifications.

"1.4.2 Physicians shall display as suffix to their names only recognised medical degrees or such certificates/ diplomas and memberships/honours which confer professional knowledge or recognises any exemplary qualification/achievements."

CAN DOCTORS WRITE BRAND NAMES OF A DRUG IN THEIR PRESCRIPTION?

Regulation 1.5 of the MCI Code of Medical Ethics does not allow doctors to write drugs by their brand names. The rule says: "1.5 Use of Generic names of drugs: Every physician should, as far as possible, prescribe drugs with generic names and he/she shall ensure that there is a rational prescription and use of drugs."

SHOULD A DOCTOR EXPOSE UNETHICAL CONDUCT IN THE INTEREST OF THE PROFESSION OR THE PATIENT?

According to Regulation 1.7 Exposure of Unethical Conduct, "A physician should expose, without fear or favour, incompetent or corrupt, dishonest or unethical conduct on the part of members of the profession."

WHAT ARE THE DUTIES OF A PHYSICIAN TOWARDS HIS/HER PATIENTS?

Chapter 2 of the Indian Medical Council Act elaborates on this issue.

"2.1 Obligations to the Sick

2.1.1 Though a physician is not bound to treat each and every person asking his services, he should not only be ever ready to respond to the calls of the sick and the injured, but should be mindful of the high character of his mission and the responsibility he discharges in the course of his professional duties. In his treatment, he should never forget that the health and the lives of those entrusted to his care depend on his skill and attention. A physician should endeavour to add to the comfort of the sick by making his visits at the hour indicated to the patients. A physician advising a patient to seek service of another physician is acceptable, however, in case of emergency a physician must treat the patient. No physician shall arbitrarily refuse treatment to a patient. However for good reason, when a patient is suffering from an ailment which is not within the range of experience of the treating physician, the physician may refuse treatment and refer the patient to another physician.

2.1.2 Medical practitioner having any incapacity detrimental to the patient or which can affect his performance vis-à-vis the patient is not permitted to practice his profession."

CAN A DOCTOR DIVULGE INFORMATION ABOUT THE PATIENT THAT HE HAS LEARNT DURING CONSULTATION?

As per Regulation 2.2 Patience, Delicacy and Secrecy, a doctor should not divulge any information about the patient that he has come across during his consultation.

"2.2 Patience, Delicacy and Secrecy: Patience and delicacy should characterise the physician. Confidences concerning individual or domestic life entrusted by patients to a physician and defects in the disposition or character of patients observed during medical attendance should never be revealed unless their revelation is required by the laws of the State. Sometimes, however, a physician must determine whether his duty to society requires him to employ knowledge, obtained through confidence as a physician, to protect a healthy person against a communicable disease to which he is about to be exposed. In such instance, the physician should act as he would wish another to act toward one of his own family in like circumstances."

WHEN CAN A PHYSICIAN DISCLOSE INFORMATION ABOUT THE PATIENT?

According to Regulation 7.14 of MCI Code of Ethics, "The registered medical practitioner shall not disclose the secrets of a patient that have been learnt in the exercise of his/her profession except:

1. In a court of law under orders of the Presiding Judge;
2. In circumstances where there is a serious and identified risk to a specific person and/or community; and
3. Notifiable diseases.

In case of communicable/notifiable diseases, concerned public health authorities should be informed immediately."

■■■■

45th Annual Meeting of the Research Society for the Study of Diabetes in India (RSSDI 2017)

CANVAS PROGRAM

Dr Bruce Neal, UK

- The CANVAS Program integrated data from two trials.
- Inclusion criteria: Patients with type 2 diabetes - HbA1c ≥7.0% to ≤10.5%; eGFR ≥30 mL/min/1.73 m^2; age ≥30 years and history of prior CV event; OR age ≥50 years with ≥2 CV risk factors (diabetes duration ≥10 years, SBP >140 mmHg on ≥1 medication, current smoker, micro- or macroalbuminuria or HDL-C <1 mmol/L).
- The CANVAS Program met its primary objective of demonstrating the CV safety and efficacy of canagliflozin.
- The data suggest a favorable benefit/risk profile with canagliflozin treatment in many patients with type 2 diabetes and high CV risk.
- During the discussion/questions session, the risk of amputation and fractures was discussed among the audience members and the speaker, and it was concluded that there has been no increased risk of fractures or amputations in patients in real clinical practice.
- The increased risk of amputation may be there only in patients who have a history of amputation.

THE INTERSECTION OF DIABETES, CVD AND CKD: THE DANGEROUS LIAISON

Dr Anoop Misra, New Delhi

- Kidney is one of the main organs affected by hyperglycemia.
- Microalbuminuria predicts progression of nephropathy, and also predicts CVD. Drug treatment of albuminuria with ACEIs or ARBs reduces progression of kidney dysfunction. Options for antihyperglycemic drug treatment become limited in CRF, particularly in those below 30 GFR.
- Among newer drugs, linagliptin retains its efficacy and could be given without need for dose modification.

VITAMIN D TOXICITY

Dr Vinod Mittal, New Delhi

Vitamin D toxicity is a rare but potentially serious and fatal condition. Generally, very high doses (nearly 50-100 times the normal dose) of vitamin D supplementation are responsible for vitamin D toxicity, especially IM injection of vitamin D - nearly 3-6 lac units every alternate day, particularly prescribed by orthopedic surgeons in elderly population after total hip replacement or total knee replacement. It is seen more commonly in elderly patients, patients with renal impairment, those on certain medications (isoniazid, thaizide, estrogens), those with granulomatous diseases like tuberculosis, sarcoidosis, etc. and lymphomas. Clinical features are due to hypercalcemia, hyperphosphatemia and worsening of renal failure.

One needs to have a high index of suspicion and do regular monitoring for vitamin D toxicity by testing 24 hours urinary calcium excretion (normal is <250 mg/day) especially if patient is taking >10,000 IU/day of vitamin D.

As vitamin D toxicity is a serious and a fatal condition, timely diagnosis and aggressive management is the key. Stop the offending use of vitamin D, add calcium disodium edetate, find and treat the cause, maintain adequate hydration by infusing IV isotonic saline, IV diuretics, IV hydrocortisone, bisphosphonates, calcitonin (nasal spray), mithramycin and dialysis in some cases.

DIABETIC HEPATOPATHY: A HEPATIC FORM OF MICROVASCULAR COMPLICATION

Dr Anuj Maheshwari, Lucknow

- Diabetic hepatopathy can be defined as a microvascular complication of diabetes presenting with microangiopathy with hepatic sinusoidal fibrosis and basement membrane collagen deposition without cirrhosis. It occurs in patients with T1DM more often than T2DM. The risk of developing diabetic hepatopathy depends on both the duration and the severity of hyperglycemia. It has been suggested that patients who take excess

insulin and treat the subsequent hypoglycemic episodes by administering glucose also promote hepatic glycogen accumulation.

- Accumulation of hepatic glycogen is promoted by high cytoplasmic glucose concentration in the presence of insulin. It occurs mostly in type 1 diabetics after receiving supraphysiological doses of insulin. It presents in metabolically decompensated conditions and in diabetic ketoacidosis states.
- Diabetic hepatopathy manifests hepatic symptoms and evidence of liver dysfunction but it is different than fatty liver as there is no steatosis and it never progresses to cirrhosis. It is reversible on achieving good glycemic control with optimum insulin therapy without causing hypoglycemia.
- Insulin pump is very good option for such patients. Diabetic diet and weight loss helps in reversal.

PRECONCEPTIONAL CARE OF WOMEN WITH DIABETES: THE 10-STEP APPROACH

Dr Jubbin Jagan Jacob, Ludhiana

1. Document use of effective contraception. **Continue contraception till HbA1c targets are met.**
2. **Dietician consultation** with individualized diet plan, educate about weight loss (if BMI >27). Advice on smoking and alcohol cessation. CHO counting (if not aware).
3. **Regular exercise** and avoidance of hypoglycemia.
4. **Optimize glycemic control:** *In type 1 diabetes:* MSII/CSII (intensive insulin regimes); consider twice-daily basal insulin; matched prandial insulin dosing; rapid-acting analogs to be considered. *In type 2 diabetes:* Stop all oral agents except **metformin;** initiate insulin if required.
5. **Monthly HbA1c. In addition,** SMBG at home at least 4-6 times daily. Overnight capillary glucose on occasion. Ketone testing for type 1 diabetes patients.
6. **Measure BP at each visit.** Target BP systolic <130 mmHg and diastolic <90 mmHg. Stop ACEIs and ARBs when contraception is discontinued. Use alternative agents e.g., methyldopa.
7. **Stop statin at discontinuation of contraception.** Screen for hypertriglyceridemia.
8. **Screen for complications.** Dilated fundus examination or retinal imaging; treat significant retinopathy prior to discontinuation of contraception. Assess degree of proteinuria and baseline renal functions. If significant overt proteinuria or eGFR <60 mL/min/1.73 m^2 present, then refer to a kidney specialist. Cardiac screening only if >35 years old or symptomatic.
9. **Screen for rubella autoimmunity.**
10. **Start on folic acid supplementation.**

CV OUTCOME TRIALS WITH DPP-4 INHIBITORS: WHAT'S NEW?

Dr Ambrish Mithal, Gurugram

CV and kidney disease are the biggest contributors to morbidity and mortality in patients with T2DM. Renal function decline is associated with increased risk of hospitalization and mortality.

Patients with T2DM and kidney disease are relatively under-represented population in CVOTs to date.

CARMELINA (CArdiovascular safety and Renal Microvascular outcomE with LINAgliptin in patients with type 2 diabetes mellitus at high vascular risk) is a long-term CVOT that is testing the impact of treatment with linagliptin vs. placebo, on top of standard of care, on CV outcomes and renal outcomes. This is a unique trial that will address important clinical questions.

CARMELINA includes the highest proportion of patients with established CKD compared with other DPP-4 inhibitor CVOTs. It will add evidence to the long-term clinical safety profile of linagliptin by including patients at advanced stages of kidney disease. It is the only DPP-4 inhibitor CVOT that will also test for renal outcomes.

PRIMORDIAL PREVENTION OF DIABETES AND ITS COMORBID COMPLICATIONS

Prof (Dr) V Seshiah, Chennai

Preventive measures against T2DM and associated CV complications should start during intrauterine period and continue throughout life from early childhood. GDM offers an important opportunity for the development, testing and implementation of the clinical strategies for prevention of diabetes and NCDs.

Insulin resistance, increased atherogenic lipid profile, inflammatory markers, hypertension and endothelial dysfunction lead to increased risk for CVD.

A substantial number of women with GDM have increased lifetime risk of developing diabetes at over three times compared to control after 16 years of index pregnancy. By 17 years of age, one-third of children born to GDM mothers have had evidence of prediabetes, T2DM, metabolic syndrome, impaired insulin sensitivity and secretion.

For diagnosis of GDM, single step testing using 75 g oral glucose and measuring plasma glucose 2-hour after ingestion is recommended. The threshold plasma glucose level of >140 mg/dL (≥140) is taken as cut-off for diagnosis of GDM.

Timely action taken now in screening all pregnant women for glucose tolerance, achieving euglycemia in them, may prevent the epidemic of NCDs. Maternal health is the link to the NCD epidemic. Low birth weight or large for gestational age birth weight leads to elevated risk for obesity, diabetes, hypertension, CVD in adult life.

There is an intergenerational transfer of risk. Postpartum follow-up is very essential and pre-GDM women should be advised against gaining weight. Similarly, their offsprings should also follow a healthy lifestyle pattern.

SETTING-UP DIABETIC CARE CLINIC: NEED OF THE HOUR

Dr Dakshata Padhye, Mumbai

Diabetes, a prevalent metabolic disease in India, increases the financial burden of patients considerably. The pillars of successfully setting up a diabetic clinic are knowledge, planning, finances, infrastructure and manpower. It is essential to pay attention to the legal and commercial aspects before setting up a specialty clinic. The necessity of updated infrastructure and teamwork cannot be ignored. Patient education is the cornerstone of management of diabetes patients.

OFFLOADING PRACTICAL PEARLS FOR PREVENTION AND CURE OF DIABETIC FOOT ULCERS

Dr Ashu Rastogi, Chandigarh

An often neglected aspect of diabetes evaluation - foot and footwear assessment in diabetic patients with neuropathy. Although there are various methods for managing diabetic foot ulcers, offloading is the ideal management strategy. Modified footwear, such as total contact casts (TCC) have been approved by ADA. However, in tropical countries like India, these casts may cause moisture locking and thus, fungal growth. Therefore, modified TCCs may be used for Indian patients, which cover lesser area of the leg. Apart from this measure, focus on patients' foot hygiene, use of appropriate shoes, proper gait and patient education and awareness is essential. Debridement is the key before dressing these ulcers and local antibiotics should be avoided in these dressings.

INSULIN SENSITIZERS IN PCOS

Dr Bindu Kulshreshtha, New Delhi

Insulin sensitizers are efficacious in the management of PCOS patients. They can be used as first-line agents for obese PCOS patients with mild-to-moderate features of oligoanovulation and/or infertility. They can be used as add-on therapy to antiandrogens for greater efficacy. Their beneficial role in metabolic syndrome gives them an upper edge to be used in preference to oral contraceptives in PCOS patients. Data with glitazones is limited and owing to their weight gaining tendency, they are not preferred.

NONINSULIN THERAPIES IN TYPE 1 DIABETES: ADJUNCTIVE ROLE

Dr Gagan Priya, Mohali

Insulin remains the cornerstone of treatment in type 1 diabetes, but most patients fail to achieve glycemic targets and experience periods of hyperglycemia as well as hypoglycemia. Weight gain, severe hypoglycemia, recurrent hypoglycemia, hypoglycemia unawareness and poor postprandial glycemic control remain significant challenges. Type 1 diabetes is characterized by α-cell dysfunction and glucagon dysregulation. Insulin resistance has been documented in individuals with type 1 diabetes. Non-insulin antidiabetic medications have been explored for their role as adjunctive to insulin therapy to improve metabolic control in type 1 diabetes. Pramlintide, an amylin analogue, is currently approved as adjunctive therapy in type 1 diabetes. The role of metformin has also been evaluated. Metformin reduces insulin dose requirement, weight and LDL-C, reduces maximal CIMT and may extend cardioprotective benefits in type 1 diabetes. Trials of GLP-1 receptor agonists have demonstrated small reductions in HbA1c levels accompanied with weight loss and reduced insulin dose, but a significantly increased risk of hypoglycemia. SGLT2 inhibitors have shown improved glycemic control with reduction in insulin dose and weight in small studies. Dual SGLT2 and SGLT1 inhibitor, sotagliflozin, is under development.

IS POSTPRANDIAL TRIGLYCERIDE DYSMETABOLISM CENTRAL TO THE DEVELOPMENT OF METABOLIC SYNDROME AND T2DM?

Dr SV Madhu, Delhi

Postprandial hypertriglyceridemia and insulin resistance (IR)/T2DM: High fat stores in ectopic

compartments have been reported at the early stage of development of type 2 diabetes as well as in IR nondiabetic obese adolescents. Significant postprandial lipemia (PPL) in first-degree relatives of type 2 diabetes patients with NGT and IGT subjects indicates that it is an independent inherited defect in postprandial TG metabolism, which occurs prior to the development of T2DM. The most direct human evidence of the causal role of triglycerides (TGs) in T2DM comes from a case report of TG-induced diabetes, where very high TG levels resulted in IR and diabetes. Complete reversal of overt diabetes and near complete reversal of IR occurred when lipid malabsorption was induced by bilio-pancreatic diversion (BPD), which substantially lowered TG levels. Studies have suggested that there is significant PPL in diabetic and prediabetic patients with a strong association with IR.

WHAT'S NEW IN DIABETIC FOOT MANAGEMENT?

Dr Ghanshyam Goyal, Kolkata

Pay attention to the basic tenets of wound care. Nothing supplants the role of good basic wound care which are - adequate offloading, adequate debridement, management of any existing infection and managing ischemia, as necessary. Wounds change over the course of treatment and hence, be prepared to change your therapy as the wound characteristics change. When considering advanced modalities, keep Indian scenario in mind - AVAILABILITY AND AFFORDABILITY. Only when conventional therapy fails, think of advanced modalities.

PROTEIN CONSUMPTION IN DIABETIC POPULATION

Dr P Janaki Srinath, Hyderabad

- Educating the diabetic patient regarding inclusion of optimal protein consumption within the recommended calorie intake is paramount.
- Recommendations for protein intake are based on individual assessment and the consideration of other health issues and implications, such as the extent of glycemic control, the presence of kidney disease, overweight, obesity and the age of the patient.
- Optimal protein intake as 20-30% of total energy can be beneficial for improving glycemic control aiding in satiety and preservation of lean body mass during weight loss in patients with diabetes and prediabetes.
- Healthcare providers should discuss the role of protein with patients, discuss ideal protein choices, food forms and portion sizes.

DIGITAL DIABETOLOGY

Dr J Jayaprakash Sai, Hyderabad

Six core elements of chronic care model: Moving from a reactive to a proactive care delivery system; self-management; decision support on evidence-based guidelines - RSSDI, ADA and IDF; clinical information system; community partnerships for affecting lifestyle changes; Team-base care. Technology as an enabler to: Better risk stratification; support decision-based systems for doctors; define care plan and managing care gaps; using technology to remind and engage patient; timely interventions to reduce risk of complications - need for a Digital Diabetes Health Care Model in India.

EYE IS THE GATEWAY FOR MICROVASCULAR DISEASES

Dr Bharat Panigrahy, Bhubaneswar

Diabetic retinopathy is the most frequent cause of new cases of blindness among adults aged 20-74 years. Screening adults with diabetes should include an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist within 5 years after the onset of diabetes for T1 and at the time of the diabetes diagnosis for T2DM, and thereafter annually. It is important to detect nerve damage at the earliest stage of diabetic neuropathy as intervention at this stage can prevent nerve degeneration or promote regeneration. Patients with nephropathy and type 1 diabetes almost always have other signs of diabetic microvascular disease, such as retinopathy and neuropathy. Retinopathy is easy to detect clinically, and typically precedes the onset of overt nephropathy in these patients. With a comprehensive ophthalmological examination every year by an expert ophthalmologist, we can get enough information about all the microvascular complications of diabetes.

VITAMIN D AND TYPE 2 DIABETES MELLITUS

Prof (Dr) CV Harinarayan, Bengaluru

Definitions: Vitamin D (25[OH]D) deficiency <20 ng/mL; insufficiency 20-30 ng/mL; sufficiency >30 ng/mL. Normal 25(OH)D levels are important for fully normal calcium absorption efficiency in the gut. Calcium absorption in the gut plateaus at 25(OH)D levels of 30 ng/mL. Vitamin D influences pancreatic β-cell synthesis, secretion and insulin sensitivity. Vitamin D may mediate the levels of extracellular and intracellular calcium ($[Ca^{2+}]i$) through a rapid response involving flux through β cells. Vitamin D deficiency

affects insulin secretion and sensitivity by its effects on $(Ca^{2+})i$. It plays a key role in ensuring preservation of extracellular calcium levels and intracellular cytosolic calcium concentration. Vitamin D supplementation - Correction of deficiency: 10,000 IU daily or 60,000 IU weekly for 8-12 weeks; 6,00,000 by IM injections once with a gap of 2 months. Vitamin D maintenance dose: 1,000-2,000 IU daily or 10,000 IU weekly or 60,000 IU once a month. This should be accompanied by calcium intake of 1 g/day in adults. Casual exposure to the mid-day sun for 15-30 minutes exposing 12% of body surface area without sunscreen will synthesize enough vitamin D for the day. Exposure of larger skin surface area is required in the elderly.

EMERGING BIOMARKERS OF ENTERPRISING CHALLENGES TO PREDICT AS WELL AS TREAT GDM

Dr M Balasubramanyam, Chennai

GDM in pregnant women is an alarming health threat to mother as well as offspring. Both GDM and its progression to type 2 diabetes could be potentially prevented by appropriate lifestyle modifications and medical management, but we need to identify the high-risk individuals. As the literature is becoming loaded with 'several of these biomarkers', the challenge is to develop, validate and pick-up a robust and reliable single or panel of biomarker. Recent Omics studies (proteomics, epigenetics, metabolomics and metagenomics) also add up novel and early biomarkers for risk prediction of GDM. Placenta is not Pleasant(!) in GDM and identification of cellular stress within the placenta has started to offer a number of placenta-derived biomarkers for GDM prediction. Despite the identification of potential biomarkers, the challenges still remain pertaining to their validation in larger cohorts and to adopting them to universally standardized lab tests, point-of-care platforms and subjecting them to Health Informatics and Clinical Utility.

EFFECTIVENESS OF AUDIOVISUAL AID IN DIABETIC FOOT EDUCATION IN OUTPATIENT SETTING: A RANDOMIZED CONTROL TRIAL

Prof Viveka P Jyotsna, New Delhi

In routine clinical practice, healthcare personnel give little/no attention to education about foot care, until patients present with a foot ulcer. On the other hand, simple health education measures can improve both the knowledge and practice regarding diabetic foot care. Both the intervention and control groups in this study were given a questionnaire to fill up. Both groups then received routine care provided by healthcare personnel in the OPD. Significant improvement in diabetic foot knowledge and foot care behavior was noted in the intervention group, compared to controls. Audiovisual aid is an effective and feasible means to improve foot care knowledge and practice. Regular reinforcement for foot care education through audiovisual aid in OPD waiting hours is a good option.

PROBLEMS AND SOLUTION FOR SCREENING OF GDM IN LESS RESOURCE SETTINGS

Dr Bhavatharini Aruyerchelvan, Erode

PROBLEMS: *For the Pregnant Mother:* She has to get ready after caring for the needs of the family members and sometimes domestic animals. Distance and time to travel. Lack of transport facilities. By this time, she will be hungry and may not be able to attend ANC in fasting state. Needs somebody to accompany-2 wages gone.

SOLUTIONS: *Need of the Hour:* Because everybody in the GH are over burdened, they always want and welcome whichever is easier and simple, at the same time useful and prevents mortality and morbidity. *Indian Problem Needs Indian Solution:* Because of all these practical problems, pregnant women are not able to come in fasting. Our Diabetes In Pregnancy Study Group of India (DIPSI) solves the problem that GCT can be done in fasting or nonfasting state and fulfils the expectations of FIGO & WHO, ie., in low socioeconomic countries like us - to do something in pregnant women depending on the resources available; to screen every pregnant woman for glucose abnormality becomes necessary to have diabetes free generation in future. Hence: Walk in test is the best. GCT which can be done in fasting or nonfasting state, i.e., a single step procedure recommended by DIPSI and approved by Govt of India, WHO and FIGO. DIPSI was started with the motto to prevent diabetes in the community by catching early as many GDM as possible.

DIABETES AND GUT

Dr Manas Kumar Panigrahi, Bhubaneswar

There is a high burden of diabetic enteropathy. Early recognition and treatment is the goal. There is a definite role of gut microbiota in pathogenesis of diabetes and diabetic enteropathy. Stem cell transplantation, fecal microbiota transplantation and endoscopic management are expected in near future.

PROGRAMMING FOR SUSTAINABLE HEALTH - LINKING MATERNAL HEALTH WITH NCD PREVENTION AND CARE THROUGH FOCUS ON HYPERGLYCEMIA IN PREGNANCY

Dr Anil Kapur, Bengaluru

Noncommunicable diseases (NCDs) and maternal health are closely linked. NCDs such as diabetes, obesity and hypertension have significant adverse impact on maternal health and pregnancy outcome and through the mechanism of intrauterine programming, maternal health has impact on the burden of NCDs in future generations. The cycle of vulnerability to NCDs is repeated with increasing risk accumulation in subsequent generations. The fetal environment represented by the mother's periconceptional and gestational health determines whether one starts life with a health 'advantage' or 'handicap', and it is on this 'foundation' that NCD risk factors play out in later life. People starting life with a 'health handicap' may be less able to withstand lifestyle risks and may be vulnerable to develop NCDs early compared to those starting with a 'health advantage'. The links between NCDs and maternal health are important and require a more integrated approach to prevention and care at the primary care level. Greater efforts are needed to create awareness and understanding about these links amongst healthcare professionals, public health experts, policymakers and funders and to develop sustainable cost-effective models to address integration at the program level. Obstetricians, family physicians, internists and pediatricians must remain vigilant and ensure that protocols for screening, diagnosis and care are adhered not only during pregnancy but also in the postpartum period. Pregnancy offers a window of opportunity to provide maternal care services, not only to reduce the traditionally known maternal and perinatal morbidity and mortality indicators but also for intergenerational prevention of several chronic diseases.

WHY ARE THICK FAT BONES BRITTLE IN DIABETES?

Dr GR Sridhar, Visakhapatnam

Imaging of the bones is often done to assess their density. In nondiabetic subjects, denser the bone, lower the risk of future fractures. In subjects with diabetes, even though the bones are dense on imaging, they are prone to fractures. The bone strength is low, despite greater density on imaging. Some antidiabetic medicines also have a propensity to lead to osteoporosis, but the following are safe in terms of bone health - metformin, sulfonylureas, DPP-4i, GLP-1 RA. Insulin should be used with care to avoid hypoglycemia.

CLINICAL ASPECTS OF PANCREATOGENIC DIABETES (TYPE 3c)

Dr Mohsin Aslam, Hyderabad

- Pancreatogenic diabetes occurs as a result of benign and malignant diseases of the exocrine pancreas. It is classified as type 3c diabetes mellitus (T3cDM) according to the current classification of diabetes mellitus by the ADA.
- T3cDM is distinct from T1DM and T2DM as it arises due to chronic inflammation, has unique clinical and laboratory parameters and is associated with high incidence of pancreatic carcinoma. The altered glucose metabolism of T3cDM ranges from mild impairment to a severe form, characterized by frequent episodes of iatrogenic hypoglycemia, referred to as "brittle diabetes", which is difficult to treat. It is not always easy to diagnose and classify a patient with T3cDM correctly. In distinguishing between the different diabetes types, the presence of islet cell antibodies is consistent with T1DM.
- In T3cDM, metformin is the initial drug of choice for oral therapy due, in part, to its insulin-lowering effects on glucose metabolism, and also due to its specific antineoplastic actions on cellular mediators of replication and protein synthesis.
- When insulin administration is required as primary therapy to adequately control hyperglycemia, adjunct therapy with additional oral agents to reduce the required insulin dose is beneficial. Pancreatic enzyme replacement therapy, in addition to improving exocrine insufficiency, may also help in controlling hyperglycemia by regulating incretin secretion.

DIABETIC FOOT: AN OUTCOME OF INCREASING LONGEVITY

Dr Ashu Rastogi, Chandigarh

India, like the developed nations, has moved from a high fertility-high mortality in the past century to a low fertility-low mortality state. Life expectancy has increased from 26.8 years in 1920 to 67.8 years in 2014. The aging population comprises a sizeable population having NCDs including diabetes mellitus. The swelling number of diabetes mellitus translates to more people with microvascular complications. With advancing age, the prevalence of neuropathy, peripheral vascular disease, increases manifolds, which themselves are risk factors for diabetic foot. Therefore, the prevalence of diabetic foot increases with increasing duration of

the disease. The lifetime risk for foot complications in patients with diabetes is 15% and contributes to significant mortality and morbidity.

CAN WE WIN THE WAR AGAINST DIABETES?

Dr Ch Vasanth Kumar, Hyderabad

Majority of the people affected with diabetes in India belong to lower socioeconomic background. They have no access to specialist care and they do not regularly monitor their health status. Most of these patients have lower BMI compared to western patients. Even the pathophysiological factors may vary in these patients and they may be relatively insulin deficient. The focus should be on these patients who are poor, either living in urban slums or in rural areas. They require regular monitoring and basic medicines and insulins to control their disease and prevent complications. There is an urgent need to train our primary care doctors, both in private and government sectors. Basic facilities like glucometers and simple lab equipment should be made available to check parameters like blood glucose, creatinine and hemoglobin. Medicines should be made available at affordable costs. The research should focus on Indian patients and try to understand the peculiarities of our patients. Finally, we have to make the diabetes treatment affordable and reach out to diabetic patients.

SECONDARY DIABETES DUE TO ENDOCRINOPATHY

Dr Kalpana Dash, Raipur

Diabetes secondary to endocrinopathies is nearly 1%. This entity refers to occurrence of diabetes secondary to hormone overproduction leading to counter-regulatory hormone production. This can cause overt diabetes or ketoacidosis. After surgical and medical intervention, there is improvement or remission of diabetes. The net metabolic outcome in patients with secondary diabetes depends on the direct or indirect impact of the underlying disorders on insulin secretion (i.e., inhibition or compensatory hyperinsulinemia), insulin-sensitivity (i.e., glucose utilization), and/or unmasking of genetic diabetes.

All endocrine disorders due to overproduction of hormones need screening for diabetes. There is an increased CV morbidity and mortality among these patients. Most of these patients need insulin therapy before surgical intervention and may be switched over to oral agents after surgery, or may not require treatment if complete remission is there.

COMBINATION THERAPY: START RIGHT!

Dr Manoj Chawla, Mumbai

Natural history of T2DM reflects underlying loss of β-cell function. To prevent/delay the loss of β-cell function, current conservative approach may not be sufficient and an approach to 'treat-to-target' may be required. In suitable newly diagnosed patients, a combination therapy to start with may be the optimum approach. The concept of 'legacy effect' also suggests that early combination therapy may create a 'good legacy' in T2DM patients, which can help over long duration in terms of lesser complications.

Starting with a combination therapy should also include the evaluation of medications. Ideally, the ones with synergistic or complimentary actions should be preferred. It should also be taken into account whether the medications are addressing the key pathophysiology or merely addressing the symptoms. The ones acting on insulin resistance as well as sustaining β-cell function can help the patients over long-term. There is emerging real-world evidence in terms of multi-country INITIAL study on early intensification, where patients were given vildagliptin+metformin to start with. Upcoming studies like GRADE and VERIFY have the potential to provide invaluable insights on benefits of starting with a combination therapy, including durability of β cells over long-term.

GDM IS A PUBLIC HEALTH ISSUE. WHAT WE CAN DO?

Prof Samar Banerjee, Kolkata

Gestational diabetes mellitus (GDM) may play a crucial role in the increasing prevalence of diabetes and obesity. The common adverse outcomes in GDM are: Stillbirth and aberrant fetal growth (macrosomia and growth restriction); metabolic problems (e.g., hypoglycemia and hypocalcemia); hematological problems (e.g., bilirubinemia and polycythemia); respiratory complications; birth trauma (e.g., shoulder dystocia). Gestational diabetes is a red flag for future GDM or type 2 diabetes in the next pregnancy. Findings suggest high diabetes and CV risks in women with previous GDM. All women should be screened for GDM, even if they have no symptoms, according to new recommendations. There should be universal early testing of Indian population because of high prevalence of T2DM. DIPSI recommends screening and diagnosis of GDM with 2-hour PG ≥140 mg/dL. This is supported by Govt. of India as a national policy. In future clinical practice, simpler and more cost-effective strategies that

do not require performing an OGTT on most pregnant women may be developed.

Preventive measures against T2DM should start during intrauterine period and continue throughout life from early childhood. GDM offers an important opportunity for the development, testing and implementation of clinical strategies for diabetes prevention. One major aim for future improvement in the outcomes of offspring of mothers with diabetes is greater awareness of these consequences related to maternal diabetes and what can be done to prevent them.

AGIs: PLACE IN THERAPY IN INDIAN T2DM PATIENTS

Dr Abhay Kumar Sahoo, Bhubaneswar

STARCH study reveals that Indian diabetics consume diet rich in carbohydrates. Carbohydrate constitutes 64.1% of total energy from diet. PPG of 62.5% diabetic population was above the target of 180 mg/dL. Efforts are needed to raise awareness on the impact of postprandial hyperglycemia (PPHG) on CV risk. Relevance of α-glucosidase inhibitors (AGIs) for Indian patients: Indian diet is rich in carbohydrates; compared to western world, this is far higher; carbohydrate load determines the postprandial rise in blood glucose. There is a need to address this high carbohydrate meal either through diet modifications or the agent, which reduces the absorption of carbohydrate; AGIs primarily take care of PPG for comprehensive control. AGIs have long track record of safety and efficacy with benefits like weight reduction, low risk of hypoglycemia and CV protection. Patients with exaggerated postprandial excursion can be treated with acarbose. AGIs with metformin: Comprehensive glycemic control.

BIONIC PANCREAS

Dr Rajeev Chawla, New Delhi

Bionic pancreas is developed by Edward Damiano and Firas El-Khatib of Boston University/Massachusetts General Hospital. A system of integrated devices to substitute endocrine pancreas by: Sensing blood glucose level; determining the amount of insulin; delivering the appropriate amount. Glucose monitoring: Various types of sensors - noninvasive, minimally invasive, invasive: Algorithm to link blood glucose levels with insulin delivery: to develop thinking like pancreas; Automatic insulin delivery system: CSII (continuous subcutaneous insulin infusion) or CIPII (continuous intraperitoneal insulin infusion). Artificial pancreas (AP) development is ongoing: Major issues are due to unphysiological route for insulin infusion and need of glucagon; insulin only AP will be more practical but to manage physiology, algorithms from technology may provide alternative; CGMS technology improvement will be must to achieve this goal.

KNOWLEDGE AND PRACTICES OF GDM

Dr Sunil Gupta, Nagpur

Principally, metformin is being more accepted by Obstetricians and less by physicians for management of hyperglycemia in pregnancy. Insulin is the drug of choice for controlling blood glucose in pregnancy. Postnatal follow-up of women with diabetes is important and should be done more aggressively.

INTERNATIONAL COLLABORATIVE RESEARCH ON DIABETES AND DEPRESSION

Prof. SK Chaturvedi, Bengaluru

Comorbid diabetes and depression is a serious public health concern. International recommendations for care are not always implemented at the local level. Evidence on the optimal ways of identifying and treating depression in people with diabetes within the local context is still lacking. International collaborative research on diabetes and depression can find answers to these issues. INTERPRET-DD is investigating these issues in 20 countries across the globe.

PATHOGENESIS OF PANCREATOGENIC DIABETES: CURRENT KNOWLEDGE

Dr M Sasikala, Hyderabad

Pancreatogenic diabetes, categorized as type 3c diabetes, arises as a result of exocrine disease to the pancreas. Most commonly identified cause of type 3c is chronic pancreatits. It is recently demonstrated that inflammation in the pancreas drives β-cell dysfunction early in the course of exocrine disease in chronic pancreatitis before the onset of clinical diabetes. Since, chronic pancreatits affects comparatively the young in India, better understanding of the progression from β-cell dysfunction to diabetes mellitus is critical to develop screening tools for early detection and intervention.

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News and Views

Initiative to Increase Insurance Coverage for Climate-related Disasters

A global initiative has been launched at the United Nations Climate Change Conference (COP23), in Bonn, Germany, with the aim of providing insurance to hundreds of millions of vulnerable people by 2020 and to increase the resilience of developing countries against the impacts of climate change. The InsuResilience Global Partnership is a major scaling-up of an initiative started by the G7 in 2015 under the German Presidency. It aims at meeting the pledge of providing cover and support to an extra 400 million vulnerable people by 2020. The Global Partnership now brings together G20 countries in partnership with the so-called 'V20' nations, a group of 49 of the most vulnerable countries including small islands like Fiji, which holds the Presidency of COP23… (*UN, November 14, 2017*).

New ATS Guidelines for Diagnosis of Lymphangioleiomyomatosis

The American Thoracic Society (ATS) and the Japanese Respiratory Society (JRS) have published additional clinical practice guidelines regarding four specific questions related to the diagnosis of lymphangioleiomyomatosis (LAM) and management of pneumothoraces in patients with LAM in the *American Journal of Respiratory and Critical Care Medicine, November 15, 2017.*

High BP During Pregnancy Increases the Risk of Hospitalization for Heart Failure

Women who develop high blood pressure during pregnancy are more likely to experience heart problems within a few years of giving birth, according to preliminary research presented at the American Heart Association's Scientific Sessions 2017 in Anaheim, California. Women who experienced any form of pregnancy-related hypertension were also more likely to be frequently hospitalized for heart failure or heart attack.

US FDA Approves New Treatment for Patients with Hemophilia A

The US Food and Drug Administration (FDA) has approved Hemlibra (emicizumab-kxwh) to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients with hemophilia A who have developed antibodies called Factor VIII (FVIII) inhibitors.

Auscultation While Standing Rules Out Pathologic Murmurs in Children

Disappearance of a heart murmur on standing is a reliable clinical tool for ruling out pathologic heart murmurs in children aged 2 years and older with a high positive predictive value of 98% and specificity of 93%, even though with a lower sensitivity of 60%, says a new study reported in November/December 2017 issue of the *Annals of Family Medicine*.

Positive Airway Pressure Therapy Improves QoL in People who have Obstructive Sleep Apnea

A study published in the November 15, 2017 in the *Journal of Clinical Sleep Medicine* has reported significant and clinically meaningful improvements in general quality-of-life (QoL) and sleep-related QoL measures after the initiation of positive airway pressure (PAP) therapy for sleep apnea, particularly in those who were adherent to PAP therapy.

Daily Drug Regimen for Treatment of TB Introduced Under RNTCP

The Ministry of Health & Family Welfare has recently announced the launch of daily regimen for tuberculosis (TB) patients across the country under The Revised National TB Control Program (RNTCP).

The Health Ministry has been providing the thrice weekly regimen for the treatment of TB, however it has now decided to change the treatment strategy for TB patients from thrice weekly to daily drug regimen using fixed dose combinations (FDCs) for treatment. This change will bring transformation in the approach and the intensity to deal with this disease which accounts for about 4.2 lakh deaths every year.

The daily FDC anti-TB drugs will be made available to private pharmacy or at private practitioners to dispense to TB patients who seek care in private sector, depending upon the convenience of patient and practitioner free of cost.

The Health Ministry will take this forward with all major hospitals, IMA, IAP and other professional

medical associations to expand the access to daily FDC to all TB patients.

The salient features of this treatment strategy are:

- Use of Ethambutol in continuation phase for all patients.
- Drugs to be given daily (as against only 3 times weekly previously).
- FDC tablets to be used which will reduce pill burden (as against separate 7 tablets previously).
- Child friendly formulations as dispersible tablets for children.
- Use of information technology (IT) enabled treatment adherence support system.

(Source: Press Information Bureau, Ministry of Health and Family Welfare, November 17, 2017)

Stressful Events can Increase Risk of Obesity in Women

Women who experienced one or more traumatic lifetime events or several negative events in recent years had higher odds of being obese than women who didn't report such stress, according to preliminary research presented at the American Heart Association (AHA)'s Scientific Sessions 2017 in Anaheim, California. The higher the number of negative life events reported by women in the last 5 years, the higher the tendency for increased odds of obesity.

FDA Expands Approval of Sutent to Reduce the Risk of Recurrence of Kidney Cancer

The US Food and Drug Administration (FDA) has approved sutent (sunitinib malate) for the adjuvant treatment of adult patients who are at a high risk of kidney cancer (renal cell carcinoma) returning after a kidney has been removed (nephrectomy). Adjuvant treatment is a form of therapy that is taken after an initial surgical removal to lower the risk of the cancer coming back.

Alectinib more Effective than Crizotinib in Asian Cancer Patients

A subanalysis of the phase III ALEX study reported November 17, 2017 at the ESMO Asia 2017 Congress in Lugano, Switzerland has shown that alectinib 600 mg twice daily is more effective than standard of care crizotinib in Asian patients with anaplastic lymphoma kinase (ALK) positive non-small cell lung cancer (NSCLC).

Cholecystectomy Done Before Weight Loss Surgery Reduces Complications in Obese Patients

A study published online October 18, 2017 in the *British Journal of Surgery* has suggested that cholecystectomy should be performed before, not during or after, the weight loss Roux-en-Y gastric bypass surgery (RYGB). A higher aggregate complication risk was observed when cholecystectomy was performed after RYGB rather than before and also when both surgeries were done at the same time.

sIL-2R Levels Better than ACE for Diagnosing Sarcoidosis in Patients with Uveitis

As reported in *JAMA Ophthalmology*, online November 9, 2017, the sensitivity and specificity of using serum-soluble interleukin 2 receptor levels alone for diagnosing sarcoidosis in patients with uveitis were 81% and 64%, respectively. Combined with chest X-ray, the sensitivity and specificity for soluble interleukin 2 receptor were 92% and 58%, respectively compared to 70% and 79%, respectively for angiotensin-converting enzyme (ACE).

New Global Commitment to End TB

Seventy-five ministers agreed to take urgent action to end tuberculosis (TB) by 2030 at the first WHO Global Ministerial Conference on Ending Tuberculosis in the Sustainable Development Era: A Multisectoral Response in Moscow.

The Moscow Declaration to End TB is a promise to increase multisectoral action as well as track progress, and build accountability. It will also inform the first UN General Assembly high-level meeting on TB in 2018, which will seek further commitments from heads of state.

The two-day conference resulted in collective commitment to ramp up action on four fronts:

1. Move rapidly to achieve universal health coverage by strengthening health systems and improving access to people-centered TB prevention and care, ensuring no one is left behind.
2. Mobilize sufficient and sustainable financing through increased domestic and international investments to close gaps in implementation and research.
3. Advance research and development of new tools to diagnose, treat, and prevent TB.
4. Build accountability through a framework to track and review progress on ending TB, including multisectoral approaches.

(Source: WHO, November 17, 2017)

GPs Trained in Compression USG can Accurately Diagnose DVT

Compression ultrasonography (USG) performed by General Practitioners (GPs) had a sensitivity of 90.0% and a specificity of 97.1% with a diagnostic accuracy for deep vein thrombosis (DVT) of almost 96%, according to a study reported in November-December 2017 issue of the journal *Annals of Family Medicine*. Trained GPs can help in the early diagnosis and thereby timely management of DVT.

FDA Approves First Telehealth Option to Program Cochlear Implants Remotely

The US Food and Drug Administration (FDA) has approved a remote feature for follow-up programming sessions for the Nucleus Cochlear Implant System through a telemedicine platform. The remote programming feature is indicated for patients who have had 6 months of experience with their cochlear implant sound processor and are comfortable with the programming process.

Exercise may Reduce Risk of Low Back Pain

Results of a systematic review and meta-analysis of controlled trials published October 19, 2017 in the *American Journal of Epidemiology* show that exercise reduced the risk of low back pain by 33% and also reduced associated disability. The study further recommends a combination of strengthening with either stretching or aerobic exercises performed 2–3 times/week to prevent low back pain.

Former Cigarette Smokers are More Likely to Use e-Cigarettes

Electronic cigarettes are more frequently used by people who recently quit smoking and alcohol drinkers, according to preliminary research presented at the American Heart Association's Scientific Sessions 2017 at Anaheim, California. E-cigarette users were 6.32 times as likely to be exposed to second-hand tobacco smoke and 4.19 times as likely to report drinking alcohol 12 times or more in the past 1 year.

A New Subcutaneous Formulation of Belimumab with Active SLE

The European Commission has approved a new subcutaneous formulation of belimumab (Benlysta) as adjunctive treatment for adults with active, autoantibody-positive systemic lupus erythematosus (SLE) with a high degree of disease activity despite standard therapy. It will be available as a once-weekly 200-mg injection from a single-dose prefilled syringe or from a single-dose autoinjector.

42nd International Congress of Military Medicine Begins

The 42nd World Congress of the International Committee of Military Medicine (ICMM) organized by the Armed Forces Medical Services (AFMS) under the aegis of the Ministry of Defence (MoD) began on Sunday. The ICMM is an international intergovernmental organization created in 1921 with its secretariat at Brussels in Belgium and currently has 112 nations as members. The 5-day event is being organized for the first time in India, and is the largest medical conference ever organised by the AFMS. The theme of this 42nd World Congress is "Military Medicine in Transition: Looking Ahead".

There are 26 thematic sessions covering diverse areas including "Terrain Specific Military Medical Support", "Health Protection and Promotion in the Military Environment", "Combat Medical Support", and "Humanitarian Aid and Disaster Relief". Workshops by international faculty on management of mass casualties, barrier nursing for hemorrhagic fevers and medical ethics in military medicine are going to be other highlights of the Congress… (*Press Information Bureau, Ministry of Defence, November 19, 2017*)

Inclisiran Lowers LDL Cholesterol for up to 1 Year

Inclisiran lowers low-density lipoprotein (LDL); "bad" cholesterol for up to 1 year in patients with high cardiovascular risk and elevated LDL cholesterol, according to results from the ORION 1 trial presented at the recent ESC Congress held in Barcelona, Spain. Inclisiran is a first-in-class investigational drug that acts by turning off PCSK9 synthesis in the liver.

Vaginal Progesterone Reduces Risk of Preterm Birth

A meta-analysis of individual patient data published November 17, 2017 in the *American Journal of Obstetrics & Gynecology* shows that use of vaginal progesterone reduces the risk of preterm birth, neonatal complications and infant death in pregnant women with a short cervix. Progesterone also significantly decreased the rate of respiratory distress syndrome, neonatal death, low birth weight and admission to neonatal intensive care units for newborns with no deleterious effects on childhood neurodevelopment.

ACOG Launches First National Multistate Collaborative on Treating Maternal Opioid Use Disorder

The American College of Obstetricians and Gynecologists (ACOG) has launched the first national

multistate collaborative to develop strategies for scalable programs to provide care and treatment for maternal opioid use disorder, which has surpassed hemorrhage and hypertension as the leading cause of maternal mortality in many states across the country. As a guide, the collaborative will use obstetric care of women with opioid use disorder, the latest bundle released by the Alliance for Innovation on Maternal Health (AIM) program.

Flu Vaccine Prevents Hospitalization in Children

According to a new research published November 17, 2017 in the journal *PLoS One*, children vaccinated against influenza are significantly less likely to experience serious complications from the virus that required hospitalization. Vaccination reduced the overall risk of hospitalization by 60%.

Study Shows Association Between Stroke Risk and Metformin in Hemodialysis Patients with Diabetes

The use of metformin is associated with stroke risk in hemodialysis patients with diabetes, suggests a study published online November 16, 2017 in the *Journal of the American Heart Association*. It was found that hemodialysis patients with ischemic stroke were more likely to use metformin 1 year before the date of stroke admission vs controls. The association was evident within 90 days before the index date.

US Tobacco Companies Asked to Run Court-ordered Ads Telling the Truth About Their Lethal Products

Starting November 26, the major US tobacco companies must run court-ordered newspaper and television advertisements that tell the American public the truth about the deadly consequences of smoking and secondhand smoke, as well as the companies' intentional design of cigarettes to make them more addictive. The ads are the culmination of a long-running lawsuit the US Department of Justice filed against the tobacco companies in 1999.

The tobacco companies must place full-page print ads in the Sunday editions of more than 50 newspapers specified by the court (newspapers without a Sunday edition must run the ads on the previous Friday). Five ads – one on each of the corrective statements – will be published over a 4-month period. The ads must also appear on the newspapers' websites. The TV ads will air on the major networks for 1 year, Monday through Thursday, between 7 pm and 10 pm The tobacco companies must also publish the corrective statements on their websites and cigarette packs, but the implementation details are still being finalized…

(Source: AHA News Release, November 20, 2017)

Salivary microRNA Levels may Identify Children at Risk of Prolonged Concussion Symptoms

Concentrations of 5 salivary microRNAs identified prolonged concussion symptoms in 42 of 50 children, an accuracy of more than 85% in a study reported online November 20, 2017 in *JAMA Pediatrics* suggesting salivary microRNA levels as an objective tool in concussion management.

Prognosis Usually not Good in Patients with Infected Diabetic Foot Ulcers, Says Study

According to a prospective observational study published November 20, 2017 in the journal *Diabetic Medicine*, clinical outcomes at 12 months for people with an infected diabetic foot ulcer are generally poor. Limb ischemia, longer ulcer duration and the presence of multiple ulcers were adverse prognostic factors.

Triptans as Migraine Treatment During Pregnancy are not Major Teratogens

Findings of a study presented at the recently concluded American Headache Society (AHS) 2017 Scottsdale Headache Symposium in Phoenix, Arizona show that triptans are not major teratogens when administered for migraine treatment during pregnancy. The study further says that when compellingly needed during pregnancy, sumatriptan as the best studied triptan appears an acceptable treatment option.

New Policy Statement on the Social and Emotional Impact of Weight Stigma on Children and Teens

In a new jointly written policy statement "Stigma Experienced by Children and Adolescents with Obesity" published online November 20, 2017, the American Academy of Pediatrics (AAP) and The Obesity Society offer guidance for pediatricians and healthcare professionals to reduce weight stigmatization and discrimination, and to educate others about the negative consequences of such actions.

Cardiorespiratory Fitness may Reduce Risk of Coronary Heart Disease

A study published November 17, 2017 in the *Mayo Clinic Proceedings* has shown that moderate-to-high level of fitness can neutralize some of the adverse effects of a high triglyceride/high-density lipoprotein (TG:HDL) ratio on coronary heart disease mortality, compared

to men with low cardiorespiratory fitness. Measuring cardiorespiratory fitness level besides the traditional risk factors gives additional information about risk of heart disease.

Nearly 21 Million People Now have Access to HIV Treatment, Says UN

About 20.9 million people now have access to the antiretroviral therapy, according to a new UNAIDS report titled "Right to health" launched in South Africa on Tuesday. The report highlights that this remarkable progress has been made possible by people living with HIV demanding their rights, strong leadership and financial commitment. The new report highlights the gaps in having access to health, while also providing some innovative examples of AIDS response. One challenge is to ensure 17.1 million people, including 1.2 million children, have access to HIV treatment, especially in the countries where new HIV infections are rising. In that regard, the report points out that new HIV infections are rising at a rapid pace in countries that have not expanded health services to those most affected. Wherever the right to health is compromised, HIV spreads, says UNAIDS… (*UN, November 21, 2017*).

US FDA Approves First Two-drug Regimen for Certain Patients with HIV

The US Food and Drug Administration (FDA) has approved Juluca, the first complete treatment regimen containing only two drugs to treat certain adults with human immunodeficiency virus type 1 (HIV-1) instead of three or more drugs included in standard HIV treatment. Juluca is a fixed-dose tablet containing two previously approved drugs (dolutegravir and rilpivirine) to treat adults with HIV-1 infections whose virus is currently suppressed on a stable regimen for at least 6 months, with no history of treatment failure and no known substitutions associated with resistance to the individual components of Juluca.

Updated ACOG Guidelines on Hospital Disaster Preparedness for Obstetricians

In an updated Committee Opinion published November 21, 2017, the American College of Obstetricians and Gynecologists (ACOG) has said that planning and collaboration are essential when disaster happens. ACOG recommends hospitals develop specific strategies for managing issues that are likely to arise during an emergency, like stabilizing and transporting obstetric patients, managing surge capacity, limited resources, power outages, sheltering-in-place and incorporating regional facilities that do not provide maternity services.

Simplified Method Allows CGM Users to Leverage Trend Arrow Data

Experts from the Endocrine Society have developed a streamlined method for using the Dexcom G5 Mobile Continuous Glucose Monitor (CGM) to help individuals (adults, children and adolescents) with diabetes maintain better control of their glucose levels, according to two perspectives published November 20, 2017 in the *Journal of the Endocrine Society*.

Any Physical Activity in Elderly Better than None at All for Reducing Cardiovascular Risk

Any physical activity in the elderly is better than none at all for reducing cardiovascular risk, according to an 18-year study in more than 24 000 adults published November 22, 2017 in the *European Journal of Preventive Cardiology*. The hazard ratios for cardiovascular events were 0.86, 0.87, and 0.88 in moderately inactive, moderately active and active elderly participants, respectively, compared to inactive people.

AHA/ACC/HRS Guideline on Management of Ventricular Arrhythmias

A new guideline for treatment of patients with ventricular arrhythmias and the prevention of sudden cardiac death has been jointly released by the American Heart Association (AHA), American College of Cardiology (ACC), and Heart Rhythm Society (HRS). The guidelines are published online October 30, 2017 in *Circulation*. The guideline includes indications for implantable cardioverter defibrillators (ICDs) for the treatment of ventricular arrhythmias and prevention of sudden cardiac death. And, also provide guidance on the use of ICDs in patients with nonischemic cardiomyopathy.

Nearly Half of the World's Busiest Airports have Smoke-free Policies

Among the 50 busiest airports in the world, 23 have smoke-free indoor policies, which means that air travelers and employees at 46% of the world's busiest airports are protected from exposure to secondhand smoke, says a report published November 22, 2017 in *Morbidity and Mortality Weekly Report* (MMWR). While the other 27 busiest airports having no smoke-free policy allow smoking in designated or ventilated indoor areas.

Airports were defined as having a smoke-free policy if they completely prohibited smoking in all indoor areas. In North America, 78% (14 of 18) of the busiest airports have a smoke-free policy; in Europe, 44% (4 of 9); in Asia, 18% (4 of 22). All four of the Asian airports with a smoke-free policy are in China. This report is the Centers for Disease Control and Prevention's (CDC) first assessment of smoke-free policies in the world's airports. … (*CDC, November 22, 2017*).

First Implanted Lens that can be Adjusted After Cataract Surgery to Improve Vision Without Eyeglasses

The US Food and Drug Administration (FDA) has approved the RxSight Inc. Light Adjustable Lens and Light Delivery Device, the first medical device system that can make small adjustments to the artificial lens' power after cataract surgery so that the patient will have better vision when not using glasses. The RxSight IOL is made of a unique material that reacts to UV light, which is delivered by the Light Delivery Device, 17-21 days after surgery. Patients receive three or four light treatments over a period of 1-2 weeks, each lasting about 40-150 seconds, depending upon the amount of adjustment needed. The patient must wear special eyeglasses for UV protection from the time of the cataract surgery to the end of the light treatments to protect the new lens from UV light in the environment.

Special Journal Issue on Global Disparities in Management of Cardiovascular Disease

The November 2017 of the journal *Circulation: Cardiovascular Quality and Outcomes* is a special issue on global disparities in management of cardiovascular disease and emphasize the continued need for collaboration and the sharing of best practices. The issues focuses on the disparities in cardiovascular care found globally and carries studies that outline findings in multiple countries.

Shoulder Decompression Surgery Offers no Advantages Over Arthroscopy

A study published online November 20, 2017 in *The Lancet* has shown that while patients treated surgically had better outcomes for shoulder pain and function compared with no treatment, arthroscopic subacromial decompression surgery for subacromial shoulder pain does not reduce pain any more than arthroscopy alone.

High-intensity Exercise Improves Memory

Six weeks of intense exercise, short bouts of interval training over the course of 20 minutes was found to significantly improve high-interference memory in a study published in the *Journal of Cognitive Neuroscience*. Brain-derived neurotrophic factor (BDNF), a protein that supports the growth, function and survival of brain cells, was found to be increased in those who had greater fitness gains.

Acute Mountain Sickness is the Most Common Type of High-altitude Illness

An article published online November 14, 2017 in *JAMA* says that acute mountain sickness is the most common type of high-altitude illness. It is a clinical diagnosis based on typical symptoms based on history of traveling to high altitudes, but it can be more difficult to diagnose in children and people with baseline health problems. Symptoms of acute mountain sickness include headache, fatigue, poor appetite, nausea, vomiting, lightheadedness and sleep disturbances that develop 6-12 hours after ascent.

Despite Progress, 180 Million Children Face Bleaker Prospects Than Their Parents

Despite global progress, 1 in 12 children worldwide live in countries where their prospects today are worse than those of their parents, according to a UNICEF analysis conducted for World Children's Day falling on November 20, 2017. According to the analysis, 180 million children live in 37 countries where they are more likely to live in extreme poverty, be out of school, or be killed by violent death than children living in those countries were 20 years ago. The report also states that primary school enrollment has declined in 21 countries, including Syria and Tanzania, due to such factors as financial crises, rapid population growth and the impact of conflicts. Children in India report feeling the most empowered with 52% of children believing their voices are heard and can help their country and that their opinions can affect the future of their country… (*UNICEF, November 20, 2017*).

Higher Physical Activity Lowers Risk of Heart Disease

Each 4 metabolic equivalent of task hours per day higher occupational and nonoccupational physical activity (approximately 1 hour/day cycling or brisk walking) is associated with a 5-12% lower risk of developing cardiovascular diseases in adults without prior heart disease, according to a study reported November 8, 2017 in *JAMA Cardiology*.

Positive Power Doppler Signal in Joint USG Indicates Risk of Clinical Flare

Patients with juvenile idiopathic arthritis in clinical remission on medication with positive power Doppler signal in joint ultrasonography are at a higher risk of developing clinical flare, suggests a prospective study published online November 13, 2017 in *Pediatric Rheumatology*. Hence, such patients should be monitored during treatment.

Paternal Depression also Influences Mental Health of Children

New research published online November 15, 2017 in *The Lancet Psychiatry* shows that depression in father also adversely affects the mental health of their adolescent children. This association was independent of, and not different in magnitude to, the association between maternal and adolescent depressive symptoms.

ADA/EASD Statement on Improving Clinical Value and Use of CGM Devices

A Joint Statement of the European Association for the Study of Diabetes and the American Diabetes Association Diabetes Technology Working Group has published recommendations for systemic improvements in clinical use and regulatory (pre- and postmarketing) handling of continuous glucose monitoring (CGM) devices to improve their safety and efficacy in achieving its potential to improve quality-of-life and health outcomes for more people with diabetes in the December 2017 issue of *Diabetes Care*.

Oral Lacosamide Approved for Use in Children with Epilepsy

The US Food and Drug Administration (FDA) has approved use of the antiepileptic drug lacosamide (Vimpat, UCB) in tablets and oral solution (not intravenous injection) in children aged 4 years with partial-onset seizures.

With Access to Clean, Modern Energy, Poorer Countries Look to Power Ahead Through Innovation

Energy is key to global development, but the world's poorest and most vulnerable nations fare up to six times worse than their more industrialized counterparts when it comes to accessing the vital resource, according to the United Nations.

In its 2017 report on the world's 47 Least Developed Countries (LDCs), focused on Transformational Energy Access the United Nations Conference on Trade and Development (UNCTAD) said that only four of them were on course to achieve internationally agreed targets on energy distribution by 2030. While they have made great strides in recent years, achieving the global goal of universal access to energy by 2030, the finish line for achieving the UN Sustainable Development Goals (SDGs), will require a 350% increase in their annual rate of electrification, said UNCTAD. "Achieving Sustainable Development Goal 7 is not only a question of satisfying households' basic energy needs," UNCTAD Secretary-General Mukhisa Kituyi said in Geneva. "That in itself has valuable welfare implications, but we need to go beyond. For electrification to transform LDC economies, modern energy provision needs to spur productivity increases and unlock the production of more goods and services."… (*UN, November 22, 2017*).

ACC Roadmap for Innovation

In a new health policy statement published in the *Journal of the American College of Cardiology* online November 20, 2017, the American College of Cardiology (ACC) has identified how to best support healthcare advances in three arenas namely, digital health (wearable, smartphone and sensor-based technologies), big data (the aggregation of large quantities of structured and unstructured health information and sophisticated analyses with artificial intelligence, machine learning and natural language processing techniques) and precision health (approaches to identify individual-level risk and the determinants of wellness and pathogenicity).

Endovascular Repair of Abdominal Aortic Aneurysm is Cost-effective and also Improves Survival

At 3 years, compared with traditional open surgery, an endovascular repair of suspected ruptured abdominal aortic aneurysm was associated with a survival advantage, a gain in quality-adjusted life years (QALYs), similar levels of reintervention and reduced costs, and this strategy was cost-effective. These 3-year results of the IMPROVE trial were published online in the *BMJ* on November 14, 2017.

CAC Scores Predict Risk for Heart Diseases in Patients with Diabetes and Metabolic Syndrome

According to a study published online November 8, 2017 in *JAMA Cardiology*, coronary artery calcium (CAC) scores had significant long-term, more than 10 years, value in prognosticating cardiovascular disease in patients with metabolic syndrome and diabetes. A coronary artery calcium score of 0 was associated

with low risk of cardiovascular disease independent of diabetes duration, insulin use, or glycemic control.

New Guideline for the Endocrine Treatment of Gender-dysphoric/Gender-incongruent Persons

The Endocrine Society has published clinical practice guideline for the endocrine treatment of gender-dysphoric/gender-incongruent persons in the November 2017 issue of the *Journal of Clinical Endocrinology and Metabolism*. The guidelines recommend that only trained mental health professionals should diagnose gender dysphoria/gender incongruence in adults. Criteria for such mental health professionals have also been outlined in the guideline.

Peripheral Blood Eosinophilia Identifies Patients at Risk for Worse Clinical Outcomes

Peripheral blood eosinophilia may be a biomarker for a group of patients with inflammatory bowel disease (IBD), with a unique inflammatory signature and at risk for worse clinical outcomes, according to a study published November 7, 2017 in the *American Journal of Gastroenterology*.

PM Reviews Steps Taken to Reduce Under-nutrition

The Prime Minister, Shri Narendra Modi, on Friday, 24th November 2017 reviewed the progress and efforts being made to prevent and reduce under-nutrition and related problems in India. The high level review meeting was attended by officials from PMO, NITI Aayog and other Ministries. The current status of malnutrition, stunting and related problems was reviewed. Successful nutrition initiatives in some other developing countries came up for discussion. The Prime Minister stressed on the need to work towards concrete objectives to reduce stunting, under-nutrition, low birth weight, and anemia. He emphasized that visible and measurable results should be seen by 2022, the 75th anniversary of independence. Towards this end, real-time monitoring towards progress of nutrition outcomes was discussed, especially in the worst performing districts… (*Press Information Bureau, Prime Minister's Office, November 25, 2017*)

Different Alcoholic Beverages Elicit Different Emotions, Says Study

According to a study published online November 21, 2017 in *BMJ Open*, different alcoholic beverages elicit different emotions, with spirits more frequently eliciting emotional changes of all types. Overall 29.8% of respondents reported feeling aggressive when drinking spirits, compared with only 7.1% when drinking red wine.

People Willing to Trade Treatment Efficacy for Reduced Side Effects in Cancer Therapies

When choosing their preferred treatment, people with chronic lymphocytic leukemia (CLL) place the highest value on medicines that deliver the longest progression-free survival, but are willing to swap some drug efficacy for a reduced risk of serious adverse events, according to a study published November 21, 2017 online in the journal *Blood Advances*.

Study Finds Many Cancers can be Prevented

An estimated 42% of all cancer cases and nearly one-half of all cancer deaths in the United States in 2014 were attributable to evaluated risk factors. Many of these cancers could have been mitigated by effective preventive strategies. Cigarette smoking had the most common association with cancer cases and deaths than any other single risk factor (20% of all cancer cases and 30% of all cancer deaths) followed by excess body weight. These findings were published online November 21 in CA: *A Cancer Journal for Clinicians*.

Intravitreous Dexamethasone does not Improve Vision in Persistent Diabetic Macular Edema

In patients with persistent diabetic macular edema, the addition of intravitreous dexamethasone to continued ranibizumab therapy reduces retinal thickness but does not improve visual acuity more than continued ranibizumab therapy alone, according to a study published online November 11, 2017 in *JAMA Ophthalmology*.

Study Links Celiac Disease to Several Medical Conditions

Findings of a study of more than 35 million people presented October 17, 2017 at the World Congress of Gastroenterology 2017 in Orlando, Florida show an association of Celiac disease with a wide range of medical conditions like liver disease, glossitis, pancreatitis, Down syndrome and autism, including other autoimmune disorders, such as type 1 diabetes, Crohn's disease and ulcerative colitis.

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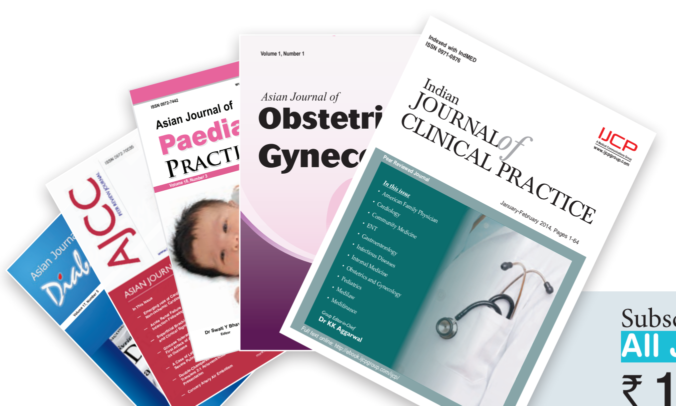

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INSPIRATIONAL STORY

The 12 Gifts of Birth

Once upon a time, a long time ago, when princes and princesses lived in faraway kingdoms, royal children were given 12 special gifts when they were born. Twelve wise women of the kingdom, or fairy godmothers as they were often called, traveled swiftly to the castle whenever a new prince or princess came into the world. Each fairy godmother pronounced a noble gift upon the royal baby.

As time went on, the wise women came to understand that the 12 royal gifts of birth belong to every child, born anywhere at any time. They yearned to proclaim the gifts to all children, but the customs of the land did not allow that. One day when the wise women gathered together they made this prophecy: Someday, all the children of the world will learn the truth about their noble inheritance…when that happens a miracle will unfold on the Kingdom of Earth.

Here is the secret they want you to know.

At the wondrous moment you were born, as you took your first breath, a great celebration was held in the heavens and 12 magnificent gifts were granted to you.

1. Strength is the first gift. May you remember to call upon it whenever you need it.
2. Beauty is the second gift. May your deeds reflect its depth.
3. Courage is the third gift. May you speak and act with confidence and use courage to follow your own path.
4. Compassion is the fourth gift. May you be gentle with yourself and others. May you forgive those who hurt you and yourself when you make mistakes.
5. Hope is the fifth gift. Through each passage and season, may you trust the goodness of life.
6. Joy is the sixth gift. May it keep your heart open and filled with light.
7. Talent is the seventh gift. May you discover your own special abilities and contribute them toward a better world.
8. Imagination is the eighth gift. May it nourish your visions and dreams.
9. Reverence is the ninth gift. May you appreciate the wonder that you are and the miracle of all creation.
10. Wisdom is the tenth gift. Guiding your way, wisdom will lead you through knowledge to understanding. May you hear its soft voice.
11. Love is the eleventh gift. It will grow each time you give it away.
12. Faith is the twelfth gift. May you believe.

Now you know about your 12 gifts of birth. But there is more to the secret that the wise women knew. Use your gifts well and you will discover others, among them a gift that is uniquely you. See these noble gifts in other people.

■■■■

Lighter Side of Medicine

HUMOR

WILL I LIVE LONGER?

Patient: Doctor, if I give up wine, women and song, will I live longer?

Doctor: Not really, it will just seem longer.

SALESMAN TO POLICEMAN

A salesman, tired of his job, gave it up to become a policeman.

Several months later, a friend asked him how he liked his new role.

"Well," he replied, "the pay is good and the hours aren't bad, but what I like best is that the customer is always wrong."

YOU DON'T HAVE THE HICCUPS

A man goes into a drug store and asks the pharmacist if he can give him something for the hiccups. The pharmacist promptly reaches out and slaps the man's face.

"What the heck did you do that for!?!" the man screams. "Well, you don't have the hiccups anymore do you?"

The man says, "No I don't, you IDIOT... But my wife out in the car still does!"

BANK NAME

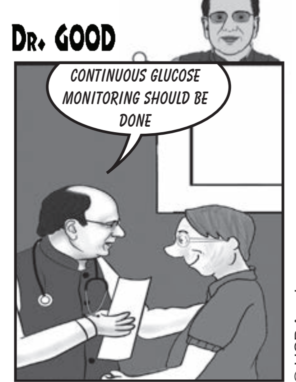
Mother decided that 10-year-old Cathy should get something 'practical' for her birthday. "Suppose we open a savings account for you?" mother suggested. Cathy was delighted. "It's your account, darling," mother said as they arrived at the bank, "so you fill out the application." Cathy was doing fine until she came to the space for 'Name of your former bank.' After a slight hesitation, she put down 'Piggy.'

WHAT'S FOR DINNER?

I have my changed my system for labeling home-made freezer meals. I used to carefully note in large clear letters, "Meatloaf" or "Pot Roast" or "Steak and Vegetables or "Chicken and Dumplings" or "Beef Pot Pie." However, I used to get frustrated when I asked my husband what he wanted for dinner because he never asked for any of those things. So, I decided to stock the freezer with what he really likes. If you look in my freezer now you'll see a whole new set of labels. You'll find dinners with neat little tags that say: "Whatever," "Anything," "I Don't Know," "I Don't Care," "Something Good," or "Food." My frustration is now reduced because no matter what my husband replies when I ask him what he wants for dinner, I know that it is there waiting.

Dr. Good and Dr. Bad

SITUATION: A type 2 diabetic male aged 49 years also developed CV autonomic neuropathy.



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LESSON: The researchers have emphasized that monitoring glucose patterns over 24-hour and not only relying on HbA1c as therapeutic target is important in patients with T2DM and CV autonomic neuropathy.

J Diabetes Complications. 2017;31(9):1389-93.

Indian
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Books

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

Articles in Books

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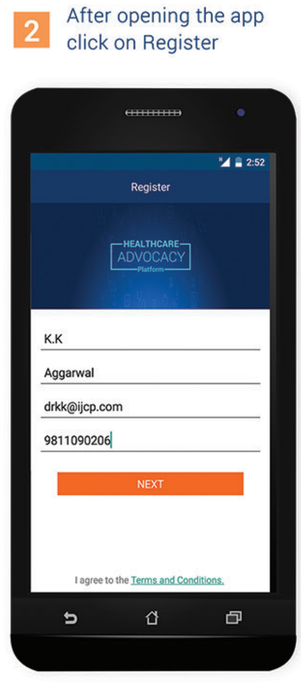

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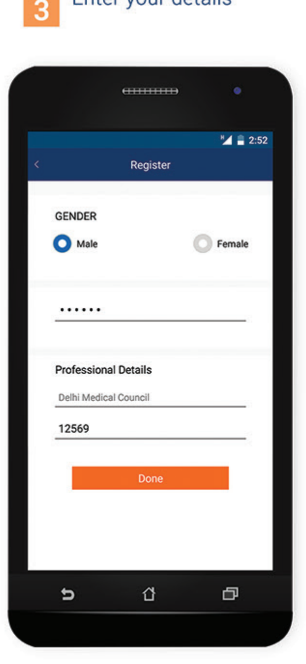

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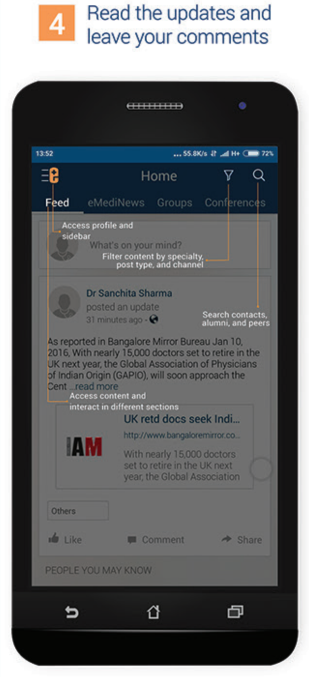

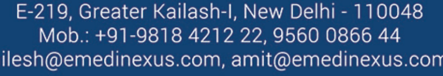

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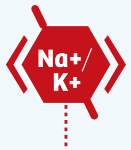

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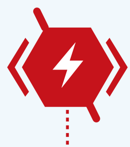

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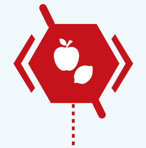

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1. Burke ER. Optimal Muscle Performance and Recovery: Using the Revolutionary R4 System to Repair and Replenish Muscles for Peak Performance. 2nd edition (revised and expanded). New York, NY: Avery (a member of Penguin Putnam Inc.); 2003; 2. Rastegar A. Serum Potassium. In: Walker HK, Hall WD, Hurst JW, editors. Clinical Methods: The History, Physical, and Laboratory Examinations. 3rd edition. Boston: Butterworths; 1990. Chapter 195; 3. Jéquier E. Carbohydrates as a source of energy. Am J Clin Nutr.1994 Mar;59(3 Suppl):682S-685S; 4. Data on file.

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