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Editorial

Inequality and Disease

Prof. (Dr.) Jyotirmoy Pal
MD, FRCP, FRCP, FICP, FACP,
WHO Fellow, Hony. Editor, JIMA

দেখ ভালো জনে রইল ভাঙা ঘরে,
মন্দ যে সে সিংহাসনে চড়ে।
ও ভাই সোনার ফসল ফলায় যে তার
দুই বেলা জোটেনা আহার,.....
হীরার খনির মজুর হয়ে কানাকড়ি নাই,.....

(a good person live in a shattered home)
(while the cruel one occupies the throne)
(those who cultivate golden crops)
(do not get meal twice a day)....
(labour of Diamond mine deprived of money)...

— Satyajit Roy
(Hirak Rajar Deshe-1980)

Evolution of Social Inequality :

Our early ancestors lived in small groups and worked actively to preserve social equality. However, as they created larger societies, inequality rose, Feudalism system evolved and Mankind started being divided into powerful and powerless fractions. Initially in human history, power was equivalent to muscle power only. But as a man talented creation of nature, started using his intellect, wisdom, manipulative power to dominate on each other. Thus, from pre-historic periods of time, socioeconomic inequality has evolved. 'Chanakya'- the Great Indian economist tried to reduce this inequality in the Ancient Indian society. King Ashoka in 3rd BC also tried to establish 'Socialized Monarchy'. Same tradition also continued in Gupta, Kushan dynasty. In Europe, Greece which is known as the birthplace of democracy and concept of socialism was touted for social inequality and sanctioned slavery. This became widened in next few thousand years and the tradition continued during Roman period. Slaves were considered as property. With the fall of Justinian Empire, Dark Age in Europe started. Human dignity and human rights were quashed by dynasties across world. But people did not react much, as they accepted it as their natural fate. Also fear from powerful administrators (Rajtantra), played a prohibiting role to react against feudalism. Slavery became rampant in Europe in medieval period.

''চিরকালই মানুষের সভ্যতায় একদল অখ্যাত লোক থাকে, তাদেরই সংখ্যা বেশি তারাই বাহন; তাদের মানুষ হবার সময় নেই; দেশের সম্পদের উচ্ছিষ্টে তারা পালিত। সব চেয়ে কম খেয়ে, কম পরে, কম শিখে, বাকি সকলের পরিচর্যা করে; সকলের চেয়ে বেশি তাদের পরিশ্রম, সকলের চেয়ে বেশি তাদের অসম্মান। কথায় কথায় তারা রোগে মরে, উপোসে মরে, উপরওয়ালাদের লাথি ঝাঁটা খেয়ে মরে-জীবনযাত্রার জন্য যত-কিছু সুযোগ সুবিধে সব-কিছুর থেকেই তারা বঞ্চিত। তারা সভ্যতার পিলসুজ, মাথায় প্রদীপ নিয়ে দাঁড়িয়ে থাকে - উপরের বাই আলো পায়, তাদের গা দিয়ে তেল গড়িয়ে পড়ে''।

There have always been one group of unseen people in society, their number is always greater, they are the carriers; they have no time to evolve as humans; they live off what their country throws away. They eat the least, they have the least to call their own, they learn less than all the others and they look after the rest; their labour is the greatest as is their misfortune. They die of disease at the slightest excuse, or of starvation and their mistreatment at the hands of those who are above them – they are deprived of every kind of comfort one needs in life. They are the stands upon which the lamp of civilization is placed, standing straight with the flame held above them – they ensure that everyone above receives light while they are covered in the drips of oil.'

— Rabindranath Tagore
(Letter from Russia)

French Revolution :

First organized protest and reform happened in French Revolution, although it was preceded by many such smaller and unorganized revolts. Underlying cause of French Revolution was failure of Ancient Regime to respond to increasing social and economic inequality, high food prices, unemployment and population explosion.

Industrial Revolution in Britain :

This time Industrial Evolution started from Great Britain. Economic activity – production, commerce, trading took the driving force in formulating social and political policies. Temptation of more and more profit made few people richer and few poorer. Usually labourers were deprived. The Industrial Revolution had a big impact on the inequality between people and countries, giving the new parameters of what is a rich or a poor country. To keep the factories, machines and workers in a good state the countries needed primary material so one of the industrialized countries, England had an idea, to extract these primary materials from the non-developed countries (colonies) and then other industrialized countries like Japan, the United States and Russia did the same strategy as England, they used the poor countries to their own benefit, and the imperialism began at this point: this was the practice extending the power of powerful countries in the poor ones, controlling the economy, production and politics, making the wealthy nations more wealthy and the poor nations poorer, creating more inequality between the social classes. So European countries engaged themselves in eshtablishing colonies (Africa, Asia, Latin America) to procure raw material for their industries at lowest possible rates and to sell their products at highest possible rates.

Protest and Revolution Against Oppression :

Much oppression was inflicted by the indigo planters on the farmers in India, which was a British colony at that time. It was supported by Zaminders of Bengal. In 1833, East India Company, the rular at that time, made an act that gave more free hand to Planters. Revolt started against oppression – "***Nilbidroha"*** Dinabandhu Mitra depicted the situation in his famous book '***Nildarpan' .*** On the other side Africa was used as exporter of Slaves to industrial Countries. But ***"Every action has its equal and opposite Reaction"***. In Europe Karl Marx and Engles came as savior of oppressed people. He stated "***Man is born free, and he is everywhere in chains***".

"When certain classes controlled the means of production, they used that power to exploit the labour for social inequality."

Just days before the outbreak of the revolutions of 1848, Marx and Engels wrote, ***"The distinguishing feature of Communism is not the abolition of property generally, but the abolition of bourgeois property".***

In the 20th century — particularly after the Russian Revolution of 1917 and the formation of the Soviet Union — social democracy and communism emerged as the two most dominant socialist movements throughout the world.

''তখনই ধরা পড়ত, দেশের ধন এত কিছু বেশি নয় যাতে সকলেরই ভাতকাপড় যথেষ্ট পরিমাণে জোটে। এখানে ভেদ নেই বলেই ধনের চেহারা গেছে ঘুচে, দৈন্যেরও কুশ্রীতা নেই, আছে অকিঞ্চনতা। দেশ - জোড়া এই অধন আর কোথাও দেখি নে বলেই প্রথমেই এই আমাদের খুব চোখে পড়ে। অন্য দেশে যাদের আমরা জনসাধারণ বলি, এখানে তারাই একমাত্র''।

— Rabindranath Tagore in his voyage to Russia

'Even if the country's entire wealth could be shared among everyone, it would not have been enough for everybody's living. As there is no inequality in this the flash of wealth is absent..so is the ugliness of poverty..but demand still prevails. As nowhere in the entire world such equality exists, this gets noticed first in this country. Unlike other countries, the common man is the only class of people who exists in this country.'

— Rabindranath Tagore (Letter from Russia)

Colonial India experienced huge advancement in Trading, infrastructure, production, westernized education system compared to Moghul dynasty. But everything was aimed for increasing Profit of east India Company or British empire. India experienced Famines, epidemics, deaths, Poverty. At the same time, there was emergence of educated Middle class. One section was Torchbearer of British ideology, whereas other Section started raising voice against social and economic disparities . Such sentiment gave birth to Indian National Congress at 28th Dec 1885 , a milestone in Indian History. Indian leadership realized without political freedom such inequality can not be removed . India under leadership of Father of Nation M K Gandhi started fight for '***Purna Swaraj'***.

Nehru realized Independent India should be synonymous to healthy India. Hardly 10 percent people were under cover of modern treatment facility. Millions of people died during epidemics. British raj was engaged only to save their own army and officials. On the other hand, The British passed Epidemic act 1894, that was discriminatory and did not consider the Indian

sentiment and applied ruthlessly culminating several riots in different parts of India. So reform was a urgent need of the Country. Fortunately before leaving, British Government set up a commission headed by Sir Joseph Bhore, membered by Dr B C roy in 1943 whose recommendation made a foundation stone in Independent India.

"No individual would fail to secure adequate care because of inability to pay."

— Bhore Committee, 1943

Inequality in Modern Terms :

Social inequality refers to disparities in the distribution of economic assets and income as well as between the overall quality and luxury of each person's existence within a society, while economic inequality is caused by the unequal accumulation of wealth.

According to the United Nations Human Development Report 2004, the gross domestic per capita (GDP) in countries with high, medium and low human development was 24,806, 4,269 and 1,184 PPP$, respectively (PPP$ = purchasing power parity measured in United States dollars).The wealthiest people in the world, which comprises, 1.8% of the global population, own 86.4% of the overall wealth.

Globalization and Social Inequality :

"Inequality is increasing in this wave of globalization"

— Nobel Laureate Eric Maskin

Globalisation increases inequality of income and wealth. changes in the workforce and in earnings between different groups are consequence of globalisation. One paradox of globalisation is that it has reduced inequality between countries but increased it within nations. Higher demand leads to higher wages for high skilled workers, but can also mean lower wages for low skilled workers.

Effect of Poverty and Inequality :

1. **Hunger :** Countries without the proper amount of food to survive.

2. **Mental state :** This is where people or the country as a whole are feeling powerless, ashamed, or humiliated. This is connected to the fact that they must rely or ask other countries for help and are unable to survive on their own.

3. **Poor groundwork :** Lack of roads, clean water, transportation, etc. meaning that they do not have a stable foundation in order to provide these things.

4. **Education :** People do not have access to proper education or any education at all.

5. **Health :** Countries are unable to provide the proper health care that many people need in order to survive.

6. **Lack of income:** People within a poor country tend to put income aside and focus on their family, physical, and environmental assets.

Introduction: What is the 10/90 Gap ?

In universe 90 percent weath enjoyed by 10 percent population. 90 percent global healthcare devoted for 10 percent people. 90 percent resource have been utilized for 10 percent diseases, those are diseases of developed country. – the so-called **'10/90 Gap'**. Virtually all diseases prevalent in low income countries particularly tropical countries are 'neglected'by physicians, government and also by the pharmaceutical industry which invests almost nothing in research and development (R&D)for these diseases. Patrick Trouiller, for example, has pointed out that of the 1,393 total new drugs approved between 1975 and 1999, only 1 per cent (13 drugs) were specifically indicated for a tropical disease.5 Research conducted by the DND Working Group and the Harvard School of Public Health in 2001 revealed that of the 20 global pharmaceutical companies surveyed, only two had research projects underway for the 'neglected' diseases of Chagas and leishmaniasis.

Neglected Diseases :

World community gave less attention towards finding effective cures and treatments for tropical infectious diseases such as leishmaniasis, lymphatic filariasis, Chagas' disease, leprosy, Guinea worm, onchocerciasis and schistosomiasis. These so-called 'neglected' diseases predominantly affected poor populations in low income countries. According to the 2002 World Health Organisation's (WHO) World Health Report, tropical diseases accounted for only 0.5 per cent of deaths in high-mortality poor countries, and only 0.3 per cent of deaths in low mortality poor countries. This figure may not be true in the sense most of the time these diseases are not reported , having lack of infrastructure to diagnose or lack of awareness among doctors who do not feel proud to be

a physician of neglected diseases. Also we teachers are reluctant to teach these diseases or feel glamorous on talking on non-communicable disease like Diabetes or Hypertension in Conferences or in lecture classes.

Most Disease in Lower-income Countries is Caused by Poverty :

A large proportion of illnesses in low-income countries are entirely avoidable or treatable with existing medicines or interventions. Most of the disease burden in low-income countries finds its roots in the consequences of poverty, such as poor nutrition, indoor air pollution and lack of access to proper sanitation and health education. The WHO estimates that diseases associated with poverty account for 45 per cent of the disease burden in the poorest countries. However, nearly all of these deaths are either treatable with existing medicines or preventable in the first place. Tuberculosis, malaria and HIV/AIDS, for example, together account for nearly 18 per cent of the disease burden in the poorest countries. Education can also play an important role in reducing the incidence of insect-borne diseases, for example by encouraging people to remove sources of stagnant water (insect breeding sites) from near their dwellings. Tuberculosis can be prevented by improving nutrition, and can be treated with DOTS therapy. Education is vital for the prevention of HIV/AIDS. Diarrhoeal diseases are caused by the poor sanitation inherent to the condition of poverty, yet are easily and cheaply treatable through oral rehydration therapy. However, diarrhoeal diseases still claim 1.8 million lives each year. Respiratory infections caused by burning biomass fuels in poorly ventilated areas also place a considerable health burden on poor people. According to the WHO, exposure to biomass smoke increases the risk of acute lower respiratory infections (ALRI) in childhood, particularly pneumonia. Globally, ALRI represent the single most important cause of death in children under 5 years and account for at least two million deaths annually in this age group. Malnutrition particularly affects people in poor countries. As a result of vitamin A deficiency, for example, 500,000 children become blind each year, despite the fact that such outcomes can be avoided by cheap, easy-to-administer food supplements.

Poverty-related diseases cause far higher levels of mortality in low-income than high-income countries. Most of these diseases and deaths can be prevented with pre-existing treatments and prevention programmes. It is estimated that 88 per cent of child diarrhoeas, 91per cent of malaria and up to 100 per cent of childhood illness, such as measles and tetanus, can be prevented among children using existing treatments. This means that up to 3 million child lives could be saved each year if these medicines could be distributed effectively to all areas of need.

Deaths caused by poverty-related diseases :

% of deaths caused by/in	High mortality low-income countries	Low mortality low-income countries	High-income countries
Infectious and parasitic diseases	34.1	24.8	2.1
Respiratory infections	9.9	8.0	3.7
Perinatal and maternal conditions	8.4	6.8	0.4
Nutritional deficiencies	1.3	1.1	0.0
Tropical diseases	0.5	0.3	0.0
Total 'poverty-related' diseases	54.1	40.7	6.2

Deaths caused by developed-country diseases :

% of deaths caused by/in	High mortality developing countries	Low mortality developing countries	developed countries
Malignant neoplasms (cancers)	6.3	9.9	21.2
Diabetes	0.6	1.5	1.7
Neuropsychiatric disorders	1.3	1.4	2.9
Cardiovascular diseases	18.9	23.4	47.8
Respiratory diseases (asthma)	4.0	6.7	5.0
Digesive diseases	2.7	3.4	3.7
Total 'developed-countries diseases	33.8	46.4	82.3

Access is the Real Problem :

Even if treatment exists there are challenges in access of preventive and curative medicines in third world countries. According to the WHO, an estimated 30 per cent of the world population lacks regular access to existing drugs, with this figure rising to over 50 per cent in the poorest parts of Africa and Asia.

The Impact of failure of this public health policy on profound in mortality. Only one-half (approximately) of sub-Saharan African children are vaccinated against childhood diseases, and in some areas that number is as low as 10%.

In British India People suffered from discrimination. Modern hospital and treatment facilities established to serve British people and to prevent spread from India to UK. Hardly 10 percent Indian people had access to modern Medicine.

"In this unfortunate country we have never had public health services in the sense in which they are understood in the West. We have a few hospitals and dispensaries , hardly one for a taluka, considering the vastness of the population. We have no facilities for the curative and preventive side of disease. ..... No country in the world is medically so badly served as India because the Government never considered the health of the people as its first and foremost concern and its national wealth, as much as it considers law and order and the police and the military to be."

— JIMA, April, 1946

The first Prime Minister of independent India Pandit Nehru realized the need for improved healthcare for the building of New India. Even before Independence in his report in 1928 public health was viewed as a constitutional right.. He did not forget to put health as an important determinant in democratic India and role was clearly mentioned in Constitution placed in Indian Parliament By Dr B R Ambedkar. Article 39(E) of the Indian Constitution contains an important provision related to public health: Article 47 places a duty on the state to raise the nutrition levels and standard of living of people of India, consider public health as a primary right for worker's health, women, and children.

Intellectual Property Rights :

Much debate on this issue of access has centred around the claim that patents held by pharmaceutical companies are a significant contributor to the dire health outcomes experienced by people in the poorest parts of the world. This law was needed indeed to meet cost of research , but at the same way Poorer people was deprived from benefit of new generation medicine. Controversy on-going in distribution of COVID vaccine to poorer countries. Financers are reluctant to waive property right with call of WHO.

Questionable Political Priorities :

The governments of low- and middle-income countries often choose to spend their scarce resources on projects and priorities that do not coincide with the basic needs and demands of their populations. Many governments, for example, choose to spend more on their militaries than they do on healthcare.

Wealth Creation as a Means to Improve Health :

Medicines also fail to reach the poor because of weak healthcare infrastructures, which are inherently the result of financial and human resource constraints.. Poverty often goes hand-in-hand with malnutrition, which again results in a host of debilitating but easily preventable diseases. Poor sanitation, a byproduct of poverty, results in a large number of deaths from diarrhoeal diseases. When poverty is reduced and eliminated, health outcomes improve. People in rich countries can expect to live longer and have better access to medical care. With greater wealth, scientists and innovators, both private and public, have better opportunities to conduct research into health and disease. With increased financial resources, more can be spent on education and to improve literacy, which in turn can promote the adoption of new technologies and ensure that these technologies are more widely diffused. Improvements in agricultural technology, for example, have led to increased food production per capita and lower food prices, even at a time when the global population has risen dramatically. When combined with more open markets and trade, these productivity increases have ensured that food has become more available to the poor. As new technologies are adopted more widely, economic growth accelerates. This in turn provides individuals and the state with the means to improve basic infrastructure, such as the provision of clean water, which in turn improves health. Health and wealth can also be mutually reinforcing: a healthier population is better able to engage in economic activities and thereby generate increased income, some of which can be spent on health. In Mymensingh (Bangladesh), for example, agricultural yields increased by 15 per cent after malaria was controlled, because farmers had more time and energy for cultivation. However, it is unlikely that good health will ever be sustained without long-term wealth creation that can pay for the ongoing improvements in water, sanitation, hospitals and medical research. Those who genuinely hope to improve the health of the world's poorest people should therefore look to wealth creation as the fundamental solution to global health problems.

"There is empirical evidence that living in unequal societies with some people being much worse off, economically and socially, tends to produce deprivations in the absolute quality of life that people enjoy."

— Amartya Sen

As the gap between rich and poor increases society gradually become more and more unhealthier. In one

hand increase in Neglected diseases other hand unusal labish life of a section of society lead to increase in lifestyle associated diseases. If fire sets in ground floor, you can not stay safe in upper floor.

India's Vision on Socialism and Healthcare :

In the 1930s, when the British ruled the country, Jawaharlal Nehru described India's situation as follows: ***"A servile state, with its splendid strength caged up, hardly daring to breathe freely, governed by strangers from afar; her people poor beyond compare; shortlived and incapable of resisting disease and epidemic; illiteracy rampant; vast areas devoid of all sanitary or medical provision; unemployment on a prodigious scale, both among the middle classes and the masses."*** On being sworn in as the first Prime Minister of independent India in 1947, Nehru called for ***"the ending of poverty and ignorance and disease and inequality of opportunity."*** Mahatma Gandhi had always insisted that India would become truly independent only when the poorest of its people would be free from human suffering. As policy Democratic Govt adopted five year plan . Initial two plan was intended towards agriculture and industrial development. As healthcare policy Govt accepted Bhore committee report and given due stress on Public health Programme to eliminate preventable diseases . Importance was also in setting up Health units /hospitals across India and universal access of healthcare free of cost .

India had poverty, poor health infrastructure legacy of 200 yrs British Raj, suffered setback from partition , population migration, famine . But Indian Leadership was kin to alleviate poverty with sincerity and sympathy.

Nehru was excited with release of **Satyajit Ray's Pather Panchali in 1955** and its compassionate portrayal of countryside poverty in India. When Nehru Nehru was moved by the film and ensured that Pather Panchali was entered in the Cannes Films festival, 1956, many critics began to denounce Ray's debut film for selling Indian poverty abroad, it was Nehru who declared that ***'if a filmmaker shows poverty with such empathy, I am all for it'.***

In seventies Prime Minister Indira Gandhi realized Poverty elimination is greatest challenge in Independent India. Wheather it is disease, pollution or population overgrowth core issue is poverty . Indira Gandhi stated at Stockholm at the launch of the NCEPC (National Committee for Environmental Planning and Coordination).

"Among all pollutants Poverty is Greatest Polluter"

— Mrs Indira Gandhi

India having strong belief in social justice and equality gave due importance in alleviating poverty. Removal of Jamindari system, land reform, Panchayeti Raj (empowerment of rural people in rural development through Democracy), midday meal programme, public distribution system, Food sequirity bill, Kanyasree etc were aimimg for restructuring social discrepencies . Ambitious India adopted plan for Universal Health Coverage by 2020.

In reality after more than seven decades of Independence, health expenditure lags far below expectation, still people are dying of starvation, more than 1000 deaths/day due to preventable diseases like Diarrhoea and Tuberculosis , a vicious cycle of poverty and ill health. Question is where lies the mistake ? Mistake in thought process of Policy makers or in Implemention ?

"Only Swasth Bharat can be a Samriddha Bharat. India cannot realize its demographic dividend without its citizens being healthy," said Mr Arun Jaitley, the Union Finance Minister while announcing the budget for 2018-19.

In 2020 need a great introspection from all stakeholders starting from Politicians, buracrates , Physicians, Medical Organizations why universal health coverage still a Gold stone bowl.

Inequality in Distribution of Health Care Provider :

The health care system in India is universal. That being said, there is great discrepancy in the quality and coverage of medical treatment in India. Healthcare between states and rural and urban areas can be vastly different. Rural areas often suffer from physician shortages, and disparities between states mean that residents of the poorest states,, often have less access to adequate healthcare than residents of relatively more affluent states. Till now rural people in many parts of India dependent on Quacks , magics and on unskilled 'die ma' for delivery. There is reluctancy on our part to provide services at Rural areas or failure on part of Government to provide minimum basic infrastructures and working environment for doctors in rural areas. India has only 0.7 physicians per 1000 persons and 1.8 nurses/ midwives per 1000 persons against the recommended norms of 1:1000 and 4:1000, respectively. Furthermore,

the distribution of health resources is rather skewed with a shortage of doctors, especially specialists in rural areas despite several governmental measures to retain doctors in rural settings. The unmet need of qualified health personnel is covered by unlicensed practitioners devoid of any medical qualifications. So inequality in distribution of health care provided made rural and poorer people more vulnerable.

Possible Inequlities in Covid 19 Vaccine Distribution :

Economic impact of the coronavirus likely to be devastating. There will be cut in development budget , more seriously in Poorer Countries, likely to push another half a billion people into poverty and exacerbate the global divide.

Poor countries fall behind race to ensure COVID 19 vaccine for their population. Rich countries are rapidly claiming the world's lion's share of future doses of COVID-19 vaccine, creating deep inequalities in global distribution.

Richard Mihigo of the World Health Organization said it's time "to make a strong appeal" for equitable access, calling it a "real problem" as some countries have ordered far more doses than needed. Intellectual Property right of some of the Pharmaceuticals may be a problem in access in cheaper cost by Poorer countries.

Despite an international agreement to allocate the vaccine equitably around the world, billions of people in poor and middle-income countries might not be immunized until 2023 or even 2024, researchers at Duke University predict. Again Challenge in poorer countries are Vaccine storage and distribution, having lack of infrastructure.

Saudi Finance Minister Mohammed al-Jadaan emphasised in meeting of G20 nations that ***"if we leave any country behind, we will be behind".***

French President Emmanuel Macron called on G20 leaders to ***"go further and faster in supporting poorer nations by donating doses, forging industrial partnerships and even sharing intellectual property"***

But ***"An ambitious effort to create a global system of vaccine equity is being undermined is a handful of countries — including those who made a commitment to equality secure as many doses as they possibly can,"***

— Elina Urli Hodges, MSPH

Dream for a New Horizon :

"ধনের ধর্ম অসাম্য"

(Wealth Create Inequality)

— Rabindranath Tagore

From the birth of civilization there is onging struggle between have and have not. Smaller, powerful section enjoyed more , oppressed larger society . Inequal distribution made the society uglier. 'Hirak Rajar Deshe' a great movie by great filmmaker Satyajit Roy was a satire against feudalism. Representative of Feudalism King Hirak raj had belief

এরা যতো বেশি পরে, ততো বেশি জানে, ততো কম মানে।
(The more they study, the more they know, the lesser they follow orders).

অনাহারে নাহি খেদ, বেশি খেলে বাড়ে মেদ।
(No harm in eating less, more food only increases flesh).

ভরপেট নাও খাই, রাজ কর দেওয়া চাই।
(Even if you don't eat food, you must pay tax)

But at end 'Ray' a strong believer of socialism dreamed end of feudalism by revolt of farmers and laborers.

"দড়ি ধরে মারো টান/রাজা হবে খান খান"

"(Pull with string / king will be demolished)"

But this dream should not be restricted in Movie or in literature.

More than 70 years have passed since independence, still the virus is alive in our society.

"How long shall we continue to live this life of contradictions? How long shall we continue to deny equality in our social and economic life? .....We must remove this contradiction at the earliest possible moment or else those who suffer from inequality will blow up the structure of political democracy"

— Dr B R Ahmedkar

We have a long walk to kill the '***dreaded virus of Mankind – Social inequality. Waiting for sunrise, waiting for discovery of Social Vaccine.'***

"চলে যাব - তবু আজ যতক্ষণ দেহে আছে প্রাণ
প্রাণপণে পৃথিবীর সরাব জঞ্জাল
এ বিশ্বকে এ-শিশুর বাসযোগ্য করে যাব আমি-
নবজাতকের কাছে এ আমার দৃঢ় অঙ্গীকার।"

**"till I am alive
remove garbage from world
will make this world comfortable to a child
Promise to a new born"**

— Poet Sukanta Bhattacharya

Review Article

Tetanus : An update on Management

Mukesh Bairwa[1], Ravi Kant[2]

Tetanus is endemic in developing countries. There is no definitive diagnostic test available for this only depends the clinical progression of disease and classical symptoms. Common clinical features includes intense muscles spasm, rigidity, and autonomic instability.The mortality depends on delay in diagnosis and other comorbidities of the patients. Prevention of disease by dressing of wound and debridement, early initiation of antibiotics and early diagnosis of the disease are the key for the survival of patient. The principal of management are the control of muscles spasm, dysautonomia, and administration of human anti tetanus immunoglobulins and ventilatory support and prevention of secondary infections. It is ethically incorrect to do and randomization studies on tetanus for the treatment options when there are already some evidence based treatment exist but this review will the best for the physician to treat a patient, based on available evidence. [*J Indian Med Assoc* 2020; **118(12):** 18-23]

Key words **: Tetanus, Rigidity, Dysautonomia, Magnesium Sulphate, Trismus.**

Tetanus is a disease that is affects the central nervous system and muscles, leads to intense muscle spasms, it's caused by the anaerobic spore forming bacteria known as Clostridium*tetani*, that is produces a toxin and commonly found in the dirty soil, saliva, dust. The clinical features of tetanus and it association with soil was well known is past. The term "lockjawor trismus (spasm of jaw muscles) is the one of the hallmark features of tetanus. Accidental tetanus are more common in underdeveloped and developing countries. The mortality rate of accidental tetanus depends on multiple factors including the age of the patients, severity of disease, types of wound, associated with involvement of other organs such respiratory and renal failure and the treatment facility availability.[1]

Tetanus is a vaccine preventable disease less common in the developed countries then under-developed world, the disease is founds in the all unvaccinated population, particularly in developing countries. The only proper treatment of traumatic injury are the mainstay of prevention of tetanus because it is difficult to eliminate the spore of clostridium tetani from the environment.

Clostridium tetani bacteria produce two exotoxins, named as tetanolysin and tetanospasmin. Tetanospasmin is potent neurotoxin that's inhibits the release of neurotransmitters from the presynaptic membrane. This toxin affects central motor system, autonomic nervous system and N-M junctions. The clinical features of disease depends of involvement of type and site of neuronal cells. Tetanus toxin inhibits release of inhibitory neurotransmitters (glycine, GABA). These inhibitory neurons helps in muscles relaxation and control the activity of motor neurons. The excess firing of motor neurons causes muscles spasm. Due to over activity of the motor neuron patient develops hypertonia and spasticity.Tetanus also affects the autonomic nervous system, develops symptoms of dysautonomia such as sweating, fever, tachycardia, labile blood pressure, cardiac arrythemias.[2]

Editor's Comment :

- **Tetanus is still common in India, early initiation of antibiotics and debridement of wound can prevent the disease**
- **Trismus and rigidity, and autonomic instability are the main features of tetanus.**
- **Diazepam, baclofen, magnesium sulphate are the main pharmacological treatment options.**
- **Mortality depends on early diagnosis, other comorbidities of the patient and availability of ventilator (ICU) facility**

Epidemiology :

It is estimated that tetanus causes 213000 – 293000 deaths worldwide each year and that it is responsible for 5-7% of all neonatal deaths and 5% of maternal deaths globally, with a case fatality rate which ranges from 6% to 72%, depending on the availability of well-equipped intensive care units.[3]

Most reported cases occur in adults. From 2009–2017, more than 60% of the 264 reported cases were among people 20 through 64 years of age. In addition, a quarter of those reported cases were among people 65 years old or older. The risk of death from tetanus is

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highest among people 65 years old or older.[4] In developing countries the immunization coverage still is not 100%, peoples are at higher risk then the developed world. The protective immunity is declines with time so booster dose required at a frequent interval. Elderly people are great risk because they have less protective antibodies.[4,5] Tetanus is endemic In India, and it remains a public health problem. Studies shows that mortality by tetanus is still high in India due to poor health facility. According to who report total around 7000 patient having tetanus in years 2018.[6]

Pathogenesis :

Clostridium tetani is spore forming obligate anaerobic bacteria, normally present in soil and gut of mammals. When it is inoculated in the tissues its transforms in a vegetative state which is rode shape. This vegetative form produces a metalloprotein known as tetanospami. Tetanospasmin binds tightly to the receptors in the spinal cord and brain after reaching via retrograde axonal and blocks neurotransmission by its cleaving action on membrane proteins involved in neuroexocytosis.[7,8]

The net effect of tetanospamin is disinhibition of anterior horn cells, motor cortex and autonomic neurons leads to muscles spasm, hypertonia and widespread of autonomic instability. The recovery and regrowth of new axonal terminals took time, so that the effects of toxin remains long-lasting.

Tetanus toxin is produce in an inactive form mediated by genes located in an intracellular plasmid. It is initially inactive polypeptide which is activated by bacterial or tissue proteases after the death of bacteria. The active form of toxin contains two chain, a heavy chain necessary for binding and entry into neurons and a light chain responsible for its toxic properties[8-10].

Heavy chains are further cleaved by pepsins into specific fragments, which individually mediate binding to specific types of neural cells. Inhibition of presynaptic neurotransmitter release is mediated via light chains. There is increase in the resting firing rate of disinhibited motor neurons and lack of inhibition of reflex motor responses to afferent sensory stimuli this leads to muscles rigidity.[10] Symptoms of sympathetic over activity occurs due to loss of neuronal control of catecholamine's by adrenal[11].

Predisposing Factors In Adults :

1. Any types of injury that causes inoculation of bacterial spores in the tissues
2. Uncontrolled Diabetes with diabetic foot
3. Sepsis and Septic abortion
4. Patients of I.V drugs abusers
5. Unsterile surgical procedure
6. Dental infection
7. Circumcision
8. Foreign body inoculation.
9. Cryptogenic Tetanus — in this type patients have signs and symptoms of tetanus but no obvious history of any type of injury is identified. Only small amount of abrasions presumed as a source of infection.

Clinical Features :

Incubation period : — depends on the distance of injury site from the CNS, its range from 3 to 22 days. Mortality is high in those patients who has short incubation period.

Clinical classification of tetanus :

1. Local tetanus : — occurs only 1% of cases, only localised to a particular muscles group that is involves in type of tetanus. In some patients this can be proceeds to in generalised form. The contraction of muscles groups may extends to many weeks then gradually subsides.

2. Cephalic tetanus : — is similar as local tetanus localised involvement of cranial nerves of facial area. Occasionally occurring with otitis media or following head injury and neurosurgical procedures.

3. Generalized tetanus : — most common type, about two third of total reported cases of tetanus in literature are of this category. The disease presented with fever, episodic tachycardia, associated with sweating and muscles spasm. First group of muscles involves are the jaw muscles leads to lockjaw (trismus). Then disease usually descends and involves neck muscles and muscles of deglutition and abdominal muscle. This may leads to difficulty in swallowing, and rigid abdomen. The muscles spasms occur frequently and remains for minutes.

The most common symptom in generalizes tetanus is trismus found in 50% of cases. Dysautonomia was found in almost 100% of patients with generalized tetanus, have symptoms of autonomic over activity. Early phases they may manifest as excessive irritability, restlessness and over sensitive to light and sound, excessive sweating, and profound tachycardia. In later phases of illness they manifest as profuse sweating, any types of cardiac arrhythmias such as VT, VF, and PSVT and labile blood pressure.

A study done by Nitin M Apte and colleagues in 1995 to demonstrate a bedside diagnostic test known as spatula test (reflex spasm of pharyngeal muscles by touching the posterior pharyngeal wall by wooden spatula). They selected 400 patient and found this test positive in 359 (94%) of patients with sensitivity of (94%) and specificity of (100%).[11]

Patients of with generalized tetanus they have

painful tonic contractions of muscles aggravated by noise and light. In the course of disease the consciousness of patients does not affect so patient felt intense pain due to muscles spasm. The spasm may also triggered by physical stimuli such as touch. Tonic and periodic spastic muscular contractions are responsible for most of the classic clinical findings of tetanus such as:

1. Stiffness of neck
2. Opisthotonus position
3. Risussardonicus
4. Rigid abdomen
5. Periods of apnoea and upper airway obstruction due to persistent contraction of the thoracic muscles and/or glottal or pharyngeal muscles
6. Dysphagia

During the tetanic spasm patient suddenly clinch his fists and jaw, the back of patient become like bow, arm flex and adduct with extension of his leg. During this phase of tetanic spasm the respiratory movement of patient is affected and he develops apnoea for some time.

Diagnosis : — The diagnosis of tetanus based clinical features. No diagnostic test available only the detail history of injury with contaminated wound and inadequate immunization may support in the diagnosis of the patient. The clinical features of tetanus mimics many other diseases.

Differential Diagnosis :

1. Drug-induced dystonia — It is characterized as abnormal rhythmic movement of neck, face, with history of drugs intake mainly the antipsychotic and antiemetic such as haloperidol. The dystonia includes the variety of movements such as torticollis, grimacing, dysarthria, oculogyric crisis. The dystonic movements usually subsides by the anticholinergic and antihistaminic drugs treatment within 30 minutesbut not in case of tetanus.

2. Malignant neuroleptic syndrome — A group of neurological symptoms characterised by, altered mental status, fever, muscles rigidity, and autonomic dysfunction. This syndrome usually develops as due to side of antipsychotic drugs both typical and atypical (haloperidol, risperidone) which act as dopaminergic receptor antagonistor withdrawal of dopaminergic drugs (levodopa,tolcapone). In this, patient has rhabdo-myolysis (increased CPK) causes renal tubular damage and renal failure. The mental status of the patient suddenly changes from agitation to deep. This syndrome is managed by bromocriptine, datrolene, cooling of body and proper hydration of patient. The presence of history of antipsychotics and rhabdomyolysis can differentiate it's from the tetanus

3. Trismus other than tetanus — Such as dental infection, deep seated neck infection, fracture of mandible neck etc.

4. Rat poisoning — Strychnine is a bitter plants alkaloid used for pesticide and rodenticide. The clinical feature of strychnine poising are similar to tetanus. Strychnine inhibits post synaptic release of neurotransmitter glycine in spinal cord and the medulla. After ingestion strychnine absorbed from the mucus surface and stomach act fast within 15 to 20 minutes leads to neuronal hyper excitability causing muscles spams similar to tetanus. This poisoning easily differentiated by history of ingestion and quick development of symptoms and can be identified by serum strychnine levels

5. Stiff man syndrome — It is an autoimmune mediated neurological disorder associated with other autoimmune diseases such as vitiligo, pernicious anaemia, diabetes, and thyroiditis. The clinical feature are similar to tetanus characterised by painful muscular rigidity. The rigidity is increased by physical stimuli such as noise, touch and sudden movement and patient is very anxious to go outside the house. Management includes diazepam and immunoglobulins rapid response to diazepam and association of other autoimmune diseases distinguish this from true tetanic spasms.

6. Management of Tetanus — Management of tetanus includes in the following headings:-

1. General Measurements

a. Admit in dark and quit room
b. Management airway, circulation, and other supportive measures
c. Well-equipped ICU

2. Wound management

a. Debridement of wound

3.Antibiotics (Adult dose)

a. Metronidazole 500mg 6 to 8 hourly
b. Penicillin G 2 to 4 MU I.V TDS4. Ceftriaxone 2g TDS if mixed infection is suspected

4.Human tetanus immunoglobulin (HTIG)

a. 3000 to 6000 units intramuscular single dose
b. 200 IU to 1,000 IU intrathecal single dose

5. Treatment of muscles spasm, Sedation and muscles relaxant

a. Dark and quit room
b. Diazepam 1 to 10 mg/kg/day3. Propofol infusion

6. Neuromuscular blockers

a. Pancuronium traditionally used
b. Intrathecal baclofen bolus 40 to 200 mcg followed by a continuous infusion of 20 mcg/hour

7. Management of dysautonomia

a. MgSO4 loading dose of 40 mg/kg for 30 minutes was used followed by a 2 g/hour infusion.

8. Prophylaxis

a. Immunization

- **General Measurements: -**Tetanus is rapidly progressive disease, when there is clinically suspicious it is recommended that patient should be admitted in ICU regardless of the severity.[12,13] A retrospective multicentre study done in France in 2017 suggestive that in high income country where ICU facility is available the mortality of tetanus is significantly less (1-year mortality 16%) compare to low income countries[14]. A Ten years retrospective study done in India shows mortality is around 42.2% in total admitted patient in general ward and ICU.[15] A study done in Bangladesh shows the mortality only 28.6% patients managed without ventilator only 2 patient out of 42 required ventilator support.[16] A Brazilian study shows that the final mortality rate 44.5%, patients those have high APACHE 2 has high mortality.[17] Another study done in Nigeria shows higher mortality rate in ICU admission probably due more sever patients admitted in ICU[18].
- **Wound management : -** All patients with tetanus will go for wound debridement to prevent further bacterial growth. There is no role of local installation of human tetanus immunoglobulins.[19]
- **Role of antibiotics : -** There is minimal role of antibiotics in treatment of tetanus. A prospective open label non randomization clinical trial done in Indonesia shows that mortality is less in patients treated with Metronidazole 500 mg thrice daily compare to penicillin group.[20] Another RCT between benzathine penicillin, metronidazole, and benzyle penicillin done in Mumbai in India shows single dose of benzathine penicillin (1.2 Million Units I.M) is equally effective as other two drugs.[21]
- **Neutralization of free toxin : -** The role of anti-toxin is to neutralise the circulating toxins and it should be given as early as possible. The human anti tetanus immunoglobulin are has better outcome then the equine anti-tetanus serum because it has lot of side effects. The various RCT shows that the intrathecal rout for administration of anti-tetanus toxin is better than intramuscular route.[22]
- **Role of intrathecal HTIG: -**A meta- analysis showed there is no difference in outcome by intrathecal therapy in neonates but has benefit in adults with tetanus.[23] Few small non randomization studies shows benefits of intrathecal immunoglobulin in view of length of hospital stay and less complications[24-26]. The dose of therapy range from 300 IU to 3000 IU. A pilot study done to assess the safety and efficacy of intrathecal immunoglobulin in tetanus showed it is feasible with less adverse effects.[27] Recently a randomization clinical trial is registered to see the efficacy of intrathecal immunoglobulins.[28]
- **Treatment of muscles spasm :-** The physical stimulus are the aggravating factors for painful muscles spasm, patient must be kept in dark sound proof room with minimal physical stimuli to prevent muscles spasm. This muscles spasm can causes respiratory arrest and exhaustion in the patients.
- **Sedation and control of muscles spasm : -** Diazepam is sedative, anticonvulsant, muscles relaxant and anxiolytic so it is the drug of choice in tetanus. A Cochrane databases study review published in 2004 that compared diazepam to other anticonvulsant such as phenobarbitone and chlorpromazine, they found better outcome in patient treated with diazepam.[29] Another comparative study done between diazepam, and combination with chlorpromazine or propranolol shown that there no additional benefit compare to diazepam alone.[30] Another study done in paediatric patients with a continuous infusion ofdiazepam (20-40 mg/kg per day) and intra-gastric phenobarbitone (10-15 mg/kg per day in 4 divided doses) shows reduction in mortality significantly.[31] A case report of severe tetanus showed effect of midazolam with propofol to reduce severe muscles spasm.[32] The continuous infusion of midazolam also effective for management of muscles spasm.[33] Diazepam is a potent GABA-ergic agonist this drug has a fast onset of action when given as a bolus, which is useful for spasm control. The dose required to provide relaxation may be high, ranging from 1 to 10 mg/kg/day according to the desired degree of relaxation. This drug can be used as a bolus (10-30 mg/hour) or a continued infusion with extra 10-mg boluses as required. Additionally, continuous infusion provides a effect more stable and allows more appropriate dose titration. Infusion of propofol may also control spasms and rigidity. Its prolonged use has been associated with lactic acidosis, hypertriglyceridemia, and pancreatic dysfunction.
- **Neuromuscular blockers :-** When sedation alone is not effective then N-M blocking agent may be use. Pancuronium is a long-acting agent, has been traditionally used. However, it may worsen autonomic instability because it is an inhibitor of catecholamine reuptake. Vecuronium can also be administered and is less likely to cause autonomic problems, but since it is short acting, it must be given as continuous infusion to provide adequate effects. Monitoring of patients on these drugs is extremely important to avoid

or recognize complications. Baclofen which stimulates postsynaptic GABA beta receptors has been used in a few small studies. The preferred route is intrathecal, and it may be given either in a bolus of 1000 mcg or by continuous intrathecal infusion. Intrathecal baclofen given as an initial bolus in a dose ranging from 40 to 200 mcg followed by a continuous infusion of 20 mcg/hour was found to control spasms and rigidity.[34, 35]

- **Management of dysautonomia : -**The pathogenesis of autonomic dysfunction is unclear only few purpose theory are given. Patient develops symptoms of sympathetic overdrive such as tachycardia and systolic blood pressure changes from minute to minutes, and may develops sudden cardiac arrest. One purposed hypothesis suggested that these symptoms are due increase catecholamine levels in the serum which may increase several times from their base line values.[36-38] However, in future studies no correlation was found between the development of symptoms and serum catecholamine levels. Second is tetanospasmin as a zinc-dependent peptidase enzyme its acts similar to ACE, excessangiotensin II in serum leads to hypertension[39,40].
- Buchanan *et al* reported in 1979 that morphine had a significant effect on reducing spontaneous sympathetic over activity in tetanus, though it had little effect on spasms.[41]
- Intra venous Morphine reduces the muscles spasm and symptoms of sympathetic over activitythe loading dose is 5 mg followed by continuous infusion of 0.05 to 0.1 mcg/kg/min or with 5-mg doses every 3 hours.
- Gregorakos et al suggested that intra venous Clonidine has reduces dysautonomia in patient compare to placebo groups.[42]
- **Beta blocker** : - suchintra venous labetalol also effective in controlling of blood pressure and tackles sympathetic overdrive.[43]
- **Role of magnesium :** - Magnesium is a physiological antagonist of calcium at cellular level has properties of vasodilation, presynaptic N-M blocking and inhibition of catecholamine release. Therefore it is very effective in controlling the symptoms of dysautonomia.[44,45] A randomized, placebo-controlled clinical trial conducted by Thwaites and colleagues in Vietnam.[46,47] In this trial, 97 and 98 patients with tetanus of comparable severity (independently verified with three different scoring systems) were allocated to receive either magnesium sulphate or placebo while receiving standard therapy (high dose diazepam for sedation replaced with midazolam as required, neuromuscular junction blockade and respiratory support when necessary). The primary outcome assessed was the need for ventilatory support within the first 7 days of magnesium therapy, which showed no difference between groups No significant difference was observed in the primary endpoint. However, a significant difference was found in the secondary endpoints, ie, reduced needs of sedation, neuromuscular blockers which were considered to be the treatment of choice for dysautonomia. Another case series (n=30) done by Mathew and et all in Chandigarh in India found that magnesium sulphate is beneficial in controlling of muscles spams and dysautonomia[48]
- **Limitations : -** There are limited options for the treatment of tetanus. It is ethically incorrect to do randomization studies on tetanus for the treatment options when there are already some evidence based treatment exist. Diazepam is easily available and safe to use so role of other benzodiazepine are not much studied. Human anti tetanus immunoglobulins are very costly and it's the definitive role for management of tetanus is not stabilized.

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as expected to do the needful while urgency needs it. The attention of the minister of health department and of the Chief Minister is earnestly drawn to look to their responsibility, as the people can't wait any more.

The country is really sick of speeches, tall talks, schemes and committees but they need action only. Independent India wants people who are alert, active, alive to their responsibilities and duties and sympathetic towards suffering humanity. No indifference, apathy and lethargy can be tolerated any longer.

No doubt there are difficulties in converting existing charitable dispensaries and hospitals vested on the local authorities by private individuals for their maintenance. But when such conversion is considered good for the sake of the people no body will object and legal difficulties may also be solved by adoption of "regulations for emergent circumstances." The Director of Health Services selected doctors and health assistants and these doctors and health assistants got training upto March last. But it is reported no other classes were taken up in April last as expected. It is further stated that those who got training are not being employed to draw their pay and allowance. Thus a great injustice has been done on the doctors and health assistants who are in great difficulty to maintain their families. Any how or other they may be immediately deputed for anti-malarial survey when they may gradually organise centres, at least 3 miles off from one another to be attended once a week for 2 to 3 hours to give medical aid, to attend village schools to educate children hygienic principles and to deliver magic lantern lectures once a week at H. E. or M. E. schools where all people may attend. If these works are taken up half the work will be organised.

It is really a difficult problem to have adequate accommodation in villages for these doctors. But from personal experience I may say that if the doctors approach rich people still residing in West Bengal villages, they will certainly accommodate them temporarily and doctors may gradually induce them to establish charitable dispensaries at their cost while the Government will contribute for the health works. Thus the plan as drafted by the Director of Health Services may be effective to give medical aid to the rural people.

During a period of 23 years in the District of Faridpur, I had to organise charitable dispensaries to raise the number of the same from 0 to 130. I had to adopt similar policy to depute doctors to certain villages to open 3 centres for treatment. Gradually local people came and provided for dispensary buildings and equipment while Union Board and District Board and Government contributed for the recurring expenditure. It is only to educate village people and to show them how they are benefited by such institutions. Everybody co-operated with the doctor. If the people insist on the Government, doctors have adequate remuneration in due course.

Local authorities have failed to manage works for the medical aid and health work. So the Government have been compelled to take up the responsibility, while the Government of India agreed to contribute. The Editor of the J.I.M.A. is certainly justified in stating that if suffering humanity cannot get the desired relief, highly paid officers of the state have no justification to continue with their inefficiency but should hand over responsibility to abler, energetic persons with wider vision and sympathetic outlook.

In West Bengal annual deaths for malaria alone comes to 1,11,000 out of a total population of 2,11,00,000. If the mortality rate is calculated at only 1 per cent, it appears that the total number of persons suffering from malaria alone comes to 1,110,000 per year. Now if we consider the economic loss due to death, treatment cost, loss of working days, funeral cost, loss of efficiency in work, it would be a fabulous sum.

Lt. Col. Sinton the late Director of Imperial Malaria Research Institute worked out these costs for whole India which comes to Rs. 10,850 lacs annually (Rs. 108.5 crores).

As regards the location of sites for 130 new Union Centres, they should be very cautiously considered. Besides the Thana headquarters and the existing charitable dispensaries within Union Board areas, they are to be established at a central place within 2 or 3 Union Board areas where people from such areas can be conveniently treated.

As regards the recruitment of doctors, it is certainly regretted that none can be expected to join on Rs. 150/- plus 45/- with quarters, as one can hardly meet monthly expenses for family at less than Rs. 300/- even in a village. There will be no difficulty in recruiting medico at the present moment while refugee doctors have got a chance for Registration and about 1000 may have registration within 31.12.49.

V

OPINION OF THE INDIAN MEDICAL ASSOCIATION ON THE CHOPRA COMMITTEE'S REPORT ON INDIGENOUS SYSTEMS OF MEDICINE

Preface

The Indian Medical Association is the representative national association of the medical practitioners of India possessing registrable qualifications in scientific or so-called 'Western' medicine and is recognised as such by the Government, the World Medical Association and the World Health Organisation of the U.N.O. The chief objects of the Association are the "promotion and advancement of the medical and allied sciences in all their different branches" and the "improvement of Public Health and Medical Education in India."

When the Indian Medical Association has to put forward its considered opinion regarding the Indi-

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genous or any other system of medicine, the Association has to bear in mind the ultimate cause for which medicine in any form or shape has to be utilised. The health of the nation and particularly the health of the poorer sections of the people in rural and urban areas is the most important consideration in the light of which such problems have to be taken into account. In this perspective the Association highly appreciates the following speech delivered by the Hon'ble Rajkumari Amrit Kaur, Minister of Health of the Government of India at the closing session of the Silver Jubilee session of the All-India Medical Conference held at Calcutta in December, 1948:

> "I viewed with grave concern the policy that is being enunciated by some of our provinces, in the matter of lowering still further the standards of qualification of your great profession. The argument advanced in favour of such action is the lack of aid to rural areas. That lack exists to our eternal shame, but to try to solve it by turning out half-baked medical personnel is to defeat the very object in view. Why should the poor men be given second best in any case? . . . Cheap Medicine and lower qualifications will not be cheaper even from the financial point of view. On the other hand, they will not only lower the standards of your profession but they will, in the long run, cause havoc to the cause of the nation's health."

The next important factors to be taken into serious consideration are the undertaking of certain responsibilities in the field of international health and the establishment of reciprocal relations with other countries of the world. Lately the Government of India has become an important member of the World Health Organization and India has been greatly benefited by this. The health services developed in this country should therefore, be such as to enable the Government of India to fulfil these international obligations. Dr. K. C. K. E. Raja, the Director-General of Health Services, Government of India has, rightly pointed out that "participation by India in the standardisation of diagnostic procedure, in the development of international standards in respect of biological, pharmaceutical and similar products or in the study and report on administrative and social technique affecting public health and preventive care will become impossible unless she (India) adopts the same system of medicine (the modern scientific system) which other nations have adopted for organization of "State Health Services".

Financial considerations would form the next important factors for judgment in such matters. The estimated cost of building and equipping a modern medical college now-a-days is well over half a crore of rupees. If separate modern teaching institutions for indigenous and other systems of medicine have to be built all over the country in addition to the new medical colleges for Scientific Medicine that are necessary, the cost of construction and equipment and recurring expenses on these is sure to prove to be prohibitive, unnecessary and wasteful.

In India, sick persons are treated by three classes of individuals, (*i*) those who possess registrable qualifications in modern scientific (western) medicine, (*ii*) those who are practitioners of the system of Ayurveda, Unani and Homœopathy and (*iii*) unqualified practitioners. It is sometimes said that in a democratic country, the individual citizen has the absolute right to take his ailments for treatment to anybody he chooses. If that be true, why a moratorium extending to a definite period of years was declared in China and Japan after which the practice of the indigenous systems in these countries would not be recognised. It may be further noted that national governments of Turkey, Iraq, Iran and Siam have also adopted an unified system of medicine based on modern sciences. Moreover, it is high time for our legislators to consider seriously the reasons for which Indigenous Systems are not recognised by the State as separate systems of medicine in any other country in the world.

Medical science is one and undivisible. It is a progressive science based on the fundamental sciences of Physics, Chemistry and Physiology and on research work carried out by scientists and medical men throughout the world. Modern scientific medicine should not be lebelled as "Western" simply because in the middle of the 19th century, medical science became progressive and was firmly established on a secure foundation initially in the western countries.

The word "Western" medicine has been used throughout the Chopra Committee's report to connote modern scientific medicine. If the stigma of "Western" or "Foreign" is applied to *allopathy* or modern medicine as practised in India to-day the stigma could equally be applied to all branches of modern science (including Physics, Chemistry and Engineering) which are being developed on the modern lines with State assistance. Moreover we cannot afford to ignore the invaluable contributions made by the eminent scientists and medical men of Japan, China, India and other eastern countries to the development of the "western" medicine.

During the British regime in India from 1757 to 1947 the health of India was of little consequence, in the eye of the Government and therefore, factors responsible for the low level of health were allowed to flourish with impunity. It is obvious that the gross inadequacy of provision by the state of adequate services by duly qualified medical practitioners in scientific medicine and the cheapness of charges made by indigenous and homœopathic practitioners and quacks for their drugs and services rendered are responsible for the continuance of these systems as well as quackery in this country. Till the other day it has been said by many that for a poor country like India, the training for the production of medical licentiates should be continued so that this cheaper class of medical practitioners would go to the villages and settle there to the benefit of the rural people. But fortunately for our country, this argument has

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been proved to be fallacious and steps have now been taken through India to stop further production of the licentiate type of doctors.

With the attainment of independence, it is just and proper to opine that measures for the protection and promotion of health of the people of our free country *should be given the highest priority in any scheme formulated by the Government*. We are strongly of the opinion that it would be unfair and unjust, on the part of the Government to deny to any one in this country the full benefit of the modern medical science merely because some other method of treatment is said to be cheaper. The question of cheapness would certainly not arise if the State can provide for employment of an adequate number of qualified medical practitioners in scientific medicine and for the establishment of a net work of modern hospitals in rural and urban areas.

We feel it is now most appropriate time for not only stoppage of further development of quackery but also of further development of practitioners of indigenous systems of medicine and homœopathy. The necessary measures should be incorporated in an act and should be passed by the legislature at an early date, and those persons trained in indigenous systems of medicine who are in actual practice now and are having their livelihood from it, should be absorbed in future Government public health scheme as public health workers after adequate and proper training.

Note on Chopra Committee's Report

The Committee on the Indigenous Systems of Medicine popularly known as the Chopra Committee, was appointed by the Government of India in December 1946 under the Chairmanship of Col. R. N. Chopra. The Committee contacted and elicited the opinion of various scientific, medical and non-medical bodies and associations of the country, in order to evolve an improved and unified system of medicine.

The Chopra Committee recommended the formation of a statutory body which when created, is to be called the National Medical Board. This Board will consist of two autonomous sections—one dealing with Western Medicine and the other with Indian Medicine. It has also recommended that the first step will be an integration of the courses of study by arranging curricula in such a way that whatever is weak in the one system is supplemented and strengthened by the strong points in the other system. The second step, according to the Chopra Committee, should be the teaching of each subject by the same teacher, instead of by separate teachers as now, giving the students an unified view of the Indian and Western Medicines. The final step the Committee says, will be the field of research where experts of Indian and Western Medicines will work side by side checking and verifying the various hypotheses and theories, either rejecting or harmonising them. If they are such that they could neither be reconciled nor rejected, they are to be used as parallel hypotheses.

The Committee has sought to create substandard medical qualifications of five or six different categories—under the plea of absorbing the existing Vaids and utilising them for mass medical relief in rural areas. They have recommended a short term licentiate course in Indian Medicine of 3 years. A still shorter course of 6 months only to absorb the existing Vaids whether trained or untrained. The highest course or the degree course will be for 5 years. All these courses are to include varying quotas of instruction from modern medicine.

There are to be different registers for different classes of practitioners in Western, and Indian Medicine, subdivided into sections for 'institutionally' trained, 'non-institutionally' trained, and 'untrained' classes of them. Heaven alone can help India and her woe-begone people if such a state of affairs be actually brought into being.

Chopra Committee's recommendations will create a complete confusion not only in the standard of medical qualification and efficiency of medical relief, but will result in a multilateral administration of public health from which order and co-ordination will entirely disappear.

The I.M.A. is of the considered opinion that the steps suggested by the Chopra Committee should be considered in the reversed order. The first step should be to sift scientifically the grain from the chaff, after careful research and then to accept the grain of established truth and reject the staff as useless and injurious. After this, the second step proposed by Chopra Committee may be taken, whereas the first step proposed by the Committee will be apparently futile, as teaching must be clear, unambiguous and absolutely free from confusion and contradiction. The question of strengthening the weak points of each system does not, therefore, arise. The experiment made in this regard in the Government school of indigenous medicine at Madras for about a quarter of a century has resulted in hopeless failure and created nothing but confusion in the minds of the alumni of this school.

Terms used in the ancient books of Ayurveda are irreconcilable in their meaning and application—and differently interpreted even by veteran Ayurvedic scholars. They cannot threrefore be profitably utilised except by students of research and history. Yet, the Committee has continuously pleaded in favour of combining in their recommended courses of study, the curricula of indigenous systems of medicine, just as they are, with merely a spattering of western medicine by way of ornamental window dressing.

Col. Sir R. N. Chopra has himself said in his book on the Indigenous Drugs of India (1933) "when it is remembered that the Ayurvedic system of medicine has been practically stationary for about 1500 years . . . one would find it very difficult to reconcile the old theories of 2000 years age . . . with the recent advance of the world in science. After imparting instructions to the Ayurvedic students in

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modern Physiology, Bacteriology, Pathology, etc., to ask to apply them therein the doctrine of *Vayu, Pittah* and *Kafa* etc. to explain the causation of disease . . . can bring nothing but chaos and discord to their minds."

The opinion of the scientists of India can be gathered from the following speech of late Sir P. C. Ray, the father of scientific research in India, delivered on the occasion of the foundation day of the Calcutta Medical College in 1940:—

"I am afraid I am looking behind me, and this has been to a great extent, the bane which has checked the progress of the country. We must now look forward and judge where we stand in the present world which is based on scientific civilisation. Although I have referred to the Ayurveda, I should say that the policy of passing off the Indigenous system of medicine as scientific systems of medicine after putting a veneer of modern medicine like Physiology and Anatomy on them does not seem to me to be the correct course. The policy should rether be to accept the Western Scientific system of medicine as the nucleus round which the tested knowledge derived from the indigenous systems of medicine may be gathered, all our knowledge should be accumulated on scientific lines."

The Committee toured over provinces and States, met practitioners and representatives of various organisations. They issued questionnaires, which also were generously responded to from different parts of the country.

It is all the more deplorable therefore that the Committee lapsed into a morass of confusion, born out of a sheer disregard for the method of synthesis advocated by medical and scientific experts such as the Indian Medical Association, the Royal Asiatic Society, the Indian Association for the Cultivation of Science and last but not least the expert opinions of patriarchal scientists such as Sir Nilratan Sircar, Sir P. C. Roy and even Sir R. N. Chopra himself.

Recommendations

It should be the duty of politicians and medical men to build up an efficient system of medical relief, on par with the modern scientific standard of other progressive countries and not to manufacture more ill-qualified practitioners—and licensed quacks—and let them loose on the public—particularly in remote and helpless rural areas. There can be no mixed teaching, half-Ayurveda, and half modern medicine. Teaching must be standardised and uniform according to the recommendations of the Indian Medical Council. The result of barrowing of powerful medicinal specifics by untrained and ill-trained members, has been quite disastrous and has inflicted "serious injury on many patients"—to the knowledge of and in the words of the Chopra Committee itself.

Uniformity in the strength and standardisation of drugs and medical appliances is quite as important as uniformity in the standard of minimum registrable qualification as laid down by the Indian Medical Council. Therefore there must be compulsory registration of pharmaceutists and compulsory examination for persons dispensing drugs.

In conclusion, we do not think it a practical proposition, nor a desirable one, to have State organisations of public health and medical relief in the indigenous systems or in a number of separate systems. Apart from the fact that it will entail too heavy a burden on the State and on the people, it will only lead to confusion and defeat the main object, viz. the welfare of the masses to whom we consider, the scientific system should be made extensively and intensively available within the shortest possible time. There should, in our opinion, be one State system, and that should be a really scientific system based on the modern advances in the field of natural sciences. We will take into it those materials in Ayurvedic and Unani as are proved to be of value by modern scientific tests and experiments; but the basic teaching should be as in modern medicine (commonly called Western Medicine), for, it is the system which is keeping pace with advancements in science and includes many subjects and branch-subjects unknown to the indigenous system or entirely lost.

In the *one* system which we advocate, so much of the materials in our old systems as are "proved" by modern tests, will, as already stated, be assimilated and should be taught to the students in the medical college and medical schools. We suggest that for the purpose proper research institutions should be established without delay with capable investigators and experts. We also suggest that every University should have a Chair of History of Medicine including Indian Medicine, with facilities of research on Ayurvedic and other indigenous medicines and with provision of beds for this purpose in a teaching hospital.

We also reiterate the memorandum submitted by us and published in Vol. II App. C 6441 of the Chopra Committee's Report and desist from reduplicating the points and issues raised therein.

The I.M.A. must warn once again against all attempts at setting back the hands of the clock of scientific progress. It will be doing a grave disservice to India's millions as also the cause of preventive and curative medicine—the noblest branch of science applied to the alleviation of human suffering.

In the best interests of the people, we demand that our national Government must not tinker and temporise with the problem but provide the people with the essential requirements of medical education and medical relief as far as possible upto the standard of other progressive countries of the world.*

*The Working Committee, I.M.A. appointed a special Sub-Committee consisting of Drs. K. K. Sen Gupta, P. K. Guha, A. K. Sen (Convener), A. D. Mukharji (co-opted) and Dr. A. C. Ukil (co-opted). The Sub-Committee formulated a preliminary report which was circulated to all Provincial Branches of the I.M.A. and the members of the Working Committee. In accordance with the opinions received the final report was drawn, endorsed by the Working Committee and forwarded to the Government of India.

Voice of the Expert

Robust Indian Healthcare Reforming towards UHC

Prof Dr S Arulrhaj
National President API
Past National President, IMA, New Delhi
Past Dean & Chief Patron, IMACGP
Dr BC Roy National Awardee

(1) Please comment on the Current Health Scenario in India in terms of service delivery.

As the Father of our Nation said "India lives in villages". Current Population of India is 1,349,841,263 (1.34 billion) as of January 23, 2018. About 72.2% of the population lives in some 638,000 villages and the rest 27.8% in about 5,480 towns and urban agglomerations.

Today Hi-tech Health Care is available in Metros and Big cities but even Basic health care (Primary care) is not available to more than 70% people living in villages.

Health Care :

Primary Care: Basic Health Care First line for routine ailments & identifying serious issues & Referral- 80%

Secondary Care: Regular Medical, Surgical, Obstetrics & Speciality care 40%

Tertiary Care: High tech Cardiac, Neuro, Gastro, Nephro& Sub speciality care. 20%

Family Doctor or Primary Care Physicians are the first rank in Health care delivery for the population. They play a vital role in Preventive health, early diagnosis and treatment of acute and chronic medical conditions with timely referral in addition to up keeping of health records of family members in the community and providing continuity of care.

Efforts by Govt of India to improve Rural/ Primary health care

1. BRMS BRHC short term health workers course recommended - **withdrawn**

2.Posting AYUSH practitioners in PHC after undergoing bridge course.

3.Permitting Lateral entry for Health sciences. **Quackery**

4.Creating Integrated System of Doctors/ Hybrid Doctors- NEP 2020 – Mixopathy

Right Efforts will be to reposition the Health system so that adequate Doctors are made available for Primary care but we are trying to sabotage the Health of Rural Indians by half backed AYUSH Doctors offering Modern Medicine.

(2) Why do you think these efforts are being made presently?

GOI Views :

1. Doctors Numbers are less
2. Doctors Not going to Rural areas
3. Modern Medicine Expensive
4. Promotion of our Ayush

Many factors may contribute to the above gap :

a. Failure to create Family Practice and Rural Health Practice Oriented Doctors by the system in place today. **MBBS as a degree has become irrelevant to the system.**

b. Paucity of Doctors. Doctor population Ratio is 1.62 per 10000 only as per WHO Norms only

Faulty Recruitment - majority

Less Production ?

c. Doctors not serving and settling in Rural areas?

d. Lack of infrastructure facilities & safety

There are two dimensions that we should not lose sight when we critically analyse this issue. A

a. The **first** and foremost is that this inequitable access is not only due to Urban and Rural divide. There are social and economic factors which are the root cause of this discrimination. Levels of literacy and gender bias play a prominent part as well. **It is not by the geographical location alone that the Rural Indian is denied access to healthcare. Poverty and social stratification take away his voice.**

b. **The second dimension is that the consideration of patient safety is supreme and any relief should address it adequately.**

The gap that exists between Urban and Rural is both in infrastructure and in service delivery. *Public sector spending accounts for less than a quarter of health spending.* There has been a sharp reduction incapital investment in Public Hospitals and gross under funding of National Health Programmes. If one goes through the direction of health planning a clear shuffling is visible between primary health care and vertical programmes. This has confounded confusion right from policy level.

But planning to fill this Gap by "Compromised Health Workers" in the name of 'Crash Course to AYUSH', Lateral entry/Hybrid Doctors will be detrimental to Health of citizen – Community Health & Life at Risk.

Two standards of Health care for the citizen of India : This is against the fundamental right of the citizen ofIndia. Blatant violation of Constitution against "Equality".

Alma Ata Declaration 1978 has said that Primary Health Care should include at least: education concerning prevailing health problems, food supply and proper nutrition, adequate supply of safe water and basic sanitation, maternal and child health care, immunization and appropriate treatment of common disease.

(3) Do you think there is a shortage of doctors in India?

- **Let us analyse the situational Facts:**

A. Doctor Indices

Total MBBS Seats and Colleges in India		
Type of Colleges	**MBBS**	
	Total Colleges	**Total Seats**
Government Colleges	280	42710
Private Colleges including Deemed Universities	262	38690
Total Seats through NEET	542	81400
AIIMS & JIPMER institutions	15 AIIMS; 2 JIPMER	1350 (AIIMS) +200 (JIPMER)
Grand Total	559	82950

NMC data as on date says annually 82,950 Medical graduates are coming out of Indian Medical Colleges. 44,190 Post Graduate seats are available in Medical Colleges.

Annualy around 39,000 Doctors sitting idle in Libraries **X 3 years and more around 1-5 lakh doctors unemployed.**

Foreign medical graduates 7500 pass out every year out of which 25% get registration in the national medical registry / year by passing the Qualifying exam.

That means 5600 x 7 years = 39200 graduates are jobless.

But we do not have Doctors to serve in Rural or Urban areas. Why? Paradox

Key reason is today's Medical Graduates are trained and oriented towards Tertiary care with no exposure to primary care.

(4) What are the challenges of rural health care?

Challenges in Rural Health

- 8% of the PHC centers do not have Doctors or medical staff
- 39% do not have lab technicians
- 18% PHCs do not even have a pharmacist.
- 66% of rural Indians do not have the access to the critical medicines
- 31% of the population travels more than 30 kms to seek healthcare in Rural India
- More than half of all residents of Rural areas live below the poverty line struggling for better and easy access to health care and services & safe drinking water
- **Health issues confronted by Rural people are many and diverse**:

- Malnutrition
- from severe malaria to uncontrolled diabetes
- from a badly infected wound to cancer
- Postpartum maternal illness and contributes to maternal mortality,
- Majority of people die due to preventable and curable diseases like diarrhea, measles and typhoid

Reality Scenario

- As compared to their pre-independence levels, all health parameters have shown remarkable progressive improvement even in Rural India.
- States like Maharashtra are now producing surplus MBBS Doctors. The Government of Maharashtra has, therefore, decided to scrap the service bond to serve Rural
- Primary Health Centres (PHCs) are the cornerstone of Rural health delivery system. The number of PHCs has increased from 77 in the first plan (1955) to 23,887 in 2011, a 300 fold increase. No new PHCs in the past 25 years.
- 30 per cent PHCs have two or more Doctors and equal number provides 24 × 7 h services. The number of doctors at the PHCs has increased from 20308 to 26329 (addition of 1,200 doctors per year) in the period 2006-2011.

Table summarizes the profile of the Nurses and Allopathic Doctors that is expected to evolve by 2022.

Projected availability of allopathic Doctors and nurses

	2011	2017	2022
Allopathic Doctors, nurses and midwives per 1000 population	1.29	1.93	2.53
Population served per allopathic Doctor	1953	1731	1451
Ratio of nurses and midwives to an allopathic Doctor	1.53	2.33	2.94
Ratio of nurses to an allopathic Doctor	1.05	1.81	2.22
http://www.planningcommission.gov.in/			

(5) Where do the Medical Profession stand ?

In the meantime, Times of India, New Delhi has come out with a message dated 8th March 2010 "Docs ready to work in Villages for PG Quota". This outcome is following a world Bank sponsored collaborative study conducted in 10 Medical & Nursing Colleges of UP. This reveals the **mindset of the young Medical Graduates of India; their willingness to work in Rural India.**

The cat is out of the Bag. Solution is ready.

Around 1,00,000 young graduates are available in India in this pool. They will solve the issue of "Rural Health Crisis" today itself.

Alternate solution suggested by Public Health Activists is to reserve 25% seats in Medical Colleges to Rural students with a guarantee to serve in Rural areas for 5 years.

The 25% Reservation system will give MBBS Doctors after 5 ½ years.

The AYUSH promoted by GOI will offer poorly qualified Mixopathy Team

But the offer by young Medical Graduates will solve the crisis today itself. Thanks to the youth Medics.

According the **Rural Health Statistics released by government of India**. As per 2016 there was a shortfall of Doctors at PHCs is only 3244 where India has currently capacity to produce 83,000 MBBS doctors per year.

The total number of posts sanctions at PHC in India only 34068 about less than half of the current number of MBBS seats. Apparently there is over supply of MBBS Doctor for whom there is no jobs in Government Sector.

Fact: There are very less sanction positions of doctors at PHC given the Indian population and high morbidity levels.

https://nrhm-mis.nic.in

The current reasons for non availability of Doctors in Rural areas are following

- Privatization of PHC in many states
- Gazetted regular services of Doctors converted into low paid adhoc contractual services by central and state agencies
- No housing and other facilities for Doctors in Rural areas
- Absence of professional satisfaction due to lack of opportunities in still development or clinical experience.

(6) Why do you think rural areas often struggle to get good medical care?

The non-availability of modern medical Doctors in Rural areas in sufficient numbers is due to multiple reasons:

1. There is less number of medical colleges in states where there is shortage of Doctors

2. The syllabi and curriculum of MBBS do not give exposure to a Medical student regarding Rural heath scenario

3. The entrance examination system NEET for MBBS itself promotes city-based candidates to get admission

4. **The Doctor population ratio is not the only criteria for better health parameters**, e.g. Sri Lanka. It is the doctor, nurse, midwife, health worker population ratio which is more important. India has better doctor population ratio, the nurse, midwife, health worker population ratio is worst.

5. The Government instead of addressing all the issues related to Public Health, is trying to solve it by a single intervention of empowering AYUSH Doctors, which is going to have a deleterious effect on public health

Health workforce shortfall has been proved above as a Myth.

Myth: The shortage of Doctors in Rural is a misplaced argument

What is our GOAL in Health?

Doctors at PHC India Rural Health Statistics Government of India	**2005**	**2016**	**2019**
Doctors at PHCs Required	23236	25354	24855
Doctors at PHCs Sanctioned	24476	34068	32824
Doctors at PHCs In Position	20308	26464	29799
Doctors at PHCs Vacant	4282	8774	7715
Doctors at PHCs Shortfall	1004	3244	1484

Healthy India through UHC built on Primary Care

Rural Health need Primary care qualified Physician and Public health worker

(7) How to resurrect and strengthen primary care in our nation ?

1. **Department of Family Medicine in UG Medical Education**

All medical colleges both Government and Private in India must have a department of Family Medicine.

We have NMC approved post graduate qualification MD in India without department of family medicine. Also DNB & Diploma in Family Medicine.

This is the key Lacuna.

2. Faculty in Family Medicine:

a) Competent Number of Family medicine DNB qualified specialities are available. They can be utilised as full time or part time Faculties.

b) Social and preventive Medicine specialities who have aptitude towards Family Medicine by Bridge course can be trained to be Faculty.

c) Public Health Specialists can be utilised the same way

d) Internal medicine and other broad specialities within interest in Family Medicine must be trained and posted.

e) Community experience should be counted towards faculty eligibility.

Faculty cadre of Family Medicine as Assistant, Reader, Professors to be created with promotional opportunities and a distinctive space in field of Medical Education& Healthcare.

3. Training in Family Medicine :

UG training in Family Medicine department in the medical college with 6 months Community training in PHC, CHC to be done. During Internship also 3 months training to be given in PHC and CHC not name sake but in real sense. Their posting in the Emergency room will help to be the first contact physicians in Medical Emergencies.

UG training in Family Medicine to be increased with at least 6 months exposure in community settings. **Community Based Education must be strengthened than tertiary carebased system.**

4. Curriculum in Family Medicine :

Like other Broad Specialties curriculum to be drawn and a separate paper in the pre final year to be included for Family Medicine.

Short term training programmes say 4-6 weeks, which can be developed by IMA-CGP and offer to in service Doctors posted at PHC/CHC as an immediate measure. These programmes can provide credits which a doctor can accumulate and get counted when undergoing PG Diploma / Degree in FM.

5. Positions in Health System :

After completion of MBBS their placement in the Health system will attract young Doctors. TO be posted in PHC, CHC, District Hospitals & NHM with large funding can utilise the MBBS doctors in the rural posting with highremuneration package.

Recruitment rules for MO/CMO position in state cadre to include special incentives for Family Medicine Specialities.

PHC (primary health centre) should be re designated as "Family Health Unit" which should provide comprehensive primary health care instead of disease focused Public health intervention.

Family physicians should be placed at front line as team leaders of the "Primary Care Teams"

Retaining programme for retainership of MBBS private doctors in rural area.

Finance and position are the key to attract Doctors in Primary care

In Developed Nations, UK, Primary care Physicians/GP are the highly paid team with good incentives. Adopt the Global best.

6. Post Graduation:

In today's demanding Health scenario every young medical graduate is compelled to do Post graduation. Now MCI approved three year institutional MD Family medicine is existing but taken by vary few because of placements. Recently Two year Diploma in Family Medicine is introduced by NBE in addition to the existing 3 year course. **No undergraduate Department but PG is available. Great . In future sub speciality courses in Family medicine can also be introduced to create status for Family Physicians.**

When Department of Family medicine with positions in the system are in place youth would prefer Family Medicine. Remuneration must be compensatory for the rural working depending on hours of working

(8) Do you think on line Post graduate Qualification in Family Medicine may be started?

E learning in the order of the day in Education globally Telelearning.

When our Prime minister is promoting Digital India, Digital PG courses must be a reality in India.

Theory (Knowledge) component will be online. Skills (Clinical) Component will be by month end clinical training in Medical colleges or Accredited Private Medical Institutions- Blended Learning.

The curriculum and syllabus will be vetted and approved by Government of India.

This approved Digital PG course of Family Medicine will attract Young Medical graduates to undertake Family medicine post graduation while continuing their self-practice or Institutional both Government and private assignments .

IMA College of General Practitioners (IMACGP) initiated by Indian Medical Association in 1963 to promote Qualified & trained Family Physicians in India, is the largest Professional body & initiated online PG qualifications in Family Medicine in the year 2013 & supporting Family Doctors (www.imaevarsity.com). First in the World .These courses to be evaluated & finetuned if necessary & approved by NMC.

This will solve the non availability of Medical Doctors in Primary care in cities and Rural areas.

Accessible and Affordable healthcare will reach for Indians.

Will also offer equitable healthcare to Indians both rural and urban as per constitution of India.

(9) What is the Role of Digital Health in supporting Primary care?

Thanks to our Visionary Prime Minister for legalising Telemedicine. Adequate Training & providing Infra at Rural & Remote areas to Family Doctors will link them with Secondary & Tertiary care centres so that time is not lost in Healthcare Emergencies & distance is managed.

In the reverse the Health workers in PHC & sub centres at village level can be linked to Primary care Physicians & offer effective Healthcare.

To be adopted actively

(10) Ayush MS to do General Surgery, ENT, Ophthalogy, urology, Thoracic & Gastro Intervention surgery. This has been proposed by the GOI vide Gazette of India, 20th, November, 2020 notification. What do you think of that?

Let them do their Ayush described surgery & not Modern Medicine Surgery

Let Modern Medicine Surgeons not teach them. Let then from Ayurveda Teachers their Surgery.

Misguided policy will cut deep into Patient Safety..
Playing with the life of common man.
Will deepen inequality
Major Community Health issue
Should not be permitted to happen
Modern Medicine is Modern Medicine
AYUSH is AYUSH

Limited resources and inequity in allocation

AYUSH allocation and utilization of central fund in CRORES

Budgetary allocation for health – the key to improving public health

- In 2015 budget, total health allocation decreased by 5.7 %

- **But out of 33,152 crore AYUSH gets 1,214 crore (3.7%)**

- **Whereas 0.5% of population use AYUSH for health care**

- The approved allocation of the AYUSH department has been increasing progressively over the years.

- The allocation of the 12th Five Year Plan of Rs.10,044 crore amounts to an increase of 235 per cent over the actual expenditure of 11th plan

Failed Experiment :

- Under NRHM, services of AYUSH practitioners are utilized for managing common childhood illness, counselling on family planning methods and as Skilled Birth Attendants (SBA).

- Allowing AYUSH practitioners as SBA will definitely result in mismanagement of new born.

- **The infant mortality rate has not decreased in the states where this has been done.**

Legal Decisives :

7.5 AYUSH Doctors in India. How to engage them in Health Care is the cause of the Healthcare Controversies; a big Agenda to be debated.

(11) what are the important Legal Verdicts on this issue?

Supreme court Judgement :

- Supreme Court Judgments that AYUSH Doctors cannot prescribe allopathic drugs are very clear in **Poonam Verma Vs. Ashwin Patel and Others (1996) 4 SCC 332**

National consumer disputes redressal commission

- Original petition no 214 of 1997

- As laid down by Apex Court in the Jacob Mathew case, we feel it is high time that Hospital authorities realize that the practice of employing non-medical practitioners such as Doctors specialized in Unani system and who do not possess the required skill and competence to give allopathic treatment and to let an **emergency patient be treated in their hands is a gross negligence.**

So taking into consideration of the Supreme Court and consumer court judgments- constitutionally and legally AYUSH practitioners should not be allowed to practice or prescribe Modern Medicine.

Primary care & now Secondary care cannot be transferred to AYUSH

(12) What is the Way Forwad?

Health to become a Constitutional Right of Indians

Health to become a Concurrent Subject

- **Budgetory Health allocation should be minimum of 5%GDP with more share to Rural health**
- Health care system has to be streamlined as **PRIMARY, SECONDARY & TERTIARY care**
- Department of Family Medicine in UG Education is the key
- Positioning of Family Physicians in Health system is needed
- Post Graduate Education in Family Medicine to be finetunes & strengthened
- **Shortfall of MBBS Doctors is a Myth. Their utilization is the failure**
- **Doctors not going to Rural Area is a procedural lapse by GOVT**.
- **A simple immediate workable solution is Reservations in NEET for Rural Candidates with bond for Rural Service for 3 years.**
- **Upgrading sub centres to PHCs** with 24X7 clinical services will provide primary care. The current structure suits India of 1950s.
- Immediate solution is utilizing the services of unemployed MBBS Doctors & Foreign Qualified Doctors for PHCs.
- **NHM** to be empowered as an Autonomous Institution.
- Doctors' recruitment to be kept in phase with the increasing population but it needs adequate Financial allocations.
- AYUSH Crash course & posting will also cost Public money spending. While spending Public money let us positively spend it.
- AYUSH to Rural India will be the greatest injustice we can do towards the Health of Rural Indians. It will be a blatant Constitutional violation too.
- Let us adopt Digital Healthcare actively to strengthen Primary care& reach to the unreached.
- Doctor must contribute as Doctor; Nurses must Contribute as Nurses; **No Lateral Entry**
- Ayush must contribute as Ayush; **No Hybrid Doctors**; citizen can choose the system they need .
- **When India is emerging as an Economic power, our health care system cannot go in a retrograde manner by not adhering to international standards in the practice of Modern medicine.**
- Primary care is Right to life
- Universal Primary care: A National Responsibility -UHC
- Empower MBBS in Primary care
- Rural health Care : A Governance issue

Universal Health Coverage (UHC) is only built on Primary care& not on Hybrid Doctors

Primary care in India to be offered by Modern Medicine qualified Doctors not by AYUSH or Hybrid Doctors.

Hence Strengthening Primary care with Modern Medicine in India is an Emergency need for moving towards Healthy India.

Thank you Prof. Dr. S. Arulrhaj for your answers. We appreciate the time taken by you and we are sure that our readers will be benefited immensely.

Original Article

Transmission and case fatality rate associated with COVID-19 in Asian countries as per Global hunger index score

Dimple Rawat[1], Sarthak Gulati[2], Shreya Gulati[3], Anshu Sharma[4], Arti Gulati[5], Vineet Kumar Kamal[6], Mahesh Kumar Seth[7], Amit Kumar[8]

Introduction : COVID-19, a new novel virus has posed an unprecedented challenge to the health care system and governments worldwide. The Global Hunger Index (GHI) could be an ideal tool to measure nutritional status among respective countries. Transmission and case fatality rate associated with COVID-19, might differ among countries classified according to GHI.

Objective : To determine the association of COVID-19 spread and case fatality rate among Asian countries classified according to GHI.

Methodology : An ecological study was done on the data reported for COVID-19 confirmed cases from Asian countries. The data were collected retrospectively considering the outcome as the number of daily reported cases, and case fatality rate caused by COVID-19 from inception till 19th April, 2020. Software STATA version 13, was used to conduct the statistical analyses. Generalized linear mixed model was used to determine the independent effect of predictor variables. P-value <0.05 was considered as statistically significant level.

Results : The generalized linear mixed model demonstrated that countries those at low risk of hunger had 2.8 times higher incidence rate ratio (IRR =2.8; 95% CI 2.01 to 4.05) and with a moderate risk of hunger had 1.7 times higher incidence rate ratio (IRR 1.7, 95% CI 1.3 to 2.1) when compared with serious and alarming GHI risk countries. Interestingly, low GHI risk countries had 50% less case fatality rate (IRR 0.5, 95% CI 0.26 to 0.94) and countries at moderate risk for hunger had 76% less case fatality rate (IRR 0.24, 95% CI 0.14 to 0.40) due to COVID-19 as compared with countries at high risk for global hunger in the Asian population, respectively.

Conclusion : More rigorous measures have to be taken by the countries with serious and alarming hunger index for reducing case fatality rate associated with COVID-19 in Asian countries.

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Key words **: COVID-19, Asia, GHI.**

Editor's Comment :

- **The findings of present study indicate that government should make rigorous health care policies to minimize the case fatality rate due to COVID-19 in countries falling under serious or alarming GHI.**

The word Corona is derived from the Latin word "crown". As the surface of this group of virus looks like a crown under an electron microscope, hence, it is given the name as CORONAVIRUS. To be precise, *Severe* Acute Respiratory Syndrome Coronavirus 2, is the cause of the current outbreak and hence, it is termed as SARS-CoV-2 and the disease was named as COVID-19 both by the World Health Organization and the International Committee on Taxonomy of Viruses on 11th February 2020[1]. The city Wuhan, in China is recognized as the origin of this outbreak.

On 29th December 2019, a cluster of similar cases of Pneumonia were identified by the Chinese authorities in the city and were determined as SARS-CoV2 and reported to WHO on 31st December 2019[2]. After China, the first case of COVID-19 was identified in Thailand on 13th January 2020. Due to its wide

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coverage, across the countries by 30th January 2020, WHO declared the outbreak as a Public Health Emergency of International Concern, and on 11th March, WHO declared COVID-19 as a pandemic (Fig 1).

The widespread of COVID-19, instils fear and anxiety because of gaps in our knowledge about its spread and behavior. The WHO, Situation Report-137 released on 5th June, 2020 reported 6535354 confirmed cases along with 387155 as fatality due to this infection and unfortunately the numbers are still rising exponentially all across the world every day.

There are several predictive models with limited validity have been reported in the literature to predict the case fatality and spread of COVID-19, however none of them have studied the impact of nutritional status of countries. Studies have shown that 'immunity as a passport to conquer COVID-19'. It is predicted that a poor nutritional status, could be the factor which might contribute to case fatality rate, but no study has been conducted till now, as per best of our knowledge to systematically study this effect.

To fill this research gap, we have conducted this cross-sectional study to determine the association of nutritional status considering the Global hunger index

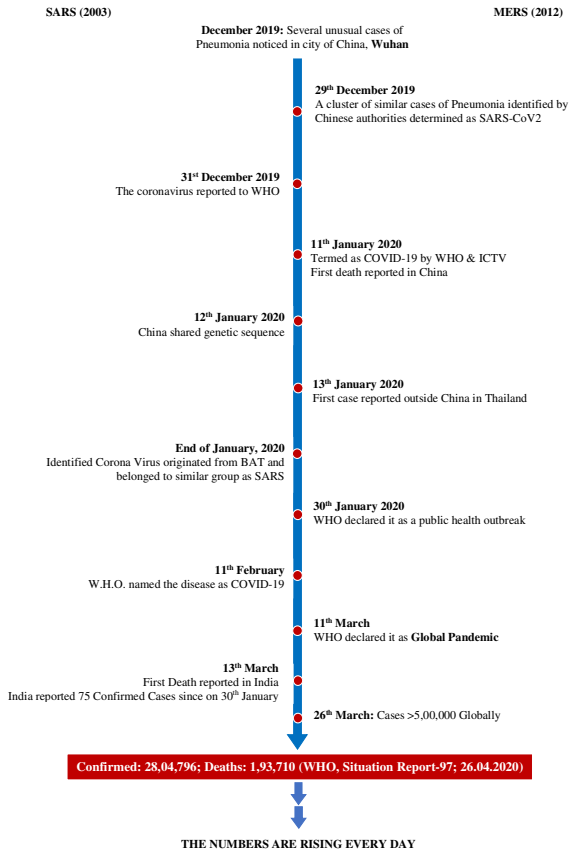

Fig 1 — Timeline of COVID-19 outbreak

(GHI) scale with number of new cases, mortality counts per day case fatality rate associated with COVID-19.

Reason to use GHI as measure of nutritional status due to:

1. GHI is based on a multidimensional approach to measure hunger.
2. COVID-19 is affecting all age-groups, therefore GHI scale is considered, because it reflects the nutritional situation of the entire population along with children.
3. The GHI is a tool to measure and track hunger and consequent undernutrition not only at the regional but also at national and global levels.
4. GHI not only reflects proportion of undernourished population; but a combination of factors which contributes to undernutrition like inadequate intake (quality or quantity) of food, poor absorption of nutrients due to infections; household food insecurity; insufficient access to maternal wellbeing or child care practices; inadequate access to health services, safe water, and sanitation.
5. GHI score are calculated each year. In the present study most recent GHI scores (2019) has been used.
6. GHI measures hunger in three dimensions: inadequate food supply (for entire population), child mortality and child undernutrition. These three dimensions are further based on four indicators including undernourishment among entire population, wasting, stunting and child mortality (Fig 2). The combination of indicators measured independently from each other reduces the impact of random measurement errors on the resulting index. The severity scale of GHI is divided into five categories: 9.9 (at low risk); 10 to 19.9 (at moderate risk); 20 to 34.9 (at serious risk); 35 to 49.9 (alarming); and 50 (extremely alarming).

There are many controversies in the existing literature regarding the immunity, economic status and status of hygiene. It's still a matter of active debate among research community. According to the "hygiene hypothesis," being too clean causes a malformation of the immune system, which may be a contributing factor for getting more prone to infectious diseases[3]. As, per the hygiene hypothesis, if the problem is being too hygiene then hypothetically the issue can be easily resolved via being unhygienic, right? But no, as it may lead to much worse. Population with high GHI are probably have low-hygiene status and disproportionally on the other hand it is predicted that people with low GHI are following better hygiene and therefore, their immunity may be affected.

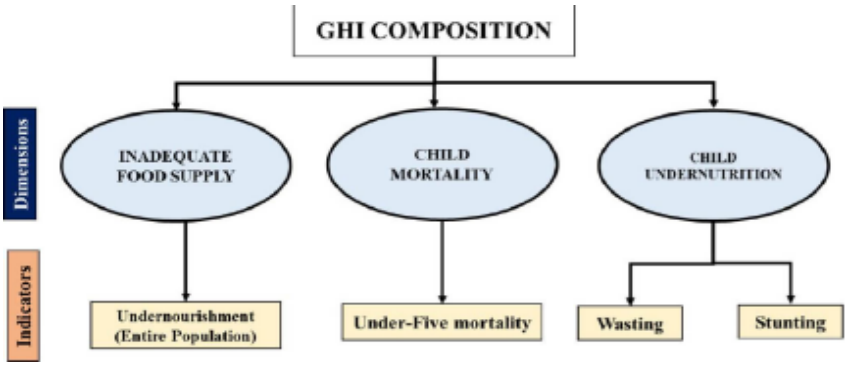

Fig 2 — Composition of Global Hunger Index

Before COVID-19 incidence, more than 820 million people went to bed hungry, and now when the nations are facing this pandemic the probability of infection rises for those who are already at risk of malnutrition which may lead to a rise in a situation of 'crisis within crisis' and when this virus is spreading in an unpredictable manner; it become necessary to study the impact of nutritional status in the individual countries in case fatality rate and spread due to COVID-19. Therefore, our study aimed to determine the association of COVID-19 spread and case fatality rate among Asian countries classified according to GHI.

Methodology :

Study design: Cross-sectional

Setting: Asian countries

Population: COVID-19 confirmed and case fatality rate cases from Asian population including all age groups and gender.

Outcome: number of new cases, and mortality counts per day due to COVID-19

Data collection: A total of 32 Asian countries with data reported for Global hunger index, confirmed cases and case fatality rate caused by COVID-19 till 19th April, 2020 were included in the study. Data was collected retrospectively from the European Centre for Disease Prevention and Control site for number of new cases and mortality counts reported per day and per country[4]. Data for global hunger index score was taken from report published in 2019 'Global Hunger Index'[5]. World meter site was used to collect data for population density and median age[6]. World Bank classification for the level of a country's income was referred[7].

Data Analysis : Since the outcome variables (number of new cases, mortality counts per day) are count (non-negative discrete number), Poisson regression is used as a standard model for analyzing such data. However, in case of over dispersion, Negative binomial regression model (NBRM) is recommended. In our case, an over dispersion test was performed to evaluate the adequacy of the NBRM over the Poisson regression model. When the ratio of variance to mean of the Poisson distribution value á (alpha) larger than one indicates over dispersion. In this study the variance was greater than the mean, and over dispersion test was significant indicated an over dispersion. Hence, the NBRM was preferred over the poison model. The effect of the association was quantified by unadjusted and adjusted incidence rate with its 95% confidence interval (CI) using univariable and multivariable negative binomial regression analysis, respectively. Data were analyzed using software STATA version 13. P value <0.05 was considered a level of signifance.

Results

A total of 32 Asian countries were included in the study (Table 1). Keeping the confirmed cases and deaths per day caused by COVID-19 as outcome, univariate regression analysis was used to study predictor and outcome relationship. The data analysis reported a significantly higher incidence of COVID-19 in countries with low risk GHI (IRR =1.74; 95% CI 1.49 to 2.04) as compared to countries with serious and alarming risk for GHI and the number of deaths was found to be significantly lower in the countries at moderate risk for GHI (IRR 0.51, 95% CI 0.39 to 0.67) when compared to countries with serious and alarming risk of GHI (Table 2).

NBRM was used to adjust the confounding effect of potential variables including number of tests done, population density and economic profile of the countries to avoid the bias of getting that countries at low risk of GHI would have high income therefore, due to better management they are having less case fatality rate. The multivariable analysis demonstrated that countries those at low risk of hunger had 2.8 times higher incidence of new cases risk (IRR =2.8; 95% CI 2.01 to 4.05) and with moderate risk of hunger had 1.7 times higher incidence (IRR 1.7, 95% CI 1.3 to 2.1) when compared with countries with serious and alarming risk for GHI. Low GHI risk countries had 50% less deaths (IRR 0.5, 95% CI 0.26 to 0.94) and countries at moderate risk for hunger had 76% less deaths (IRR 0.24, 95% CI 0.14 to 0.40) due to COVID-19 as compared with countries at high risk for global hunger in Asian population, respectively. We also observed 9% less deaths per day (IRR 0.91, 95% CI

Table 1 — *List of countries included in the study along with mortality percentage*

Country	Global Hunger Index	Case fatality	Incidence	Case fatality rate%	Average case fatality rate%
Armenia	Low risk	20	1291	1.5	**1.8**
Azerbaijan	Low risk	18	1373	1.3	
China	Low risk	4636	83803	5.5	
Georgia	Low risk	4	388	1.0	
Iran	Low risk	5031	80868	6.2	
Kazakhstan	Low risk	17	1654	1.0	
Kuwait	Low risk	6	1752	0.3	
Kyrgyzstan	Low risk	5	673	0.7	
Mongolia	Low risk	0	31	0	
Saudi Arabia	Low risk	92	8274	1.1	
Thailand	Low risk	47	2733	1.7	
Turkey	Low risk	1890	82329	2.2	
Iraq	Moderate risk	81	1482	5.4	**2.2**
Jordan	Moderate risk	7	413	1.6	
Lebanon	Moderate risk	21	672	3.1	
Malaysia	Moderate risk	88	5305	1.6	
Myanmar	Moderate risk	5	107	4.6	
Oman	Moderate risk	6	1180	0.5	
Sri_Lanka	Moderate risk	7	254	2.7	
Uzbekistan	Moderate risk	5	1495	0.3	
Vietnam	Moderate risk	0	276	0	
Afghanistan	Serious risk	30	908	3.3	**2.4**
Bangladesh	Serious risk	84	2144	3.9	
Cambodia	Serious risk	0	122	0	
India	Serious risk	507	15712	3.2	
Indonesia	Serious risk	535	6248	8.5	
Laos	Serious risk	0	19	0	
Nepal	Serious risk	0	31	0	
Pakistan	Serious risk	159	7993	1.9	
Philippines	Serious risk	382	6078	6.2	
Timor-Leste	Serious risk	0	18	0	
Yemen	Alarming risk	0	1	0	

Table 2 — *Crude association of GHI with number of new cases and deaths per day due to COVID-19*

Outcome	GHI Risk	p-value	Unadjusted IRR	95% CI
Number of new cases	At low risk	0.000	1.74	1.495 to 2.041
	At moderate risk	0.001	1.32	1.123 to 1.559
Mortality counts	At low risk	0.091	1.21	0.969 to 1.523
	At moderate risk	0.000	0.51	0.390 to 0.674

0.87 to 0.94) and 5% less incidence of reported cases per day (IRR 0.95, 95% CI 0.93 to 0.97) in countries with each year decrease in the average median age of subjects of respective countries (Table 3).

Discussion

We observed that case fatality rate caused by COVID-19 was significantly lower among countries which were at low to moderate risk of global hunger index with reference to countries which were at serious or alarming risk of GHI. In our analysis as expected we observed that 50% less deaths per day in countries with lower risk for hunger and 76% less deaths per day due to COVID-19 in countries with moderate risk for hunger with reference to countries which were at serious or alarming risk for hunger. Many confounding factors for this of study may not be adjusted in the model could explain the difference in the effect size observed in the low and high risk countries. A possible reason for less deaths per day observed in the low and moderate risk for GHI countries could be due to a high percentage of population in the low GHI countries is calorie sufficient and has dietary diversity which indicates that majority of the people in population have better overall nutritional status which may lead to the better immune system to fight with infections like COVID-19, and that is why a large percentage of people though may test positive for COVID-19 but it may not lead to mortality as their immune systems are strong enough to cope with it.

On the other hand, the population in countries with high GHI score where a high percentage of people eat poor quality diets and are calorie deficit, and hence suffer from various deficiency diseases already have a weak immune system which may not fight against the COVID-19 virus leading to high mortality rates.

Presently the world is in the grip of the pandemic COVID -19, a new novel virus and new things are far more complicated to understand initially. However, a few studies have been done in understanding the importance of nutrition in COVID-19 patients.

A paper published by Barazzoni R *et al*,[8] mentioned that patients with worst outcomes and higher mortality are reported to include immunocompromised subjects and malnourished people in general are at risk of developing factors which contribute to morbidity and mortality in chronic and acute diseases. Having a good nutritional status and preventing or treating malnutrition is likely to lower the complications in patients who

Table 3 — *Results of multivariable negative binomial regression analysis*

Variable	Number of new cases per day IRR	95% CI	p-value	Mortality counts per day IRR	95% CI	p-value
Alarming and serious	Reference			Reference		
Low Risk GHI score ≤9.9 (At low risk)	2.8	2.01 to 4.05	<0.001	0.5	0.26 to 0.94	0.033
Moderate GHI Score 10.0 to 19.9 (At moderate risk)	1.7	1.3 to 2.1	<0.001	0.24	0.14 to 0.40	<0.001
Median Age	0.95	0.93 to 0.97	<0.001	0.91	0.87 to 0.94	<0.001

Adjusted for number of tests done, population density and economic profile of the countries

are at nutritional risk and might be diagnosed as COVID-19 positive[8].

A recent study published in 'The Lancet' pointed out that COVID-19 can be accompanied with fever, nausea, vomiting and diarrhea[9]. All these symptoms may impair the food intake and absorption of nutrients in an individual. Thus, having a good nutritional status is beneficial for people to combat the severe complications of COVID-19. The nutritional status of an individual is an important factor in the outcome of a variety of different infectious diseases[10]. A recently published study on influenza pandemic highlighted the importance of nutrition in variations in morbidity and mortality figures[11].

Median age of the countries people could be an important confounder for the predictor and outcome relationship as shown by a recently published study in 'The Lancet Infectious Diseases'[12] done on COVID-19 positive patients in 38 countries found that risk of death from the disease increased with each decade of age. Therefore, we have adjusted the confounding effect associated with median age of the people living in the respective countries.

Many recent studies have highlighted the importance of good nutrition in building a strong immune system to fight against diseases like COVID 19. Based on these findings, a balanced dietary approach should be given prime importance along with the first-line treatment not only to treat any disease but also in building up a good nutritional status. The findings of the present review reinforce the concept of importance of good nutrition in fighting the infections than those with moderate or poor nutrition.

Conclusion : More rigorous measures have to be taken by the countries with serious or alarming hunger index for reducing case fatality rate associated with COVID-19 in Asian countries.

Limitation of the Study : This study has few limitations.

1. A detailed patient information regarding clinical outcomes, was not available at the time of analysis.
2. Although our findings are applicable for Asian countries, on the other hand it provides the homogeneity in findings.
3. The testing policies in the respective countries could be an important confounder for the predictor-outcome relationship although we have adjusted, the number of test done in respective countries for COVID-19 diagnosis.
4. Percentage of the elderly population (high risk for case fatality due to COVID-19) were not accounted in the current study, which would have affected the predictor-outcome relationship.
5. The effect of the lockdown could not be adjusted in the generalized linear mixed model generalized linear mixed model which could be an important confounding variable for the objective of this study.

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Original Article

Prevalence of Peripheral Arterial Disease in Middle Aged (40 years and above) Diabetic Patients and Its Correlation with Carotid Intima-media Thickness in North 24 Parganas District Hospital

Arnab Bhattacharyya[1], Kajal Chandra Ray[2], Tapan Haldar[3], Naga Jyothi Kondra[4]

Background : Diabetes Mellitus (DM) is an independent risk-factor of coronary artery disease (CAD). Over thirty million people have been diagnosed with diabetes in India (Diabetes.co.uk). The CPR (Crude Prevalence Rate) in the urban and rural areas in India are approximately 9% and 3% of the total population respectively. North 24 Parganas District of West Bengal is one of the most populated Districts of India (second only to Thane District of Maharashtra). As per 2011 census, the population of North 24 Parganas approximates about one crore (rural 4275724 and urban 5807128). In spite of the high disease burden (as per national average of Diabetes Mellitus), very few studies have been conducted till now regarding the diabetic population of North 24 Parganas, West Bengal.

Methods : A descriptive cross-sectional study has been conducted in North 24 Parganas District Hospital, Barasat, to find out the prevalence of peripheral arterial disease (PAD) by ankle-brachial index (ABI), in middle aged(40 years and above) diabetic patients and to find out the correlation with carotid intima-media thickness (CIMT), as they often co-exist with coronary artery disease (CAD), cerebrovascular disease or other complications of Diabetes Mellitus.

Results : Coronary atherosclerosis is often clinically silent with serious morbidity and mortality at its first presentation. In the present study, the mean age was 53.87 years, mean duration of DM was 6.76±5.78 years, with 70% of patients having abnormal ABI values (=0.9) and 46% of patients having abnormal CIMT (>0.8). They were correlated with each other, so as to assess the degree of atherosclerosis.

Conclusion : It may be concluded that measurement of carotid intima media thickness is an important tool to assess the burden of atherosclerotic complications of Diabetes Mellitus.

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Key words **: DM, CAD, CPR, PAD, ABI, CIMT.**

CAD is the leading cause of death in DM[1]. Diabetes is able to impair morphological and functional characteristics of the vascular wall and this condition plays as precursor of atherosclerotic disease[2]. The chronicity of DM affects many organs, systems and is responsible for the majority and mortality associated with the disease. Chronic complications can be divided into vascular and non-vascular complications. The vascular complications of DM are further divided into micro-vascular (retinopathy, neuropathy and nephropathy) and macro-vascular complications (CAD, cerebrovascular disease, PAD). The chronic complications usually do not become apparent until the second decade of hyperglycemia. However, since type-2 DM has a long asymptotic period of hyperglycemia, many individuals, suffering from type-2 DM have complications at the time of diagnosis.

PAD of the lower extremity is primarily the clinical manifestation of systemic atherosclerosis and atherothrombosis. With the advent of atherosclerosis, there is change in intima-media thickness(IMT) of the arterial wall along with inflammation[3]. PAD is commonly seen in type-2 DM and occurs almost three time more frequently in individuals with DM, compared to the age

Editor's Comment :

- **Carotid doppler is perhaps the only non-invasive method of diagnosing burden of atherosclerosis and at the same time a study regarding its correlation with ABI is simple and inexpensive method of community survey of macrovascular complications of diabetes mellitus.**

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and sex matched non-diabetics and it often coexists with cerebrovascular disease or coronary artery disease and therefore it is associated with poor prognosis and increased risk of morbidity and mortality[4].

Several studies have demonstrated that patients with PAD are at risk of adverse cardiovascular events compared to those individuals without PAD[5]. Coronary atherosclerosis is often clinically silent with serious morbidity or mortality as its first manifestation[6]. Patients with PAD, therefore, have an increased risk of myocardial infarction (MI), stroke and death[7,8]. The current concept of PAD is established by non-invasive tests such as, ankle-brachial index (ABI) and carotid intima-media thickness (CIMT) measurements, even before the onset of clinical symptoms[9].

Type-2 diabetes appears to confer an excess risk of cardiovascular events. Atherosclerosis is one of the primary, patho-physiological processes, underlying ischaemic cardiovascular events[10]. CIMT is strongly associated with the risk of MI and stroke in asymptomatic older adults. ABI is reliable indicator of high coronary risk and significantly related to the presence of PAD[11]. Cardiovascular risk prediction in asymptomatic individuals is mainly based on the level of cardiovascular risk factors incorporated in scoring equations. Improvement in cardiovascular risk prediction is needed and may be established by including a measure of pre-clinical atherosclerosis in the risk prediction algorithms, because atherosclerosis underlying the cardiovascular events develops over decades and has a prolonged asymptomatic phase, during which it is possible to modify the course of the disease. Measurement of CIMT has been proposed to be added to cardiovascular risk-factors to improve the individual risk assessment[12]. B-mode scan-imaging offers the ability to examine the pre-symptomatic lesion.

The patho-physiological mechanisms, by which arterial insufficiency develops, is based on the presence of arterial stenosis that progresses naturally to cause complete occlusion of the artery. Atherosclerosis is a complex process that involves endothelial dysfunction, lipid disturbance, platelet activation, thrombosis, oxidative stress, vascular smooth muscle activation, altered matrix metabolism, remodeling and genetic factors. There is role of inflammation in all stages of development of atherosclerosis and among the bio-markers of inflammation, C-reactive protein (CRP) is associated with both the development of PAD and impaired glucose regulation. Again, the flow-distribution at the arterial bifurcation hastens the process.

Aims and Objectives

The study was conducted in North 24 Parganas District hospital, Barasat, so as to assess the prevalence of PAD in middle-aged (40 years and above) diabetic patients and to find out its correlation with common carotid artery intima-media thickness (CCA-IMT).

And for this to occur —

(1) ABI was measured in middle-aged diabetic patients to detect PAD.

(2) Common carotid artery intima-media thickness was measured by carotid doppler study.

(3) Correlation between CCA-IMT and PAD was done.

Materials and Methods

A hospital-based study of seventy middle-aged (40 years and above) diabetic patients was conducted in North 24 Parganas district hospital, Barasat, Kolkata-124, from 1st April 2015 to 31st March 2016 (12 months). Patients with established CAD, patients symptomatic for PAD and patients with ABI>1.5 (because of arterial calcification with false high blood pressure) were excluded from the study. For this study, age, sex, duration of DM, systolic blood pressure of upper and lower limbs, ABI, carotid-IMT, presence of neuropathy and relevant biochemical parameters of all patients of study group were recorded.

Sample Size with Calculation

The study was a descriptive, cross-sectional one. The number of subjects required for this study was 70.

As per study by YJV Reddy, MV Nagabhusana, Aravind Sosale, Edward. Jude, *et al* in South India on 200 rural and 400 urban patients with type-2 DM. Prevalence of ABI in type-2 DM was 17.8% ie, ($p<0.01$). The formulae used for sample size calculation are as follows:

Sample size in descriptive study is calculated from

$$n = \frac{(Z_{\alpha/2})^2 \times p \times q}{l^2}$$

l	-	precision in absolute term
	-	Is considered as -9
p	-	proportion from previous study
	-	is considered as -17.8%
q	=	100-p = 100-17.8 = 82.2
Z	-	normal standard deviate
$Z_{a/2}$	=	1.96 (considering 95% confidence interval, its value would be 1.96)
$(Z_{a/2})^2$	=	1.96×1.96 = 3.84

$$n = \frac{(Za/2)^2 \times p \times q}{l^2}$$

therefore,

Minimum sample size is found to be 70

Statistical Methods

Statistical analysis was performed with the help of software sas9.2, spss 15.0, stata 10.1. Using this software, basic tabulations and frequency distributions

were prepared. The mean and standard deviation were also calculated. Chi-square test was used to test the association between different study variables. Pearson correlation (r) was calculated to find the correlation between the different variables of the study. Significance level was set at 0.05, confidence interval was at 95% level. $p<0.05$ was considered statistically significant and CIMT were measured using doppler ultrasound Acuson X150 with 8 linear array MHz transducer and a sphygmomanometer. All measurements were performed in the supine position after 10 minutes of rest. The sphygmomanometer cuff was tied just above the elbow in arms and just above the medial malleolus in legs. The ultrasound transducer was used to locate arterial doppler signal distal to the cuff. The systolic pressure of the posterior tibial artery and brachial artery were measured bilaterally. Then for obtaining ABI highest systolic pressure of posterior tibial artery was divided by the highest systolic pressure in the brachial artery.

ABI values were interpreted as follows: abnormal (ABI=0.9), borderline (ABI 0.91-0.99), normal (1.00-1.4) or non-compressible (ABI=1.4).

Carotid intima-media thickness was carried out in common carotid artery, with the subject in supine position, neck-extended and head slightly turned to the direction opposite to the carotid artery, being examined. CIMT was measured in the far wall of common carotid artery, around 1cm below carotid bifurcation using high resolution B-Mode ultrasound machine with a linear array transducer of 8 MHz It is calculated as distance between the leading edges of lumen intima interface and media adventitia interface. Multiple measurements of ABI and CIMT were performed to improve the precision and eliminate the risk of error by measuring both the non-invasive measures.

CIMT values were recorded as: normal(<0.8mm), abnormal (>0.8mm).

Patients were divided into PAD and non-PAD groups on the basis of ABI values. Data have been analyzed accordingly and the prevalence of PAD in patients with type-2 DM were found out. Then with further statistical analysis, the correlation of PAD with carotid IMT and various other parameters of diabetes were found out.

Results And Analysis

Of the total 70 cases recorded from IPD and OPD of North 24 Parganas District Hospital, Barasat were as follows:

(a) mean age-53.87 years (±8.95).

(b) mean systolic BP of lower limbs-117.17mm of Hg (±11.15).

(c) mean systolic BP of upper limbs-135.68mm of Hg (±13.93).

(d) mean ABI-0.87(±0.07).

(e) mean IMT-0.80(±0.06).

(f) 38.57% of patients were suffering from neuropathy.

(g) 25.7% of subjects were suffering from DM and hypertension.

(h) Out of 70 patients, 32 patients were less than/equal to 50 years of age. 24 patients were 50-60 years of age. 11 patients (61-70) and only 3 patients (71-80).

(i) 51.4% of total subjects were with duration of diabetes less than/equal to 5 years. 27.1% belonged to 6-10 years of duration and subjects having DM more than 15 years were only 4.

(j) 70% of subjects were having ABI=0.9.

(k) 46% of subjects were having IMT>0.8.

(l) Out of 49 patients, having ABI=0.9, 25 patients were suffering from peripheral neuropathy and out of 21 patients having ABI >0.9, only 2 patients suffered from peripheral neuropathy. The chi-square statistics is 10.6833.p-value is .001081. The result is significant at $p<0.01$.

(m) Among total subjects, 74.2% (52) were non-hypertensive with 44.3% (31) subjects having ABI values =0.9. Among all subjects, 25.7% (18) were hypertensive and identified with ABI=0.9. The result is significant as the p-value is 0.001271($p<0.01$).

(n) Among 46% of subjects having IMT>0.8, 21.4% subjects were hypertensive. The test is significant at chi-square statistics 13.81, p-value 0.00201($p<0.01$).

(o) The chi-square statistics is 18.7538 and p-value is 0.000878 ($p<0.01$)- showed that most of the subjects with duration of DM more than 5 years were identified with ABI=0.9- which is significant.

(p) Out of 21 patients having ABI>0.9, only 3 patients were recorded as IMT>0.8, whereas, out of 49 patients having ABI=0.9, 29 patients were recorded as IMT>0.8. The chi-square statistics is 11.9408. The p-value is 0.000549. The result is significant at $p<0.01$.

(q) 92.85% (65) patients were having FBS=126mg/dl, 84.28% (59) having PPBS=200, 18.57% (13) having low HDL and 30% (21) having high triglyceride and high LDL levels.

Discussions

So, in this descriptive cross-sectional study, mean duration of DM was 6.76(±5.78) years with 51.4% patients were of less than 5 years duration and only 5.7% of patients belong to long duration (16-20 years).

Patients were divided into two groups : ABI (=0.9) and (>0.9). 70% among total patients were having ABI less than/equal to 0.9. 46% of total patients were identified with intima media thickness>0.8. Among these (CIMT>0.8), 41.42% subjects were having ABI=0.9. The result was highly significant as $p<0.01$.

The study could be compared with the study done by Pendekar S *et al*[5], where the mean age was 55.2 years (53.87 years in present study), with 68.9% cases with established CAD, proven by angiography; out of which, 64% were having abnormal ABI values, thus predicting the future risk of CAD.

The study could also be compared with Jasmine Kaur Chawla *et al*[10], which showed that type-2 DM group had higher mean CIMT as compared to the control groups. That study concluded that CIMT had association with ABI and duration of type-2 DM.

In the present study, 74.28% of all subjects were not having any other predisposing factors like hypertension; 25.71% were having hypertension with DM. Among 74.2% of non-hypertensives, 44.3% were having ABI=0.9 and 30% were having ABI>0.9. 25.7% hypertensives were identified with ABI=0.9.

61.42% of total subjects were not having peripheral neuropathy and 38.57% were having peripheral neuropathy.

Among all the patients with less 50 years of age, 11.42% were with IMT>0.8, indicating that increase in age could be correlated with increased IMT. The study also showed that there was significant correlation of IMT>0.8 with hypertension. Most of the subjects, whose duration of DM was more than 5 years, were identified with ABI=0.9. And it also showed that there was significant correlation between ABI=0.9 and IMT>0.8.

The study covered only North 24 Parganas District Hospital (Barasat) and not any other Government Hospital in the District and hence it did not reflect the true load of DM and its complications in the district. However, it suggested a way of preventing the complications of DM (viz. CAD) in a less expensive and less time-consuming way and the simple procedures could also be applied for community-based survey.

Summary and Conclusion

Among the total subjects, 70% of diabetic subjects were found with ABI=0.9, 30% of the subjects were with ABI>0.9. Among the 70% of diabetic subjects, 35.71% were found to be associated with peripheral neuropathy. The result is significant as the p-value is 0.001.

Among the total subjects, 46% were found with IMT>0.8mm. The result is significant as p-value is 0.0005. This indicates that ABI value=0.9 was strongly associated with increased carotid intima media thickness. The study also showed most of the diabetic subjects with age 40 years and above have abnormal ABI and an associated increased CIMT.'

Subjects with increased CIMT had increased risk of atherosclerotic complications.

Thus, it may be concluded that measurement of carotid intima media thickness is a simple, inexpensive, time-saving procedure that may be used to measure the degree of atherosclerotic burden and complications of diabetes mellitus.

Limitations

The study is Institution (District Hospital) based – and so the sample size is small; as a result, some data may be exaggerated or there may be under-reporting.

Funding : None

Conflict of Interest : None

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Original Article

Epidemiological Review and Sensitivity Patterns of CBNAAT Testing for Tuberculosis in a Teaching Hospital of Eastern India

Madhab K Mandal[1], Udas Chandra Ghosh[2], Sudipta Mondal[3], Atanu Roy Choudhuri[4], Md Hamid Ali[5]

Introduction : CBNAAT facilities utilizing the molecular method of TB diagnosis yields substantially higher rates of diagnosis than conventional methods.

Methods : We conducted an observational record review study of CBNAAT samples received at a teaching hospital of Eastern India and analyzed the type of source patients, the nature of health facility sending such samples and the outcomes of CBNAAT testing across the subpopulations of TB patients.

Results : 2453 Pre DR TB and 1950 Pre TB patients comprised our study population, with 87.5% being HIV negative. 50.5% Pre DR TB and 13% Pre TB patients had CBNAAT positivity. CBNAAT positivity was 50.2% in new sputum negative and 44.5% in new sputum positive samples, while it was 74.8% in Pre DR TB and 12.9% in Pre TB samples, the figures being statistically significant. However, the incidence of Rifampicin resistance did not differ among most subpopulations in the study.

Conclusions : CBNAAT remains a crucial diagnostic tool in TB detection campaigns. Rifampicin resistance was not rare in the study and spanned all subgroups included in this study.

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Key words **: Pre TB, Pre DR TB, CBNAAT, Rif resistance.**

Tuberculosis (TB) caused by Mycobacterium tuberculosis (MTB) bacteria is an important public health issue around the globe. Routine diagnostic methods for MTB include acid-fast bacilli (AFB) microscopy, MTB culture, conventional polymerase chain reaction (PCR), and GeneXpert® MTB/RIF assay.

The efficiency of MTB culture using the LJ medium has been demonstrated to detect MTB when 10 viable bacilli per mL of sputum were present.[1] GeneXpert MTB/RIF assay is one of the most advanced and rapid PCRbased methods recommended by WHO in 2010 for the detection of MTB DNA and rifampicin resistance. It is based on a hemi-nested real-time PCR assay utilizing five molecular beacon technology spanning the rpoB gene 81-bp rifampicin resistance determining region (RRDR).[2] The early detection of the MTB and RIF/DR in TB suspects is crucial for disease management and to control the disease transmission from person to person and the emergence of drug-resistant tuberculosis (DRTB). Moreover, studies have shown that CBNAAT facilities utilizing the molecular method of TB diagnosis yields substantially higher rates of diagnosis than conventional methods.[3]

Editor's Comment :

- **CBNAAT testing for Tuberculosis yields positive results in both sputum positive as well as negative samples.**
- **Rif resistance among CBNAAT positive samples are more common in Pre DR TB than among Pre TB subjects.**
- **PLHIV are most susceptible to harbor Rif resistance.**
- **Sputum negative samples are more likely to harbor Rif resistance than sputum positive samples.**

Material and Methods

This study was conducted at Murshidabad Medical College, Berhampore, a tertiary referral center catering to large parts of West Bengal and the adjoining areas of Bihar, Jharkhand and Bangladesh. This was an observational record review study from the sputum CBNAAT test records conducted at the TB clinic of our institution. Records of all sputum samples received from June 2018 to July 2019, both inclusive were collected and tabulated to obtain information about the source and type of patients as well as of the outcome of the test results.

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The source of patient referral was either the hospital IPD or OPD, or from private facilities, Tuberculosis units (TU) or the ART center of our institution.

The patients presenting for sputum CBNAAT testing were categorized as per RNTCP guidelines into Pre TB (those with no exposure to ATD, without HIV positivity and with no contact with MDR TB) and to pre DR TB (those with previous exposure to ATD, with HIV TVB co-infection or with contact with MDR TB), into the following subgroups:

- Pre TB
  - Pre TB NSN (New sputum negative)
  - Pre TB NSP (New sputum positive)
- Pre DR TB
  - Pre DR TB Contact MDR (NSN, NSP)
  - Pre DR TB FU (Follow up) (NSN, NSP)
  - Pre DR TB PLHIV (with HIV TB coinfection) (NSN, NSP)
  - Pre DR TB RT (returned to treatment after default) (NSN, NSP)

Results

This was an observational record review study of all cases presenting for sputum CBNAAT testing at Murshidabad Medical College, West Bengal, India, during the period June 2018 to July 2019. Data regarding gender distribution, source of referral for the sputum CBNAAT testing, suspected pulmonary or extra pulmonary involvement, HIV status of the population being tested and the CBNAAT test result were recorded and analyzed to yield statistical information.

The study spanned a period of 14 months from June 2018 to July 2019, both inclusive, during which a total of 4403 patients (2953 males, 1450 females, 67.1% and 32.9%, respectively) were tested at our facility, giving a male : female ratio of 2.04 : 1.

The patients were classified into two broad groups as per the RNTCP nomenclature into Pre TB cases (1950 cases, with no prior exposure to ATD, to HIV or to contact with MDR TB) and Pre DR TB (2453 cases) with previous exposure to ATD (treatment completed on follow up or returned to treatment after treatment discontinuation), HIV positivity or contact with MDR TB (Fig 1).

These cases were further subdivided into NSN and NSP cases. It was observed that the NSN cases were significantly more among Pre DR TB PLHIV (146 *versus* 84) and Pre DR TB RT (458 *versus* 154) and equitably distributed among Pre DR TB Contact MDR (50 versus 46) and Pre DR TB FU (769 *versus* 746). However, among Pre TB cases, NSP patients outnumbered NSN cases (1151 *versus* 799) (Fig 2 and 3).

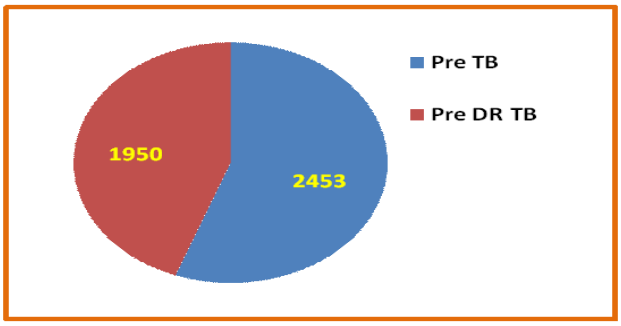

Fig 1 — Distribution of study population (n = 4403)

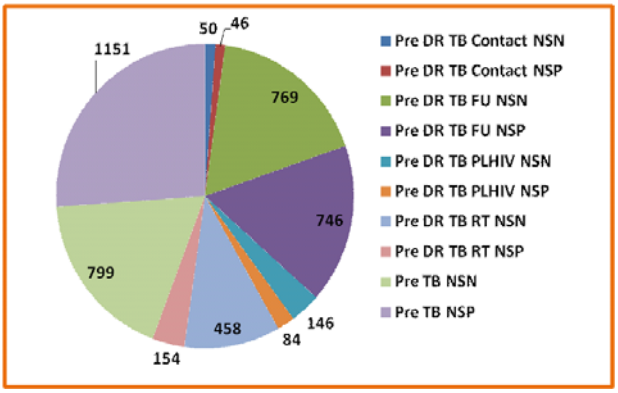

Fig 2 — Distribution of patient categories in study population (n = 4403)

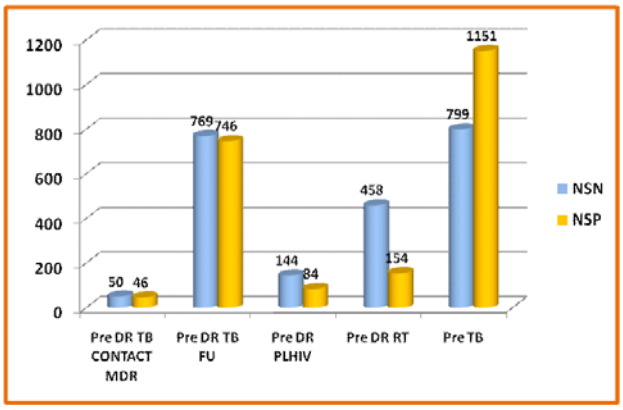

Fig 3 — Distribution of NSN and NSP cases across study sub-populations

The health facility from which patients were referred for CBNAAT testing were tabulated. 49% and 26.6% patients were referred from the OPD and IPD respectively of the study institution, followed by 11.6% from the TB units, 8.7% from private facilities and 4.1% from the ART center of our hospital. The hospital OPD generated relatively more DR TB suspects than pre TB cases (57.4% *versus* 38.4%) while the ART center referred more Pre TB cases than DR TB suspects (7.6% versus 1.3%) (Table 1).

Our study included patients who were referred for sputum CBNAAT testing. Predictably, the study

Table 1 — *Source of referral for patients tested for sputum CBNAAT*

	IPD	OPD	Private	TU	ARTC	Total
Pre DR TB Contact MDR :						
NSN	11	22	11	6	0	50
NSP	8	25	8	5	0	46
Total	19(19.8%)	4749%)	19(19.8%)	11(11.4%)	0	96(100%)
Pre DR TB FU :						
NSN	149	401	72	147	0	769
NSP	138	422	31	153	2	746
Total	287(18.9%)	823(54.3%)	103(6.3%)	300(19.8%)	2(0.1%)	1515(100%)
Pre DR TB PLHIV :						
NSN	33	68	7	16	22	146
NSP	14	50	3	9	8	84
Total	47(20.4%)	118(51.3%)	10(4.3%)	25(10.9%)	30(13%)	230(100%)
Pre DR TB RT :						
NSN	73	250	43	89	3	458
NSP	35	68	8	43	0	154
Total	108(17.6%)	318(52%)	51(8.3%)	132(21.6%)	0	612(100%)
Pre DR TB Total	561(22.9%)	1409(57.4%)	183(7.7%)	268(10.9%)	32(1.3%)	2453(100%)
Pre TB :						
NSN	196(24.5%)	343(42.9%)	38(4.8%)	142(17.8%)	80(10%)	799(100%)
NSP	413(35.9%)	405(35.2%)	163(14.2%)	101(8.8%)	69(6%)	1151(100%)
Total	609(31.2%)	748(38.4%)	201(10.3%)	243(12.5%)	149(7.6%)	1950(100%)
Study population	1170(26.6%)	2157(49%)	384(8.7%)	511(11.6%)	181(4.1%)	4403(100%)

population predominantly involved suspected PTB patients (4223 out of 4403 patients, 95.1%) with less than 5% cases with clinical suspicion of EPTB. This predominance of PTB patients was evident in all sub population in this study (94.8% in MDR Contacts, 98.4% in follow up patients, 83.3% in PLHIV, 98.4% in returned to treatment, and 94.7% in pre TB group). The highest incidence of EPTB was seen in the PLHIV population (11.7%). Excluding the patients with a prior diagnosis of HIV, the prevalence of HIV sero-positivity was 14.2% in Pre TB patients, and 3.6%% in pre DR TB RT. The overall prevalence of HIV was 11.1% in pre DR TB patients, 14.2% in pre TB patients and 12.5% in the entire study population (Table 2).

Out of the 4403 samples tested in our study, CBNAAT was negative in 50.9%, while 2207 (47.4%) of sputum samples provided positive test results. The overall CBNAAT positivity was 74.8% in pre DR TB group and 12.9% in the pre TB group, summing up to a diagnostic yield of 47.4% in the study population.

Sensitive and Rif resistant MTB was detected in 45.3% and 2.1% samples respectively. The incidence of negative CBNAAT samples was highest among Pre TB (85.5%), Pre DR PLHIV (56.1%) and Pre DR TB RT (45.9%) cases. Rif resistance was seen in 2.1% of our cases, with Pre TB and Pre DR TB sub-populations showing resistance figures of 0.5% and 3.4% respectively. The highest incidence of Rif resistance was seen in Pre DR TB PLHIV (8.3%) (Table 3). CBNAAT testing yielded highest results in follow up cases (90.2%), followed by defaulters returning to treatment and PLHIV patients (50.5% and 43% respectively).

We further analyzed our study population into sputum negative and sputum positive samples. There were 1116 new sputum negative (NSN) cases (1004 Pre DR TB, 112 Pre TB) and 971 new sputum positive (NSP) cases (831 Pre DR TB, 140 Pre TB) in our study, giving a case detection rate of 50.2% among NSN cases and 44.5% among NSP cases (Fig 5). The CBNAAT positivity rate was significantly higher among Pre DR TB patients (70.6% in NSN, 80.7% in NSP) than among Pre TB patients (14% in NSN, 12.2% in NSP) (Table 4).

Table 2 — *HIV status and pulmonary versus extra pulmonary TB*

	HIV +	HIV -	PTB	EPTB	Total
Pre DR TB Contact MDR :					
NSN	0	50	45	5	50
NSP	0	46	46	0	46
Total	0	96(100%)	91(94.8%)	5(5.2%)	96(100%)
Pre DR TB FU :					
NSN	4	765	747	22	769
NSP	18	728	744	2	746
Total	22(1.5%)	1493(98.5%)	1491(98.4%)	24(1.6%)	1515(100%)
Pre DR TB PLHIV :					
NSN	146	0	119	27	146
NSP	84	0	84	0	84
Total	230(100%)	0	203(88.3%)	27(11.7)	230(100%)
Pre DR TB RT :					
NSN	17	441	448	10	458
NSP	5	149	154	0	154
Total	22(3.6%)	590(96.4%)	602(98.3%)	10(1.7%)	612(100%)
Pre DR TB Total	272(11.1%)	2181(88.9%)	2387(97.3%)	66(2.7%)	2453(100%)
Pre TB :					
NSN	50	749	696	103	799(100%)
NSP	227	924	1151	0	1151(100%)
Total	277(14.2%)	1673(85.8%)	1847(94.7%)	103(5.3%)	1950(100%)
Study population	549(12.5%)	3854(87.5%)	4234(96.2%)	169(3.8%)	4403(100%)

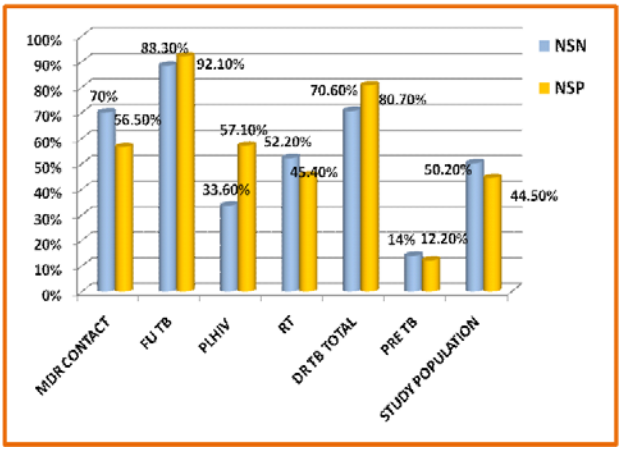

Fig 4 — CBNAAT positivity in NSN and NSP samples

We analyzed our data to see if the rate of CBNAAT positivity was different among various study subpopulations. Considering the Pre DR patients, CBNAAT positivity was higher among NSN than NSP (80.7 and 70.6) and this was statistically significant. Such statistically significant differences were also observed between Pre DR TB NSN and Pre TB NSN (70.6% and 14.0%), Pre DR TB NSP and Pre TB NSP (80.7% and 12.2%), and Pre DR TB and Pre TB (74.8% and 12.9%), but not between Pre TB NSN and Pre TB NSP (14.0% and 12.2%) patients (Table 5).

Resistance to Rif is a major area of clinical interest. This was less than 5% among all subpopulations in the study, except for a resistance of 19.2% among PLHIV and 6.5% among pre DR TB RT subjects (Table 6). Rif resistance was seen in 27.5% of Pre DR PLHIV NSN, 11.4% of Pre DR PLHIV NSP, 7.1% of Pre DR RT NSP, 6.3% of Pre DR RT NSN, 5.5% of Total Pre DR NSN cases, and 5.4% of all NSN cases in the study. In all remaining categories, the incidence of Rif resistance was less than 5% (Table 7, Fig 5). However, there was no statistically significant difference in Rif resistance between Pre TB NSN and Pre DR TB NSN, Pre TB NSP and Pre DR TB NSP, NSN and NSP or Pre TB and Pre DR TB subgroups (Table 8).

Discussion

It has been seen that, in a low-resource high-burden setting like India, CBNAAT has a great impact in holding off treatment where empiric ATD is often used [4]. The simplicity, high sensitivity and specificity for Rif resistance detection makes CBNAAT a very attractive tool for diagnostic of MTB and RIF resistance in MDR cases [5]. There has been little documentation regarding the utilization of CBNAAT from Eastern India ever since the Government of India adopted this technique and incorporated into the protocol of the RNTCP.

Our study had 44.4% of Pre TB cases suggesting that new TB suspects are yet to be routinely referred for CBNAAT testing. The predominance of Pre DR TB cases (Contact MDR, PLHIV, FU and RT) reflects the trend among clinicians to offer CBNAAT only to those

Table 3 — *Distribution of CBNAAT test result across the study subpopulations*

	Sensitive	Resistant	Not detected	Indeterminate	Error	Total
Pre DR TBContact MDR	60(62.5%)	1(1%)	32(33.3%)	3(3.1%)	0	96(100%)
Pre DR TBFU	1323(87.3%)	43(2.8%)	130(8.6%)	1(0.1%)	18(1.2%)	1515(100%)
Pre DR TBPLHIV	80(34.8%)	19(8.3%)	129(56.1%)	1(0.4%)	1(0.4%)	230(100%)
Pre DR TBRT	289(47.2%)	20(3.3%)	281(45.9%)	8(1.3%)	14(2.3%)	612(100%)
Pre DR TBTotal	1752(71.4%)	83(3.4%)	572(23.3%)	13(0.5%)	331.3%)	2453(100%)
Pre TBTotal	243(12.5%)	9(0.5%)	1668(85.5%)	6(0.8%)	24(1.2%)	1950(100%)
Study population	1995(45.3%)	92(2.1%)	2240(50.9%)	19(0.4%)	57(1.3%)	4403(100%)

Table 4 — *CBNAAT positivity in study sub-populations*

MDR Contact NSN (n = 50)	35 (70%)	MDR Contact NSP(n = 46)	26 (56.5%)
FU TB NSN (n = 769)	679 (88.3%)	FU TBNSP(n = 746)	687 (92.1%)
PLHIV NSN (n = 146)	51 (33.6%)	PLHIV NSP(n = 84)	48 (57.1%)
RT NSN (n = 458)	239 (52.2%)	RT NSP(n = 154)	70 (45.4%)
Pre DR TB Total NSN (n = 1423)	1004 (70.6%)	Pre DR TB Total NSP(n=1030)	831 (80.7%)
Pre TB NSN (n = 799)	112 (14%)	Pre TB NSP(n = 1151)	140 (12.2%)
Total NSN cases in the study (n = 2222)	1116 (50.2%)	Total NSP cases in the study(n = 2181)	971 (44.5%)

Table 5 — *CBNAAT positivity among various study subpopulations*

Variables	CBNAAT Test		Total No (%)	χ^2, df	p value
	Positive No (%)	NegativeNo (%)			
Pre DR TB NSP	831 (80.7)	199(19.3)	1030(100)	32.4981, 1	0.000
Pre DR TB NSN	1004 (70.6)	419(29.4)	1423(100)		
Pre DR TB Total	1835 (74.8)	618(25.2)	2453(100)		
Pre TB NSN	112 (14.0)	689 (86.0)	799(100)	1.3902, 1	0.238
Pre TB NSP	140 (12.2)	1011(87.8)	1151(100)		
Pre TB Total	252(12.9)	1700(87.1)	1952(100)		
Pre DR TB NSN	1004 (70.6)	419(29.4)	1423(100)	656.1168, 1	0.000
Pre TB NSN	112 (14.0)	689 (86.0)	801(100)		
NSN Total	1116(50.2)	1108(49.8)	2224(100)		
Pre DR TB NSP	831 (80.7)	199(19.3)	1030(100)	1033.1208, 1	0.000
Pre TB NSP	140 (12.2)	1011(87.8)	1151(100)		
NSP Total	971(44.5)	1210(55.5)	2181(100)		
Pre DR TB	1835 (74.8%)	618 (25.2)	2453 (100)	1668.6549, 1	0.000
Pre TB	252 (12.9%)	1698 (87.1)	1950 (100)		
Study population	2087 (47.4%)	2316 (52.4)	4403 (100)		

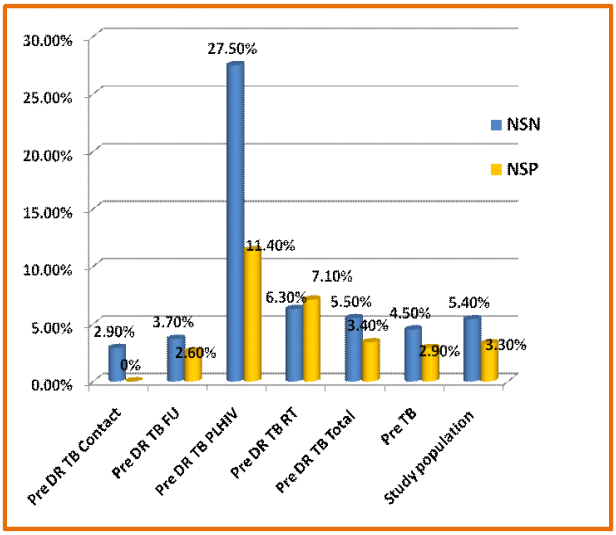

Fig 5 — Incidence of Rif resistance (n = 4403)

DR TB suspects. Further awareness generation amongst the medical and paramedical community is essential to counter this selection bias in future.

75.6% of our patients were referred from the study institution itself (49% from OPD and 26.6% from IPD services) while the neighboring TB units and private sector health facilities contributed 11.6% and 8.7% of our study patients. This is a dismal figure and indicates poor orientation to CBNAAT testing among the health care providers.

As mentioned, less than 5% of our cases were suspect EPTB cases. This raises the question of subjecting other clinical specimens for CBNAAT. Specimens that can be sent for testing include respiratory specimens such as sputum, bronchial or tracheal aspirates, broncho-alveolar lavage and gastric lavage as well as extra pulmonary specimens like tissue biopsy including lymph node, pus from abscess, CSF, ascitic and pericardial fluid, pleural fluid [6]. CB-NAAT testing for TB on other samples such as stool, urine and blood is not recommended [7].

50.9% of our patients had negative CBNAAT results, raising the question of patient selection before utilizing this facility. However, in high burden countries like India, where diagnosis of TB remains a clinician's nightmare, this figure reflects the utility of CBNAAT to rule out TB, unless histopathological examination proves otherwise.

Table 6 — *MTB detection rates by CBNAAT and incidence of Rif resistance among CBNAAT positive samples*

	CBNAAT positivity	Rif resistance (% of CBNAAT positive samples)
Pre DR TB Contact MDR (n=96)	61 (63.5%)	1 (1.6%)
Pre DR TB FU (n = 1515)	1366 (90.2%)	43 (3.1%)
Pre DR TB PLHIV Total (n =230)	99 (43%)	19 (19.2%)
Pre DR TB RT Total (n =612)	309 (50.5%)	20 (6.5%)
Pre DR TB Total (n = 2453)	1835 (74.8%)	84 (4.6%)
Pre TB NSN (n = 799)	112 ((14%)	5(4.5%)
Pre TB NSP (n = 1151)	140 (12.2%)	4(2.9%)
Pre TB Total (n = 1950)	252 (12.9%)	9 (3.6%)
Study population (n = 4403)	2087 (47.4%)	93 (4.5%)

The prevalence of HIV in our study was 12.5%, with a higher prevalence of resistance in this subgroup (19.2% among CBNAAT positive samples). In a study from Pune in Western India using line probe assay, the authors documented prevalence of MDRTB, INH mono- resistance and Rif resistance at 12.5%, 9% and 2.5%, respectively. The prevalence of MDRTB among new and relapsed patients was 8.8% and

Table 7 — *Incidence of Rif resistance in new sputum negative (NSN) and new sputum positive (NSP) samples*

New sputum negative (NSN)				New sputum positive (NSP)			
	Sensitive	Resistant	Total		Sensitive	Resistant	Total
MDR Contact NSN (n = 50)	34(97.1%)	1(2.9%)	35	MDR Contact NSP (n = 46)	26(100%)	0	26
FU TB NSN(n = 769)	654 (96.3%)	25(3.7%)	679	FU TBNSP(n = 746)	669(97.4%)	18(2.6%)	687
PLHIV NSN(n = 146)	37 (72.5%)	14(27.5%)	51	PLHIV NSP(n = 84)	43(89.6%)	5(11.4%)	48
RT NSN(n = 458)	224 (93.7%)	15(6.3%)	239	RT NSP(n = 154)	65 (92.9%)	5(7.1%)	70
Pre DR TB Total NSN (n = 1423)	949 (94.5%)	55(5.5%)	1004	Pre DR TB Total NSP (n = 1030)	803(96.6%)	28(3.4%)	831
Pre TB NSN(n = 799)	107 (95.5%)	5(4.5%)	112	Pre TB NSP(n = 1151)	136 (97.1%)	4(2.9%)	140
Total NSN(n = 2222)	1056 (94.6%)	60 (5.4%)	1116	Total NSP(n =2181)	939 (96.7%)	32(3.3%)	971

Table 8 — *Difference in the incidence of Rif resistance in study subpopulations*

CBNAAT positive	CBNAAT Test		Total No. (%)	χ^2, df	p value
	Sensitive No(%)	Resistance No(%)			
Pre TB NSN	107 (95.5%)	5 (4.5%)	112 (100)	0.2036, 1	0.651
Pre DR TB NSN	949 (94.5%)	55 (5.5%)	1004 (100)		
Total NSN	1056 (94.7)	59 (5.3)	1115 (100)		
Pre TB NSP	136 (97.1%)	4 (2.9%)	140 (100)	0.0987, 1	0.753
Pre DR TB NSP	803 (96.6%)	28 (3.4%)	831 (100)		
Total NSP	939 (96.7)	32 (3.3)	971 (100)		
NSN	1056 (94.6%)	60 (5.4%)	1116 (100)	5.3349, 1	0.020
NSP	939 (96.7%)	32 (3.3%)	971 (100)		
Total	1995 (95.6)	92 (4.4)	2087 (100)		
Pre TB	243 (96.4)	9 (5.6)	252 (100)	0.4763, 1	0.490
Pre DR TB	1752 (95.4)	83 (4.6)	1835 (100)		
Total	1997 (95.6)	92 (4.4)	2089 (100)		

23.1%, respectively[8]. More importantly, the detection rate of TB with CBNAAT is much higher than with sputum microscopy and this most evident with HIV co-infection where sputum negative TB is common. In a study of 100 patients from New Delhi, the case detection rate was 11% with microscopy and 40% with CBNAAT[9]. Apart from HIV, we also found a high prevalence of resistance in Pre DR TB RT patients who defaulted on ATD at some point of time. This trend is not unique to India and has been witnessed in Vietnam, Thailand and Rowanda[10-12].

The sub-analysis of patients into NSN and NSP categories was unique to our study. Interestingly, both Pre DR TB and Pre TB cases had higher rates of resistant organisms being detected in the NSN populations (5.5% versus 3.4% and 4.5% versus 2.9%) respectively. This deserves further analysis and research and raises the possibility of prior treatment leading to both less sputum positivity and higher rates of drug resistance. Last, but not the least, a conspicuous finding in our study is the low rates of CBNAAT positivity among Pre TB NSP cases (12.2%). Pre DR RT cases (45.4%), Pre DR Contact MDR NSP cases (56.5%) and among Pre DR TB PLHIV NSP cases (57.1%). This is a matter of serious concern and poses the strong possibility of false positive sputum microscopy and raises quality assurance issues on our minds. Further studies are essential to throw more light on this matter. The statistically insignificant differences in Rif resistance among our study subgroups indicate that Rif resistance is not isolated to any particular patient category and needs to be borne in mind across the spectrum of health care services.

Conclusion

We conclude that CBNAAT testing is essential in resource restricted setting not only to confirm the presence of MTB infection but also to rule out tuberculosis in clinically suspected cases. Moreover, an overall resistance of 2.1% in the study population from a predominantly rural part of Eastern India and a resistance figure of 3.4% among Pre DR TB suspects contributes important information to the rising incidence of drug resistance TB in this part of the world.

Lacunae

The OPD and IPD patients included in our study were not subdivided on the basis of the department of origin, which would have reflected the relative levels of sensitization among the medical personnel across the departments. This study with a sample size of more than 4000 reflects a wide population base. However multivariate analysis was not performed which could have added to the statistical power of the study.

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Conflict of Interest : None

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Original Article

Study on Secondary *versus* Tertiary Prophylaxis in Hemophilia Children under 12 Years of Age in a Tertiary Care Hospital in Eastern India

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Background : Prophylaxis in hemophilia is the standard of care in developed countries for prevention of further bleeding and to preserve joint functions, thereby improving quality of life. The goals of prophylaxis are minimal or 'zero bleeds', no joint deformity and near normal life. The present study was aimed to study the outcome of secondary versus tertiary prophylaxis with a lower dose in hemophilia A and Hemophilia B children under 12 years of age.

Methods : The present prospective study was conducted over a period of 18 months. Total 34 patients were included in the study. Hemophilia A (HA) patients were started prophylaxis with recombinant Fc fusion long acting factor VIII at 15 IU.kg^{-1}.dose^{-1} twice weekly and hemophilia B (HB) with recombinant Fc fusion long acting factor IX at 30 IU.kg^{-1}.dose^{-1} once weekly. Outcome measured in terms of median annualized bleeding rate (ABR), hemophilia joint health score (HJHS) and child activity.

Results : Among 34 patients included in the study, 28 (82.3%) patients were HA and six (17.7%) were HB. Mean age of patients was 6.82 years for HA & 6.5 years for HB. Median ABR reduced from 15.6 to 1.9 bleeds/year. HJHS in case of secondary and tertiary prophylaxis at first visit were 12.83±3.09 and 15.72±1.6 and in fourth visit (at 18 months) were 6.66±3.11 and 8.86±1.45 respectively. None developed inhibitors during study. Child activity measured in terms of combined mean of school activity participation (SAP) score and daily activity (DA) score improved in secondary and tertiary prophylaxis from 1.455±0.12 and 2.46±0.11 in first visit to 6.09±0.33 and 5.39±0.23 in fourth visit respectively.

Conclusion : When compared, secondary prophylaxis is better than tertiary prophylaxis in children. In resource constraint countries where availability of CFC is an issue, prophylaxis can be individualized and the goals can be achieved by using even smaller doses.

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Key words **: Hemophilia, Children less than 12 years, Low Dose Prophylaxis, Long Acting Factors.**

Editor's Comment :

- **The standard of care in hemophilia is prophylaxis.**
- **Goals of prophylaxis are minimal or 'zero bleeds', no joint deformity and near normal life.**
- **Prophylaxis can be individualized and the goals can be achieved by using even smaller doses.**
- **Long acting factors are helpful in decreasing the frequency of administration.**

The two most common and serious congenital coagulation factor deficiencies are Hemophilia A (Factor VIII) and Hemophilia B (Factor IX), both inherited as X-linked recessive characters. Clinical manifestations of Hemophilia A (HA) and Hemophilia B (HB) are more or less same.[1] The reported incidence is 1 in 10,000 births for HA and 1 in 50,000 births for HB. Depending on how much working clotting factor is in the blood, hemophilia is classified as mild (5%-40%), moderate (1%-<5%) and severe (<1%). Bleeding may occur at any site but the hallmark of hemophilic bleeding is joint bleed (hemarthrosis). Spontaneous bleeding generally occurs in severe hemophilia, in moderate form prolonged bleeding occurs with minor trauma whereas prolonged bleeding occurs with major trauma and surgery in mild hemophilia.[1,2] Repeated joint bleeds with suboptimal treatment ultimately leads to disability due to chronic arthropathy and contracture.[1] Other than hemarthrosis, bleeding in muscle (especially psoas bleed) and CNS are also common. Different complications of hemophilia (may be related to disease- synovitis, chronic hemophilic arthropathy, pseudotumour or related to therapy - development of inhibitors & transfusion related

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infections) in the long run causes decrease in quality of life (QoL) and increased morbidity. In hemophilia, prophylaxis is considered as the optional care to prevent further bleeding and to preserve joint function and thus improving QoL.[3] In this contexts, a study was conducted in children of <12 years of age with HA & HB who were given secondary and tertiary prophylaxis to determine QoL in relation to joint mobility and its effect in their social life and school activity. Thus, the study aimed to compare the outcome of secondary versus tertiary prophylaxis in respect to joint involvement and child activity.

Material and Methods

This prospective study was conducted in the Departments of Hematology & Department of Pediatrics Medicine at Nilratan Sircar Medical College, a Tertiary Care Hospital in Eastern India over a period of 18 months (January, 2018 to June, 2019).

Patients included in the study were- (a) three to 12 years of age, (b)after two or more bleeds into large joints (large joints= knees, ankle, elbow, hips and shoulders) and before the onset of joint disease documented by physical examination and imaging studies (secondary prophylaxis arm)[2], (c)after the onset of joint disease documented by physical examination and imaging studies (tertiary prophylaxis arm)[2], (d)all severe cases (factor level <1%) and moderate cases with factor level<2%, (e)previously treated patients (history of at least 50 documented EDs to FVIII or FIX in HA and HB respectively. Participants excluded from the study were : (1) Children less than three years of age and of and above 12 years, (2) children having other associated bleeding disorders, (3) history of, or currently detectable, inhibitor, (4) history of anaphylaxis associated with either FVIII or FIX.

After taking proper consent from legal guardians, a total of 34 patients were enrolled in the study. The following variable were studied and recorded for individual patients — (a) type of Hemophilia- HA or HB, (b) factor VIII & IX level at diagnosis, (c) age at starting prophylaxis, (d) number of joint bleeds at the start of prophylaxis, (e) level of inhibitor (Bethesda unit), (f) straight X-ray of involved joint(s) in selected cases. HA patients were started with low dose prophylaxis[4,5] with recombinant Fc fusion long acting factor VIII (rFVIIIFc) (ELOCTATE) at 15 $IU.kg^{-1}.dose^{-1}$ twice weekly (Monday and Friday) and HB patients started with low dose prophylaxis[6] with recombinant Fc fusion long acting factor IX (rFIXFc) (ALPROLIX) at 30 $IU.kg^{-1}.dose^{-1}$ once weekly (Friday); both for 18 months. In cases of break through bleed, they received recommended dose[2] of Coagulation Factor Concentrates (CFC) depending on site.

Outcome measured in terms of median ABR, HJHS and also child activity was measured in terms of School Activity Participation (SAP) score and Daily Activity (DA) score according to Beijing Children Hospital (BCH)[7] assessment scale.

SAP score :

- score 0 (unable to have activities beyond classes)
- score 1 (able to walk around in school yard)
- score 2 (participation in exercise drill and stretching)
- score 3 (participation in non-contact sports such as swimming or jogging)
- Score 4 (participation in contact sport such as basketball, but not in competition).

DA score :

- score 0 (wheelchair bound)
- score 1 (can work slowly)
- score 2 (walking plus one activity such as swimming or jogging)
- score 3 (walking plus two or more additional activities)
- Score 4 (no activity limitation).

Improvement in SAP score and DA score was noted as :

- poor (no change),
- mild (≤2 scores increase)
- moderate (>2 scores increase)
- Good (full increase from score 0 to 4).

School absenteeism (days/month) was also noted. HJHS and child activity score as per BCH scale[7] noted at 4 different time points- first visit (zero month), second visit (at 6 months), third visit (at 12 months) and fourth visit (at 18 months).

Statistical analysis : Data were entered into a Microsoft excel spread sheet and then analyzed by SPSS20 and GraphPad Prism version 5. Data were summarized as mean & standard deviation for numerical variables and count and percentage for categorical variables. Data were distributed in skewed fashion. But as they suffice the criteria of Robust Means of Equality & Levene statistics (that is homogenicity of variables not been disrupted), so we performed unpaired t test, Mann-whitney u test, one way ANOVA and Spearman Rho correlation test.

Observations

Among 34 patients, 28 (82.3%) patients were HA and six (17.7%) were HB. All the children included in the study were male except one female diagnosed as

HB. Definite history of another member affected in the family present in 26% cases. Mean age at diagnosis in case of Hemophilia A is 16.82±14.2 months and Hemophilia B 18.50 ± 14.36 months. Mean age of patients recruited for the study was 6.8 years for HA & 6.5 years for HB. Among the 34 patients, 15 (44.1%) patients were in severe category and 19 (55.9%) were in moderate category. Median ABR reduced from 15.6 to 1.9. Total 22 patients (HA-20 and HB-2) had a total of 38 target joints where knee joint was the most predominant site and there was resolution in all target joints. The HJH scores of each visit in case of secondary and tertiary prophylaxis are shown in Fig 1; in first visit, the mean HJH score was 12.83±3.09 and 15.72±1.6 (p=0.03) respectively. At second visit, the mean HJH score for secondary and tertiary prophylaxis are 10.66±3.20 and 13.04±1.73 (p=0.043). At third visit, the mean HJH score for secondary and tertiary are 8.41±2.84 and 10.68±1.49 (p=0.024). At fourth visit, the mean HJH score for secondary and tertiary prophylaxis are 6.66±3.11 and 8.86±1.45 (p=0.046).

During the course of study, in no case there was development of inhibitors (BU<0.6). With prophylaxis, school absenteeism (days/month) reduced by 90.3% (13.38 to 1.29). Improvement in child activity measured as combined mean value of SAP score and DA score as per BCH[7] scale was 1.455±0.12 at first visit and 6.09±0.33 at fourth visit in the secondary prophylaxis arm versus 2.46±0.11 at first visit and 5.39±0.23 at fourth visit in the tertiary prophylaxis arm (p= 0.0001).

Discussion

The term 'prophylaxis' is defined as "treatment by intravenous injection of factor concentrate in anticipation of and in order to prevent bleeding" that should be regular and continuous [defined as the intent of treating for 52 weeks/year and receiving a minimum of an a priori defined frequency of infusions for at least 45 weeks (85%) of the year under consideration].[2,8] Because of recurrent joint bleeds, there is permanent joint deformity that mainly affects the quality of life. Prophylaxis is known to prevent recurrent joint bleed and thus reduce the severity of hemophilic arthropathy and considered as the standard of care for young children in developed countries.[8,9] In contrast, lack of adequate therapy (in terms of prophylaxis) results in rampant disability in persons with hemophilia (PwH) in resource constraints countries.

With prophylaxis, in the present study, median ABR reduced from 15.6 to 1.9 (reduction by 87.8%). Mandal PK *et al*[5] earlier had studied in adultson tertiary prophylaxis with low dose rFVIIIFc and had shown a decrease in mean ABR of 3.6 bleed/year compared to 37.8 bleed/year on 'ondemand therapy'. Gulshan S *et al*[10] studied on low dose rFVIIIFc prophylaxis in children up to 12 years of age with HA and had shown a reduction in median Annual Joint Bleeding Rate (AJBR) by 85.76% (from 14.5 to 2.2bleed/year) in comparison to 'on demand therapy'. Pasi KJ *et al*[11] reported median ABR of 2.3 bleed/year in children <12 years with HB (≤2 IU/dl) who were given weekly prophylaxis with rFIXFc at a dose of 20-100 IU/Kg. Khayat CD[12] reviewed two prospective randomized studies on efficacy and safety of once-weekly prophylaxis (100 IU/kg) with recombinant factor IX (nonacog) in adolescents and adults with HB and shown reduction of ABR by 89.4%.

A target joint is defined as a major joint with three or more bleeding episodes in a consecutive 3-month period. Target joint resolution is defined as two or less bleeds in a 12 months period. In the present study, 22/34 PwH (HA-20/28 and HB-2/6) who had a total of 38 target joints at baseline achieved target joint resolution in all cases after rFVIIIFc and rFIXFc prophylaxis. O'Hara J *et al*[13] reported 551 PwH with 692 target joints and concluded thattreatment of 'target joints' should be an important target while managing hemophilia.

In the present study, total 34 children were on either secondary or tertiary prophylaxis and the outcome was measured by the HJHS and BCH assessment tool. As noted in the result section and shown in Fig 1, mean HJHS of each visit in case of secondary and tertiary prophylaxis had shown p-value of 0.03, 0.043, 0.024 and 0.046 in the first, second, third and fourth visits respectively and all were statistically significant. And there was a significant reduction in HJHS from 12.83 to 6.66 (reduction=48.1%) and from 15.27 to

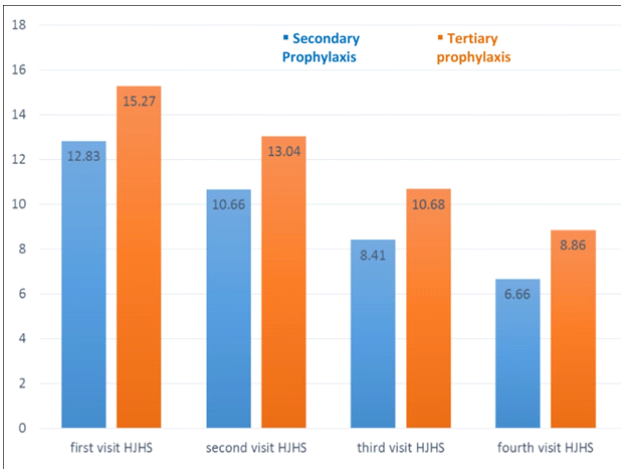

Fig 1 — Mean HJH score in first visit and subsequent visits in case of secondary and tertiary prophylaxis

8.86 (reduction=41.9%) in secondary and tertiary prophylaxis respectively. Thus, the reduction in HJHS in secondary prophylaxis (48.1%) was better than in tertiary (41.9%) prophylaxis. Payal V *et al*[14] from Jodhpur, India studied 56 cases of PwH, had shown mean HJHS of 6.78 ± 9.04 and significant positive correlation with age of patient (p=0.0001). They suggested that, prophylaxis should be tailored based on bleeding pattern and age of patients rather than clotting factor levels. When compared to 'on-demand' therapy, secondary/tertiary prophylaxis has clearly shown a significant reduction of 93.63% and 93.89% in the studies from India by Gulshan S *et al*[10] and Sidharthan N *et al*[4]. In the study from Eastern India by Gulshan S *et al*,[10] in severe HA children the mean HJHS at presentation was 8.3 that significantly reduced with regular and continuous prophylaxis. In the study by Sidharthan N *et al*[4] from South India mean HJHS at presentation was 14.9 that also significantly reduced with regular and continuous secondary/tertiary prophylaxis. Study by Kar A *et al*[15] conducted at five different centers in India measured the prevalence of disability in PwH. Their study had shown that, only nine(6.8%) out of 148 persons(aged 5-55 years) with severe HA, were free of disability. Of concern was that in the age group of 5-12 years, only 14.3% patients were disability-free. A significant association was found between the socioeconomic status of the family and the severity of disability; the study highlighted the need to provide CFCs in sufficient amounts to prevent disability.

In the present study, school absenteeism (SA) across secondary/tertiary prophylaxis groups reduced by 90.3% (13.38 to 1.29days/month). Gulshan S *et al*[10] reported a reduction in SA by 86% (17.38 to 2.42 days/month) after prophylaxis. The improvement in child activity as measured by combined mean of SAP score and DA score was statistically significant (p=0.0001) in secondary prophylaxis as compared to tertiary one. Study from China by Wu *et al*[7] showed improvement of SAP score of poor, mild, moderate and good in 25%, 75%, 0% and 0% cases respectively and in the study by Gulshan S *et al*[10] it was 5%, 57%, 38% and 0% respectively. Wu *et al*[7] showed improvement in DA score of poor, mild, moderate and good in 31.03%, 58.62%, 3.4 and 6.8% cases respectively and it was 17%, 40%, 43% and 0% respectively in the study by Gulshan S *et al*[10].

None of the cases (0/34) in the present study had shown development of inhibitors. There is no reports of development of inhibitors in recent studies from India by Mandal PK *et al*[5] with rFVIIIFc in adults and Gulshan S *et al*[10] in children <12 years. In the study on the safety and efficacy of rFIXFc by Pasi KJ *et al*[11] in the Phase 3 B-LONG (adults/adolescentse ≥12 years) and Kids B-LONG (children<12 years) studies of subjects with hemophilia B, no inhibitors were observed. In contrast to Swedish[16] protocol (25–40 IU.kg^{-1}.dose^{-1} thrice weekly) and Dutch[17] protocol (15–25 IU.kg^{-1}.dose^{-1} thrice weekly), many centers[4,5,10] in India had used low dose prophylaxis (10–20 IU.kg^{-1}.dose^{-1} twice weekly) with a significant net reduction in factor consumption with comparable outcome. Moreover, both the supplied products used in the present study were long acting preparations with extended half lifes[11,18] and that minimized number of hospital visits (notably weekly one visit for HB) and this was reflected by very good compliance in all patients.

Another important issue discussed in many of the studies on prophylaxis in hemophilia is cost that was not an issue in this study as both rFVIIIFc (ELOCTATE) and rFIXFc(ALPROLIX) they received were donated by WFH Humanitarian Aid; thus not affected the compliance of patients. The study period was long in comparison to many such other published studies.

Conclusion

CFC replacement in terms of prophylaxis is the optimal therapy for prevention of recurrent joint bleed and therefore to improve child activity. When compared, secondary prophylaxis is better than tertiary prophylaxis in children in terms of outcome such as-ABR, HJHS and child activity scores. Overall, the results are very encouraging and promising but, warrant larger studies in the study population to provide adequate information for planning of prophylaxis.

Limitations of the study :

We observed several limitations in the present study as follows —

- Small sample size (especially in case of hemophilia B); it should be done in larger sample size hence the results may be inadequate.
- In few children aged 3-6 years (ie, preschool age), there was some difficulty in assessment of child activity as per BCH assessment tools and for the reason, we had to omit the parameter of school absenteeism which is studied by many others
- Socioeconomic status, parental education status and feasibility of home based therapy that indirectly reflects the success of prophylaxis therapy, were not assessed in the present study.
- Did not measure quality of life (QoL) as measured by other study tools for kids.

Informed Consent : Informed consent was obtained from the legal guardians of all individual

children included in the study.

Conflict of Interest : No Conflicts of Interest declared by any author

Source of Funding : The present study was conducted using ELOCTATE (Biogen Inc, Cambridge, MA 02142) and ALPROLIX (Bioverativ Therapeutics Inc, Waltham, MA 02451 USA, US License #2078). Both the products were provided to the patients as a support programme of World Federation of Hemophilia (WFH) Humanitarian Aid.

Source of support : None

Ethics approval : The study was approved by the institutional ethical committee.

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I have had dreams and I have had nightmares, but I have conquered my nightmares because of my dreams

— **Jonas Salk, *American Physician who developed the Polio Vaccine***

Original Article

A Prospective Study of 200 Patients Admitted in a Tertiary ICU with Severe Acute Respiratory Infection to Develop a Pretest Probability Score of COVID 19 Infection, COV-SARI Score

Pratibha Dileep[1], Parin Patel[2], Chintan Dhebar[3], Kapil dev Thakkar[3], Kushal Shah[4], Parikh Harsh Kashyap[5], Harsh Shah[6]

Background : COVID-19 infection is the worst and biggest pandemic the world is facing.The biggest challenge is to identify the infection at the earliest and isolate these patients at the earliest. Availability of reverse transcriptase polymerase chain reaction (RT-PCR) is very limited especially in developing countries and sometimes it takes lot of time to get the results.This study was aimed to detect suspected COVID-19 infection by Clinico-Radiological Co-relation till the nasopharyngeal swab test results are available.

Material and Method : We conducted a prospective study of 200 patients who came consecutively to the intensive care unit (ICU) with severe acute respiratory infection (SARI) at Zydus Hospital Ahmedabad. We collected clinical data as per the protocol and subjected all of them to High resolution chest tomogram (HRCT Thorax). We devised a Pretest probability score, COV-SARI score to determine the positive predictability of COVID 19 infection.

Results : Based on the prevalence of symptoms, history and COVID-19-reporting and data system (CO-RADS) score a simplified score of 17 was devised. Based on the statistical analysis of the data a cutoff score of <9 or >9 was determined. Patient with COV-SARI Score^{3}9 has sensitivity 89.4% and positive predictive value 73.07% and Negative predictive value 90.62% and specificity 75.6%.

Conclusion : This score can be a very good screening tool and quarantine these patientstill the results of RT-PCR is available.

[*J Indian Med Assoc* 2020; **118(12):** 54-7]

***Key words*: COVID-19, SARS-COV-2, Pretest Probability Score, CO-RADS Score.**

COVID-19 infection started in December 2019 from Wuhan in China and took the world by storm as a pandemic by mid-March 2020. By the time of this writing more than 238million cases have been confirmed worldwide and more than 800,000 deaths have been reported. More than 250 countries are affected by this deadly infection irrespective of their geography, economy and medical facilities. India saw its first case in January 2020 but increasing numbers started in middle of March. By now India has reported more than 3million cases with around 59500 deaths.

Editor's Comment :

- **Considering the seriousness and pandemicity of the COVID 19 infection, the need of the hour is to have a simple clinical score to predict probability of COVID 19 infection.**
- **This simple score can easily predict the probability of COVID 19 infection, along with HRCT thorax till the results of RTPCR are available with good sensitivity and specificity.**

On January 30th, 2020 the World Health Organization (WHO) declared the outbreak a Public Health Emergency of International Concern and on March 11th, 2020, declared it a pandemic[1].

The gold standard for COVID-19 diagnosis relies on Severe acute respiratory syndrome Coronavirus-2 (SARS-CoV-2) RNA detection by reverse transcription polymerase chain reaction (RT-PCR) through nasal and oropharyngeal swabs (sensitivity of the RT-PCR ranges between 56 to 83%)[2].

Many centres in the world including India did not have many labs to do the swab test.Swab tests are also dependent on the quality of swab collection,

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transport medium and the test kits. Besides this, in many small centres, the test results take about 36-48 hours for the results to be available. Hence a quick handy tool would be very useful to suspect COVID-19 infection and in immediately isolating the patients for further treatment.

This study was aimed to detect suspected COVID-19 infection by Clinico-Radiological Co-relation till the nasopharyngeal swab test results are available.

We started collecting data prospectively from 17th May2020 onwards for 200 patients who came to Emergency Department with Severe Acute Respiratory Infection (SARI) to devise a Pre-testpredictability Score-COV-SARI Score by clinical and radiological correlation.

Aim

A Prospective study of 200 patients presenting with Severe Acute Respiratory Infection (SARI) in Zydus Hospital ICU to devise a Clinico-Radiological scoring system to predict the probability of COVID-19 infection (COV-SARI SCORE).

Material and Methods

A prospective study was designed to include all those patients who were admitted to Zydus Hospital Isolation Intensive care unit (ICU) with Severe Acute Respiratory Infection (SARI) above the age 18 years.

Zydus Hospital is a 500 beddedtertiary care Multi-speciality hospital situated in Ahmedabad, Gujarat, India.

200 consecutive patients were studied from the period from 17th May 2020 to 12th July 2020.

Inclusion criteria :

All the patients coming to Zydus Hospital Isolation ICU with Severe Acute Respiratory Infection (SARI) above the age 18 years.

Exclusion criteria :

1. Patients with interstitial lung disease or any pre-existing structural lung disease
2. Pregnant patients

A detailed demographic data with clinical history as per the protocol were collected. All the patients were subjected to HRCT thorax and CO-RADS scoring was done.

Following scoring system was adopted as per our clinical judgement (Table 1).

All these patients were subjected to RT-PCR testingfor COVID-19 by taking a swabeither and/or from throat, nasopharynx, endotracheal tubes or Broncho-alveolar lavage (BAL). If the RT-PCR was negative, it was repeated after 24 hours in cases where the clinical suspicion was strong and the COV-SARI Score was ≥9.

Table 1 — *COV-SARI Scoring System*

		Point
History of COVID Positive Contact		1
Previous hospitalization in last 4 weeks		1
Co-Morbidities	None	0
	1	1
	≥2	2
Symptoms		
Fever >100°F		2
Cough		2
Breathlessness		2
GI Symptoms		1
CNS / or Others		1
CT CO-RADS SCORE		1-5 (maximum -5)
TOTAL		17

Data Collection :

For all the eligible patients, demographic data (age, sex, residence), history of contact with COVID-19 patients, travel to and from COVID-19 affected countries, past medical history and co-morbid conditions like diabetes, hypertension, malignancy, chronic kidney disease etc. were recorded. Presenting symptoms as per the chart and HRCT thorax findings with CO-RADS scoring were recorded.

In March 2020, Dutch Association of Radiology prepared a CT scoring system (Table 2).

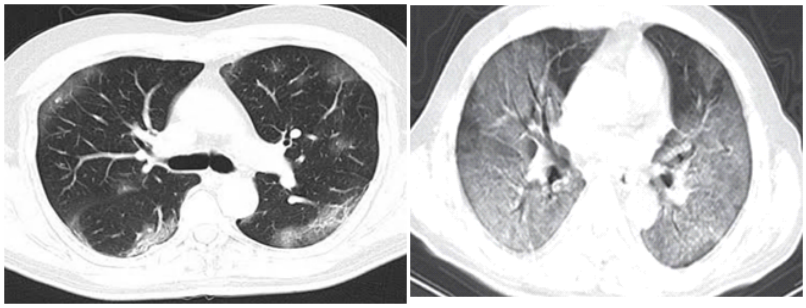
Typical findings of HRCT chest in COVID-19:[3]

1. Multifocal ground glass opacities (GGO)
2. Peripheral and basal distributions
3. Unsharp demarcation
4. Vascular thickening
5. Crazy paving
6. Ground glass and consolidation (Reverse halo)
7. Spider web

Based on above features all the CT scans were reported by a single senior radiologist who was blinded to the clinical details.

Table 2 — *CORADS classification- level of suspicious of COVID- 19 infection*

CO-RADS1	No	CT findings normal or noninfectious abnormality
CO-RADS 2	Low	Abnormality consistent with infection other than COVID-19
CO-RADS 3	Intermediate	Unclear whether COVID-19 present
CO-RADS 4	High	Abnormality suspicious of COVID-19
CO-RADS 5	Very High	Typical COVID-19 infection
CO-RADS 6	RT-PCR positive	



Classical radiological features of COVID-19 pneumonia

Statistical analysis :

Two hundred patients were classified into COVID-19 positive and COVID-19 negative groups according to RT-PCR test results. 85 patients were COVID-19 positive and 115 patients were COVID-19 negative. Data is entered in MS Excel spreadsheet. Qualitative data is expressed by using descriptive statistics as percentage, Chi square test is applied to check statistical association in cross tabulation that made comparison between two qualitative data. P value less than 0.05 is considered as statistically significant.

Ethics committee approval :

As this was an observational study and did not require any intervention, Institutional no objection certificate was obtained with a waiver of patient consent. However, complete confidentiality of the patient information was maintained at all times.

Results :

In a period of 57 days, we screened all the 200 patients who were admitted to ICU Isolation.Out of 200 patients, 85 patients were RT-PCR positive and 115 patients were RT PCR negative.Out of these 85 patients, COVID 19 contact history was positive only in 7 (8.2%) patients, while it was not seen in 78 (91.7%) patients.

Majority of the patients had respiratory symptoms 69/85 i.e. 80%. Fever was seen in 63/85 (74.12%). Coughwas seen in 41/85 (48.24%). Breathlessness seen in 69/85 (81.18%). 23.5% (20/85) had Gastrointestinal (GI) symptom, 8.2% (7/85) had CNS symptoms and 56% had other symptoms like extreme weakness, change / loss of taste / loss of smell etc (Fig 1).

In our study no patient who had CO-RADS 1 score was found to be RT-PCR positive. CO-RADS 2 score in 6/85 (7%). CO-RADS 3 score seen in 2/85 (2.35%). CO-RADS 4 score seen in 8/85 (9.81%). CO-RADS 5 score wasseen in 69/85 (81.18%) patients (Fig 2).

40/85 (47%) patients had history of previous hospitalization in last 1 month while 45/85 (53%) did not have history of hospitalization.15/85 (17.6%) patient had no co-existing co-morbidities while 25/85 (29.4%) had one co-morbidity and 45/85 (53%) had 2 or more than 2 co-morbidities (Tables 3&4).

Discussion

This study was designed to quickly and accurately screen the patients of SARI. As many centres in India at the time of this study did not have facility to do RT-PCR and the test needed particular expertise in collecting the specimen. In remote areas the sample had to be transferred to another centre and it use to take 24-36 hours for the results to be available.

As this score involved clinical history and symptoms with CT scan scoring, within a couple of hours the score was ready.

As this study, ≥9 score has sensitivity 89.4% and specificity of 75.6% with a positive predictive value of 73.0% and negative predictive value of 90.62%. This is a good screening tool in a centre where RT-PCR facilities are not easily available.

In our score, heavy weightage is given to CO-RAD scoring because ours is a tertiary care centre and mainly a referral centre, hence patients normally report after 5-7 days of illness and hence most of these COVID-19positive patients showed CORAD Score [3]4.

Use of CTchest alone as a primary screening tool

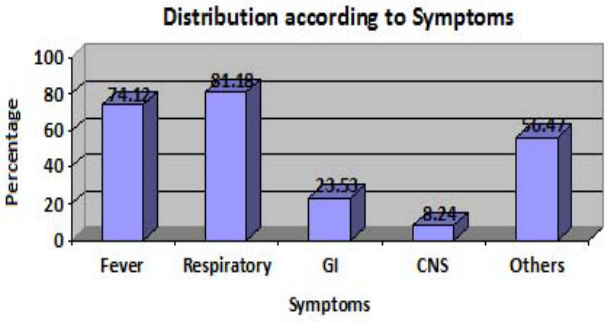


Fig 1 — Distribution of patients according to symptoms

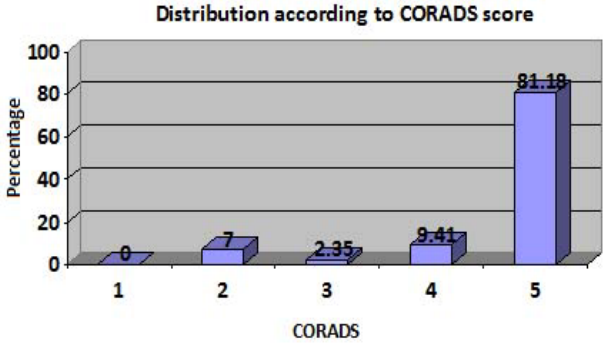


Fig 2 — Distribution of patients according to CT CO-RADS score

Table 3 — *Characteristic of patients*

		COVID-19 RT-PCR Positive(n)	COVID-19 RT-PCR Negative(n)	Total	P Value
Age	≥55 Years	64	77	141	0.2012
Sex	Male	53	74	127	0.772056
History of Exposure	Present	7	0	7	
Symptoms	Fever	63	43	106	<0.00001
	Cough	41	21	62	<0.00001
	Breathlessness	69	56	125	<0.00001
	GI Symptoms	20	49	69	0.005017
	CNS Symptoms	7	38	45	0.000033
	Others	48	48	96	
CT Co-rads Score	1-3	8	99	107	<0.00001
	4-5	77	16	93	<0.00001
H/O Previous Hospitalization in Last 4 Weeks	Yes	40	44	84	0.212692
Co-morbidity	None	15	19	34	0.834106
	1	25	33	58	0.912147
	≥2	45	63	108	0.796179
Cut-off Score	≥9	76	28	104	<0.00001

P value <0.05 is statistically significant

Table 4 — *Sensitivity and specificity calculated according to various cut-off score*

Cut-off Score	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
8	96.47%	53.91%	60.74%	95.38%
9	89.41%	75.65%	73.07%	90.62%
10	80.0%	87.83%	82.93%	85.59%
11	75.29%	93.04%	88.88%	83.59%

must be discouraged as in mild disease orin early disease CT is likely to be negative. CT can be a good modality in patients with worsening respiratory status. However, it improves pre-test probability in more severe cases[4].

This is aneasy to calculate score hence easy to implement even at the junior level and is easily reproducible.

We hope that this score is used as a screening tool in areas where RT-PCR is not easily available. Places where RT-PCR is available, this scoring system can help in isolating the suspected patients till the report become available.

Our study and this score has certain limitations. If patient comes early in the course (less than 5 days) of illness, the score may not pick up all cases. Sample size is small and there is no focus on lab investigations including the lab studies like lymphopenia, thrombocytopenia, raised C- reactive protein (CRP) etc. Including the lab results in study could have been a good idea[5].

CO-RADS scoring has a limitation that it becomes positive only after 5-6 days, hence if patient presents early in course of illness the score can still be negative.

Our centre has a very busy Nephrology unit and many of chronic kidney disease (CKD) patients who came with acute severe volume overload had high COV-SARI Score, as these patients had high CO-RADS scoring and hence COV-SARI Score falsely was very high.

Besides these two groups, this score is a very good and simple clinico-radiological screening tool to predict possibility of SARI due to COVID- 19 infection.

Summary :

To conclude this simple bedside score combined with radiological scoring can be a very simple and effective and above all a quick screening tool for the patients who present with SARI till the swab results are available.

Acknowledgements :

We acknowledge the entire department of Critical Care Medicine in helping us for providing patients, Mr. Hitesh Chauhan, Mr.Rushikesh Kansara for providing help in statistical analysis, and special thanks to Dr Dileep S. Iyengar for his help in writing this manuscript.

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Conflict of Interest : None

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Original Article

A Preliminary Clinico-epidemiological Depiction of COVID-19 Outbreaks of South Bengal

Kripasindhu Gantait[1], Kalimujjaman Molla[2], Abhijit Mishra[2], Saumya Shankar Sarengi[3], Nandan Bandyopadhyay[4], Rabilochan Maji[2], Pabitra Kumar Mandal[5]

On account of the rapid spread of coronavirus infection across India over the last few months, a fervid need is there for the evaluation of the epidemiological trends of the affected individuals. There is no definite pharmacological molecule for coronavirus disease (COVID 19) so far. Our article is aimed to was to make out the disease outline and fend off further spread and grow- management strategies. Diagnosis was made on the basis of real time reverse transcription -polymerase chain reaction test (RT-PCR). Clinico-demographic and biochemical and laboratory parameters were taken from different hospitals of Paschim Medinipur district, West Bengal. A total of 112 diagnosed cases of COVID-19 were included as study subjects, among which 72 patients were asymptomatic whereas 40 patients were symptomatic on admission. The calculated mean age was 31.9 years with male predominance. The major presenting symptoms included cough (13%), fever (12.5%) and shortness of breath (11%). Majority patients (88.4%) had no comorbidity. Our study suggests that patients with Covid19 may remain asymptomatic or symptomatic. So we need to isolate them.

[*J Indian Med Assoc* 2020; **118(12):** 58-61]

***Key words*: Corona, Covid 19, Cough, Comorbidity.**

In December 2019 a novel member of human infective agent newly identified in Wuhan, China, known as the coronavirus. Later it was named as coronavirus disease 2019 (Covid-19). The causative agent for COVID 19 is severe acute respiratory syndrome coronavirus 2 (SARS CoV 2), a novel coronavirus that has wrecked a havoc and declared as an expansive global pandemic by the WHO on 11th March 2020.

It was established that the SARS-CoV-2 belongs to the beta-coronavirus 2b lineage in the phylogenetic tree. By examining the full-length genome of SARS-CoV-2, it was discovered that this novel virus shared 87.99% identity sequencing with the bat SARS like coronavirus[1], and it shared ~80% identity nucleotide with the original SARS epidemic virus[2]. Based on the preliminary information of this novel virus, it is considered that SARS-CoV-2 is the third zoonotic human coronavirus of the century[3]. Furthermore, clinical evidences have advocated that this virus is transmissible from person to person[4,5]. The structure of the 2019-nCoV is very similar to bat corona viruses[6]. There is much debate regarding the origin of the infection, but the transmission is believed to be started from the Huanan Seafood Wholesale Market[7].

Editor's Comment :

- **The novel coronavirus disease has myriads of presentation.**
- **Fever, cough and shortness of breath are the major clinical presentation.**
- **Testing and isolation is paramount importance to prevent the spread of infection.**

The clinical range of COVID 19 differs, ranging from mild to moderate symptoms of non productive cough, fever, headache, anosmia, rhinorrhea, sore throat, difficulty in breathing, vomiting and loose motion to signs and symptoms complex of pneumonia, respiratory failure, acute respiratory distress syndrome (ARDS) and dysfunction of multiple organ system[8].

The aim of our study is to narrate the epidemiological trends of these patients ranging from their demoghraphic profile, clinico-laboratory evaluation and treatment outcome.

Materials and Methods

All patients diagnosed with Covid-19 infection

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admitted to the different Hospitals of Paschim Medinipur, West Bengal from 7th June to 30th June, 2020 were enrolled.These hospitals have been deputed for isolation and management of COVID 19 patients according to the existing Government protocol. The hospital staffs involved in the management of COVID 19 patients have taken all preventive measures. A suspected case is defined as "symptomatic or asymptomatic patient with travel history to states with COVID 19 patients over the previous last 14 days, or who had exposed themselves to COVID 19 positive patients in the community," were admitted in these hospitals or observed in quarantine centres respectively. The nasopharyngeal and throat swabs were being tested at the Department of Microbiology in Midnapore Medical College using reverse transcription polymerase chain reaction (RT PCR) to confirm SARS CoV 2 infection. All laboratory confirmed cases were included in the present study. Furthermore, the demographic data, medical and exposure history, subjacent comorbidities, clinical findings, laboratory parameters, chest X-ray and treatment measured were recorded.

This hospital based observational descriptive study was conducted in the different Hospitals of Paschim Medinipur, West Bengal. One hundred and twelve (112) COVID 19 patients were enrolled to find the epidemiologic trends. The quantitative variables and qualitative measures were defined with mean ± standard deviation (SD) and proportion respectively. The frequencies of categorical variables were compared using the chi-square test as appropriate. Statistical analyses were performed using JASP software (Version 0.13.0.0). The tests with P value of <0.05 were considered statistically significant.

Observations

A total of 112 patients diagnosed as COVID-19 were included in this study, among which 72 patients were asymptomatic whereas 40 patients were symptomatic on admission. The average time period needed for RT PCR conversion from positive to negative test profile was 9 ± 5.63 days. The mean age for all patients was 31.9 years with SD ± 12.89 years and about 83.9% of patients were male. The demographic profile of study patients is depicted in Table 1. Majority patients were migrant labourer (81%) from different states of India. The number of patients coming from different regions of the district of Paschim Medinipur is represented in the map (Fig 1).

The clinical profile is summarized in Table 2. Of note, 64% and 36% patients were asymptomatic and symptomatic respective. Common clinical manifestations in the order of frequency being cough (13.5%), fever (12.5%), shortness of breath (11%), headache (3.5%), diarrhea (3.5%), nausea(2.5%), sore throat (2%) and weakness (2%) respectively. Thirteen patients (15%) had coexisting comorbidities including diabetes mellitus type 2 (five patients), Hypertension

Table 1 — *Demographic Profile of the COVID -19 patients (n=112)*

Variable	Level	Frequency	Total	Proportion	x^2	p
Gender	Male	94	112	0.84	51.57	<0.001
	Female	18	112	0.16		
Age group	12-39	81	112	0.723	82.53	<0.001
	40-60	26	112	0.232		
	>60	5	112	0.045		
Education	No education	6	112	0.054	240.34	<0.001
	Primary	99	112	0.884		
	Secondary	5	112	0.045		
	Higher	2	112	0.018		
Marital status	Married	82	112	0.732	24.14	<0.001
	Single	30	112	0.268		
Family size	2-5	40	112	0.357	21.72	<0.001
	6-10	56	112	0.500		
	>10	16	112	0.143		
Resident	Native	21	112	0.187	43.75	<0.001
	Migrant	91	112	0.813		

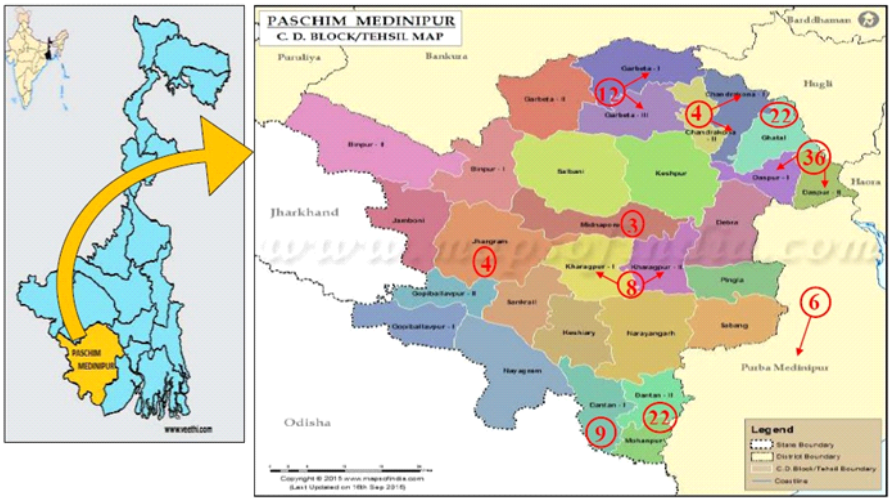

Fig 1 — Map of the district of Paschim Medinipur. Represents the number of patients coming from different regions of Paschim Medinipur

Table 2 — *Clinical profile of the COVID 19 patients (n=112)*

Variable	level	Frequency	Total	Proportion	X^2	p
Symptoms :						
Asymptomatic	Present	72	112	0.643	9.14	<0.005
	Absent	40	112	0.357		
Cough	Present	15	112	0.134	60.04	
	Absent	97	112	0.866		
Shortness of breath	Present	12	112	0.107	69.14	
	Absent	100	112	0.893		
Fever	Present	14	112	0.125	63	
	Absent	98	112	0.875		
Sorethroat	Present	2	112	0.018	104.14	
	Absent	110	112	0.982		< 0.001
Diarrhea	Present	4	112	0.036	96.57	
	Absent	108	112	0.964		
Nausea	Present	3	112	0.027	100.32	
	Absent	109	112	0.973		
Weakness	Present	2	112	0.018	104.14	
	Absent	110	112	0.982		
Headache	Present	4	112	0.036	96.57	
	Absent	108	112	0.964		
Comorbidities :						
Comorbidities	Present	13	112	0.116	66.04	
	Absent	99	112	0.884		
CVA	Present	2	112	0.018	104.14	
	Absent	110	112	0.982		
Hypertension	Present	3	112	0.027	100.32	< 0.001
	Absent	109	112	0.973		
Type 2 Diabetes	Present	5	112	0.045	92.89	
	Absent	107	112	0.955		
Chronic Obstructive Pulmonary Disease (COPD)	Present	3	112	0.027	100.32	
	Absent	109	112	0.973		

(three patients), chronic obstructive pulmonary disease (three patients) and cerebrovascular accident [CVA] (two patients) (Table 2).

Table 1 and Table 2 represents demographic and clinical profile of COVID 19 patients respectively (n = 112). There are significant differences in the distribution of COVID 19 patients within variables.

Out of 112, 4 patients had lower oxygen saturation on room air and they needed oxygen and rest did not require any oxygen support. All patients who needed

Fig 2 — Bilateral pneumonitis (L>R) including consolidation with effusion in left.

oxygen support were male and had history of being chronic smoker. 3 out of 4 patients requiring oxygen support had one comorbidity in the form of COPD. Rest one had diabetes and developed bilateral pneumonitis (Fig 2) after infection with SARS CoV-2. He was received treatment in combination with hydroxychloroquine and antibiotics (Azithromycin + Ceftriaxone) and turned negative on the 6th day of treatment. He was discharged and advised home quarantine for 14days and is doing well in follow up.

All basic investigations were done of symptomatic COVID 19 patients and revealed abnormal chest x-ray (one), leukocytosis (two) and high random blood sugar (one).

All patients were being treated empirically in combination with hydroxychloroquine and azithromycin and discharge satisfactorily.

Discussion

This study included 112 patients with Covid-19 in the the age group of 12-39 years comprising 72% of them. Our study results simulate that reported by Bhandari *et al*[9] but younger than the age group reported by Wang *et al*[10] (56.0 years), Chen *et al*[11] (55.5 years) and Huang *et al*[12] (49.0 years).

Most of our study subjects were male (83.9 %) that simulates the study results reported by Huang et al and Chen *et al* which revealed 75.0% male predominance but a bit higher than that of Wang *et al* (54.3%) and Bhandari *et al*[13](65.6%) .

In our study 64% patients had no symptoms at

presentation which was more than that reported by Bhandari *et al* (33.33%).Cough was the commonest symptom(13%) followed by fever (12%) and respiratory distress (11%) in our study that was similar to Bhandari et al but fever was the commonest symptom reported by Chandra *et al*[14](69.47%), Wang *et al* (91.7%) and Guan *et al*[15] (87.9%).

In our study, though fever, cough, and shortness of breath are the common symptoms, it has comparatively lesser frequency because of majority patients (64%) were asymptomatic.

Lastly, at the epilogue, we want to say that asymptomatic patients pose a major epidemiological risk for the society as they have the capability to spread the infection silently. So we need to isolate them.

Funding : None

Conflict of Interest : None

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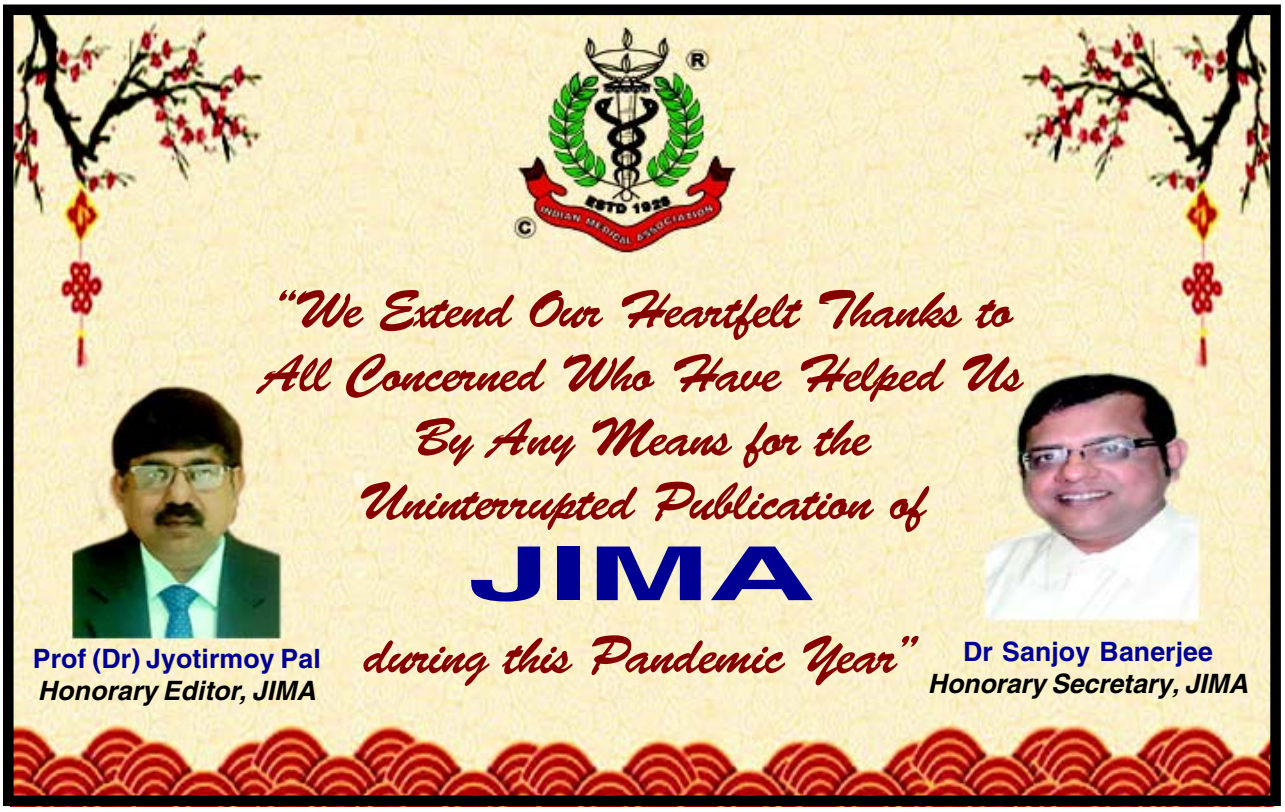
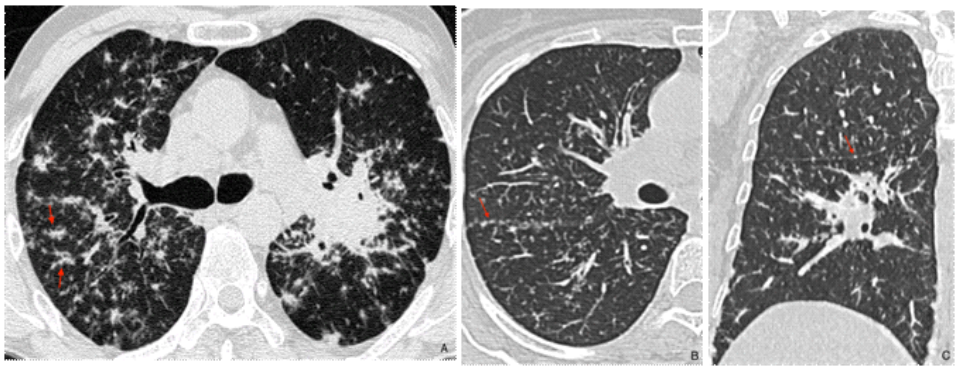


Image in Medicine

Bhoomi Angirish[1], Bhavin Jankharia[2]

Quiz 1

CT scan images of the chest of 2 different patients.



Questions :

(1) What is the diagnosis?

(2) What is the pathophysiology of this pattern?

(3) What are the imaging features of sarcoidosis?

Answers :

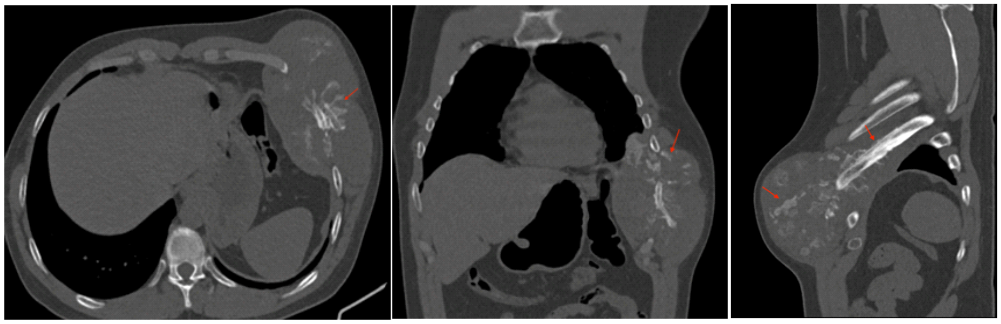
(1) Eribronchovascular (arrow in A) and perifissural (arrow in B,C) nodules are seen, suggestive of pulmonary sarcoidosis.

(2) The distribution of sarcoid granulomas is mainly along the peribronchovascular lymphatics and to a lesser extent in the interlobular septae and subpleural locations.

(3) Sarcoidosis commonly presents as symmetric hilar and mediastinal lymphadenopathy. Calcification is common in lymph nodes and may present in eggshell, punctate or amophous pattern. There is a wide spectrum of pulmonary parenchymal features ranging from perilymphatic nodules, alveolar sarcoidosis and pulmonary fibrosis.

Quiz 2

A 46 year old man presented with rapidly growing swelling in left lateral chest wall since 3 months.



Questions:

(1) What is the diagnosis?

(2) What are the common locations of this lesion?

(3) What are the imaging features of this lesion?

Answers :

(1) An osteolytic lesion with large soft tissue component showing calcified matrix is seen involving left 8th rib. These imaging findings favour diagnosis of chondrosarcoma of rib, which was confirmed on biopsy.

(2) The common locations of chondrosarcoma are long bones like femur, pelvis, ribs, spine, scapula and sternum.

(3) Chondrosarcomas are osteolytic lesions showing intralesional calcifications (most commonly rings and arch or popcorn calcification). Permeative appearance of bone is seen in high grade tumours. Endosteal scalloping, cortical remodelling and periosteal reaction are useful in distinguishing between an enchondrma and low-grade chondrosarcoma.

Picture This by Jankharia, Mumbai, Maharashtra
[1]MD, DNB (Radiology)
[2]MD, DMRD (Radiology)

Student's Corner

Become a Sherlock Homes in ECG

M Chenniappan[1]

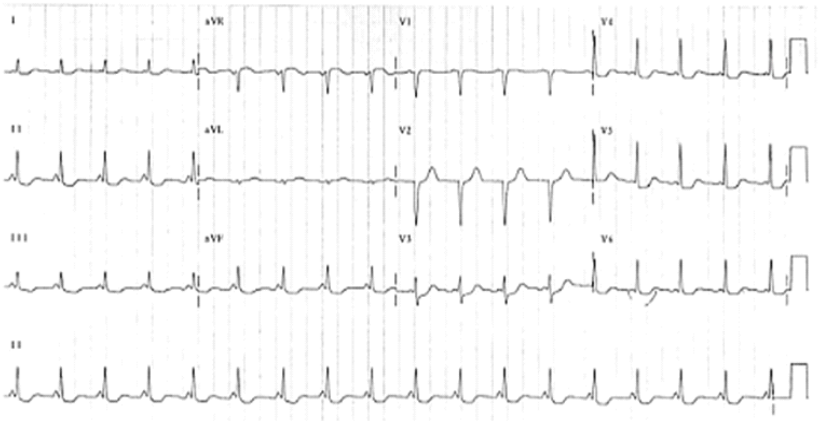
Series 7 :

ECG

"This is the ECG of 60 year old patient with rest chestpain.

Previous ECGs are not available.

"Carefully Note and Read"



1. What are the ECG findings?
2. Why is this clue?
3. What are practical implications?

ECG FINDINGS :

The main finding in this ECG is short PR with no delta wave or wide QRS. In addition there is anterior ST depression and avR ST elevation. The anterior ST changes and avR ST elevation is suggestive of Left main coronary artery critical occlusion.

THE CLUE :

In the presence of short PR, with upright P in LII, L III, avF with no delta wave,we can suspect James Pathway pre excitation which is by passing the AV node and then conducting through normal pathway, hence the narrow QRS. But only in the presence of h/o palpitation and documented episode of tachycardia it is called "Lown Ganong Levine syndrome"(LGL syndrome). So this ECG you cannot interpret as LGL syndrome without history. The name given to this type of ECG isCoronary Nodal Rhythm. (CNR). That's why the clue of "Carefully Note and Read" (CNR) is given. The figure 60A explains the approach to short PR.

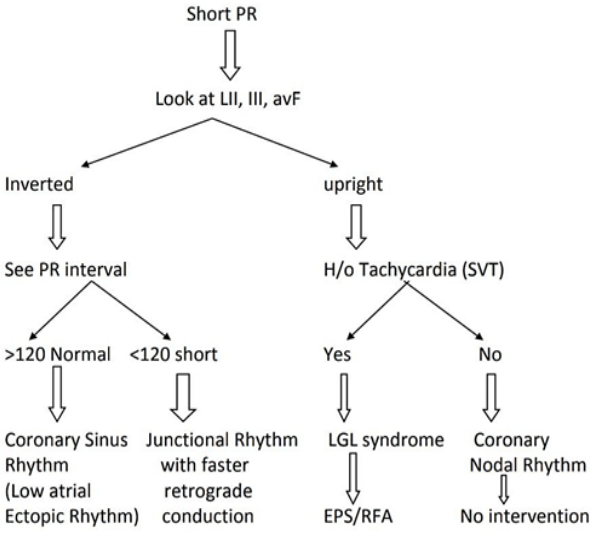


Fig.60 A — APPROACH TO SHORT PR

PRACTICAL IMPLICATIONS:

The immediate management in this ECG is for ST depression and avR elevation by doing immediate coronary angiogram and suitable revascularisation. The short PR interval does not need any intervention. If the patient develops tachycardia, then EP studies and Radio Frequency ablation may be planned.

[1]Adjunct Professor, Dr MGR Medical University, Tamilnadu; Senior consultant cardiologist, Tamilnadu; Ramakrishna Medical Centre, Apollo Speciality Hospital, Trichy

Case Report

Tele Consultations in Dermatology — New Experience and A Report of Lockdown Dermatology in COVID 19 Scenario

Sudip Das[1]

Amidst unprecedented lockdown for last 40 days, because of global pandemic of Corona virus, patients as well as clinicians of multiple specialities were at a loss. But medical council and various associations stepped in to allow teleconsultation. I did a survey on my dermatology patients and results were that what we perceive as emergency, is not by patients. Sexually transmitted diseases did not go down in lockdown.

[*J Indian Med Assoc* 2020; **118(12):** 64-5]

Key words **: Teleconsultation, Covid 19, Lockdown, Dermatology.**

Teleconsultation is defined as synchronous or asynchronous consultation using information and communication technology to omit geographical and functional distance. Its goals are for diagnostics or treatment between two or more geographically separated health providers[1]. the objective of teleconsultation projects is to increase access to and quality of healthcare delivery in a cost efficient manner[2].

The janta curfew was declared by Prime Minister on 22 march with total number of cases in India reported was only 45 per day, the state of west Bengal went into lockdown from next day and well before 24 may, when national lockdown was announced.

Patients and doctors started to shut their clinics over concerns of safety of patients, staffs, family members as the situation grew grimmer. There was a call for something, and a forbidden fruit (teleconsultation) was reintroduced .

Case Report

Various platforms like medsign, lybrate, docon, navya, medisign all came into picture selling doctors a platform for videocalling and keeping online records.some, like me made an innovation asked patients to send clinical photo on whatsapp no, enumerate her problems, pay teleconsultation fees on pay Tm, google payand bank transfer. consultation was given on email, whatsapp or mailed to patients from platforms. The patients across globe consulted including Nepal and Bangladesh, though very few. Patients were frantically calling for consultation from lockdown zones also.

We registered at platforms like DOCON and lybrate, whereby patient paid fees and problems discussed on video call. prescriptions done online and mailed by platforms. The otherway was patients whatsapped clinical photo, paid fees on pay T m, phone pay or did a bank transfer provided by the doctor. The doctor then called the patient on google Duo or made normal calls, had discussion the prescription was then written on normal prescription pad, scanned and send on mail and whatsapp (Figs 1 & 2).

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Accepted on : 17/10/2020

Editor's Comment :

- **During lockdown when the patient doctor contacts were severly jeopardised in the context of fear, social distancing teleconsultations have become an important tool in the setting of this pandemic.**
- **The government and medical council of India, premium institutions like All India Instituteof Medical sciences, New Delhi, PGI chandigarh all resorted to teleconsultations.**
- **It may not be a substitute of physical consultation, but despite limitations it is an useful tool in pandemic set up.**

Results

Request or enquiry were made by patients on whatsapp or mobile no seventy percent were follow up patients. Remaining were new patients who got information from other patients, referred by other doctors or got from internet including social media Actual teleconsultation was done in 44 percent of patients enquiring, rest refused as they were sceptical of teleconsultation, did not have digital payment ways. One patient who had consulted earlier, called up and said he was stuck in interior of Assam and had difficult times was provided free consultation.

In a span of 30 days, 7 days post lockdown we started to record the cases seen via teleconsultation and DOCON PLATFORM. The total number of cases seen were 94 in a 30 days period, which was approximately 13-14 percent of normal patients seen in this period. We analysed the data, out of 94 patients 38 were female patients and 56 were male patient (Table 1).

The misclenous group included a potpourri of cases of scabies (4), popular urticaria (3), ingrowing toe nail (2), herpes zoster (3), urticaria (5), hair disorders namely alopecia areata (2), Telogen effluvium (6). Trichitillomania (1). Interestingly, we had 3 cases of TSDF topical steroid damaged face. Four cases, of autoimmune collagen vascular disorders (3 of scleroderma and one of dermatomyositis) reported for treatment. The remaining

Fig 1 — Secondary syphilis lesion with Biettes collarette

Fig 2 — Tinea corporis in a lady in waist region

cases included acute paronychia, folliculitis, bed sores, miliria rubra and one case of hirsutism.

To our assessment only 18 out of 98(18.36%) had compelling reasons to call (acute paronychia, hidraneditis suppuritiva, scabies, urticaria and popular urticaria had compelling reasons to seek teleconsultations. If you take STD cases – one was a 19 year old boy with MSM (men having sex with men) activity presenting with palmar lesions with Biettes collarette and subsequently confirmed with VDRL positive in 1:32 titre and TPHA POSITIVE. He was however HIV negative. Two had candidial balanitis, one was old and one new, both diabetic for more than 3 years. Two males (both follow up) was on recurrence of herpes lesions. One female patient complained of vulvovaginal discharge and was treated by syndromic management.

Table1 — *Distribution of Cases*

Diseases	New/old	Percentage of total
Dermatophytosis	9/5	14/98-14.28 percent
Psoriasis	2/5	5/98-5.1 percent
Hidraneditis suppuritiva	1/3	3/98-3.06 percent
Dermatitis	18/22	22/98-22.44 percent
Acne, melasma and other cosmetic problems	4/7	7/98-7.14 percent
Misclenous	10/50	50/98-51.02 percent
STD	2/6	6/98-6.12 percent

Discussion

Teleconsultation remains a useful tool in post COVID 19 lockdown management. But its use can be extended to patients who stay in other parts of country and cannot regularly follow up. In todays busy world even patients cannot report for regular visits, so customising teleconsultation will be a step forward.Besides in post covid era, it will remain a safe way of consultation.

The dermatologist perception of emergency and patients perception are different. Some consider even melasma as an emergency. But people are not yet digital friendly as less than one third od queriesdid convert to digital practice. This is due to fear of digital payments,wheather doctor will see him properly. More public awareness will be required in post covid scenario in popularising teleconsultation, look after its legalities and use judiciously.

The android smart mobile phones can very well be used by doctors to facilitate and review good quality images and save valuable time of all to provide treatment[3], more important in this COVID 19 scenario.

But in some cases like aesthetic procedures, managing SJS, dreadly diseases like DRESS, Type 2 lepra reactions, this will never be useful.The author is of opinion that teleconsultation can be a good follow up and useful in primary diagnosis in a limited number of cases.

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Case Report

An Unusual Case of Recurrent Respiratory Failure

Pushpita Mandal[1]

Myasthenic crisis is a complication of myasthenia gravis characterized by worsening of muscle weakness, resulting in respiratory failure that requires intubation and mechanical ventilation. Advances in critical care have improved the mortality rate associated with myasthenic crisis. This article is about the atypical presentation of a case of recurrent respiratory failure which was finally turned out to be a case of myasthenic crisis. Therapeutic options including mechanical ventilation and pharmacological management is also discussed here.

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***Key words*: Myasthenia gravis, Autoimmune diseases of the nervous system, Myasthenic crisis, Neurocritical care clinical specialty.**

Myasthenia gravis (MG) is an autoimmune disease commonly affecting middle-aged female populations[1]. This disease is mediated by a type-II antibody reaction in which antibodies directed against post-synaptic nicotinic acetylcholine receptors attack the myoneural junction and damage the post-synaptic membrane via complement fixation. This results in the failure of action potential propagation across the neurons, eventually leading to a neuromuscular weakness without stiffness[2]. Classically, the anticholinergic autoantibodies target the extraocular muscles, leading to fluctuating muscular fatigability, predominantly resulting in bilateral diplopia and ptosis, which is typically worse at the end of the day. It constitutes more than half the cases[1]. Bulbar weakness, leading to dysphagia and dysarthria, has been rarely described as the initial complaint, more commonly in the elderly male population[2].

Case Report

A 68 yrs old male was admitted with increased shortness of breath in our ICU in February 2020. He had background history of type 2 DM, hypertension,COPD. He was a prolonged smoker and received chemotherapy and radiotherapy for mucoepidermoid carcinoma of the tongue earlier. He had a history of cough, cold and shortness of breath on exertion for last 3-4 days. Following which he developed Bells' palsy (difficulty in closing left upper eyelid).

On Examination :

He was tachypnoic (RR>30),tachycardic, and suddenly became unresponsive and bradycardic in the CT scan department (while undergoing HRCT thorax) requiring intubation and ventilation.CXR was suggestive of widening of mediastinum with right lower zone opacity. ABG was suggestive of type 2 respiratory failure. But after a couple of hours he became totally conscious alert and wanted to pull out the tubes. On the next morning he got extubated .

Editor's Comment :

- **Myasthenia gravis (MG) is often complicated by respiratory failure, known as a myasthenic crisis. However, most of the patients who develop respiratory symptoms do so during the late course of disease and have other neurological signs and symptoms. However, in some patients respiratory failure is the initial presenting symptom.**
- **In this case of a 68-year-old male with MG who presented with isolated respiratory failure as his first presenting symptom as illustrated by this case, it is important to consider neuromuscular disorders in cases of unexplained respiratory failure.**

Course in the Hospital :

But again by the evening he had drowsiness, ABG was suggestive of type 2 respiratory failure (ABG-pH 7.29, pCO2 82, pO2 53, HCO3 39.4), he was put on BIPAP initially at (14:6), then increased to (16:6),but ultimately required reintubation and ventilation. HRCT scan of thorax was suggestive of suspected lung mass and right whole lung collapse. FOB (fibreoptic bronchoscopy) was suggestive of right lower lobe bronchus totally plugged with thick secretion, which was aspirated and sent for culture and there was no evidence of any endobronchial growth. BAL fluid culture was suggestive of growth of MDR klebsiella which was sensitive to colistin only, so intravenous colistin was started.He gradually improved and got extubated after 2 days.

But again on next morning, on morning round he was found to have difficulty in neck holding, there was increased drooling of saliva, weakness of proximal muscle and left sided ptosis. He reqired reintubation by the evening due to bradycardia,desaturation and one episode of convultion. Neurologist decided to do EEG, lumbar puncture and NCV at bedside. His acetylcholine receptor antibody level was sent also.

- His CSF showed cell count of 2(all lymphocytes), protein 40mg/dl, sugar 150mg/dl.
- His NCV report showed (normal distal latencies,

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reduced CMAP amplitudes and reduced conduction velocity of bilateral median, ulnar, tibial & common peroneal nerve, All F responses of both upper and lower limbs were absent, bilateral soleus H reflexes were absent, bilateral median, ulnar, sural SNAPS were absent…final impression was **bilateral axonal type sensory motor polyneuropathy involving all four limbs.**

As it was 3rd time intubation it was decided that tracheostomy will be done, but later on it was decided to give him a trial of IVIG infusion 400mg/kg/day for next 5 days. Gradually his neurological status improved, neck holding got better, he was put on oral steroids in high dose. Got extubated after 5 days. He was put on appropriate antibiotic as per culture sensitivity report. His BAL galactomannan was also very high (value 2.71, normal reference range was negative <.50, positive>=.50). So he was put on voriconazole intravenously 400 mg twice daily for 1 day then 200 mg twice daily for next 14 days. By this time his acetyl choline receptor antibody report came which showed positive result in **high titre(59.8). (**Reference value for positive was>0.50).

So our diagnosis **was an atypical variety of myasthenia presenting with myasthenic crisis with sensory motor axonal polyradiculoneuropathy.** He was put on pyridostigmine 60 mg tds, oral steroid and mycophenolatemofetil.

But unfortunately again after 2 days he had started showing weakness of respiratory muscles, so again required reintubation, this time it was decided to put him on plasmapheresis. Nephrologists gave the regimen for plasmapheresis.

He received plasmapheresis for total 5 days,and then gradually over a period of another 2-3 days his respiratory parameters got improved and he got extubated and discharged subsequently.

Discussion

Myasthenia gravis is an autoimmune disorder causing skeletal muscle weakness, most commonly in the eyes, bulbar muscles, limbs, and respiratory muscles[1]. Whilst it usually presents with ocular symptoms or dysarthria, dysphagia and fatigable chewing, our patient presented with difficulty in breathing, needing recurrent ventilatory support[3]. This case illustrates importance of considering uncommon causes for common presentations, when it does not fit in with the diagnosis.

This patient had myasthenia gravis presenting with respiratory failure due to respiratory muscle weakness. Several studies have reported respiratory muscle weakness in patients with generalised myasthenia gravis[9,10]. **This case is unusual in that :**

• The respiratory muscles were affected predominantly and patient had no prior history of progressive neuromuscular weakness or increasing fatiguability symptom at the end of the day.

• There was associated sensory-motor-axonal polyradiculoneuropathy.

• Acetyl choline receptor antibody was present in high titre and patient required both IVIg and plasmapheresis

Epidemiology :

• Although data are limited, the proportion of patients with myasthenia gravis who experience at least one myasthenic crisis may be as high as **10 to 20 percent** and the annual risk of myasthenic crisis among patients with myasthenia gravis is approximately **2 to 3 percent**. In 13 to 20 percent of patients who present with myasthenic crisis, it is the first manifestation of myasthenia gravis. Most myasthenic crises occur in the first few years after the diagnosis of myasthenia gravis, when the disease is often in its most active phase.

• Clinical features:Patients who develop myasthenic crisis typically experience increasing generalized or bulbar weakness as a warning. Occasionally, patient presents with respiratory insufficiency out of proportion to limb or bulbar weakness. In a report of 44 patients who developed 63 episodes of myasthenic crises, the crisis began with generalized weakness, bulbar symptoms, or weakness of respiratory muscles Myasthenia gravis is most frequently associated with antibodies against acetylcholine receptors (AChR) in the post-synaptic motor end plate. A second form of myasthenia gravis, usually seen in young women, involves antibodies against muscle-specific tyrosine kinase (MuSK). A third group of patients has antibodies to neither AChR nor MuSK, and these patients are considered seronegative. Clinically, these patients are similar to patients with AChR antibodies. Overall, women are twice as likely as men to be affected. A bimodal distribution of myasthenic crisis is seen[11,12]. An early peak prior to age 55 affects women 4:1, whereas a later peak after age 55 affects women and men equally[4].

Advances in mechanical ventilation and critical care have been paramount in improving mortality associated with myasthenic crisis.

Precipitants of Myasthenic Crisis :

The most common precipitant is infection. One series documented infection in 38% of patients presenting with myasthenic crisis; most commonly, the infection was bacterial pneumonia followed by a bacterial or viral upper respiratory infection[8].

Other precipitants include aspiration pneumonitis, surgery, pregnancy, perimenstrual state, certain medications and tapering of immune-modulating medications. Other antecedent factors include exposure to temperature extremes, pain, sleep deprivation, and physical or emotional stress. Approximately one-third to one-half of patients may have no obvious cause for their myasthenic crisis[4].

Numerous medications may exacerbate MG[15,16], including quinidine, procainamide, α-adrenergic antagonists, calcium channel antagonists (verapamil, nifedipine, felodipine) magnesium,antibiotics (ampicillin, gentamicin, streptomycin, polymyxin, ciprofloxacin, erythromycin), phenytoin, gabapentin, methimazole, α-interferon, and contrast media[5]. These medications should be used cautiously in myasthenic patients, especially after surgery. Any medication suspected of precipitating myasthenic crisis should be discontinued.

Although corticosteroids can be used in the treatment of

MG, initial treatment with prednisone led to an exacerbation of MG in almost half of patients in 1 series. The incidence of myasthenic crisis resulting from corticosteroids ranges from 9%-18%. Thus, commencement of corticosteroids for the treatment of MG should always occur in a hospital setting, where respiratory function can be monitored.

Of the 46 episodes of MC, extubation failure occurred in 20 (44%), including 9 of 35 episodes (26%) of reintubation. Male sex, history of previous crisis, atelectasis, and intubation for more than 10 days were associated with extubation failure[7]. Lower pH and lower forced vital capacity on the time of extubation, atelectasis, and bilevel intermittent positive airway pressure use after extubation predicted the need for reintubation[16]. Atelectasis showed the strongest association with both end points.

Conclusions

Extubation failure is relatively common in patients with MC. Atelectasis is the strongest predictor of this complication[17].

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For the birth of something new, there has to be a happening. Newton saw an apple fall; James Watt watched a kettle boil; Roentgen fogged some photographic plates. And these people knew enough to translate ordinary happenings into something new.

— Sir Alexander Fleming

Case Discussion in Medicine

Reversal of Diabetes Autonomic Neuropathy with Intense Treatment Monitoring — A Case Study

Shambo Samrat Samajdar[1], Shatavisa Mukherjee[2], Shashank Joshi[3], Santanu Kumar Tripathi[4]

Diabetic autonomic neuropathy (DAN) is a significant marker of adverse cardiovascular, renaland cerebrovascular outcomes in diabetic patients. According to the American Neurological Society guidelines, screening for autonomic dysfunction should be carried out immediately afterthe diagnosis of type 2 diabetes (T2DM) and repeated every 5 years thereafter. Patients with poor glycemic control, cardiovascular risk factors and other micro- andmacrovascular complications of diabetes are at a greater risk. The present case describes a 56 year olddiabetic male presenting with complaints of tingling sensation in limbs and symptoms of gastroparesis. Proper history taking, effective screening for autonomic neuropathy and further work-up addressed the complaints within 3 months.

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***Key words*: Diabetes Autonomic Neuropathy (DAN), Type 2 Diabetes Mellitus, Ewing's Tests, Gastroparesis**

Diabetic autonomic neuropathy (DAN) is a significant marker of adverse cardiovascular (CV), renal and cerebrovascular outcomes in diabetic patients. According to the American Neurological Society guidelines, screening for autonomic dysfunction should be carried out immediately after the diagnosis of type 2 diabetes (T2DM) and repeated 5 years thereafter. Patients with poor glycemic control, with cardiovascular (CV) risk factors and with other micro- and macrovascular complications of DM are at a greater risk. For all T2DM patients, cardiovascular autonomic neuropathy (CAN) must be ruled out even in resource constraint settings[1]. The reversal of autonomic neuropathy features in T2DM with intense glucose monitoring has been reported, only sparingly[2]. Probability of such reversal depends on several factors including the time since diagnosis of diabetes, treatment compliance, presence of cardiovascular risk factors etc. We present here a case of partial reversal of autonomic neuropathy in just 3 months of intense monitoring of glycemic control.

Case Report

A 56 year old gentleman, a known patient of T2DM for 15 years, attending the Diabetes Clinic, presented with complaints of insidious-onset tingling sensation in right lower limb and decreased sensation in both lower limbs. Probing elicited the history of thermal injury (blister) in right foot, failing to sense the temperature of hot water. He was also hypertensive, on medications for 5 years. He was a cigarette smoker for 30 years. On presentation, his diabetes regimen included insulin (H Mixtard 30/70) - 24 U before breakfast and 14 U twice daily 30 minutes before each meal, besides twice daily dosing of vildagliptin 50 mg and metformin 500 mg. Further, he was also receiving single oral daily dosing for each of atorvastatin 20 mg, amlodipine 5 mg, amitriptyline 25 mg and vitamin B12 1500 mcg. His BMI was noted to be 22.8 kg/m^2 and CBG 56 mg/dl. The patient had a history of pre-lunch severe hypoglycemia and two episodes of hospitalization, in the last 6 months. He also gave a history of fall while walking, 5 months back, post-meal abdominal pain, bloating even with small food intake,

Editor's Comment :

- **Consider routine screening for DAN in all T2DM patients diagnosed for 5 years.**
- **Go for early detection and prompt treatment of DAN.**
- **A composite assessment of Valsalva ratio, inspiratory/expiratory RR interval ratio and focused history is useful as a surrogate marker to detect gastroparesis.**
- **In presence of gastroparesis, re-adjust insulin timing to avoid post-meal hypoglycemia.**
- **Medication reconciliation and deprescribing, as needed, are useful.**
- **Just good glycemic control can delay or ameliorate gastroparesis in T2DM patients.**

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incomplete bladder emptying since last 10 months and recurrent loose motion (night time) for last 6 months. Patient had a disturbed sexual life for last 5 years due to erectile problem.

Investigations for glycemic status showed HbA1c 10.9%, FPG 86mg/dl, and PPPG324 mg/dl. On examination, fine touch with 10 gm mono-filament was diminished on toes, heels and dorsum of feet, but perceived normally in all meta-tarsal heads in both limbs. Vibration sense (128 Hz) was also found diminished in both great toes and medial malleoli, but was intact in both knees. Screening for Diabetes Autonomic Neuropathy (DAN) was performed that involved five simple tests as proposed by Ewing et al [3]and the findings were suggestive of loss of autonomic neurofunction, particularly the parasympathetic neurofunctional integrity (Table 1). A diagnosis of DAN with features of CAN and gastroparesis was made.

A thorough reconciliation of medications was done. Both vildagliptin and amitryptiline were omitted andamlodipine was substituted with telmisartan. Oral domperidone thrice a day was added. The patient was counselled for change in insulin regimen and dose adjustments of insulin was donewith premix insulin(30/70) 22U before breakfastand 16 U twice daily just before meals. An hourlyCBGcheck for 4 hours post meal, for 2 weeks, was advised.The follow-up visit was scheduled after 3 months.To optimize compliance, the patient was telephonically counselled every week.

Onreassessment after 3 months, there was a marked improvement in the gastroparesis symptoms. No episode ofhypoglycemia was experienced. The post-meal hourly CBG check in the initial 2 weeks revealed good post-meal glycemic control. The HbA1c was7.4%. The DAN screening tests were repeated and the findings were suggestive of subtle improvement in all the parameters (Table 1).

Discussion

DANis a frequent chronic complication of DM with potentially life-threatening outcomes. Despite its significant negative impact in quality of life in the affected, it has been one of the least recognised and comprehended complications of diabetes. DAN may affect many organ systems throughout the body, eg, Gastrointestinal (GI), Genitourinary (GU), and Cardiovascular (CV). Major clinical manifestations of DAN thus include resting tachycardia, exercise intolerance, orthostatic hypotension, constipation, gastroparesis, erectile dysfunction, sudomotor dysfunction, impaired neurovascular function, and hypoglycemic autonomic failure[4]. GI disturbances are common and may includeenteropathy, gastroparesis, constipation, diarrhea, and fecal incontinence. Gastroparesis should be suspected in individuals with irregular glucose control and in presence of post meal hypoglycemia. In this present case, patient was initially taking insulin 30 minutes before breakfast, but owing to gastroparesis there was delayed food absorption which led to recurrent post breakfast hypoglycaemia. Considering pharmacokinetics of human insulin (onset of action ~ 30 minutes) and existing gastroparesis, this patient was advised to take insulin just before the meals which reduced the incidents of hypoglycaemic events. This report highlights the importance of reconciliation of existing treatments and individualizing treatment as necessary in a given patient. Dose of insulin should be titrated as per pre and post meal CBG values, but one needs to monitor CBG for longer duration, may be up to 4 hours, as in this case. A single 2-hour post meal CBG value may prove misleading, particularly in presence of gastroparesis.

Ideally, DAN related gastroparesis should be identified by gastric emptying scintigraphyof a radiolabeled solid meal, that evaluates motor function

Table 1 — *Findings of DAN Screening*

Test	Description	Baseline	After 3 Months	Normal
Expiration/ inspiration (E/I) ratio	The patient was asked to take deep breaths for 10 minutes with frequency about 6 breaths/min.	1.05	1.3	≥1.2
Valsalva maneuver	The patient was asked to blow into the special manometer to maintain the pressure at about 40 mmHg for 15s.	1.1	1.16	>1.2
Postural heart rate response : maximum-minimum (30:15 ratio)	Heart rate was measured in the horizontal position and again two minutes later after standing upright.	1	1.09	>1.03
Postural blood pressure response	Blood pressure (mm of Hg) :			
	lying down	130/66	140/76	
	1 min after standing upright	130/80	130/80	
	3 min after standing	122/82	132/82	
	5 min after standing	126/82	136/82	
Isometric handgrip test (dynamometer)	Blood pressure (mm of Hg) :			
	beforehandgrip	130/66	140/76	
	5 min post handgrip	167/72	167/86	
	Difference between DBP (mm of Hg)	6	10	

of stomach and quantifies the emptying of the meal. However, such tests are broadly unavailable in resource constrained settings. Cardiac autonomic neuropathy (CAN) assessment can be an indirect marker of probing gastroparesis. In the present case, based on elicited history and clinical examination, a provisional diagnosis of diabetic gastroparesis was made. Our DAN screening findings emphasizing changes in Valsalva and deep breathing ECG suggested parasympathetic dysfunction, which serves as an indirect surrogate marker for detection of DAN associated gastroparesis.

The American Diabetes Association recommends the use of the Ewing's tests in the diagnosis of DAN. Ewing's tests are simple and doable in resource-constrained settings also. Thus DAN screening using Ewing's tests can be integrated in routine monitoring of T2DM patients. Both expiration-inspiration ratio and Valsalva maneuver measure the ability of the vagal nerve to slow the heart rate during procedures which increase heart rate. The Valsalva maneuver represents both sympathetic and parasympathetic components. The isometric handgrip test and postural blood pressure show changes in sympathetic function and involve principles of baroreflex-mediated blood pressure fluctuations[5].

Diabetic gastroparesis needs dietary modification, glycemic control, de-prescribing, if needed of drugs which may have detrimental effects on gut motility, and specific pharmacotherapy. In this patient we de-prescribed vildagliptin, amitryptiline and amlodipine. Generally incretin based therapy and alpha glucosidase inhibitors are withdrawn if patients are suffering from diabetic gastroparesis. There exists a controversy with use of metformin due to its gastrointestinal side effects. However, insulin resistance is known to contribute to diabetic gastroparesis and metformin ameliorates it. Many physicians thus prefer to continue it with close monitoring. In the present case, metformin was continued. Amitryptiline and amlodipine, due to their anticholinergic potential,tend to further worsen gastroparesis. The anticholinergic burden of different concomitant medications in T2DM patients should be assessed using appropriate tools, and those with high burden score should better be omitted after a risk-benefit analysis. Prokinetic drugs like metoclopramide, domperidone or acotiamide are sometimes required. In the present case, domperidone was used.

Hyperglycemia itself delays gastric emptying, even in the absence of neuropathy or myopathy. Generally, it is mediated by reduced phasic antral contractility and the induction of pyloric pressure waves.[6] Hyperglycemia antagonizes ameliorating effects of prokinetic agents. Glucose levels should be maintained below 180 mg/dL, which would help to avoid inhibiting gastric myoelectric control and motility. Continuous Glucose Monitoring (CGM) canseamlessly assess glycemic control andcan guide insulin injection timing in presence of gastroparesis. However, use of CGM was not feasible in our facility. In order to minimize occurrences of dysglycemic episodes, what is needed is employing individualized intervention. In this case, prompt glycemic control helped in reversing gastroparesis and CAN related abnormalities. Both the sympathetic and parasympathetic derangement were corrected within 3 months. The reversal of autonomic neuropathy features in T2DM with intense glucose monitoring has been reported, only sparingly[2]. However, our experience with this patient is not in conformity with other reported studies[7] where prolonged period of improved control failed to reverse established autonomic dysfunction of diabetes. Nonetheless, with lessons from the index patient, we resolved to routinely screen all T2DM patients diagnosed for more than 5 years, for DAN, and to institute closertreatment monitoring and control with a hope of avoiding and/or reversing of such complications. An early detection of autonomic dysfunction in T2DM patients can encourage the physician to improve metabolic control, thus ensuring better treatment outcomes.

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Pictorial CME

Persistent Hypoglossal Artery — A Rare Vascular Anomaly

K Mugundhan[1],Viveka Saravanan R[2], Jeyaraj K Malcolm[3], Sakthi Velayutham S[3], P R Sowmini[3], M Sathish Kumar[3]

Fourty Years old male, non alcoholic, not a known hypertensive who presented with sudden onset of severe headache. Neurological examination was normal. CT brain and MRI brain showed left frontal white matter and external capsule hemorrhage. Patient improved well.Since patient had recurrent attacks of headache, Digital subtraction angiography was done to look for any aneurysms and A-V malformations. It revealed bilateral persistent hypoglossal artery (Fig 1&2) and absence of vertebral arteries (Fig 3).

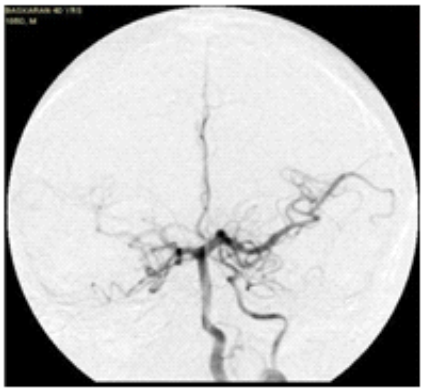

Fig 1 — DSA showing Left Persistent hypoglossal artery (AP view)

Fig 2 — DSA showing Right Persistent hypoglossal artery (Sagittal view)

Fig 3 — DSA showing absence of left vertebral artery

Discussion

Persistent hypoglossal artery is a rare carotid – basilar anastomosis with reported incidence between 0.03 % and 0.26 % on cerebral angiography[1]. During embryogenesis, two longitudinal arteries are formed along the basal surface of hindbrain. These vessels are supplied by anastomotic channels that connect them to the internal carotid arteries. They are trigeminal, otic, hypoglossal and pro- atlantal segmental arteries. With the development of posterior communicating artery and vertebro basilar system, these channels regress. The hypoglossal usually arises from internal carotid artery at C1 – C2 vertebral level and runs dorsally and lies lateral to hypoglossal nerve to enter the hypoglossal canal and then into posterior fossa to join basilar artery. Both vertebral arteries are absent or hypoplastic in these cases.

Identification of this vessel is important before carotid endartectomy or skull base surgery because both anterior and posterior circulation is dependent on arterial supply of internal carotid artery. Formation of atherosclerotic plaque and aneurysms has been reported in persistent hypoglossal arteries because of altered flow dynamics[2].The detection and investigation of persistent hypoglossal artery is of clinical importance, since its presence has been related with a spectrum of diseases. It can also be recognised as an incidental finding in cerebral angiography as in this case.

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Pictorial CME

A Girl with Seizure Disorder

Nandini Chatterjee[1], Mrinal Kanti Roy[2]

A twelve year old girl born full term to non-consanguineous parents presented with recurrent generalized seizures for last 4 years. She had learning disability, delayed milestones and difficulty in walking. There is no history of birth trauma, antenatal or perinatal complications except delayed cry after birth.

On examination, she had mental retardation, upper motor neuron signs in left upper and lower limbs and mild deviation of mouth to the right.Bilateral carotid pulsations were normal.

Her investigations revealed an abnormal EEG suggestive of generalized seizure disorder (Fig 1). The MRI showed hemi - atrophy of the right cerebral hemisphere (Fig 2) with ipsilateral dilatation of the lateral ventricle. Thickening of the calvarium was noted on the right (Fig 3) along with prominence of right mastoid air cells. (Fig 4) A diagnosis of Dyke Davidoff Masson Syndrome was made.

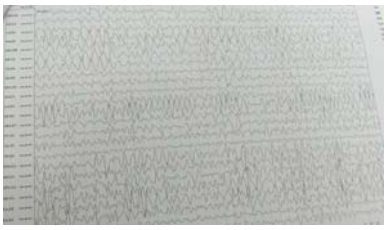

Fig 1 — EEG demonstrating generalized seizure disorder

Fig 2 — Hemiatrophy of right cerebral hemisphere with ipsilateral dilatation of the lateral ventricle

Fig 3 — Thickening of the calvarium of the right side

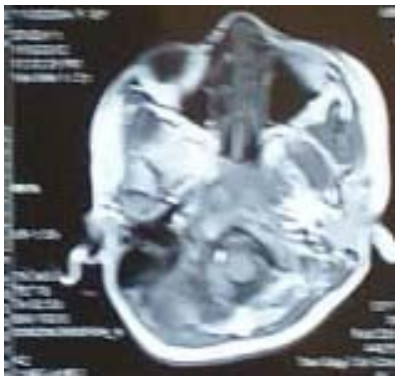

Fig 4 — Prominence of the right mastoid cells

Childhood Cerebral Hemi-atrophy Syndromes may be congenital or acquired. Acquired causes include trauma, perinatal infections as well as Rasmussen encephalitis[1], ischemia, neoplasia and radiation injury. Some disorders like Sturge Weber Syndrome[2] neurofibromatosis, Parry Romberg Syndrome[3], Silver Russel Syndrome may also present with cerebral hemi-atrophy.

The Dyke Davidoff MassonSyndrome, is characterized by mental retardation, epilepsy, hemiparesis andpsychiatric manifestations. There is hemi-atrophy of the cerebral hemisphere, ventricular dilatation with calvarial thickening, along with overpneumatization of mastoid and paranasal sinuses[4]. The calva rial changes signify that the cerebral atrophy happened early in life as ¾th of brain growth occurs before 3 years of age. The acquired causes lack the osseous changes.

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History : Remembering the Stalwart

Rudrajit Paul, Jayati Mondal

Dr Vithal Nagesh Shirodkar was, in his day, one of the most famous Gynecologists of the world. He was born in 1899 in Goa and passed his MBBS from Grant Medical College, Bombay in 1923. He passed MD in 1927 and FRCS in 1931. His entire professional life was spent in Bombay. By 1940, he had become the Professor of Midwifery and Gynecology at his Alma Mater.

Dr Shirodkar was a gifted surgeon of world renown. He pioneered the surgical techniques for genital prolapse. Another of his path-breaking contributions in the field of Obstetrics was the cerclage operation of the cervix to prevent second trimester abortions. By 1955, his pioneering technique had become world famous as "Shirodkar Operation". Dr Shirodkar was one of the first doctors in India to realize the importance of video recording of surgeries and he meticulously recorded his procedures. These were shown in European conferences like the one in Paris in 1951, to critical acclaim.

Vithal Nagesh Shirodkar

Picture taken from an article by Purandare CN et al. in 2012

Dr Shirodkar had numerous indexed publications and also contributed chapters in international textbooks of Gynecology and Obstetrics. In 1963, he was invited to New York to perform his surgery in front of an American audience. This was a rare achievement for a doctor of a country which had become independent only 16 years ago. His other notable contributions were those in the fields of tuboplasty and creation of neovagina. One of his most famous papers was published in JIMA:

Shirodkar VN — Surgical treatment of female sterility. *JIMA* 1957; **29:** 56-7.

It can be safely commented that along with Dr SubodhMitra and Dr SubhasMukhopadhyay, Dr Shirodkar was instrumental in cementing the position of Indian Gynaecology in the world stage.

There is hope in dreams, imagination, and in the courage of those who wish to make those dreams a reality.

— **Jonas Salk,** ***American Physician who developed the Polio Vaccine***

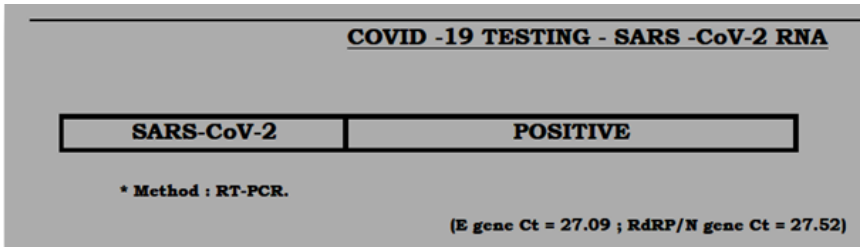
Essential Update

CT Value in the RT-PCR Report : What does it mean?

Rudrajit Paul, Jyotirmoy Pal

The Covid-19 pandemic has revolutionized the field of medicine over the last one year. It was just one year ago, on 31st December, 2019 that the first case of novel coronavirus was reported from Wuhan, China. Now, after one year, this new virus has left a trail of death and mayhem in all the continents. One of the significant paradigm shifts in this pandemic has been the widespread use of molecular genetic tests. In the previous epidemics like scrub typhus, dengue or malaria, the diagnosis was mainly done by antigen or antibody tests. But Covid-19 is the first pandemic (besides the small outbreak of swine flu in 2009) where the main diagnostic modality is a genetic test. For internists, this is a new domain and they have to get used to the technical terms. One such frequently used term: **CT** is described here.

Let us look at a Covid-19 test report of a recent patient:



Right below the RT-PCR positive report, the Ct value is written for two different genes. The full form of this is **Cycle Threshold**. In RT-PCR, the clinical material is subjected to repeated cycles of DNA amplification to reach a threshold of detection. Ct is the number of cycles required for the fluorescent signal to reach this threshold. Thus, if the nuclear material in the sample is high, it will get amplified easily with less number of cycles, that is, the Ct value will be low. So, lower the Ct value, more the amount of DNA/RNA in the clinical sample; in other words, more the viral load.

Usually, the instruments used for clinical purpose perform around 40 replication cycles per sample. If nothing is detected by 40 cycles, the sample may be considered to be negative for clinical purpose.

The two genes mentioned here are E: envelope protein and RdRP: RNA-dependent RNA polymerase. If only one gene target is used for PCR detection, the test will be faster. But accuracy will be less. Most Indian laboratories are using two gene targets (as shown in this report).

What is the Ct value for considering high viral load? This cut-off is still debatable and different authors have mentioned different cut-offs from 25 to 29. When do you consider a test to be negative? This is again debatable. While some authors define a threshold of 35, others consider higher values to determine negativity.

The Ct value may vary with the kit used, the method of sample collection and the temperature at which the sample is transported. Thus, at present, there is no clinical significance of this number. Low values can identify high viral load, BUT IT DOES NOT CORRELATE WITH PROGNOSIS, CHANCE OF PROGRESSION OR INFECTIVITY of that person. Clinicians should not give undue importance to this number. Patients should be treated mainly based on clinical judgement.

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Essential Update

Emotional Intelligence : A Paradigm Shift

Niranjan Shendurnikar[1], Tushar Shah[2]

Among the emerging health concerns for the physical and mental well-being of children, adolescents multiple biological, psychological, social, cultural, environmental and economic factors have a potential influence for the attainment of the health and well-being on an individual. Since renowned psychologist Daniel Goleman published his pioneering book 'Emotional Intelligence' in 1995, interest continues to grow in what is considered to be an indispensable component not only of achieving one's potentialbut life satisfaction and success too.[1] While the focus had earlier remained on the academic achievement during the growing years of childhood, emotional regulation was largely ignored. Not only the intelligence quotient (IQ) but emotional intelligence (EI) is considered twice as a strong predictor of than IQ of later success. In Goleman's own words, emotional intelligence is the capacity for recognizing our own feelings and those of others, for motivating ourselves, and for managing emotions well in us and in our relationships.[2] Emotional intelligence describes abilities distinct from, but complementary to, academic intelligence or purely cognitive capacities measured by the intelligence quotient.It is the ability to notice and understand the emotions and channelize the action on those emotions in an effective direction[1].

During the last few years, Emotional intelligence (EI) gained further attention as it has a promise to be applied as an intervention for the set of skills that can be taught to enhance coping resources and promote the well-being. When the child or an older person appreciates the steps in thinking and learning processes, EI is akin to Global Positioning System (GPS) which assists him/her to navigate the way around the potential/real obstacles and find a right path towards the destination/goal. These set of perceptions and skills can be learnt right from early childhood to the grown-ups.

The five components of emotional intelligence as identified by Goleman are: self-awareness, self-regulation, internal motivation, empathy and social skills. The self-awareness is about knowing one's own feelings at a particular time and how those feelings and moods can affect others. Once the possible consequences of acting on an impulse are considered beforehand, it's a manifestation of responses to the emotions (self-regulation). Motivation is another step which helps one to accomplish tasks/goals in spite of distractive or negative which may be there in a given situation. Understanding the others' feelings from their perspective and making a sincere effort to put oneself in other's shoes is what Empathy about. But it is not just about understanding the emotions of others but also a timely ability to express the reciprocal sensitivity to them, too. Social skills are an integral part of healthy relationships in the sphere of family, community and society[1].

A recent study of 912 high school students in Spain (2020) on relationship between emotional intelligence, social skills and peer harassment observed a positive relationship between EI and social skills. In turn, social skills reflected a negative relationship with respect to bullying ($p < 0.001$). The authors recommended the need to implement the educational programs focused on the development of emotional intelligence in the classroom, as a means to try to stop bullying behaviors in the classroom[3]. Further, the connection between EI and a range of positive outcomes across the academic, social, psychological and career domains among adolescents has been well-documented in several research studies in the past decade. A recent study of adolescents in 2015 found that yoga, which can increase mindfulness, helped improve student's emotional regulation capacity.[4]

Emotional intelligence isn't set into a particular frame and can be a part of learning over a period of time with help from others. As the child grows, the capacity for emotional self-regulation can improve thereby helping to learn the strategies to eliminate or avoid disturbing situations and thus solve the problem. The parents and family members are most suited to help learn their children learn emotional intelligence skills as the kids grow, develop and mature. While all the emotions are acceptable, all the behaviors and

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reactions are not and that is why awareness of the child's feelings and having a label for them (such as upset, disturbed, distressed, shy or joyous, hopeful, excited) makes a good beginning. Empathy makes them understand and validate their feelings to be open to listening, reasoning and help them in finding a solution. As children continue to grow, new challenges are a part of learning and hence healthy coping and problem-solvingskills need to become a part of ongoing process. Parents consistently need to have mandatory family talk time and sharing their own experiences and limitations withchildren, praising them for their sincere efforts and creating a supportive environment without over reaction and guilt tripping to build up EI.

During the last few years, the concept of EI has extended beyond childhood and adolescents to youths including medical undergraduates. A descriptive Study on emotional intelligence, perceived stress and academic performance of Sri Lankan medical undergraduates was conducted in the University of Colombo. It concluded that higher EI was associated with better academic performance amongst final year medical students. In addition, a higher EI was observed in those who had a higher level of self-satisfaction and self-perceived stress was lower in those with a higher EI. Enhancing the EI might help to improve academic performance among final year medical students and also help to reduce the stress levels and cultivate better coping during professional life in the future[5]. With a paradigm shift medical educators have been among the many advocates for developing EI as a leadership competency for physicians. They have endorsed a need for emotional intelligence in physician leadership development, mentoring and advancement within academic medicine, and developing effective social networks within the healthcare field. *Several studies from India and abroad have* **perceived** stress and burnout as by-products of residency programs and stressful schedules thereof of resident doctors[6]. In such settings EI works as an adapting and coping tool and can become an explicit part of medical education and training programs. Besides EI has a potential to be a strong foundation to maintain and foster well-being, health and performances in challenging work environments even in the years ahead. Time has come to acknowledge emotional intelligence as a mainstream skill!

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The reward for work well done is the opportunity to do more.
— **Jonas Salk, *American Physician who developed the Polio Vaccine***

Future Technology

Rudrajit Paul

The Future :

[The post-Covid world will be radically different from the near past. Especially in Medical Science, there will be a lot of changes. There will be a lot more use of technology for diagnostic, therapeutic and also, communication purposes. This new section, started from December 2020, will highlight these new technologies for the busy physician.]

Video Calling :

After Telemedicine became legal in India in March 2020, there has been an increasing trend in the use of video consultation for medical purposes. Thus, the physician of tomorrow must be adept in the use of video calling technology. This is now used not only for patient consultation, but also in medical teaching. In fact, throughout 2020, in all medical colleges of India, all classes and seminars were held through video calls only. Many multi-speaker national conferences were also held via this medium. Slowly, people have become used to this technology and it is highly likely that in the post-Covid world, this trend will continue.

There are a lot of video calling Apps. Some are free while others require subscription.

1. Zoom : This is one of the most popular Apps. There are free and paid versions. The free version allows meetings up to 40 minutes. The paid versions allow more participants and much more meeting hours. Usually, the host of the meeting will create a meeting ID (called raising) and send the id and password to other participants. Everyone else can join using those credentials. Sometimes an e-mail/Whatsapp link is sent and just clicking on the link will take you to the live meeting.

2. WhatsApp video call : We are sure that all readers of this article use WhastApp and also know how to use the video calling feature. As of now (Dec, 2020) up to 8 participants are allowed in one call. There is no limit on time and it is completely free. This is good for tele-consultations but not good for lecture classes.

3. Google Meet : This is free for 100 participants up to 60 minutes. Anyone with a Google account (which we are sure all of our readers have anyway) can start a Google Meet meeting. The link can be sent to the participants.

4. Microsoft Teams : This has free and paid versions. For the free version, up to 100 people can join and meeting can be up to 60 minutes. The paid versions allow much more flexibility. This App also allows cloud storage.

5. Facetime : This is the inbuilt App for iPhone users. Maximum users: 32

6. Facebook Messenger : This also allows up to 50 users and unlimited time. But it would be unadvisable to use it for official purposes.

Most of the Apps used here are extremely easy to use. To join a meeting, one just needs to download the App and type in the passcodes. To be a host, we need to create accounts (like any other social media website). One needs to have high-speed internet connection for these Apps.

Etiquettes for video calling : —

- During a video calling session, we should remember that it is a public event. Thus our dress (even if we are at home) should be as required for a formal meeting
- When one attendee is speaking, others should keep their devices in the “mute” mode
- The backdrop of the speaker should be such that no domestic details (like someone doing domestic chores) are unnecessarily revealed
- Video calls are mostly taking place from home. But the attendees have to make sure that other family members are not creating distractions. If needed, keep the video mode “off”.
- It is rude to leave midway during a speech.
- It must be remembered that when “screen sharing” option is used, the home screen of the device becomes public. Thus, it must be ensured that the home screen does not contain any offensive images or personal details.
- For those who will be doing regular video lecture sessions, it may be advisable to have a corner of the home or clinic decorated to look “official”.
- A person may have some objects or pictures at home which may be offensive to some other people. Such artefacts should never be in the backdrop during the video call.
- The “chat” feature of video calling Apps are for relevant discussions only.

Perspective

Pulse oximeter as a household instrument : Does it help or aggravate the situation ?

Rudrajit Paul, Jyotirmoy Pal

With the advent of the current Covid-19 pandemic, there have been a lot of changes in our daily life. Common medical concepts like hypoxia, ARDS and acquired immunity have entered public discourse and there has been a surge in the sales of portable medical instruments for home use. In September, *The Tribune* newspaper reported that medical stores in North India were selling 800-1000 Oximeters a month. An e-commerce website of India registered a 300% increase in the demand for portableOximeters all over the country.

Such portable personal care medical instruments are quite useful. They help the patients in taking charge of their own health and makes telemedicine easier. Any epidemic with high morbidity like Covid-19 will always overwhelm the existing health infrastructure and a significant number of the patients will be managed at home. For such cases, home-use medical instruments are highly recommended. In fact, many state governments in India (like West Bengal) have officially recommended home monitoring of oxygen saturation in their official guidelines.

However, sudden surge in the use of a new technology also gives rise to some confusion and miscommunication. As the common public started using this new device, there was a lot of misunderstanding. For example, it was very common for people to get alarmed at mere one point drop in the SpO_2 reading. Many a doctor in India has been the recipient of frantic calls from patients, who had become anxious about their readings dropping from 99 to just 98%!

In the author's experience, some people also thought that SpO_2 was something that can be compared between patients, as an indicator of recovery. The author even had to face a situation where two patients in a family were given the same treatment for Covid and both got clinically better. But one of them had SpO_2 of 99% while the other had 96%. This second person got very depressed that she was "not getting better" like her other family member. Also for example, for anyone recovering from Covid, if the family members found the SpO_2 dropping from 98% to 96% in one day, they would get unduly anxious that "the disease was coming back". It becomes very difficult to explain the concept of "normal range" as opposed to a single "normal value" for human body parameters. In another situation, a person had 99% oxygen saturation, while his other family members had SpO_2 between 94 and 97. This person thought that he was "healthier" than his family. So, instead of trying to understand the nuances of this parameter, most people had a simplistic explanation for the machine reading. Many people started doing breathing exercises like "Pranayama" with the hope that deep breathing would raise the SpO_2 value.

The pulse oximeter has been recommended for use in confirmed Covid cases only. However, many people without any illness also bought it and started using it for screening purposes. For any minor sneeze or pharyngitis, or a little dyspnoea (may be even due to anxiety), they would use the meter; and if the value fell below their expectations, they would be seeking medical consultation. In a time when the health sector is already stretched to its limit, such unwanted influx of "patients" is highly undesirable. Many people have started equating health with oxygen content of the blood and even repeated reassurances would sometimes fail to convince them that they had no disease. This is somewhat similar to the overuse of blood pressure instruments or weight scales at home.

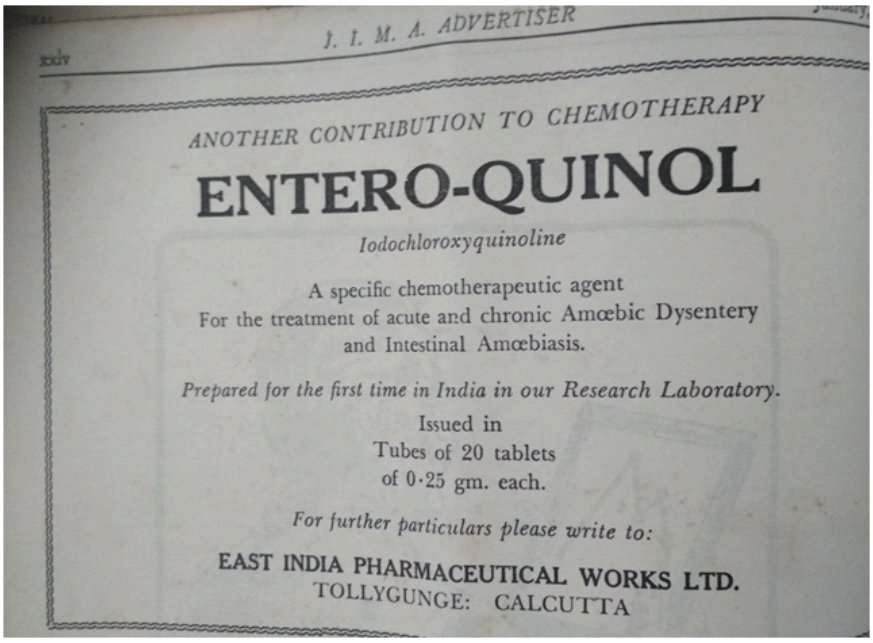
The interaction between man and machine is always a fascinating study for the medical anthropologist. The study gets even more intricate when the machine in question is a medical device. In the author's experience, the common person often develops an unassailable faith in the readings displayed on the LCD screen. The questions of technical error or biological variations are often relegated to the background. Instead of paying heed to the overall feeling of well-being, it becomes an obsession to check the machine readings repeatedly to get assured of health. People try to transfer their anxiety on to that device and the LCD screen reading becomes the beacon of hope.

Ads from the Past

Over the Counter Remedy for Dysentery

Rudrajit Paul, Jyotirmoy Pal

This is an advertisement from January, 1946. But this medicine is very much available even today in all chemist shops of the country and is freely sold over the counter.



Iodochloroxyquinoline was an Amoebicide first used in the 1930s. This drug directly kills the intestinal trophozoites. It gives quick symptomatic relief and is very cheap. Thus, this drug has a sort of cult following among the common public in India and many Indians, on getting the first symptoms of diarrhoea or dysentery, would start this medicine on their own. In spite of being rejected by modern physicians for over four decades due to its documented side effects, this drug enjoys a steady popularity even today, bolstered by word of the mouth. Although the trade name remains the same, the composition is now slightly altered to Quiniodochlor. It still contains Iodine, which raises possibility of interaction with thyroid function.

Between 1955 and 1970, there were tens of thousands of cases of subacutemyelo-optic neuropathy in Japan. Epidemiological data linked the disease to the use of Clioquinol, a drug similar to enteroquinol. This led to a worldwide ban on further use of the drug and most modern texts would not even mention this chemical compound, let alone the dosage. But in India, people have continued to use this drug (using any dose they think convenient) and there has not been much report of adverse reactions. At the time in the 1970s, when huge number of cases was reported from Japan, only 10 odd cases could be reported over a period of 10 years from Bombay (Wadia, JJ Hospital).

Quinodochlor has additional antifungal properties, which could be useful in dermatological diseases like P. versicolor. But since all research into the drug stopped after the ban, there is no way of knowing its efficacy for these alternative indications. Since millions of people in India are using this drug without prescription and not much side effects are coming out, it may be worthwhile to look into the reuse possibilities of this extremely cheap medicine.

Drug Corner

Ivermectin as a Chemo-prophylactic Agent against COVID-19: A Consensus Statement

Surya Kant[1], Harsh Rastogi[2], VK Arora[3], AG Ghoshal[4], Ravi Wankhedkar[5], Prasanta Mohapatra[6], Pradhyut Waghray[7], Alladi Mohan[8], Pradeep Bhowmik[9], Agam Vora[10], Mangesh Tiwaskar[11], Jayesh Lele[12], Amit Gupta[13], Parthiv Mehta[14], Ketan Mehta[15], Arvind Ghongane[16], Bhavin Shah[17], Shuchin Bajaj[18], Bhupesh Dewan[19]

Under the aegis of Academy of Advanced Medical Education, apanel comprising of Infectious Disease Specialists and pulmonologists with years of experience met on August 30, 2020; September 22, 2020 and October 13, 2020. Based on the currently available evidence, the panel reached at a consensus that a dosage regimen of ivermectin with dose ranging from 200-400mcg/kg bw, can be used prophylactically (12 mg for below 60 kg, 18 mg for 60-90 kg, and 24 mg for >90 kg of body weight) against COVID 19. First three doses of 12 to 24mg, ivermectin should be given 72 hours apart and then once monthly. Four groups of individuals are recommended for prophylactic treatment; healthcare workers (Corona Warriors), asymptomatic close contacts of confirmed COVID-19 cases, individuals residing in containment zones andhigh risk groups: like diabetes, obesity, cardiac disorders, immunocompromised patients including HIV positive cases and individuals above 60 years of age.

[*J Indian Med Assoc* 2020; **118(12):** 81-5]

***Key words*: COVID-19, Ivermectin, Prophylaxis, SARS-CoV-2.**

Currently, with more than 7 million confirmed coronavirus disease 2019 (COVID-19) cases, India ranks 2nd in the world.[1] This has resulted in an immense burden on both national economy and healthcare set-up. To tackle this issue, ideal approach would be prevention of COVID-19, therebydecreasing the total number of cases.[2]

With the launch of COVID-19 vaccine being a distant

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dream, repurposing of already approved drugs present a realistic approach. Introduced in 1980s, as an anthelmintic agent, ivermectin has a known safety profile with low incidence of adverse events, when administered orally.[3] Simultaneously, its antiparasitic, antiviral, immunomodulatory, and anti-cancer activity were discovered and it has been termed as a wonder drug.[4,5]

Recently, researchers from Australia provided the first evidence of action of ivermectin against severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2).[6] Subsequently, ivermectin is being used globally as a prophylactic and therapeutic agent against COVID-19 and is undergoing various randomized controlled trials.[7-14]

Academy of Advanced Medical Education held panel discussions on August 30, 2020 and September 22, 2020 under the guidance of Prof. Dr V K Arora in presence of following Infectious Disease Specialists

Prof Dr Agam Vora, Prof Dr AG Ghoshal, Prof Dr Surya Kant, Prof Dr Ravi Wankhedkar, Prof Dr Prasanta Mohapatra, Prof Dr Pradhyut Waghray, Dr Harsh Rastogi, Prof Dr Alladi Mohan, Prof Dr Pradeep Bhowmik, Dr Mangesh Tiwaskar, Dr Jayesh Lele, Dr Amit Gupta, Dr Parthiv Mehta, Prof Dr Ketan Mehta, Dr Arvind Ghongane, Dr Bhavin Shah, Dr Shuchin Bajaj and Dr Bhupesh Dewan.

Rationale for using Ivermectin as a Chemo-prophylactic agent :

(1) Following an *in-vitro* experiment by Caly *et al*, multiple mechanisms of action have been proposed that suggest anti-SARS-CoV-2 activity of ivermectin.

(a) It has been proposed that ivermectin does not target any specific viral protein, but rather acts by inhibiting the binding of importin-α (IMPα) to importin-β1 (IMPβ1). Moreover, it acts by targeting the IMPα/β1 heterodimer, resulting in its dissociation.[15] This dissociation hampers binding of Impα/β1 to the viral protein, thereby preventing it from entering the nucleus. This leads to reduced inhibition of the antiviral responses, resulting in a normal, more efficient antiviral action.[6]

(b) The initial transfer of IMPα/β1 heterodimer to cell nucleus results in initiation of the viral life cycle. This suggests that prior inhibition of importin receptor leads to decreased rate and intensity of viral growth. This may also decrease the chances of infectionof non-infected host cells. Similarly, when administered in the early phase of infection, ivermectin halts the nuclear transportation of IMPα/β1 heterodimer resulting in decreased severityand duration of disease,as well as attenuated spread of infection.[16]

(c) Another study has highlighted that ivermectin has a significantly better binding affinity for SARS-CoV-2 proteins than doxycycline and shows a perfect binding site to the interacting regions of Spike-RBD and angiotensin converting enzyme 2 (ACE2). This indicates that ivermectin might be acting by interfering in the interaction of spike with ACE2 and inhibiting the viral entry in to the host cells.[17]

(d) Ivermectin has been described to act as an ionophore. It generates pores in biological membrane of SARS-CoV-2, disturbs its hydro-electrolyte balance, and exerts antiviral action.[18]

(e) Recently, 'catch and clump' hypothesis has been proposed. The SARS-CoV-2 catches CD147 receptor on red blood cells (RBCs) and endothelial cell. Following thisbinding, RBCs forms clumps with other RBCs, leucocytes, platelets, and endothelial cells resulting thrombotic complications. It has been assumed that ivermectin acts by competitively binding the spike proteins of SARS-CoV-2 and prevents the formation of clumps, thereby exerting anti-thrombotic action.[19]

(f) Ivermectin is proposed to act on four important drug targets, spike protein, RNA-dependent RNA polymerase, 3-chymotrypsin- and papain-like proteases of SARS-CoV2.[20]

(2) In an *in-vitro* experiment, Caly *et al*. demonstrated that a single applicationof ivermectin (5 μM) could eliminate 99.98 % viral RNA within 48 hours in SARS-CoV-2 infected Vero/hSLAM cells. Moreover, it is worth highlighting that no cytotoxicity was observed at this high concentration.6

(3) Over the past 30 years, ivermectin has demonstrated a favourable safety profile in humans.[21]A study involving healthy adult individuals evaluated the safety and tolerability of escalating doses of ivermectin and reported that safety and tolerability of ivermectin was comparable to placebo, even at dose that were 10 times the maximum approved dose.[22]

(4) Finally, ivermectin is included in the 21st WHO Model List of Essential Medicine 2019 and also finds place in the National List of Essential Medicines of various member nations.[23] This had resulted ineasily availability of ivermectin at reasonably affordable price in major areas of the world.

Ideal Candidates for Chemo-prophylactic Therapy:

- The healthcare workers (corona warriors including doctors, para medics, nurses and support staff like persons associated with morgue, crematorium, ambulance, security at health care etc)
- Asymptomatic close contacts of confirmed

COVID-19 cases including family members, household workers, immediate neighbors, care takers, office and business staff etc.

- Individuals residing in containment zones : Red Zone as declared by appropriate authorities or area with overcrowded residences with multiple COVID confirmed cases or buildings and colonies having confirmed cases on home quarantine.
- High risk group : People with comorbidities like uncontrolled Hypertension, uncontrolled diabetes, obesity, cardiac disorder, immune compromised diseases including HIV, elderly people with frailing immunity are ideal candidates for chemo-prophylactic therapy.

Ivermectin acts by suppressing the replication of SARS-CoV-2 within 24-48 hrs, it decreases the risk of contracting the COVID-19.[6] Ivermectin can be beneficial and provides considerable protection in these candidates and this has been confirmed by the findings of recently completed clinical trial.[24]

Pharmacokinetics – Rationale for dosing & frequency for prophylaxis :

Ivermectin is highly lipophilic, and rapidly absorbed (Tmax = 4 hours). It binds strongly to plasma proteins (93 %), and has a predilection for sequestration in tissues (Volume of distribution~3.5 L per Kg).[25] Following single doses of 30 to 120 mg, AUC and C_{max} were generally dose proportional, with T_{max}~4 hours and $t_{1/2}$~18 hours (range 12-36 hours). The geometric mean AUC of 30 mg ivermectin was 2.6 times higher when administered with food. Geometric mean AUC ratios (day 7/day 1) were 1.24 and 1.40 for the 30 and 60 mg doses, respectively, indicating that the accumulation of ivermectin given every fourth day is minimal.[26] Based upon the half-life range of 12-36 hours, once a week dosage schedule can be justified for prophylaxis, but due to paucity of safety data on frequent weekly dosing, the academy advocated the use of once monthly dosage schedule. This regimen may be modified to more frequent dosing, once we get more experience on the molecule and its long term safety.

Clinical Safety :

Ivermectin has been well tolerated when administered as a single dose of 800 µg per kg,[27] and multiple dose of 1,600 µg per kg over 12 weeks,[28] and 1,600 µg per kg over 13 days.[29] In a recent meta-analysis, Navarro *et al* compared the safety of standard (up to 400 µg per kg) and high dose (up to 800 µg per kg) ivermectin and reported no significant differences between them in terms of frequency or intensity of adverse events.[30] Moreover, long-terms follow-up studies have reported that ivermectin in a dose of 400 µg per kg does not result in increased incidence of death amongst elderly.[31,32]

However, ivermectin is contraindicated in pregnant women and its safety and efficacy is not established in children weighing less than 15 kg.[33]

Hydroxychloroquine (HCQ) was initially recommended as a chemo-prophylactic agent in COVID-19. However, it should be avoided in cases with ischemic heart disease, as it has been found to be associated with cardiotoxicity and results in prolongation of QTc interval and cardiac arrhythmias.[34,35] Moreover, in severe and critical COVID-19 cases with diabetes, use of HCQ is associated with the risk of hypoglycaemia.[36,37] In these two subset of cases, HCQ is contraindicated. Comparatively, ivermectin has no such contraindications and can be given in high doses without any safety concerns.

Prophylactic Clinical Trials :

Currently, only one clinical trial (NCT04422561) evaluating the efficacy of ivermectin, as a prophylactic agent, in asymptomatic close family contacts (N = 340) of COVID-19cases is complete (unpublished data). It is a randomized, open label, phase 2/3 study, in which individuals in Ivermectin group (N = 203) received 2 doses [dose of 15 mg per day (40-60 kg), 18 mg per day (60-80kg), and 24 mg per day (>80kg)] of tablet ivermectin72 hours apart, while individuals in Control group (N = 101) were observed without prophylaxis. At the end of the study, the protection rate was 92.6% and 41.6% in the Ivermectin and Control group, respectively. This finding suggests that two doses of tablet ivermectin provided considerable protection in asymptomatic close family contacts.[24]

As of Sep 2020, there are 5ongoing clinical trials (NCT04446104, NCT04447235, NCT04527211, CTRI/2020/05/025333, and CTRI/2020/06/026232) evaluating the efficacy and safety of ivermectin as a chemo-prophylactic agent against COVID-19.[7-11] Variable doses of ivermectin are being evaluated in these trials and ranges from single dose of 200 µg per Kg (CTRI/2020/06/026232) to weekly dose of 200 µg per Kg for 7 weeks (NCT04527211).

Indian Prophylactic Guidelines :

On August 6, 2020, the Government of Uttar Pradesh Government had released a guideline regarding prophylactic use of ivermectin against COVID-19. As per the guideline, the close contacts of COVID-19 cases are recommended ivermectin tabletsin a dose of 200 µg per Kg body weight on Day 1 and Day 7, 2 hours following the dinner. While, in healthcare

workers, ivermectin tablet is recommended in a dose of 200 µg per Kg body weight on Day 1, Day7, Day30, and then monthly, 2 hours following the dinner.[38]

Recently, on September 29, 2020, the Government of West Bengal introduced ivermectin as a chemo-prophylactic agent against COVID-19. As per the guideline, once daily dose of 12 mg ivermectin is recommended on Day 1, Day 7, and then monthly.[39]

Global Prophylactic Guidelines :

In Brazil, for healthcare workers, the authorities have recommended ivermectin tablet 6 mg per 30 kg body weight for two days, and then every 15 days. While, in case of individuals at risk of COVID-19, other than healthcare workers, single dose of ivermectin (6 mg per 30 kg body weight) followed by every 15 days is recommended.[40]

In Peru, healthcare workers and other individuals at risk are recommended a single dose of 6 mg/mL ivermectin suspension in a dose of 1 drop (200 µg) per Kg body weight, with maximum dose of 50 drops.[41]

Consensus Statement :

In light of the exigent circumstances, absence of a clearly safe and effective therapeutic agent/vaccine and theemerging evidence, especially a recently completed randomized control trial (RCT) in Egypt, the panel reached at a consensus that

- Ivermectin is economical, easily available, safe & is well tolerated drug and does not have any significant drug to drug interaction & it may be considered as a chemo prophylactic drug against COVID 19
- A dosage regimen of ivermectin with dose ranging from 200-400mcg/kg bw,can be used prophylactically (12 mg for below 60 kg, 18 mg for 60-90 kg, and 24 mg for >90 kg of body weight). First three doses of 12 to 24mg, ivermectin should be given 72 hours apart and then once monthly.

Four Group of Individuals are Recommended for Prophylactic Treatment :

1. **Healthcare workers (Corona Warriors)-** may receive prophylaxis till COVID 19 continues to be a public health problem.
2. **Asymptomatic close contacts of confirmed COVID-19 cases-** 3 doses 72 hours apart followed by one additional dose if the index case continues to shed the virus for a longer period of time.
3. **Individuals residing in containment zones :** for at least one month after the area is declared green zone or at least one month after the last case is cured in that area / building or colony
4. **High risk groups:** like diabetes obesity, cardiac disorders, immunocompromised patients including HIV positive cases and individuals above 60 years of age – Till COVID 19 continues to be a public health problem

Panel emphasizes that due to paucity of evidence, this recommendation is preliminary and shall be revised based on the availability of new safety and efficacy data. The panel firmly believes the urgent requirement of awell-designed RCT involving healthcare workers, asymptomatic close contacts of confirmed COVID-19 cases, individuals residing in containment zones and high risk groups. The panel also feels that ivermectin may be combined with other drugs like Zinc, Vitamin C and Vitamin D3 to enhance the overall prophylactic benefit.

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Drug Corner

Association between Benign Prostatic Hyperplasia and Metabolic Syndrome : A Clinical Update

Ketan M Desai[1]

The prevalence of metabolic Syndrome (MetS) in men with benign prostatic hyperplasia (BPH) as reported by Asian Studies was 26.7% to 55.4%, Men with MetS have higher prostate volume and higher prostate growth rate. Insulin resistance, increased visceral adiposity, low androgen high estrogen levels, low grade inflammatory state, dyslipidemia are all contributory factors. The treatment options include lifestyle modification, alpha 1 adrenoreceptor blocker, 5 alpha reductase inhibitors, PDE5 inhibitors. Combination of 5 α reductase inhibitors and α-blockers provides relief to LUTS and prevents progression of BPH.

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Key words **: Metabolic Syndrome, BPH, Combination therapy.**

In benign prostatic hyperplasia (BPH), there is an enlargement of the prostate gland characterized by the formation of hyperplasic nodules in prostate, and related lower urinary tract symptoms (LUTS).[1,2] It is highly prevalent among middle-aged and elderly men. The only two principal determinants known earlier which increases the BPH risk were aging and androgens. But, recent evidence suggest that there are number of modifiable risk factors such as obesity which have an important role in the development of BPH.[2] An association was observed between BPH and metabolic syndrome (MetS), or its components.[3]

The prevalence of MetS in men with BPH as reported by the Asian studies were 26.7% to 55.4%.[1]

*Metabolic syndrome is a complex disorders related to metabolic abnormalities*such as obesity, hypertension, dyslipidemia, insulin-resistance with compensatory hyperinsulinemia, and glucose intolerance.[2] *These metabolic abnormalities can lead to development of BPH and lower urinary tract symptoms (LUTS) in men.*[1]

The prevalence of MetS in men with BPH as reported by the Asian studies were 26.7% to 55.4%.[1]

As per the recent study, *men with MetS have higher total prostate volume*, by difference of 1.8-10.2 mL and *significantly higher prostate growth rate*than those without MS.[1,4] The number of MetScomponents an individual possess is positively associated with risk of BPH. Also, men with BPH have substantially greater odds of having metabolic syndrome. In the same way, men present with MetScould also be assessed for LUTS/BPH, this would help to improve quality of life and also to identify men at risk of BPH progression.[3]

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Editor's Comment :

- **An association has been found between benign prostatic hyperplasia and metabolic syndrome.**
- **Three hit mechanism of prostatic inflammation, metabolic changes and altered sex steroid levels lead to prostatic hyperplasia.**
- **Therapy should involve lifestyle changes, α-blockers, 5α reductase inhibitors and PDE 5 inhibitors for BPH and LUTS.**

Pathophysiology of MetS and BPH :

Though epidemiological data suggests the link between MetS and BPH/LUTS but, the exact biological pathways are still unclear. Several key factors have been identified and postulated to be responsible in such pathophysiological processes are listed below.[1]

(a) Insulin resistance :

Insulin is a growth factor for prostatic epithelial cells. Directly or indirectly hyperinsulinaemiathrough obesity and its altered hormone metabolism can increase genestranscription involved in sex hormone metabolism. It increasesthe risk of BPH by increasing the amount of androgen and estrogen entering prostatic cells. Also, insulin-like growth factor 1 (IGF-1) promote prostate epithelial growth and associated with BPHrisk. Due to homology of insulin receptor with IGF receptor, *insulin can bind to IGF receptor and activate the IGF signaling pathway to promote the prostatic growth.*

(b) Increased visceral adiposity :

Obesity increases the aromatase activity which further increases estradiol production which inhibits gonadotropin secretion and the production of

testosterone. This hypogonadal obesity cycle results in an increased estrogen to androgen ratio leads to hypogonadal state. *Each kg/m^2 increase in BMI leads to 0.41 mL increase in prostate volume.* As compared to non-obese patients, obese patients had a 3.5-fold increasedrisk of an enlarged prostate.One of the study have reported that obesity increases the BPH risk by 28%.

(c) Sex steroid :

Like MetS, low androgen and high estrogen levels were also observed in menwith LUTS and BPH. The smooth muscle hyperplasia increased with lowdihydrotestosterone (DHT) level in the transition zone of the prostate. Hyperinsulinaemiacan indirectly cause BPH by its effect on obesity and sex hormones. This *sex hormones can increases the BPH risk by activating DNA synthesis and cellular proliferation due to their androgenic actions in the prostate*.

(d) Dyslipidaemia :

In BPH patients, low level of HDL-C and high levels of total cholesterol and low density lipoprotein cholesterol (LDL-C) were observed than in controls. While, one study reported no significant association between total cholesterol, HDL-C, triglycerides, triglyceride to HDL-C ratio and the risk of BPH.

(e) Chronic low grade pro-inflammatory state:

The chronic low grade inflammation, with elevated levels of inflammation markers for instance, C-reactive protein (CRP), pro inflammatory cytokines such as tumor necrosis factor-α (TNF-α), interleukin (IL)-8, IL-6, and IL-1 was associated with MetS. In prostate inflammatory infiltrates, the T-cell activities can result in stimulation of stromal and epithelial cell proliferation that is sustained by an autoimmune mechanism. Chronic inflammation induced tissue damages and consequent chronic process of repetitive wound healing may lead to the development of BPH nodules.

(f) Three-hit mechanism :

A three-hit hypothesis has been proposed by Vignozzi *et al* on the pathogenesis of BPH under metabolic influence. An induced prostatic inflammation (first hit) can be auto sustained or overlapped by metabolic changes (second hit) and sex steroid aberrations (third hit). The combined actions of two or three hits result in overexpression of Toll-like receptors, transformation of prostatic cells into antigen-presenting cells, activation of resident human prostate-associated lymphoid tissue and over production of growth factors thus, contributes to the prostate remodeling and enlargement.[1]

Overlapping symptoms of BPH :

As reported, LUTS has multiple causes, it is important to understand that LUTS in men maynot be caused by the prostate.There is an overlap of both obstructive voiding symptoms and storage symptoms for most men with LUTS (Fig 1). Certainly, it isthe storage symptoms but, not the voiding symptoms which is associated with prostate enlargement. In men with BPH, they are the most troublesome group of LUTS.[5]

Since, the symptoms of OAB and LUTS secondary to BPH overlap, it is possible that LUTS in most of the men who suffer from this condition may be due tothe bladder dysfunction.[6]

For the patients with bothersome voiding and storage LUTS at low risk of progression, the standard pharmacologic treatment should be a α1-Adrenoreceptor (α1-AR) antagonist.While, the combination alpha blocker (α1-AR antagonist) plus anti-muscarinic agent is an appropriate and valid treatment option for patients with voiding and persistent storage symptoms, providing their post-voiding residual is ≤200 mL.[5]

Treatment Options of MetS-Associated BPH/LUTS:

Multiple new treatment modalities for symptomatic BPH have arisen over the last decade. The treatment options-ranges from watchful waiting to open surgery. This range is as broad as the BPH spectrum of symptoms. The aim of BPH therapy is to improve quality of life by providing symptom relief and increasing maximum flow rate as well as reducing disease progression and the development of new morbidities.[7]

Current therapy for BPH/LUTS is largely based on the use of á-adrenergic receptor blockers, and 5-α_1 reductase inhibitors. Current EAU guidelines recommends α_1-blockers and 5-α reductase inhibitors for the treatment of men with moderate-to-severe LUTS. It also suggest the usefulness of lifestyle modifications.[8]

■ Lifestyle Modifications

Lifestyle intervention emerges as a novel opportunity for the prevention and treatment of BPH.[1]The type of diet and level of physical activity affect the prostate

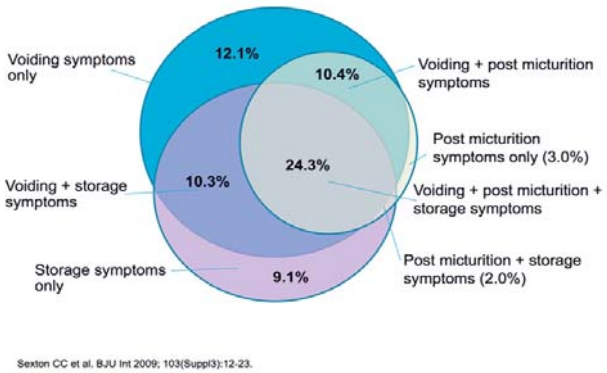

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Fig 1 — Most men have both voiding and storage symptoms.[5]

health in the aging male, most probably reducing risk factors such as MetS, hypogonadism, and inflammation. Some of the evidence have suggested that high consumption of red meat and a high fat diet increased the BPH risk. Also, high vegetables consumption reduces the risk of BPH.Physical activity reduces the risk of prostate enlargement, LUTS, and LUTS-related surgery. Increasing walking by 3 h/week decreases the risk of BPHby 10%.[8] While, moderate to vigorous physical activity can reduce BPH risk up to 25% as compared to a sedentary lifestyle.[1]

■ Watchful Waiting

It is a management strategy in which the patient is monitored by the physician without receiving any active intervention.

■ Alpha one adrenoreceptor blockers (α_1- AR blockers)

It is the first line treatment option for the symptomatic relief of BPH. Presently, α_1-adrenoreceptor antagonists are common for treating BPH related LUTS. They relax the smooth muscle of the prostate by blocking α_1-receptor mediated sympathetic stimulation.Currently available α_1-blockers arenonselective α_1-blockers, terazosin, doxazosin, and alfuzosin, and the highly selective α1A-blocker, tamsulosin. They are well-tolerated drug class but, cardiovascular side-effects can occur and can lead to serious morbidity such as falls and fractures. While, the safety of tamsulosinis better documented than other α_1-AR antagonists in such risk groups in LUTS/BPH patients.

■ 5-alpha reductase inhibitors (5ARIs)

It inhibit the conversion of testosterone to DHT which is the primary androgen involved in both normal and abnormal prostate growth. Currently available 5 ARIs for the management of BPH arefinasteride and dutasteride. The only available 5 ARIs which inhibit both type 1 and type II 5 α-reductase is Dutasteride which induces a more profound reduction of serum DHT in the range of 90–95% compared with 70-75% for finasteride.[7]

■ PDE-5 Inhibitors (PDE5i)

PDE5i reduce moderate-to-severe LUTS in men with or without ED. Accordingly, tadalafil (5mg once daily) has been approved by the US Food and Drug Administration and the European Medical Agency (EMA) for the treatment of male LUTS in Europe.[8]

■ Combination therapies

Most of the guidelines suggested the combination of 5-áreductase inhibitors or and α-blockers as appropriate treatment for patients with LUTS with demonstrated prostatic enlargement. The combination has the potential to address the concern associated with mono therapy. Also, the 4-yr CombAT data suggest the long-term use of dutasteride and tamsulosin combination therapy in men with moderate-to-severe LUTS due to BPH and prostatic enlargement.[7]

The Combination therapy provide relief from symptoms and also reduces the risk of BPH progression, it means increase of the symptom score, surgical treatment due urinary retention, urinary incontinence, urinary tract infection and renal failure.[9]

■ Minimally invasive therapies

In minimally invasive therapies (MITs) the prostate gland is heated by various means (electrical, microwave, laser). Insertion can be directly into the prostate via a needle or into the urethra via a catheter, probe or endoscope.[7]

■ Phytotherapy

One of the several phytotherapeutic agents available for the treatment of BPH is Cernilton which is prepared from the rye-grass pollen Secalecereale. It is used worldwide by millions of men and is a registered pharmaceutical product. Evidences suggests that Cernilton is well tolerated and improves overall urological symptoms, including nocturia.[7]

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Mediquiz

Series - 11

HIV infection (in recognition of *World AIDS day* : 1st December)

Rudrajit Paul
Quiz Master

(1) From 2020, the Government of India is introducing Dolutegravir in the ART regimen. Which group does this new drug belong to?
a. Integrase inhibitor
b. Reverse transcriptase inhibitor
c. Entry inhibitor
d. Protease inhibitor

(2) According to the new NACO guidelines, what is the CD4 count below which HAART is to be started?
a. 200
b. 350
c. Irrespective of the value
d. 500

(3) Isospora belli is an opportunistic pathogen causing diarrhea in HIV infected persons. What is the treatment of this infection?
a. Nitazoxanide
b. Cotrimoxazole
c. Ciprofloxacin
d. HAART

(4) A 39 year old man, known HIV infected, presented with progressive ataxia and fatigue. Also, he had some slurring of speech and right knee jerk was brisk. MRI of brain revealed plaques in the white matter in cerebellum and upper cervical spine. What is the treatment of this condition?
a. Acyclovir
b. HAART
c. Pyrimethamine
d. Methylprednisolone

(5) Which of the following is not a clinical stage 4 condition in HIV?
a. Cerebral toxoplasmosis
b. Peritoneal tuberculosis
c. HIV wasting syndrome
d. Hairy leukoplakia

(6) According to NACO guidelines, which are the two commonest causes of brain SOL in HIV positive persons in India? (choose two of the following)
a. Tuberculosis
b. Penicillium spp.
c. Toxoplasmosis
d. Cryptococcoma
e. MAC infection of the brain

(7) According to the NACO 2018 document, HIV care in India has the target for three "zero"es by 2024. What are these three "zero"es?
a. New case, new drug resistance, new opportunistic infection
b. New case, new death, discrimination
c. New death, discrimination, mental health problems
d. New case, lost to follow up, drug development

(8) In the diagnosis of HIV infection, if the first test is positive but the second test comes negative, what should be the next course of action?
a. Declare the result as negative
b. Declare the result as indeterminate
c. Do a third test
d. Do nothing for now, repeat test after 1 month

(9) For a person with HIV infection on cotrimoxazole prophylaxis, which laboratory tests are needed for monitoring?
a. Liver function test
b. No specific test
c. Complete hemogram and LFT
d. Complete hemogram, reticulocyte count and folic acid levels

(10) A person presented with fever and seizures. On further testing, cryptococcal meningitis was diagnosed. Also, the person was found to be HIV+ve. What should be the ideal treatment sequence?
a. Start ART and anti-fungals simultaneously
b. ART is started only after completion of full course for Cryptococcus
c. ART started first, followed 2 weeks later by amphotericin
d. Start ART after initial 4 weeks of amphotericin and clinical stabilization

(11) A person is newly diagnosed to be HIV +ve. On initial assessment, she is found to have hemoglobin level of 7.3 g/dl. Other parameters are normal. What is the best course of action regarding HAART initiation?
a. First give blood transfusion to raise Hb to 10; then start ART
b. First give iron and folate tablets
c. Clinically assess; if nothing else is found as a cause of anemia, start ART
d. Do a bone marrow study to assess the aetiology of anemia before starting ART

(12) What were the outcomes of the HPTN 052 trial?
a. Early ART can prevent premature death
b. Early ART can prevent HIV transmission
c. Early ART can prevent neurological progression
d. Early ART can prevent opportunistic infections

(Answer : Page 91)

Letters to the Editor

[The Editor is not responsible for the views expressed by the correspondents]

Challenges in Medical Education in India

Sir, — Voice of expert "Medical Education-Vision 2020" by the famous Dr. Gurpreet S. Wander (JIMA, Vol-118, No-11, November, 2020) is an extensive, excellent and timely article. As India marches towards an exciting new future, medical education is expected to play pivotal role in overall development agenda especially the public health care in post Covid-19 era. But presently unregulated growth of private medical colleges under the influence of privatization and corporatization has become a very lucrative business, mired by gross inadequacies compromising standards of medical education. One revolutionary measure of National Eligibility-cum-Entrance Test (NEET) has miserably failed to rationalize admissions on merit and eliminated capitation fee as private medical colleges have obnoxiously increased their fee to match the capitation fee, ever decreasing cut-off marks has compromised merit. I think, medical education in India is at crossroads, may be on the verge of collapse because of several important challenges faced by medical education such as an exploding number of private medical colleges, skewed distribution, devaluation of merit in admissions, increasing fees making medical education out of reach of the most, an alarming shortage of teachers, increasing ghost faculty culture, gross shortage of patients in most of private institutions, increasing concept of dummy patients, contract to pass all students in private medical colleges, poor internship training because of PG entrance test and most importantly the miserable failure of Medical Council of India to enforce guidelines so much so that even after several complaints with photographic proofs, MCI failed to order even an inquiry and let a local medical college continue including PG courses inspite of gross deficiencies that everyone knows why. Corruption was the main reason for scraping MCI and formation of National Medical Commission which may or may not prove its utility with time. I think medical education is most neglected subject and requires revolutionary short, intermediate and long term measures including a substantial and separate budget for medical education focusing on public medical education and improving standards of education in most of the private colleges. It is really good that prestigious journal, JIMA has published Dr. Wander's vision 2020, a step forward to bring medical education into focus and sensitize other professional organizations towards challenges faced by medical education. I feel, medical education should find a prime place and no one has the right to commodify it, otherwise it is going to destroy India's public health care system.

MD (Medicine), FICP, FCSI, FACP, FIACM. Health and Human Rights activist, Bathinda 151001, Punjab

Prof. Dr. Vitull K. Gupta

IMA Covid Martyrs Data

Sir, — As the COVID-19 pandemic has worsened worldwide, health care workers including the doctors worked tirelessly for the care of the patients and some even continued after their retirement. These lives are indeed a reminder to the general population of the relentless dedication and service of those people who did not stop their work even if the number of cases and deaths were increasing.

Death in the line of duty is the doctor's ultimate sacrifice, which may be compounded when physicians unknowingly infect family members The general public may not comprehend the importance of self-isolation measures to contain the COVID-19 pandemic until a physician dies fighting the virus.

Results :

IMA Covid Data : Doctors Martyrs Age Factors

Less than 35yrs	:	25
Above 35 - 50yrs	:	84
Above 50-60yrs	:	214
Above 60-70yrs	:	295
Above 70yrs	:	88
Total Martyrs	:	706

The analysis of results showed that the total COVID related Doctors deaths in India till 11th December, was 706. With available data of infected doctors and confirmed data of number of doctors deaths the Case Fatality Rate must be high nearly 10 times. We are able to arrive at a figure of doctors patients mortality ratio in India 1:202.

Out of 706 doctors died, 690 were practicing doctors 98% while 14 were resident doctors 2 were house surgeons. This highlights the fact the mainly senior doctors succumbed because of comorbid conditions & long exposure and insufficient preventive measures. The age range of the deceased doctors was 24 - 88years. The percentage of death below 30 was 1.6% below 40 years was 6.6% below 50 years it was 15.4% The percentage of fatalities below 60 was 46% while 54% deaths among doctors above 60. The average age of doctors at death was 60-68 years with a median age of 60 years.

General Practitioners bore the brunt of virus infection 59%. This could be attributed to lack of preparedness & preventive equipments like PPE & long exposure. Among the specialists Paediatricians, General surgeons, obstetricians and anaesthesiologists, orthopaedic surgeon, ENT surgeons, radiologists lost their lives. The super specialists who lost their lives comprised of Neurosurgeons, Neurologists….

The state wise distribution of doctor deaths showed that the highest deaths were in Tamil Nadu, Andhra Pradesh, Gujarat, Maharashtra and Karnataka.

We have also found that number of COVID 19 deaths among doctors were at peak during September and started declining (Graph). This is because of growing knowledge regarding COVID 19 & use of social distancing, PPE and

other precautions.

The team sadly recollect the sacrifice of our own Chairman of IMA COVID DATA Dr Gangadara Rao from Andhra Pradesh who died of COVID 19 inspite of all his vigilant measures we salute him.

I thank all the JDN members who worked tirelessly in collecting the details and forming an authentic IMA COVID MARTYRS DATA of India.

National Co.ordinator, **Dr KM Abul Hasan**
IMA Covid Martyrs Data

Prediction of Cardiovascular Events in Patients with Chronic Kidney Disease By Serial B- Type Natriuretic Peptide Levels. (JIMA , Vol 118, October 2020)

Sir, — The authors have rightly enlightened us regarding the role of serial estimation of B- type natriuretic Peptide level in prediction of cardiovascular event in patients with CKD as BNP are important factor in evaluation of Left Ventricular hypertrophy and dysfunction which are strongly found in Patient with CKD...

The study has also rightly pointed the role of serial estimation of BNP Level as pre evaluation level can be higher in many cases due to other Factor.

As BNP level can be influenced by age, sex , BMI and atrial fibrillation And other factors and echocardiogram is better indicator for cardiac Status detection so if we correlate BNP levels with echocardiogram Finding and cardiovascular outcome that will reveal the role of BNP Value in prediction of cardiovascular events.

Furthermore BNP levels can be higher in patients with persisten tatrial fibrillation And heart faliure so inclusion of atrial fibrillation as variable would

Emphasize us to detect the role of BNP in prediction of future cardiovascular Outcome.

Junior Resident **Dr Moni Sankar Bhattacharjee**
Department of General Medicine
R.G.Kar Medical College, Kolkata

Medical Education — Vision 2030 (JIMA, Vol 118, No 11, November, 2020)

Sir, — I would like to congratulate Prof (Dr) Gurpreet S Wander for enlightening us regarding the changes brought in the field of medical education sinceindependence of India-through the last 70 years.

The article has rightly stated thatpublic and private sectorsneed to work together hand in hand to raise the level of medical education in India.

It has been mentioned aptly that the approach and attitude of the younger Indian doctors have changed where they are more keen towards proper documentation asthe working environment has become more demanding, transparentand audited.

The article has highlighted the reforms brought in medical education withtheintroduction of national eligibility cum entrance test (NEET), which hasbrought uniformity across the country for admission and the national exit test (NEXT), which is scheduled to start from next year, will be used as the basis for postgraduate admissions- which will emphasise on the need to learn clinical skills.

The author emphasised on the importance of long answer questions instead of MCQs for testing of clinical skills in the present examination system. He has also rightly stated the need of a special area of curriculum for pandemic situations.He has also explained how the preservation of clinical skills along with technological advancements are jointly required for better patient care.

The article has rightly pointed out the need tocontinue focus both on non communicable diseases (NCDs) and communicable diseases as NCDs account for more than 50% deaths in our country.

The author also aptly highlighted the importance of soft skills in the MBBS curriculum as started by the National Medical Commission (NMC). The area of primary care needs upliftment in India, so that our primary care physicians are at par with global specialists.

He has also correctly emphasised on the blend of virtual seminars and face to face learnings in institutions as the future of curriculum and will help in optimisation of costs and increased interactivity.

The article has correctly stated on the adequate requirements of proper training and communication so as to successfully transition to e-learning platforms.

He has also rightly commented on the positively changing doctor patient relationship due to the effective representation of the IMA.

The author has rightly portrayed the changing relationship between a doctor and the patient where the patients are more aware and thus demand transparency and open discussions which involve active discussion between the doctor and his patient.

He has rightly stated in this article that putting doctors in the decision making team instead of only making them their subordinates will help the IMS(IndianMedical Services)in making many important decisions regarding healthcare much easier.

Thus, this article has been very enlightening to the medical fraternity all over the country regarding the changes in medical education and its probable impact in the future.

Assistant Professor **Dr Atanu Chandra**
Department of General Medicine
R.G.Kar Medical College

Answer : Mediquiz

(1) A	**(2) C**	**(3) B**	**(4) B**
(5) D	**(6) A & C**	**(7) B**	**(8) C**
(9) B	**(10) D**	**(11) C**	**(12) B**

Forbidden classes of substances:
Anabolic steroids ; Growth factors e.g Erythropoietin
Diuretics ; Stimulants like Ephedrine, Ecstasy;
Glucocorticoids ; Cell and gene doping;
Opioids like Morphine ; Cannabinoids;
Food supplements like Creatine and metabolic modulators

***Beta-agonists are allowed only in inhaled form

DOPING IN SPORTS MEDICINE

CLASSES OF DRUGS	HOW THEY HELP IN SPORTS	LONG TERM EFFECTS
Anabolic steroids	Increase muscle mass Prevent muscle breakdown Increase aggression	Hypertension Hirsutism Depression Testicular atrophy
Erythropoietin	Increase oxygen carrying capacity	Dehydration Thrombosis
Ephedrine	Decrease fatigue Increase alertness Ergogenic effect	Hypertension Insomnia Arrhythmia; Psychosis

HOW TESTING IS DONE?

Urine and/or blood collected anytime and anywhere
The urine collection process is **observed** by a chaperone
The samples are divided into two: A and B. Sample A is tested first. If doubt, B sample is tested

When is a substance considered to be a performance enhancing agent and is banned?

It has the potential to enhance sport performance
It represents a health risk to the athletes
It violates the spirit of sport

Caffeine was banned till 2004; But now allowed

Further information: https://www.wada-ama.org/

Composed by Rudrajit Paul and Jyotirmoy Pal for JIMA

JOURNAL OF THE INDIAN MEDICAL ASSOCIATION

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January – December, 2020

ABBREVIATIONS USED

(C) Correspondence,(CDM) Case Discussion in Medicine, (CR) Case Report, (CS) Case Series , (DC) Drug Corner, (Ed) Editorial, (FA- Commt. from Expert) From Archive Comment from Expert, (HM) History of Medicine, (IM) Imaging in Medicine, (JCW) Journey of COVID Warrior, (KU) Knowledge Update, (MH) Medical History, (NA) Newer Advances, (OA) Original Article, (ORA) Original Research Article, (PCME) Pictorial CME, (RA) Review Article, (SC) Student's Corner, (SRA) Systemic Review Article, (Spl C) Special Correspondence, (THP) Take Home Points, (VE) Voice of the Expert

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WE THANK ALL THE HON'BLE REFEREES WHO CONTRIBUTED FOR JIMA DURING THE YEAR 2019-2020

JIMA SALUTES THE MARTYRS WHO SACRIFICED THEIR LIVES IN THE FIGHT AGAINST COVID-19 PANDEMIC

Andhra Pradesh


Dr KV Rama Rao

Covid Martyrs from Andhra Pradesh whose photographs are not available:
Dr Laxminarayana, Dr Maj Gopala Rao, Dr Patibandla Sivaji, Dr Seetaramaiah, Dr Venkata Rao, Dr Tirupataiah, Dr Venkataiah, Dr.Basava Rao, Dr.D.S.Koteswsra Rao, Dr.Mukherjee

Assam

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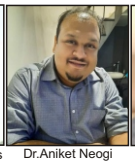
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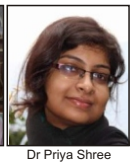
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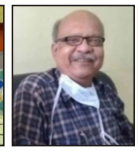
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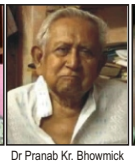
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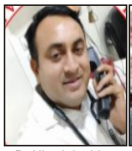
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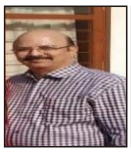
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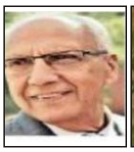
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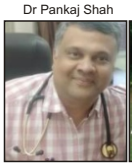
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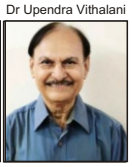
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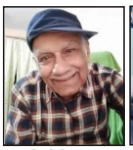
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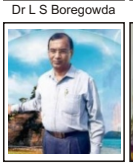
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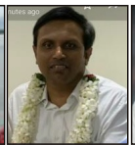
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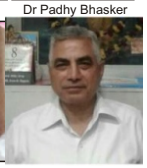
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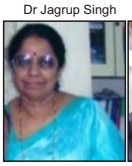
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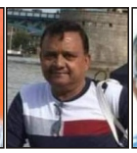
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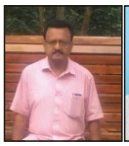
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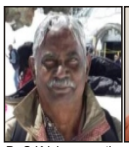
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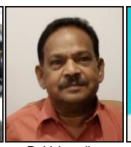
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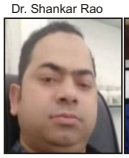
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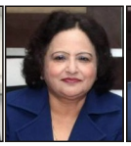
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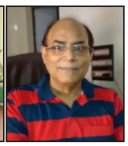
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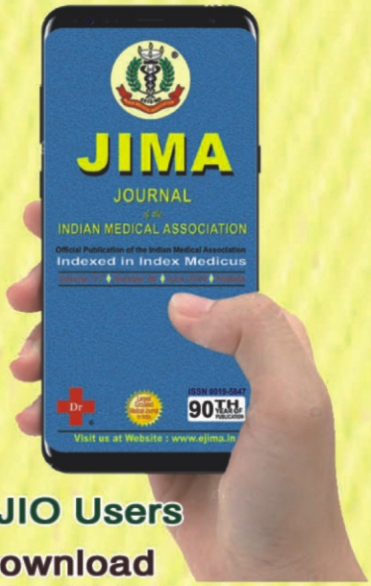

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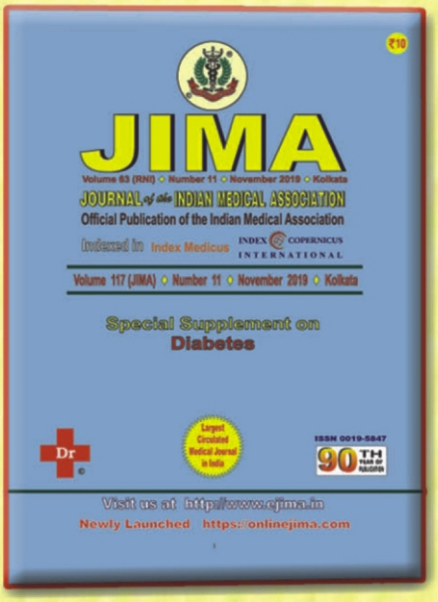

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