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Editorial

Artificial Intelligence and Medicine

Let me start this editorial with a quiz. Name a living being with minimalized size as compared to the towering elephant or a sky-scraping giraffe or name an animal which is not worthy of even carrying even a fraction of the load bearing ability of an ant but yet the undeniable ruler of the world. The answer might bamboozle some of you for a fraction of a second…..well the answer is HUMAN BEING. Still this species of life is the SUPREMO of all creatures. He is the CREATOR, THE SUSTAINOR AND EVEN THE DESTROYER like the trinity Hindu gods BRAHMA, BISHNU AND MAHESWARA. But how? Only because he has at his disposal a supremely functional grey matter called INTELLIGENCE which he uses with deftness and dexterity to overcome all hurdles of existence and make life as easy as a cake walk for all of his kith and kins. But Life, at all his nooks and corners, has in store for us lots of new challenges and surprises lying in ambush. These, we need to confront with all gumptions. Thus man has been in constant perusal to go beyond his frontiers of achievements and sought new means to be victorious. We are now in the age of Machine Intelligence or Artificial Intelligence (which henceforth in this article will be called by its acronym AI) which has increased the capacity of human decision making manifolds and within a bat of an eyelid.

Now What is AI ?

Isaac Asimov, the revered author of science fiction conceived of an idea of AI and machine learning and introduced it into his fiction way back in 1940.[1]Thereafter that the wing of fantasy slowly began to be analyzed in terms of its practical feasibility and during the mid half of the previous century AI was founded as an academic discipline.

Going by the terminology, the term artificial intelligence (AI) refers to human-alike intelligence demonstrated by a computer, robot, or other machine. In popular terms, artificial intelligence is the ability of a computer or machine to ape the capabilities of the human mind—learning from examples and experience, recognizing objects, understanding and responding to language, making decisions, solving problems—and combining these and other capabilities to perform functions a human might perform, such as greeting a hotel guest or driving a car.

All of the above functions using AI are definitely laudable but the use of AI in medical science to me should attract the maximum kudos as it makes the difference between life and death by early detection of diseases ensures healing before the nemesis. But how are these two distinctly different fields of study correlate and work in harmony? Let us discuss in detail. Medical artificial intelligence (medical AI)

primarily deploys computer techniques to aid clinical diagnoses and suggest treatments. AI has the capacity of detecting meaningful correlation in a dataset and is widely used in oodles of clinical situations to diagnose, treat, and predict the results. The application of AI has tremendous potentials in the following fields[2]:

(i) Artificial Intelligence Techniques in Medicine

(ii) Data Mining and Knowledge Discovery in Medicine

(iii) Medical Expert Systems

(iv) Machine Learning-Based Medical Systems

(v) Medical Signal and Image Processing Techniques

Avila-Garcia et al.[3] exhibited the use of a neural network-based multiscale Gaussian matching filter for detection and segmentation on coronary angiogram X-ray images and in the process quickened and perfected the results of image classification.

Cui et al.[4] exhibited a cascaded neural network composed of a Tumor Localization Network to localize the brain tumor from slices of MRI images and an Intra-Tumor Classification Network to label tumor regions. With advanced technologies being applied it has the potential to generate better and more perfect results. This is a boon for the doctors and the suffering patients.

Fu et al.[5]demonstrated results of using a Convolutional Neural Network (CNN) to recognize strabismus. Trained by and from the data collected by an eye-movement tracker, and after analyzing a large number of GaDe images, their CNN could recognize successfully strabismus.

Chan et al.[6]trained a support vector machine to perfectly detect common pneumothorax using the local binary patterns derived from a multiscale intensity texture analysis on the chest X-ray images.

Chen et al.[7]introduced a clinical decision support system to augur fractures in hip bones and vertebrates engendered by medications for treatments of chronic respiratory diseases. The system uses integrated genetic algorithm and support vector machine trained by balanced datasets acquired from random and cluster-based undersampling methods, parallelly tested with imbalanced datasets.

Yap et. al.[8]demonstrated the use of state-of-the-art computer vision object detection algorithm on Breast Ultrasound (BUS) lesion localisation to improve the lesion detection by the use of IoU (equivalent to Dice Coefficient Index, which is commonly used in lesion segmentation) as it is more reliable when compared to the detected point.

As rightly said by one, in near future a patient might be visiting a computer before visiting a doctor for detection of diseases. Now let us zero in on a sensitive issue. To err is human and doctors being human can make mistakes or misdiagnose diseases which can be fatal to their patients. In fact, this problem is so severe that "medical mistakes are now estimated to kill up to 440,000 people in U.S. hospitals each year, making preventable errors the third leading cause of death in America behind heart disease and cancer."[9]Currently, doctors are not given incentives to consult with each other. Patients too burn a hole in their pocket to get a second opinion. One AI application, created by the Human Diagnosis Project (Human Dx), aspires to solve the problem. The app has an interface where physicians can raise a clinical question, their working diagnosis and even upload images and test results of the case they are acting upon. Using the app, the physician can request help from specific colleagues or the wider network of doctors who are empanelled to the Human Dx community. Within a few days, the app's AI consolidates all the responses received into a single report. In this waythe app can act with dexterity without the hazards of setting up a formal, expensive, external consultation.

What can be more relevant than the use of AI during the COVID19 pandemic? AI has the potential to improve the planning, treatment and reported outcomes of the COVID-19 patient, being an evidence-based medical tool. AI can easily track the spread of the virus, identifies the high-risk patients, and is effective in controlling this infection in real-time. It can also forecast mortality risk by analyzing the previous data of the patients. AI does this by population screening, medical help, notification, and suggestions about the control of infection.

This article can attain a stupendously huge length if I go on discussing about the advantages of the use of AI in health care sector. To cut it short, let me come back to the note with which I started this article. Man is the greatest creation of nature and He has provided man with the best place (our earth) to live and prosper on. But how can man show his gratitude to Nature? An idiom effectively gives the answer – "WHAT YOU ARE IS A GIFT OF

NATURE BUT WHAT YOU BE IS A GIFT TO NATURE". Intelligence actually is the device which has been gifted by nature to humanity to help him supersede others and infringe into the hitherto unbounded territories of achievements. After honing up his intelligence on the anvil of practical challenges of living on this hostile world man has unleashed his acquired skill to step into the next frontier that is AI OR MACHINE LEARNING. Let us all hope that this application will make the world we live in if not the heaven but close to utopia.

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Original Article

Diagnostic Value of Serum Adenosine Deaminase (ADA) in Tuberculous Lymphadenitis

Mihir Kanti Adhikari[1], Shohael Mahmud Arafat[2], Mehruba Alam Ananna[3], Md Atikur Rahman[4], Hasan Imam[5], Shah Mohammad Mohaimenul Haq[6]

Background: Tuberculosis is one of the major infectious disease in Bangladesh and also a re-emergent disease in the developed world. Extra-Pulmonary Tuberculosis (EPTB) comprises a significant share of all cases of tuberculosis and tuberculous lymphadenitis is the commonest form. It often requires FNAC or biopsy of lymph node to reach a final diagnosis of tuberculous lymphadenitis, which is invasive, expensive, and needs an advanced setting. Estimation of ADA in different body fluid and serum has been suggested as a quick, cheap, and reliable test for tuberculosis.

Materials and Methods: This was a cross-sectional observational study, conducted in Bangabandhu Sheikh Mujib Medical University Hospital over a two year period and included 68 participants, divided equally into two group e.g. tuberculous lymphadenitis and a healthy comparison group. As tuberculous lymphadenitis, only newly diagnosed cases, labeled on the basis of histopathological findings of epithelioid granuloma with caseation necrosis were included. Serum ADA concentrations were estimated by enzymatic method and compared between groups.

Results: The mean serum ADA concentration was found to be 25.52±7.11 U/L in tuberculous lymphadenitis group, which was significantly higher (p=0.000) than that of the healthy comparison group (14.82±3.85 U/L). Three different cut-off values of serum ADA (18.25 U/L, 20.45 U/L, 22.15 U/L) were used to determine the best predictive value for the diagnosis of tuberculous lymphadenitis. Sensitivity and specificity of these cut off values were 91.2% and 82.4%, 79.4% and 88.2%, 67.6% and 97.1% respectively.

Conclusions: It is clearly denoted by the study that, tuberculous lymphadenitis patients has significant higher serum ADA then the healthy comparison group. This result indicates that serum ADA can be used as a useful adjunct in the diagnosis of tuberculous lymphadenitis with conventional investigations.

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Key words **: Serum ADA, Adenosine deaminase, Tuberculous lymphadenitis, Socio-demography of Tuberculous Lymphadenitis, Sensitivity and specificity of serum ADA.**

Tuberculosis (TB) is one of the oldest diseases that is affecting human over centuries. It is a virulent infectious disease worldwide and a re-emergent disease in the current developed world. TB lymphadenitis constitutes about 35 percent of extra-pulmonary tuberculosis (EPTB) and it is 15 to 20 percent of all cases of tuberculosis[1]. It is almost exclusively caused by Mycobacterium tuberculosis in Bangladesh.[2] Non-tuberculous mycobacterial (NTM) infection is rare here and also uncommonly reported from India[1].

Editor's Comment :

- Tuberculous lymphadenitis (LNTB) is the most common form of EPTB.
- Diagnosis of LNTB needs invasive procedure and technically demanding histopathological study.
- Estimation of ADA in body fluids has been established as a diagnostic tool for tuberculosis.
- This study has shown that estimation of serum ADA is also useful in diagnosis of LNTB.

The diagnosis of tuberculous lymphadenitis is usually based on clinical presentation, radiological findings, and positive tuberculin or Boston Consulting Group (BCG) tests. If Fine Needle Aspiration Cytology (FNAC) or biopsy of enlarged lymph node reveals granulomatous lesion with caseous necrosis along with positive mycobacterial stain and culture, it helps to confirm the diagnosis. In Bangladesh, AFB positivity has a high association with caseation necrosis[3]. Conventional Acid-Fast Bacillus (AFB) smears have low sensitivity and it requires a long time for M tuberculosis to become evident in culture. Waiting for culture result to start treatment was found to be associated with higher mortality in tuberculous peritonitis[4]. So, the finding of granuloma with caseation necrosis is often considered final for the diagnosis of tuberculous lymphadenitis and treatment initiated. In many other cases, the difficulties regarding obtaining biopsy specimen and histopathological study leads to empirical anti-tuberculous therapy. It is, therefore becomes

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imperative to find out some rapid and useful tests for the diagnosis of tuberculosis.

Adenosine deaminase (ADA) is associated with purine catabolism. It controls proliferation and differentiation of T lymphocytes.The most important isoforms of ADA, are ADA-1 and ADA-2, which are located on different gene loci[5]. ADA-2 appears to be found only in monocyte ADA1 in all cells[6]. The sensitivity and specificity of ADA depend on the prevalence of tuberculosis in the population. In the regions with a high incidence of tuberculosis, ADA appears to be a useful marker for early diagnosis of tuberculosis. ADA-2 found to be the predominant isoforms in tuberculosis accounting for 80-90% of the activity. The isoenzyme ADA-1 is elevated in the presence of empyema and para-pneumonic effusions[7].

The value of ADA as a diagnostic marker of tuberculosis has been established in numerous studies, especially in tuberculous pleural effusion, ascites, and pericardial effusion. An elevated pleural fluid ADA level predicts tuberculous pleuritis with the sensitivity of 90-100% and the specificity of 89-100%[8]. Dwivedi *et al* (1990) described the sensitivity of 100% and specificity of 96.6% at an ADA level >33 U/L for early diagnosis of tuberculous peritonitis, another study by Gupta *et al* (1992) shown 95% sensitivity and 94.1% specificity at an ADA level >30 U/L[9,10]. In South Africa, a prospective study showed an ADA cut-off level of 40 U/L resulted in a test sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic efficiency of 84%, 80%, 91%, 66%, and 83%, respectively in tuberculous pericarditis[11]. Koh *et al* (1994) studied pericardial fluid ADA level along with histopathology of pericardial biopsy and found a cut-off level of 40 U/L has the sensitivity of 93% and the specificity of 97% in the diagnosis of tubercular pericardial effusion, which is similar to the study by Mathur *et al* (2006) that showed 100% sensitivity and 83.3% specificity[12,13].

Bangladesh is a country with a high tuberculosis burden. FNAC from lymph node and biopsy is only available in the advanced hospitals that lack in number. Furthermore, tuberculous lymphadenitis involving internal structures like mediastinal or intra-abdominal lymph nodes, CT guided or laparoscopic approach is required, which is technically demanding and difficult even in advanced centers. With such limited resources, an ideal test for tuberculosis should be economic, minimally invasive, of high accuracy and quick to perform. ADA is a simple and inexpensive colorimetric test that can be done easily with limited resource and short training. The study was intended to assess the usefulness of serum ADA in the diagnosis of tuberculous lymphadenitis.

Materials and Methods

This cross-sectional observational study was conducted in the Department of Internal Medicine BSMMU from March, 2015 to February, 2017. The study included 34 patients of tuberculous lymphadenitis over 18 years and older, of both gender. Another age and gender match 34 healthy individuals were added as a comparison group. Convenient sampling technique was adopted and subjects were chosen as per inclusion and exclusion criteria. Patients presented with constitutional features of tuberculosis, like fever, weight loss, anorexia with lymphadenopathy were considered for lymph node FNAC or biopsy. Epitheloid granuloma with caseous necrosis was labeled as tuberculous lymphadenitis. Participants who had pulmonary tuberculosis or extra-pulmonary tuberculosis along with tuberculous lymphadenitis were excluded as well as metabolic derangements like hepatic, renal or electrolyte abnormality, organic or inorganic psychosis, or current pregnancy. Before starting anti-tuberculous chemotherapy, serum ADA was measured by adenosine deaminase assay kit supplied by Diazyme laboratories, CA, USA in the laboratory of the Department of Microbiology of BSMMU. Ethical clearance was obtained from the institutional review board of BSMMU and informed written consent was taken from all patients. Data were compiled and analyzed by Statistical Package for the Social Sciences (SPSS). Continuous variables were analyzed using Student t-test and one way ANOVA, when and where appropriate, categorical variables were compared using the chi-square test. A p-value <0.05 was considered statistically significant. A Receiver Operating Characteristic (ROC) curve was used to determine the sensitivity and specificity of serum ADA for the diagnosis of tuberculous lymphadenitis.

Results

In this study, the age range of the tuberculous lymphadenitis as well as healthy controls ranged from 18 to 60 years, the mean (±SD) age was 29.94 (±12.13) years and 30.24 (±10.21) years respectively. Among the respondents, in both of the groups' majority were female (70.6%) (Table 1). In tuberculous lymphadenitis group, majority of the respondents (94.10%) had fever, other predominate symptoms were loss of appetite (79.4%), weight loss (82.4%), and pain in lymph nodes (20.6%). Symptoms like cough, nausea and vomiting were present in 11.8% of patients. In this group, 8 (23.5%) of 34 participants had a history of contact with smear positive pulmonary TB patients, while 1 (2.9%) of them had a previous

Table 1 — *Socio-demographic Characteristics of Participants (n=64)*

Demographic characteristics	Tuberculous lymphadenitis (n=34) Frequency (%)	Healthy control (n=34) Frequency (%)
Age (Years) :		
18-20	10 (29.4%)	10 (29.4%)
21-40	17 (50.0%)	17 (50.0%)
41-60	7 (20.6%)	7 (20.6%)
Mean age (±SD)	29.94 (±12.13)	30.24 (±10.21)
Gender :		
Male	10 (29.4%)	10 (29.4%)
Female	24 (70.6%)	24 (70.6%)
Residence :		
Rural	15 (44.1%)	19 (55.9%)
Urban	19 (55.9%)	15 (44.1%)

history of tuberculosois. In this group, most of the patients (73.5%) presented with single regional lymphadenitis and cervical lymph nodes were mostly affected (95.8%). The largest lymph nodes were >2cm in 50% of patients. Consistency was firm in the majority (85.3%) of patients, 44.1% of them had matted lymphadenitis. Cold abscess with discharging sinus was found in 14.7% of cases.

In tuberculous lymphadenitis group, mean serum ADA concentration was found to be 25.52 (±7.11) U/L and in the healthy comparison group it was 14.82 (±3.85) U/L (Table 2). In the male participants, mean serum ADA was 26.23 (±10.12) U/L and in the female, it was 25.22 (±5.66) U/L.

The receivers operating characteristic (ROC) curve was utilized. The area under the curve (AUC) was significant (0.935). The sensitivity and specificity of serum ADA in the diagnosis of tuberculous lymphadenitis for different cut off values were estimated (Table 3 and Fig 1).

Discussion

Tuberculous lymphadenitis is the most prevalent form of extra-pulmonary tuberculosis. The final diagnosis needs FNAC or biopsy, and is difficult due to the invasiveness of the procedure and its unavailability is the low resource setting. Estimation of ADA in different body fluids is a simple method of investigation and is proved to be diagnostic. Previous studies have also shown the usefulness of serum ADA in pulmonary tuberculosis and in limited cases of Extrapulmonary Tuberculosis (EPTB).

Among the respondent, in tuberculous lymphadenitis group, most were females (70.6%), such female predilection has also been reported by previous studies[14,15]. Most (79.4%) of respondents of this group was within 18 to 40 years of age. Many previous studies also reported its predominance in children and young adults[14,15]. Majority of the respondents (94.10%) of this group had fever, but objective evidence of raised body temperature was found in 55.90% of cases. It can be explained by the natural history of disease; tuberculosis causes evening rise of temperature but as most of the cases was taken from outdoor at morning, elevated temperature couldn't be demonstrated. In tuberculous lymphadenitis group, most of the patients (73.5%), presented with single regional lymph node enlargement, among them cervical lymph node involvement was most common (95.8%), which is consistent with previous studies[15,16].

Table 2 — *Comparison of Serum ADA Concentrations (U/L) between Study Groups (n=68)*

Group	Mean (±SD)	Min	Max	P value	t
Tuberculous lymphadenitis	25.52(±7.11)	14.10	41.30	0.000[a]	7.714
Healthy group	14.82(±3.85)	8.30	23.90		

a = Independent sample t test was done.

Table 3 — *Sensitivity and Specificity of Serum ADA (U/L) at Different Cut Off Values in Tuberculous Lymphadenitis*

Cut of value of serum ADA	Sensitivity	Specificity
18.25 (U/L)	91.2	82.4
20.45 (U/L)	79.4	88.2
22.15 (U/L)	67.6	97.1

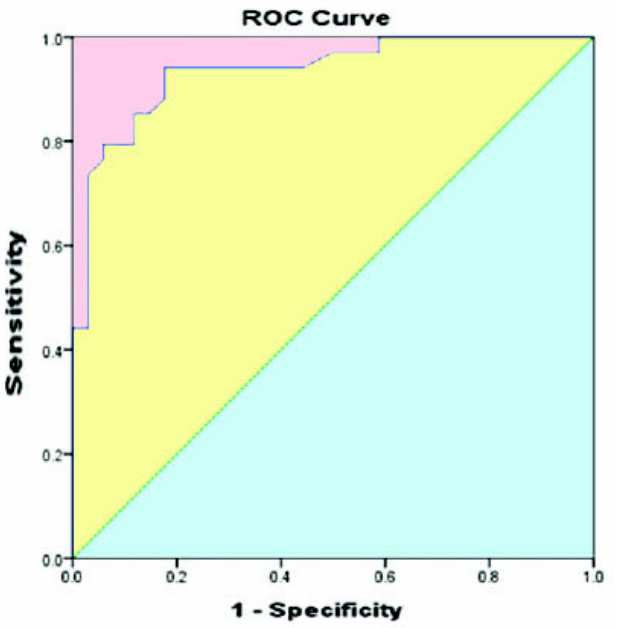

Fig 1 — Receiver operating characteristic (ROC) curves showing the sensitivity and specificity of serum ADA level

In this study, mean serum ADA concentration was found to be significantly higher in tuberculous lymphadenitis group (25.52 ±7.11 U/L) than the healthy comparison group (14.82±3.85 U/L) (p=0.000). This finding is consistent with a previous study who found mean serum ADA concentration as 20.2 (±3.64) U/L and 14.95 (±3.22) U/L in tuberculous lymphadenitis and healthy control respectively.[17] Giusti (1984) have also shown serum ADA in healthy population as 17.05 (±3.75) U/L[18]. Another study in Belgrade, Serbia, Stevanovic et al. (2011) found serum ADA concentration 31 (±11) U/L in a group of patients of extrapulmonary tuberculosis, of whom 27% was tuberculous lymphadenitis[19]. A recent study described elevation of serum ADA level to a range of 31-40 U/L in 65% of cases and 41-60 U/L in 20% of cases in a group consisting of 30 cases of tuberculous lymphadenitis[20]. These concentrations were much higher than the findings of the current study.

Three different cut-off values of serum ADA (18.25 U/L, 20.45 U/L, 22.15 U/L) were used to determine the best predictive value for the diagnosis of tuberculous lymphadenitis in the current study. Sensitivity and specificity of these cut off values were 91.2% and 82.4%, 79.4% and 88.2%, 67.6% and 97.1% respectively. Receivers operating characteristic (ROC) curve shown area under the curve (AUC) was significant (0.935) (Fig 1).

We admit few limitations of our study like small sample size and

convenient sampling technique. For the diagnosis of tuberculous lymphadenitis, the case definition of the presence of granuloma with caseation necrosis in FNAC or biopsy was used. Serum total ADA was measured in this study, which is less specific than ADA 2 for the diagnosis of tuberculous lymphadenitis.

Conclusions

This study clearly demonstrated significant elevation of serum ADA concentration in the tuberculous lymphadenitis patients in comparison to the healthy control. This result indicates that serum ADA can be a useful adjunct in the diagnosis of tuberculous lymphadenitis with conventional investigations. To overcome the limitations of this study a large scale multicenter study with random sampling and using culture positivity of Mycobacterium tuberculosis from FNA or biopsy material of lymph nodes as gold standard can be done. Serum ADA 2 concentration, which is more specific to tuberculosis, can also be measured.

Contributions :

Adhikari MK,[1] designed the study, data collection tools, collected, compiled, cleaned and analyzed the data, and drafted and revised the paper. Arafat SM,[2] designed the study, and revised the paper. Ananna MA,[3] analyzed the data and revised the draft. Rahman MA,[4] collected and compiled the data, and drafted the paper. Imam H,[5] collected and compiled the data. Haq SM,[6] collected, compiled, cleaned and analyzed the data.

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Competing interests : None declared.

Ethical Clearance : Ethical clearance was obtained from the Institutional Ethics Committee.

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Original Article

Study of Neurologic Manifestations of Hyponatremia with Special Reference to Unusual Rare Manifestations

Nishtha Jain[1], Vijay Sardana[2], Dilip Maheshwari[3], Bharat Bhushan[4], Sunil Kumar Sharma[5]

Background : The normal serum sodium concentration ([Na+]) in the human body ranges from 135 to 145 mEq/L and is maintained by renal mechanisms. A serum [Na+] less than 135 mEq/L is usually defined as hyponatremia. A significant hyponatremia can lead to various neurologic manifestations. Overcorrection of hyponatremia can lead to neurological deterioration secondary to Osmotic Demyelination Syndrome (ODS). This study was done to see the various neurologic manifestations in patients with hyponatremia and to study outcome after treatment.

Objective : The objective of this study is to evaluate the common and rare neurological effects of hyponatremia and to correlate them with different range of serum sodium levels and also to study the outcomes including recovery and adverse effects after correction. Differences in the neurological manifestations of hyponatremia in young(<50 yrs) and old(>50yrs) patients were also studied.

Methods : 200 patients were included who were admitted with symptomatic hyponatremia.

Results : Mean age of presentation of patients was 63.89 years. Most of the patients were having comorbid conditions which included Hypertension, Diabetes Mellitus, Hypothyroidism, Chronic Liver Disease, Chronic Renal Disease, Epilepsy, Schizophrenia, Coronary Artery Disease, Stroke and Rheumatoid Arthritis. The neurologic manifestations of the patients included encephalopathy, followed by extrapyramidal features, generalised tonic clonic seizures, ataxia and focal seizures. Rare manifestations included ataxia and focal seizures. A strong association between sodium levels <120 meq/l and generalised tonic clonic seizures as presentation was found. ODS was observed in seven patients.

Conclusion : Hyponatremia is very frequent in elderly. It is mostly associated with multiple comorbid conditions and can present with varying manifestations. Proper recognition of the condition is important as it is a potential treatable condition.

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Key words **: Hyponatremia, Comorbidities, Neurologic manifestations, Adverse effects.**

The normal serum sodium concentration (Na+) in the human body ranges from 135 to 145 mEq/L and is maintained by renal mechanisms that regulate the excretion of water[1]. Abnormality of water excretion and intake, or, less often, an rise in urinary sodium excretion will raise the body water content relative to the body sodium content, thereby reducing the serum (Na+). A serum (Na+) less than 135 mEq/L is usually defined as hyponatremia[1]. The disorder occurs in 15 to 22% of hospitalized patients and is the most common fluid-electrolyte disorder among hospitalized patients[2].

Hyponatremia is divided in three Groups, viz: (i) mild hyponatremia: it is defined as serum sodium level between 130 - 135 mmol/L; (ii) moderate hyponatremia: it is defined as serum sodium level between 125-130 mmol/L and severe hyponatremia: it is defined as serum sodium level less than 125mmol/L[3].

Water gain due to hypotonicity leads to swelling of the brain. Partial restoration of brain volume occurs within a few hours as a result of cellular loss of electrolytes (rapid adaptation). The normalization of brain volume occurs through loss of organic osmolytes from brain cells (slow adaptation). Low osmolality in the brain persists despite the normalization of brain volume. Normal osmolality is restored by correction of hypotonicity risking damage to the brain. Too rapid correction of hyponatremia can lead to irreversible brain damage. Therefore correction of hyponatremia must take into account the chronicity of the condition. Acute hyponatremia (duration less than 48h) can be safely corrected more quickly than chronic hyponatremia[4].

Editor's Comment :

- **Symptomatic hyponatremia is mostly prevalent among the elderly.**
- **Presence of comorbidities is an important determinant.**
- **Commonest neurological manifestation is encephalopathy and seizures are common when sodium level is less than 120 meq/l.**
- **Gradual correction is the norm to avoid Osmotic Demyelination Syndrome (ODS).**

Patients with mild hyponatremia (plasma sodium 130-135 mmol/L) of any duration are usually asymptomatic. Nausea and malaise are the earliest symptoms. Headache, restlessness and disorientation occurs as the sodium concentration falls below 115-120 mmol/L. With severe and rapidly evolving hyponatremia, seizures, coma, permanent brain damage, respiratory arrest, brain stem herniation and death may occur.

Hyponatremia is important to recognize because of the common occurrence and potential morbidity and mortality. The economic impact of hyponatremia on the patient and the health care facility is evident by longer duration of stay, higher risk of death and disability

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and increased cost of care.

So this study is planned to be carried out in all the patients with symptomatic hyponatremia and to focus on the rare neurologic manifestations attributable to it and observe the outcomes including recovery and adverse effects which can be helpful to recognise the rarer manifestations caused by it and to see the correlation between the sodium levels and the severity of manifestations for making further protocol for management of hyponatremia. There has been many studies on hyponatremia in the geriatric population but there is not much literature available in young patients and also there are no studies comparing the manifestations and adverse effects of hyponatremia in young patients (<50 years) and old patients (>50 years). So in this study we will also focus on the differences, if any, in the neurological manifestations of hyponatremia and outcome of correction between young (<50yrs) and old (>50 yrs) patients.

Aims and Objectives

The objective of this study is to evaluate the common and rare neurological manifestations of hyponatremia and to correlate them with different range of serum sodium levels and also to study the outcomes including recovery and adverse effects after correction. Differences in the neurological manifestations of hyponatremia in young(<50 yrs) and old(>50yrs) patients were also studied.

Materials and Methods

This study was conducted in the Department of Neurology for a period of one year (2017- 2018) after getting clearance from ethical committee. 200 patients were included from adults admitted with symptomatic hyponatremia. All patients were included after written informed consent. Patients with symptomatic hyponatremia were given intravenous infusion of hypertonic saline, in order to increase of 6 mmol/L over 24 hours (not exceeding 12 mmol/L) and 8 mmol/L during every 24 hours thereafter to bring sodium level to 130 mmol/L. The following equation was used to gauge an expected change in serum sodium (Na) with respect to characteristics of infusates used : Change in serum Na = [(infusate Na + infusate K) - serum Na] / [Total body water +1] Close monitoring of serum electrolytes (ie, every 2-4 h) to avoid overcorrection was done.

Inclusion Criteria — Patients above 18 yrs of age with serum sodium levels < 130 meq/l presenting with neurological complaints were included in this study.

Exclusion Criteria — Patients with abnormal Cerebrospinal Fluid (CSF) examination, any structural cause found responsible for the neurological condition, chronic liver disease (Grades B and C according to Child-pugh classification), Glomerular filtration rate (GFR) below 10% of normal[5] and any other metabolic abnormality eg, hypoglycemia which can cause similar clinical manifestations.

Statistical Analysis — The categorical variables were compared by Chi-square test. The t-test was used to compare the variables between the two groups. The p-value<0.05 was considered significant. All the analysis was carried out on Statistical Package for the Social Sciences (SPSS) 20.0 version.

Results

During the study period, a total 200 patients of symptomatic hyponatremia were enrolled after considering the inclusion and exclusion criteria mentioned above. Patients were treated according to the treatment protocol described and the serum sodium levels were closely monitored.

The maximum number of patients were above 50 years of age. Mean age of presentation was 63.89 years. Majority of patients in the study population were males (60.5%).

Most of the patients (76.5%) were having various comorbid conditions which included Hypertension (61.5%), Diabetes Mellitus (28.5%), Hypothyroidism (5.5%), Chronic Liver Disease (4%), Chronic Renal Disease(6.5%), Epilepsy (1.5%), Schizophrenia (2%), Coronary Artery Disease (9.5%) and Stroke (19.5%) and Rheumatoid Arthritis (1%).

The mean serum sodium levels at the time of admission were 121.40 meq/l, the minimum level being 90 meq/l and the maximum level was 130 meq/l at presentation. 34% patients had serum sodium of 126-130 meq/l at presentation, 35% had 120-125 meq/l at presentation while 31% patients had serum sodium levels of <120 meq/l at the time of admission. The neurologic manifestations of the patients included encephalopathy (86%), followed by extrapyramidal features in form of rigidity and bradykinesia (10%), generalised tonic clonic seizures (9.5%), ataxia (4%) and focal seizures (1%). The frequency distribution of the various neurologic symptoms according to Serum Sodium levels and age is shown if Fig 1 and 2 respectively.

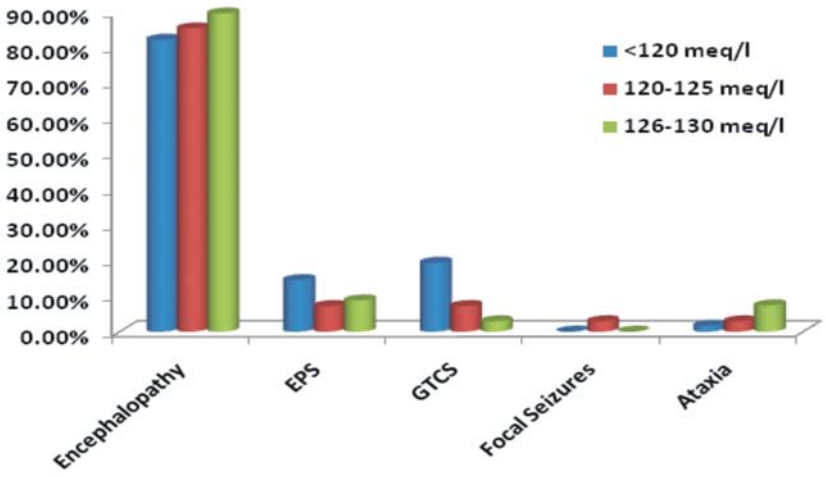

Fig 1 — Distribution of various neurologic manifestations at different Serum Sodium levels
EPS- Extrapyramidal symptoms, GTCS- Generalised Tonic Clonic Seizures

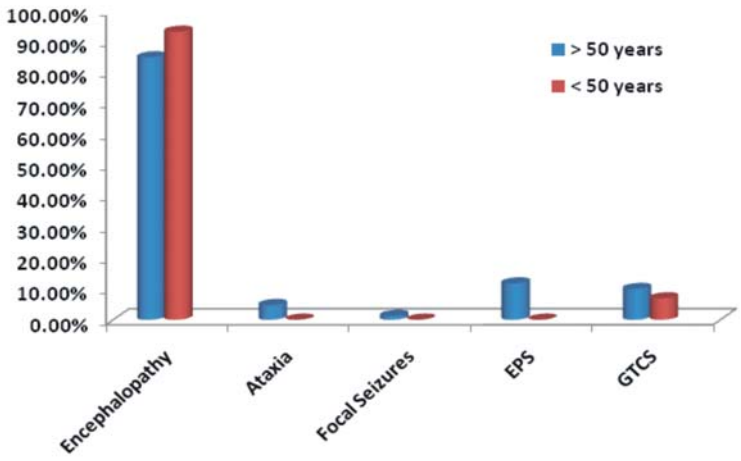

Fig 2 — Distribution of Various Neurologic Manifestations According to Age Distribution.
EPS - Extrapyramidal symptoms, GTCS - Generalised Tonic Clonic Seizures

As far as the neurologic manifestations are concerned, there was no statistically significant difference found between the patients who were less than 50 years of age when compared to the patients older than 50 years (Table 1).

When the association between the serum sodium levels at admission with neurologic manifestations at admission were compared, a strong association between sodium levels <120 meq/l and generalised tonic clonic seizures as presentation was found. No other neurologic manifestation was found to have any association with range of serum sodium levels (Table 2).

Seven patients developed adverse effects of treatment given in form of ODSwhich was found secondary to faster rate of correction of serum sodium levels and most of these patients were referred from the peripheral centres after neurological deterioration. Five of these patients had involvement of pons and two had involvement of basal ganglia and presented with extrapyramidal symptoms. The distribution of the neurological side effects seen is shown in Fig 3.

Table 1 — *Distribution of various neurologic manifestations according to age distribution*

Neurologic Manifestation	Patients >50 years (%)	Patients <50 years (%)	P value
Ataxia	4.7	0	0.235
Focal Seizures	1.2	0	0.558
Encephalopathy	84.8	93.1	0.233
Extrapyramidal symptoms	11.7	0	0.052
GTCS	9.9	6.9	0.605

GTCS- Generalised Tonic Clonic Seizures.

Table 2 — *Distribution of Various Neurologic Manifestations According to Serum Sodium Levels at Admission*

Neurologic manifestation	Mean Sodium levels without concerned manifestation (meq/l)	Mean Sodium levels with concerned manifestation (meq/l)	P value
Ataxia	121.24	125.12	0.121
Focal Seizures	121.40	121.00	0.935
Encephalopathy	119.11	121.77	0.059
Extrapyramidal symptoms	121.42	121.20	0.892
GTCS	122.01	115.58	<0.001*

GTCS - Generalised Tonic Clonic Seizures.
* - Statistically significant

Discussion

This was a prospective observational study carried out in the patients admitted with symptomatic hyponatremia with neurologic manifestations. A total of 200 patients were enrolled during the study period and were observed for neurologic symptoms attributable to hyponatremia and also for recovery and adverse effects.

We have enrolled the patients with hyponatremia under three categories on the basis of serum sodium levels ie, <120 meq/l, 120-125 meq/l and 126-130 meq/l. Patients with levels more 130 meq/l were not enrolled as most of these were not having any neurologic manifestations at presentation. We also divided the study population according to age (more than or less than 50 years) for assessing any correlation between age of presentation and neurologic manifestation.

The most common neurologic manifestation seen in the study population was encephalopathy followed by extrapyramidal symptoms, GTCS, Ataxia and focal seizures. Patients with serum sodium levels less than 120 meq/l were found to have more propensity to have GTCS as compared to patients with higher serum sodium levels at presentation. There was no statistically significant difference found between serum sodium levels and any other neurologic manifestation. Most of the patients in the study were older than 50 years of age with multiple comorbidities. The various comorbidities may predispose the patients to hyponatremia by decreasing oral intake or because of certain medications prescribed such as diuretics, antiepileptics etc.

There was no statistically significant difference found between the neurologic manifestations of patients who were less than 50 years of age when compared to the older population. Seven of the patients developed adverse effects attributed to the correction of sodium levels in the form of osmotic demyelination syndrome involving pons in five and basal ganglia in two patients. Most of these patients were referred from primary care physicians after deterioration in neurological status, so it may possible that they did not follow the proper treatment protocol for sodium correction.

There has been many studies for evaluating the patients of hyponatremia. In a study by Nankabirwa *et al*[6], the patients enrolled were older than 60 years of age and were having heart failure who were taking loop diuretics. The most common symptoms in the study were falls, altered behaviour and mentation and the risk

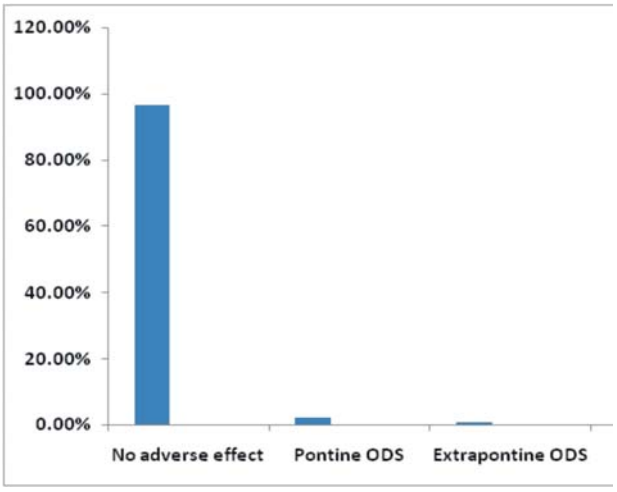

Fig 3 — Frequency distribution of adverse effect in the study population
ODS- Osmotic Demyelination Syndrome

factors most commonly associated included hypertension and heart failure. In the present study also most of the patients were more than 50 years of age and were having hypertension as the most common comorbidity with encephalopathy as the most common neurologic manifestation.

In a study by Rao *et al*[7], 100 patients with symptomatic hyponatremia were studied. Most frequent symptoms included drowsiness, lethargy, confusion, seizures and coma. The co-morbid conditions associated were Hypertension (69%) and diabetes mellitus (51%). The common cause of Hyponatremia was Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH) followed by drugs of which diuretics was the main culpriit.

In a study by Patil *et al*[8], it was concluded that hyponatremia is most common in critically ill patients admitted to ICU. Most etiological factors involved in it are severe sepsis, renal failure, liver cirrhosis, trauma, hypothyroidism, and hypocortisolism. Neurological manifestations include seizures, reduced consciousness level, confusion, unsteadiness, and falls.

In a study by Paniker *et al*[9], a total of 100 patients were included. The mean age of patients in the study was 55.05 years. The most common neurologic symptoms included confusion, tremors, hallucinations, seizures, psychosis, coma. In this study the authors have also seen the manifestations at different serum sodium levels. Seizures were noted in moderate to severe hyponatremia. In the present study also we found that the seizures were more common in patients with lower levels of serum sodium levels.

Similar results were seen in study by Gopinath *et al*[3]. Among the 50 patients with hyponatremia, 42% of encephalopathy patients had metabolic encephalopathy. Majority who developed hyponatremia had age between 61 to 80 years. Clinical profile of patients with hyponatremia was revealed and most of the patients with hyponatremia were observed having confusion followed by nausea/vomiting, delirium, seizure. The common co-morbid conditions for hyponatremia were hypertension 55.93%, diabetes mellitus 43.85%, and chronic renal failure 35.29%.

Similar to all these studies, the present study also showed the association of hyponatremia with multiple comorbidities and old age. Also the most common neurologic manifestation was encephalopathy and the incidence of seizures increased with decrease in serum sodium levels. But in none of the previous studies the comparison was done between the patients of age less than and more than 50 years. Also extrapyramidal symptoms were not described as major neurologic manifestation in any of the previous studies. Along with in none of the studies the frequency of adverse effects with correction of hyponatremia was studied.

Conclusion

Hyponatremia is a common dyselectrolytemia disturbance seen in the elderly. It is mostly associated with multiple comorbid conditions associated with decreased oral intake and multiple medications. Proper recognition of the condition is important as it is potential treatable condition with very less incidence of adverse effects secondary to treatment and if left untreated will lead to serious neurologic outcomes. Primary care physicians should be educated regarding the protocol of sodium correction in cases of hyponatremia so that incidence of ODS can be reduced.

Source of Support : Nil
Conflicting Interest : None
Ethical Clearance : Ethical clearance was obtained from the Institutional Ethics Committee.

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Original Article

Antimicrobial Susceptibility Profile of *Staphylococcus aureus* Isolates Obtained from Skin and Soft Tissue Infections : A Real-World Study Based on a Large Diagnostic Laboratory Data

Manmohan Singh[1], Gifty Immanuel[2], Aarathy Kannan[3]

Introduction : Skin and soft tissue infections (SSTIs) are infections of the epidermis, dermis, or subcutaneous tissues caused by the microbial invasion of the skin and underlying soft tissues.India reported an incidence rate of SSTIs to be 18.21/1000 person-years.The susceptibility of *Staphylococcus aureus* to prescribed antimicrobials varies widely across the geographic regions due to increasing resistance. This study aims to assess the susceptibility profile and trends by utilizing the diagnostic laboratory-based data from multiple centers across India.

Methods : Itis an observational retrospective study conducted on secondary data retrieved from multiple diagnostic laboratories located across different Indian states. A total of 6142 specimens of *Staphylococcus aureus* from different skin and soft tissue samples, were included in the study.The included samples were from different specimen categories such as pus swab, breast abscesses, skin scrapping, bedsore swab, hand swab, nipple discharge and nail scrapping. Only the records of the patients, who attended diagnostic labs between Jan 2010-Dec 2019, were considered for the analysis.

Results : Overall, 29252 specimens (pus swab, breast abscess, skin scrapping, bedsore swab, hand swab nipple discharge and nail scrapping) of SSTIs were considered, out of which, 6142 were found to be positive for *Staphylococcus aureus* and were included in the final analysis.Susceptibility of *Staphylococcus aureus* was found to be highest for 1stgeneration cephalosporins (84.7% & 88% for cephalexin and cephazolin respectively), followed by 79.5% for second generation cephalosporin (cefuroxime) and 53.8% for third generation cephalosporin (cefixime). For other two commonly used antimicrobial agents, clindamycin&amoxicillin-clavulanic acid in SSTI susceptibility was found to be 78.5% and 66.1% respectively. *Staphylococcus aureus* was found to be highly resistant to amoxicillin (sensitivity 7.4%).

Conclusion : This study highlighted the increase in resistance to the newer generation antimicrobial agents and there are significant regional differences in sensitivity patterns of culture isolates.

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***Key words* : Skin and soft tissue infections, SSTIs, *Staphylococcus aureus,* Susceptibility.**

Skin and soft tissue infections (SSTIs) are defined as infections of the epidermis, dermis, or subcutaneous tissues caused by the microbial invasion of the skin and underlying soft tissues. These infections have highly variable presentations, severity, etiologies are frequently observed in clinical practice[1]. According to a study conducted on the general population in the USA, the estimated incidence rate of SSTIs was found to be 24.6 per 1000 person-years[2]. Another study reported an estimated prevalence of 7-10% of SSTIs amongst hospitalized patients[3]. Further, a study highlighted SSTIs as the third most diagnosed disease condition in emergency care settings after chest pain and asthma[4]. A study conducted on patients visiting the Emergency Department of Tamil Nadu, India reported an incidence rate of SSTIs to be 18.21/1000 person-years[5].

The infections contributing to the purulent type of SSTIs are carbuncles, furuncles and abscesses while non-purulent infections include cellulitis, erysipelas and necrotizing fasciitis[1]. Further, SSTIs can be classified into other categories like the mild, moderate and severe type of infections[6]. Severe purulent infections show symptoms like tachycardia, rise of temperature (>38ºC), tachypnea and abnormal count of White Blood Cell (WBC). Moderate non-purulent infections of mild type include erysipelas or cellulitiswith systemic symptoms of infections[7].

Editor's Comment :

- Continuous surveillance of AMR remains the key step in detecting spatiotemporal deviation in resistance patterns.
- Abandoned antimicrobials can be resurrected and repositioned for the chemotherapy of skin infections with resistant organisms.
- Physicians' clinical decision trees and algorithms should be guided by real-time data studies.

The spectrum of SSTIs ranges from mild infections such as pyoderma to life-threatening infections. The possible reasons for this can range from the inappropriate medical management or the presence of other co-morbidities such as diabetes and immunocompromised conditions like HIV/AIDS[6]. *Staphylococcus aureus* is the causative organism of a large percentage of SSTIs (39%) and blood infections (22%)[8]. It is capable of evading antimicrobials and host defenses by multiplying and persisting in

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biofilms formed on surfaces of the prosthetic devices in the hosts[9].

SSTIs are common, and the emergence of resistant *Staphylococcus aureus* isolates limits the available treatment options[10,11]. Monitoring the spatiotemporal variations of antibiotic resistance is crucial component of any antimicrobial stewardship program[12].

Material and Methods

Study Objectives :

To understand the sensitivity profile of *Staphylococcus aureus* isolated from clinical specimens of skin and soft tissue infections against commonly used antimicrobial agents such as cephalexin, amoxicillin, amoxicillin-clavulanate, cefuroxime, clindamycin, cefazolin and cefixime by using laboratory-based culture and sensitivity data.

Research Design and Methods :

Study type :

This is an observational retrospective study conducted on secondary data retrieved from multiple diagnostic laboratories located across different Indian states.

Study platform :

Skin and soft tissue infection culture and sensitivity data retrieved from multiple diagnostic laboratories located across four different Indian regions; East (Assam, Bihar, Jharkhand, Manipur, Tripura, Orrisa, West Bengal, Andaman and Nicobar Island), West (Goa, Gujarat, Rajasthan, Madhya Pradesh, Maharashtra), North (Chandigarh, Delhi, Haryana, Himachal Pradesh, Jammu & Kashmir, Uttar Pradesh, Punjab, Uttarakhand) and South (Andhra Pradesh, Karnataka, Kerala, Tamil Nadu, Telangana) was retrieved and utilized in the study.

Sampling Method and Sample Size :

A total of 6142 specimens of *Staphylococcus aureus* from different skin and soft tissue samples, were included in the study.The included samples were from different specimen categories such as pus swab, breast abscesses, skin scrapping, bedsore swab, hand swab, nipple discharge and nail scrapping. Only the records of the patients,who attended diagnostic labs between Jan 2010-Dec 2019, were considered for the analysis. Samples with missing variables like age, sex were excluded from the analysis.

Data Analysis :

Data was analyzed using Microsoft Excel and R Studio Open 3.5.3. Detail of descriptive variables such as mean age, gender distribution etc. was provided in the study. The culture sensitivity indices were described in the form of proportions. Categorical variables such as gender and sensitivity were presented as percentage/proportions and compared using the Chi-square test/ Fischer exact test. Statistical significance was considered at $p<0.05$. Percentage sensitivity was calculated by dividing total number of sensitive samples by total samples. Samples with intermediate sensitivity were also considered as resistant.Sensitivity patterns were analyzed across age, gender, states, regions and time (Year).

Ethical Issues :

Confidentiality of subjects was maintained by using anonymized and de-identified data only.

Results

Descriptive Statistics :

A total of 29252 specimens (pus swab, breast abscess, skin scrapping, bedsore swab, hand swab nipple discharge and nail scrapping) suggestive of SSTIs were considered for this study (Fig1A). Out of total 29252 specimens, 6142 were found to be positive for *Staphylococcus aureus* and were included in the final analysis. Most of samples were from pus,6074 (98.89%), followed by breast abscess 54(0.87%) and rest 14(0.22%) from other categories such as skin scrapping, bedsore swab, hand swab, nipple discharge and nail scrapping (Fig 1B). A total of 44.7% samples were from females and 55.3% from males. Most of the samples, 2582(42%) were from young adults (>18-45years), followed by 1635(26.8%)from older adults (>45-60years), 1371(22.5%) from elderly (>60years) and 554(9%) from the pediatric population (0-18years) (Table 1).

The samples included in the study were obtained from different parts of India, but majority of the samples were from Maharashtra1757(28.6%) followed by Kerala1187(19.3%), Madhya Pradesh 836(13.6%), Uttar Pradesh 541(8.8%), Delhi 322(5.2%),Karnataka 288(4.7%), Chandigarh 228(3.7%), Tamil Nadu 201(3.3%), Punjab 177(2.9%), Assam 172(2.8%) and rest 15.2% from other states (Table 2). Table 2 highlights the state-wise positivity rate of culture for *Staphylococcus aureus.*The analysis demonstrated highest positivity rate of culture for *Staphylococcus aureus* in Chandigarh (228 positives out of 667 samples; 34.18%), followed by Maharashtra (1757 positives out of 5380 samples; 32.66%) and least positivity rate in Other States (207 positives out of 3918 samples; 5.28%).

Table 3 provides the gender-wise susceptibility pattern of *Staphylococcus aureus* to various antimicrobial agents.

On conducting analysis across the different age groups, the susceptibility pattern of *Staphylococcus aureus* to none of the

Table 1 — *Descriptive Details of Overall Samples*

Specimen	Pus	Breast abscess	Others	Total
Age and gender wise distribution of *Staphylococcus aureus* positive samples				
Male N (%)	3392(55.8%)	2(3.7%)	2(14.3%)	3396(55.3%)
Female N (%)	2682(44.2%)	52(96.3%)	12(85.7%)	2746(44.7%)
Total	6074(100%)	54(100%)	14(100%)	6142(100%)
Age-wise distribution of samples with positive culture				
0-18 Years	552(9.1%)	2(3.7%)	(0%)	554(9%)
>18-45 years	2528(41.6%)	44(81.5%)	10(71.4%)	2582(42%)
>45-60 Years	1628(26.8%)	7(13%)	(0%)	1635(26.6%)
>60 Years	1366(22.5%)	1(1.9%)	4(28.6%)	1371(22.3%)
Total	6074(100%)	54(100%)	14(100%)	6142(100%)

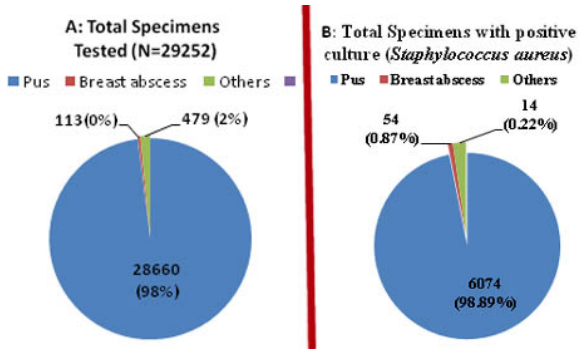

Fig 1 — Pictorial representation of the (A) Total specimens tested and (B) Total specimens with positive culture for Staphylococcus aureus

antimicrobial agent except for amoxicillin-clavulanic acid showed a statistically significant difference (P<0.05).

The analysis was performed to identify the comparative susceptibility pattern of *Staphylococcus aureus* across the different regions and states of India. The susceptibility varied significantly across the different regions for all the antimicrobial agents except for amoxicillin (P< 0.05) (Table 3). Table 4 presents the state-wise susceptibility pattern of Staphylococcus aureus to various antimicrobial agents. Maximum susceptibility (95.6%) of Staphylococcus aureus was found to be highest for cefazolin (1st generation cephalosporin) in Haryana, followed by Maharashtra (94.2%) and cephalexin (1st generation cephalosporin) in Kerala (91.8%). From the analysis it was found that *Staphylococcus aureus*was resistant to amoxicillin in West Bengal (sensitivity 4.7%), followed by Maharashtra (sensitivity 3.5%).West and South Zones have better susceptibility profile of *Staphylococcus aureus* for most of the antimicrobial agents.

Fig 2 provides the antimicrobial sensitivity status of *Staphylococcus aureus* to different antimicrobials across pus, breast abscess and other samples. For pus specimens which included majority of test samples,susceptibility of *Staphylococcus aureus* was found to be highest for 1st generation cephalosporins (84.7% & 88% for cephalexin and cephazolin respectively), followed by 79.5% for second generation cephalosporin (cefuroxime) and 53.8% for third generation cephalosporin (cefixime). Susceptibility for other two commonly used antimicrobial agents, clindamycin & amoxicillin-clavulanic acid in SSTI was found to be 78.5% and 66.1% respectively. *Staphylococcus aureus* was found to be highly resistant to amoxicillin (sensitivity 7.4%).

The year-wise susceptibility trend provided a clear picture of the dynamics for the past ten years (Fig 3).The antimicrobial susceptibility of*Staphylococcus aureus* to cephalexin in year 2010-2011 was 68.97%, 2012-2013; 95.59%, 2014-2015; 91.22% followed by 78.88% in 2016-2017 and then 82.16% in 2018-2019. Similarly, for cefazolin in year 2010-2011 was 79.59%, 2012-2013; 82.19%, 2014-2015; 87.93% followed by 88.49% in 2016-2017 and then 90.91% in 2018-2019 (Table 5).

Discussion

The result from this study suggests that the first-generation

Table 2 — *State-wise Distribution of Samples with Positive Culture and State-wise Positivity Rate of Culture Tested for Staphylococcus Aureus*

States	Pus	Breast abscess	Others	Grand Total
Maharashtra	1721(28.3%)	32(59.3%)	4(28.6%)	1757(28.6%)
Kerala	1185(19.5%)	2(3.7%)	(0%)	1187(19.3%)
Madhya Pradesh	822(13.5%)	7(13%)	7(50%)	836(13.6%)
Uttar Pradesh	540(8.9%)	(0%)	1(7.1%)	541(8.8%)
Delhi	322(5.3%)	(0%)	(0%)	322(5.2%)
Karnataka	287(4.7%)	0%	1(7.1%)	288(4.7%)
Chandigarh	224(3.7%)	3(5.6%)	1(7.1%)	228(3.7%)
Tamil Nadu	200(3.3%)	1(1.9%)	(0%)	201(3.3%)
Punjab	177(2.9%)	(0%)	(0%)	177(2.9%)
Assam	172(2.8%)	(0%)	(0%)	172(2.8%)
Haryana	107(1.8%)	8(14.8%)	(0%)	115(1.9%)
West Bengal	110(1.8%)	1(1.9%)	(0%)	111(1.8%)
Himachal Pradesh	56(0.9%)	(0%)	(0%)	56(0.9%)
Rajasthan	53(0.9%)	(0%)	(0%)	53(0.9%)
Jammu & Kashmir	33(0.5%)	(0%)	(0%)	33(0.5%)
Goa	15(0.2%)	(0%)	(0%)	15(0.2%)
Jharkhand	11(0.2%)	(0%)	(0%)	11(0.2%)
Manipur	11(0.2%)	(0%)	(0%)	11(0.2%)
Andhra Pradesh	8(0.1%)	(0%)	(0%)	8(0.1%)
Uttarakhand	8(0.1%)	(0%)	(0%)	8(0.1%)
Gujarat	4(0.1%)	(0%)	(0%)	4(0.1%)
Bihar	3(0%)	(0%)	(0%)	3(0%)
Telangana	2(0%)	(0%)	(0%)	2(0%)
Andaman & Nicobar	1(0%)	(0%)	(0%)	1(0%)
Orissa	1(0%)	(0%)	(0%)	1(0%)
Tripura	1(0%)	(0%)	(0%)	1(0%)
Grand Total	**6074 (100%)**	**54 (100%)**	**14 (100%)**	**6142 (100%)**

States	Positivity Rate	Total Samples
Chandigarh	228 (34.18%)	667
Maharashtra	1757 (32.66%)	5380
Karnataka	288 (32.54%)	885
Kerala	1187 (29.89%)	3971
Madhya Pradesh	836 (25.49%)	3280
Delhi	322 (22.79%)	1413
Tamil Nadu	201 (22.02%)	913
Assam	172 (14.65%)	1174
Uttar Pradesh	541 (14.32%)	3779
Punjab	177 (12.38%)	1430
Haryana	115 (6.06%)	1898
Others	207 (5.28%)	3918
West Bengal	111 (20.40%)	544
Grand Total	**6142 (21.00%)**	**29252**

Table 3 — *Comparative Susceptibility Patterns of Staphylococcus Aureus to Various Antimicrobial Agents among Male and Female and Different Regions*

Gender	Amoxicillin clavulanic acid	Amoxicillin	Cefazolin	Cefixime	Cefuroxime	Cephalexin	Clindamycin
Female	1481(67.5%)	79(10.1%)	924(87.3%)	299(52.8%)	793(80.2%)	481(83.6%)	1504(79.5%)
Male	1819(65.3%)	86(4.7%)	1076(88.2%)	449(53.7%)	1007(79%)	587(85%)	1917(77.6%)
Total	3300(66.2%)	165 (7.3%)	1600 (87.8%)	748(53.3%)	1800(79.6%)	1068(84.4%)	3421(78.4%)
P-value	0.18	0.18	0.56	0.82	0.55	0.52	0.20
Region	**Amoxicillin clavulanic acid**	**Amoxicillin**	**Cefazolin**	**Cefixime**	**Cefuroxime**	**Cephalexin**	**Clindamycin**
East	267(59.6%)	77(5.2%)	50(62%)	9(11.1%)	93(59.1%)	18(66.7%)	298(67.8%)
North	353(56.4%)	(0%)	176(63.6%)	142(47.9%)	142(62%)	197(79.2%)	1293(72.9%)
South	271(29.9%)	4(25%)	71(84.5%)	162(49.4%)	59(61%)	518(87.5%)	328(82.3%)
West	2361(72.7%)	83(8.4%)	1657(91.1%)	433(57.3%)	1505(83.2%)	335(83.6%)	1453(84%)
P-value	<0.05	0.29	<0.05	<0.05	<0.05	<0.05	<0.05

Table 4 — *State-wise susceptibility pattern of Staphylococcus aureus to various antimicrobial agents*

States	Amoxicillin clavulanic acid	Amoxycillin	Cefazolin	Cefixime	Cefuroxime	Cephalexin	Clindamycin
Assam	166(66.3%)	8(0%)	6(100%)	(0%)	7(85.7%)	(0%)	172(74.4%)
Chandigarh	144(78.5%)	(0%)	68(72.1%)	85(61.2%)	53(67.9%)	26(69.2%)	217(80.6%)
Delhi	172(39%)	(0%)	65(56.9%)	46(23.9%)	48(52.1%)	144(86.8%)	299(77.9%)
Haryana	48(62.5%)	(0%)	45(95.6%)	2(100%)	2(50%)	1(0%)	112(80.4%)
Karnataka	67(19.4%)	(0%)	4(25%)	78(71.8%)	13(84.6%)	77(67.5%)	168(82.1%)
Kerala	97(54.6%)	(0%)	5(100%)	13(23.1%)	4(75%)	390(91.8%)	1(100%)
Madhya Pradesh	795(49.6%)	(0%)	378(80.2%)	62(32.3%)	455(74.3%)	(0%)	363(87.3%)
Maharashtra	1539(84.2%)	57(3.5%)	1252(94.2%)	370(61.6%)	1023(86.7%)	335(83.6%)	1019(84.1%)
Others	45(82.2%)	35(20%)	35(100%)	8(12.5%)	43(88.4%)	8(37.5%)	196(60.2%)
Punjab	7(57.1%)	(0%)	(0%)	7(57.1%)	17(70.6%)	2(50%)	134(67.9%)
Tamil Nadu	101(10.9%)	10%)	58(86.2%)	70(30%)	39(48.7%)	49(85.7%)	149(81.2%)
Uttar Pradesh	29(48.3%)	(0%)	43(60.5%)	4(25%)	21(61.9%)	24(50%)	491(72.5%)
West Bengal	90(48.9%)	64(4.7%)	41(53.7%)	3(0%)	75(57.3%)	12(83.3%)	100(58%)

Table 5 — *Susceptibility Trend of Staphylococcus Aureus to Various Antimicrobials from Year 2010 to 2019*

Year	Amoxicillin clavulanic acid	Amoxi-cillin	Cefazolin (1st Generation cephalosporin)	Cephalexin (1st Generation cephalosporin)	Cefuroxime (2nd Generation cephalosporin)	Cefixime (3rd Generation cephalosporin)	Clindamycin
2010-2011	107(96.26%)	-	49(79.59%)	29(68.97%)	110 (91.82%)	88(85.23%)	113(92.92%)
2012-2013	307(96.09%)	-	292 (82.19%)	159 (95.60%)	209(92.34%)	74 (89.19%)	207(86.96%)
2014-2015	536(84.33%)	-	439 (87.93%)	262(91.22%)	133 (82.71%)	86(72.09%)	477(83.65%)
2016-2017	1050(55.05%)	-	747 (88.49%)	461 (78.31%)	555(70.81%)	307(37.79%)	959(80.08%)
2018-2019	1300(58.31%)	7.27% (165)	473(90.91%)	157 (82.17%)	793(80.08%)	193(41.45%)	1665(73.93%)

cephalosporins, cefazolin(87.8%) and cephalexin(84.4%) demonstrated the highest antimicrobial activity against *Staphylococcus aureus* followed by second generation cephalosporins, cefuroxime(79.6%) and clindamycin (78.4%).On the other hand, other antimicrobials such as amoxicillin-clavulanic acid (66.2%), cefixime (53.3%) showed moderate activity while sensitivity was very low for amoxicillin (7.3%).

Staphylococcus aureus associated SSTIs were more prevalent in males (55.3%) compared to females (44.7%). The male preponderance observed in our study is like the results reported

by multiple other studies[13,14]. The odds of being a carrier for *Staphylococcus aureus* were also high among males (odds ratio of 1.38 {1.31–1.46})[14,15]. There is no defined explanation for a higher risk and different immune response in males and in females[16,17].

The results in our study demonstrated susceptibility of *Staphylococcus aureus* to cephazolin was maximum (95.6%) in Haryana followed by Maharashtra (94.2%) and for clindamycin it was maximum (87.3%) in Madhya Pradesh, followed by Maharashtra (84.1%). A prospective study conducted by RS Phakade *et al*, in a tertiary care center in Mumbai, Maharashtra enrolled eight hundred and twenty patients with community-acquired (CA) SSTIs. Susceptibility patterns of *Staphylococcus aureus* to antimicrobials (cephazolin: 100%, clindamycin: 97%) tested were in congruence to our findings[18].

Majority of the antimicrobial agents showed better activity in South and Western Zone. Similarly, ICMR AMR Surveillance report 2017 concluded that the prevalence of antimicrobial resistance varies across different regional locations[19].

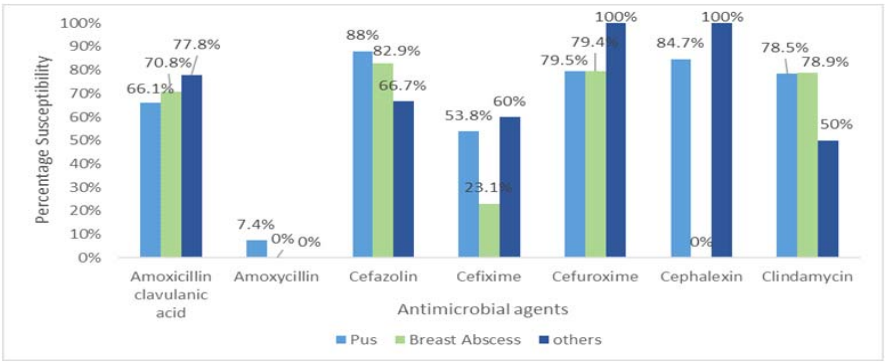

Fig 2 — Comparative susceptibility patterns of Staphylococcus aureus to various antimicrobial agents across different specimen

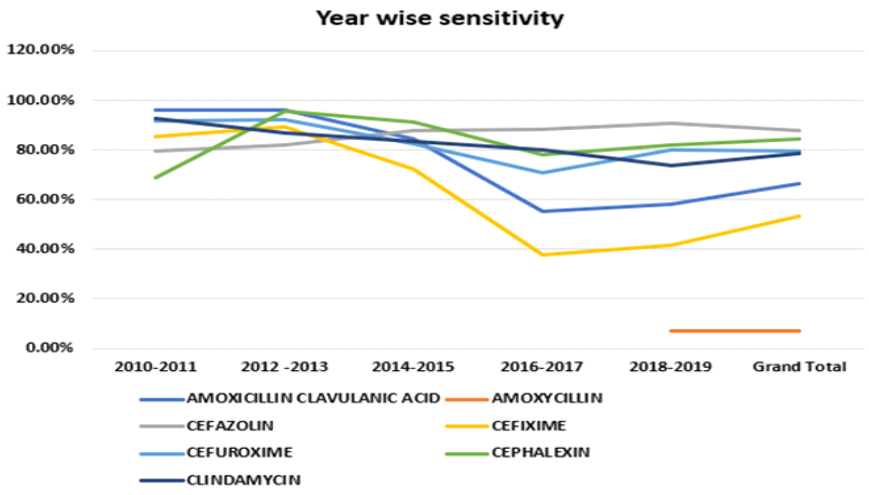

Fig 3 — Line diagram showing Susceptibility trend of Staphylococcus aureus to various antimicrobials from year 2010 to 2019

The ICMR guidelines reported 78.7% antimicrobial sensitivity toclindamycin, followed by cefoxitin (64.2%), oxacillin (51.6%), trimethoprim-sulfamethoxazole (61.2%),erythromycin (47.2%) and ciprofloxacin (27.6%), and recommended first-generation cephalosporins in *Staphylococcus aureus* associated SSTIs[20].

Clindamycin is prescribed alone or in combination with other drugs such as cefazoline and amoxicillin-clavulanate as empirical therapy, for the treatment of SSTIs[6,20]. But,an increase in the prevalence of resistance to clindamycin has been observed in recent times amongst *Staphylococcus aureus*[21,22]. A study from tertiary care centre in north-east India reported inducible resistance (10.70%) and constitutive resistance (16.88%) in *Staphylococcus aureus* isolates[22].

A hospital in Southern India assessed sensitivity percentage of*Staphylococcus aureus* isolates from OPD and IPD settings pertaining to both, community-acquired and hospital-acquired skin infections. The study documented high resistance for penicillins (85.4%) and amoxicillin-clavulanic acid (41%)[23]. Similarly, high resistance (97.7%) to penicillins was documented in hospital settings of Andhra Pradesh[24]. The results of this study are consistent with resistance observed for amoxicillin (92.6%) and amoxicillin-clavulanic acid (33.9%) in our study. An increase in resistance for clindamycin from 2.61% (2009) to 17.11% (2015)[25] was noted.

The results from present study support older or first-generation cephalosporins, cefazolin and cephalexin are emerging antimicrobials for treatment of SSTIs and these trends must be considered while developing empirical therapy.

Limitations :

The study was limited in a way as clinical information such as prior exposure to antimicrobials, prescriptions provided to patients after confirmation of infections, follow up data of patients and details of settings whether OPD, IPD or ICU were unavailable (as data has been retrieved from diagnostic laboratory).

Conclusion

Real-time surveillance is the key to understand spatiotemporal trends of antimicrobial resistance. There are several significant findings, which need to be considered during the management of *Staphylococcus aureus* associated skin and soft tissue infections at the clinic level.

(1) There is increasing resistance to the newer generation

antimicrobial agents but at the same time older generation drugs are improving and showing better activity.

(2) There is significant regional differences in sensitivity patterns of culture isolates and samples from Southern and Western India showed high sensitivity.

Source of Support : Nil
Conflicting Interest : None

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Original Article

Study on Loss of Protection Sense in Type 2 Diabetes Mellitus with Special Reference to TSH Value within Normal Range

Sourav Kumar Bhakta[1], Saumik Datta[2], Arnab Roy[1], Partha Pratim Mukherjee[3]

Peripheral neuropathy is estimated to affect around half of people with diabetes. Thyroid dysfunction is found in 4-17% in Type- 2 Diabetes. T2DM with Hypothyroidism is more likely to have peripheral neuropathy. We planned this study to find correlation of Thyroid-stimulating Hormone (TSH) level (within normal range) with loss of protection sense (LOPS) in T2DM. It had been observed that those with TSH ≥3 mIU/ml had 5.47, 2.59, 2.96, 3.08, 10.25, 4.56, 2.51 times more risk of having abnormal VPT (VPT>25), absent ankle jerk, absent vibration sense , absent pin prick sense , abnormal 10-MFT, abnormal skin and musculoskeletal status of foot, respectively comparing to those with TSH <3 mIU/ml. Overall, those with TSH ≥3 mIU/ml were observed at 14.82 times more risk of having LOPS comparing to those with TSH <3mIU/ml .

[*J Indian Med Assoc* 2021; **119(3):** 27-30]

Key words **: Diabetic neuropathy, Hypothyroid, VPT, LOPS.**

Diabetes mellitus is a major health problem with rising prevalence globally. Diabetic peripheral neuropathy is the most common cause of neuropathy worldwide. Some Diabetic patients may present with spontaneous discomfort. But, neuropathic symptoms poorly correlate with sensory loss[1].

Prevalence of thyroid dysfunction in diabetes is higher than that of general population. Thyroid dysfunction is found in up to a third of patients with Type 1 Diabetes Mellitus (T1DM)[2] and 4-17% with Type 2 Diabetes Mellitus (T2DM)[3].

Peripheral neuropathy in hypothyroidism is correlated with segmental demyelination. It results from a basal metabolism disorder of Schwann cells[4]. T2DM with Sub Clinical Hypothyroidism is more likely to have Diabetic peripheral neuropathy and it is due to incipient axonal alteration presented in hypothyroidism[5].

But, association between TSH level within normal range and loss of protection sense in T2DM had not been comprehensively studied. So, we planned this study to find out whether there is any correlation of TSH level (within normal range) with loss of protection sense (LOPS) in type 2 Diabetes Mellitus.

Materials and Method

This cross sectional study had been conducted in Calcutta National Medical College and Hospital, Kolkata for a period of 1 year on 100 type 2 diabetic patients attending Endocrine OPD.

Exclusion Criteria :

- T1DM
- Ulcerated foot
- Gestational Diabetes Mellitus (GDM)

Editor's Comment :

- Result of Thyroid function test in every case of Type 2 Diabetes Mellitus has to be interpreted more carefully when TSH is at high normal range.
- A larger longitudinal prospective case control study may tell us whether thyroid hormone replacement to keep TSH value within 3 mu/L will be more effective to preserve protective sense in foot of persons living with Type 2 Diabetes Mellitus by avoiding additive effect of thyroid related neuropathy.

- HbA1c≥9%,
- HIV
- Serum TSH >5 mIU/L
- eGFR<30 ml/min/1.73m^2
- Malignancy
- Hypothyroid, Graves' disease, Multinodular goiter, Thyroiditis
- Sick patient
- H/o heavy metal exposure.

After taking careful history regarding duration of diabetes, addiction, neuropathic symptoms, past history of ulcer and other macro and microvascular complication, we focused in foot examination. Dermatological assessment was done for skin status; such as color, thickness, dryness, cracking, fungal infection between toes, ulceration, calluses/blistering. We also looked for any foot deformity like claw toes, prominent metatarsal heads, Charcot joint and muscle wasting.

Neurological assessment was done with 10-g monofilament, 128-Hz tuning fork. Pinprick sensation, ankle reflexes and Vibration Perception Thresholds (VPT) were assessed. Any abnormal test among these suggests LOPS.

Vibration Perception Threshold Test :

Biothesiometer gives a semiquantitative assessment of VPT. Stylus of the instrument was placed over six different places (First toe, 1st, 3rd, 5th metatarsal head, instep, and heel) on both feet with patient lying supine. Amplitude was increased until patient

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detected vibration. Resulting number is known as the VPT. The final value had been taken as per average of twelve readings. A VPT >25 V was regarded as abnormal.

Laboratory investigation : Serum TSH, free T4, T3 was estimated by chemiluminescent immunoassay.HbA1c was estimated using High Performance Liquid Chromatography (HPLC) system.

Statistical Analysis :

Categorical variables were compared across the groups using Pearson's Chi Square test for Independence of Attributes/ Fisher's Exact Test as appropriate. Continuous were compared across the groups using Mann-Whitney U test. Associations between continuous variables were captured using Spearman's Rank Correlation Coefficient. Multivariate analysis had been done using Binary Logistic Regression Method. The statistical software SPSS version 20 had been used for the analysis.

Results

Different characters of study population had been described in Table 1.

Abdominal obesity (waist-hip ratio of more than 0.85 for females and 0.9 for males) was present in around 78% of patients. The mean HbA1c was 7.03 ± 1.3%, whereas 41% of persons had HbA1c value of >7%.The mean creatinine was 0.86 ±0.21 mg/dl. Average e GFR 90.62 ± 20 (ml/min/1.73 m²). 54% ,41% and 5% having STAGE 1, 2, 3 CKD, respectively .Nearly 46 % patients had microalbuminuria and 7% having macroalbuminuria .The mean LDL C was 93.33 ± 21.88 mg/dl and 86% persons had a serum LDL level above >70 mg/ dl.

Positive symptoms and negative symptoms were complained by 74% & 29% of patients, respectively. Foot care awareness was not present in 67%. History of ulcers present in 20% of patients. Abnormal skin status of foot was found in 68% of patients which included mostly cracking (44%) ,dry skin (35%), deformities (10%) callus (30%), fungal infection (5%). LOPS was found in 63% of group.

On examination, 58% had loss of sensation on 10 g SW monofilament testing .51% patients had abnormal VPT (>25). 36% had abnormal ankle reflexes and 33% of subjects had reduced/ absent vibration perception with 128 Hz tuning fork. 31% had absent pinprick sensation.

Mean VPT was 25.84± 11.60.It was higher (mean VPT = 32.27 ± 9.86) in LOPS group (n 63) comparing with those without LOPS (mean VPT=14.91±2.77) with p value < 0.001.

Age, Duration of diabetes, waist hip ratio, TSH, eGFR, LDL cholesterol, Urine ACR had significant association with LOPS by univariate analysis.Hypertension, addiction (alcohol /smoking) , BMI, waist circumference, FBS, PPBS, HbA1c were not significantly associated with LOPS using univariate analysis.

Those with TSH≥3(mIU/ml) were at 4.56 times more risk of having abnormal skin status (OR:4.56 ,CI:1.79-11.62) and 2.51 times more abnormal musculoskeletal status (OR:2.51 ,CI:1.04-6.03) comparing to those having TSH<3(mIU/ml) and both were statistically significant (p = 0.001 & p = 0.037 respectively).Though foot deformities were 2.67 times (OR:2.67, CI:0.65-10.97) more in patients having TSH≥3(mIU/ml), but it was not statistically significant.

Table 1 — *Distribution of variables of study population*

Variables	Mean ± SD or n (%)
Age (Years)	50.39 ± 8.17
Duration of T2 DM(Years)	6.92 ± 5.95
Gender :	
Male	48
Female	52
History of Hypertension	20
Family history of diabetes	68
Smoker	32
Alcoholic	22
SBP(mm of Hg)	130.92 ± 11.83
DBP (mm of Hg)	80.49 ± 7.97
BMI (kg/m²)	23.32 ± 2.82
Waist Circumference(cm)	88.02 ± 8.61
Waist Hip Ratio	0.94 ± 0.07
VPT	25.84 ± 11.60
FBS(mg/dl)	134.01 ±40.41
PPBS(mg/dl)	196.72 ± 63.79
HbA1c %	7.03 ±1.30
TSH (mIU/ml)	3.11 ± 1.81
e GFR (ml/min/1.73 m²)	90.62 ±20.19
LDL (mg/dl)	93.33 ±21.88
Urine ACR (mg/gram)	70.54 ± 93.87

Table 2 — *Multivariate logistic regression analysis for the association of factors for Loss of protective sense (LOPS)*

	p Value	Odds Ratio	95% C.I. for Odds Ratio	
			Lower	Upper
Age	0.155	1.124	0.957	1.320
Gender	0.959	0.941	0.093	9.525
Duration of Diabetes	0.429	1.118	0.848	1.473
Alcoholic	0.309	0.200	0.009	4.425
Smoker	0.737	0.595	0.029	12.250
INSULIN	0.162	0.082	0.002	2.730
Waist circumference	0.012	0.761	0.615	0.941
Waist Hip Ratio	0.005			
BMI	0.121	1.488	0.900	2.461
TSH	0.003	2.984	1.447	6.152
HbA1C	0.478	0.735	0.313	1.722
FBS	0.160	0.975	0.941	1.010
PPBS	0.468	1.008	0.987	1.029
eGFR	0.664	1.012	0.959	1.068
LDLC	0.157	1.035	0.987	1.085
Urine ACR	0.054	1.053	0.999	1.111
Constant	0.013	0.000		

Those with TSH≥3(mIU/ml) were at 14.82 times (OR:14.82, CI: 5.01-43.87) more risk of having LOPS comparing to those with TSH <3(mIU/ml) and this was statistically significant (p <0.001).

TSH had a significant positive correlation with VPT (P <0.001).

Multivariate logistic regression analysis had shown TSH, waist hip ratio, waist circumference as independent correlates of LOPS.

Discussion

The overall prevalence of LOPS was 63% in our study. This is similar to a study carried out by Kulkarni *et al*[6]. They observed 60% prevalence of diabetic neuropathy[6]. Reported prevalence of foot at risk from another center in north India was 66.9%[7] which is also similar to this study. A higher prevalence of LOPS in this study was also compounded with lack of awareness about foot care. 64.2% of patients having LOPS did not have foot care awareness.

Most abnormal test in this study was 10 -g MFT followed by abnormal VPT (>25) which was also similar to finding of Kishore S *et al*[8].

The use of VPT (cut-off of ≥24.5V) for the diagnosis of neuropathy has been well validated by clinical studies with a sensitivity and specificity of 80% and 98%, respectively[9].

In this study there is significant association of age, duration of diabetes, systolic blood pressure, waist-hip ratio, TSH, PPBS, Cr, eGFR, Urine ACR with abnormal VPT (VPT > 25),which is similar to study by Lakshmana N *et al*[10]. But, multivariate logistic regression analysis found that only TSH had a statistically significant relationship with high VPT(>25).

A significant correlation of Urine ACR with VPT supports the concept of coexistence of other microvascular complications like nephropathy along with neuropathy.

Table 3 — *Multivariate logistic regression analysis for the association of factors for VPT >25*

	p Value	Odds Ratio	95% CI for Odds Ratio	
			Lower	Upper
Age	0.051	1.124	0.999	1.264
Gender	0.638	0.667	0.124	3.594
Duration of Diabetes	0.065	1.197	0.989	1.449
Alcoholic	0.856	0.822	0.100	6.759
Smoker	0.654	1.530	0.238	9.859
INSULIN	0.054	0.113	0.012	1.039
Waist circumference	0.686	0.972	0.847	1.116
Waist Hip Ratio	0.134	27965.941	0.043	18168510895.124
BMI	0.966	1.008	0.691	1.472
TSH	0.009*	1.823	1.164	2.857
HbA1C	0.693	0.870	0.435	1.737
FBS	0.783	0.997	0.973	1.021
PPBS	0.180	0.988	0.972	1.005
eGFR	0.610	1.010	0.973	1.047
LDLC	0.554	0.991	0.963	1.021
Urine ACR	0.365	1.004	0.995	1.013
Constant	0.066	0.000		

This study showed that advanced age was significantly associated with LOPS and it was similar to the finding across India[11-14].

Longer duration of diabetes had been identified as a statistically significant risk factor and 1.18 times more likely to develop LOPS compared to shorter-duration . It was in accordance with many neuropathy prevalence studies[14,15].

Smoking is an important risk factor . We found that smokers are 1.79 times more at risk of having LOP. However, smoking and alcohol intake were not statistically significantly associated with LOPS in our study.

Those having BMI≥23 kg/m² were at 1.19 times more likely to develop LOPS compared to patients with BMI of <23 kg/m² but BMI and LOPS have no statistically significant association.

The waist-hip ratio had a positive association with LOPS on multivariate analysis, but BMI and LOPS had no statistically significant association. This again proves discordance between Obesity and BMI in the Indian population which is well known to us.

This present study did not show association of LOPS with HbA1c. This is supported in other studies[16,13]. Though, it was observed that the risk of neuropathy had an association with HbA1c in study by Kumar HK *et al*[14]. HbA1c of that[14] study was (8.7± 1.8) % which is higher than HbA1c (7.03 ±1.30) % of our study. This fact can explain the discordance.

This study found no association of LDL with LOPS on multivariate analysis. However, insulin taken for the treatment had a significant association with LOPS.

Table 4 — *Association of clinical variables of foot examination & LOPS with TSH*

Variables	(*n*=37) *n* (%)	OR	95% CI for Odds Ratio		p value
			Lower	Upper	
VPT>25					<0.001
TSH <3	16(31.3)	1			
TSH ≥3	35(68.7)	5.47	2.32	12.88	
Absent Ankle Jerk					0.025
TSH <3	13(36.1)	1			
TSH≥3	23(63.9)	2.59	1.11	6.01	
Absent Vibration sense					0.013
TSH <3	11(33.3)	1			
TSH ≥3	22(66.7)	2.96	1.24	7.09	
Absent pinprick test					0.012
TSH <3	10(32.3)	1			
TSH ≥3	21(67.7)	3.08	1.26	7.51	
Absence of 10-g MFT					<0.001
TSH <3	17(29.3)	1			
TSH ≥ 3	41(70.7)	10.25	3.94	26.65	
Presence of LOPS					<0.001
TSH <3	19(30.2)	1			
TSH ≥3	44(69.8)	14.82	5.01	43.87	

Among the LOPS group, 65% of patients had microalbuminuria. The prevalence of microalbuminuria was only 13.5% in those not having LOPS. However,multivariate analysis did not show any significant association.

TSH showed a significant association with VPT >25.The mean TSH of our study is 3.11 ± 1.81 mIU/ml .Those with higher TSH are at 1.82 times more risk of having VPT > 25 .

In this present study, there was a positive association of TSH with LOPS (coefficient of 1.093 in multivariate analysis) and those with higher TSH levels were at 2.98 times more risk for having LOPS (OR 2.98, CI: 1.44–6.15).

It had been observed that those with TSH≥3 mIU/ml had 5.47, 2.59, 2.96, 3.08, 10.25, 4.56, 2.51 times more risk of having abnormal VPT (VPT>25), absent ankle jerk, absent vibration sense, absent pin prick sense, abnormal MFT, abnormal skin and musculoskeletal status of foot, respectively comparing to those with TSH <3 mIU/ml.

Those with TSH≥3 mIU/ml were at statistically significant 14.82 times (OR:14.82, CI: 5.01-43.87) more risk of developing LOPS.

So, present study observed higher prevalence LOPS though TSH was within normal limit.

TSH had a significant positive correlation with VPT (p <0.001) which was similar to study by Pramanik *et al*[17]. They included overt hypothyroidism in their study along with subclinical hypothyroidism. We excluded even subclinical hypothyroid population and found a positive correlation between VPT >25 and TSH.

Limitations:

We have not considered Type 1 Diabetes Mellitus.

We have not considered secondary hypothyroid.

We have not considered Free T4 and T3 value for analysis and interpretation.

Conclusion

Loss of Protective Sense was detected in 63% of our study population. We observed that TSH was an independent predictor of LOPS. Patients having LOPS showed a higher TSH level, even when TSH value was within normal range. To our best knowledge, it is the first study to report correlation of TSH (within normal range) with diabetic foot at risk.

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Conflict of Interest : None

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Review Article

COVID-19 Pandemic : Impacts on General Surgical Practices

Abhimanyu Basu[1], Anshu Kumar[2]

Introduction : SARS CoV-2 virus is a novel RNA virus, and many of its characters and behaviours are yet to be explored. During this COVID-19 pandemic, there are inundation of recommendations and guidelines. Most of the recommendations have advised postponement of non-essential elective surgery. We continued our emergency and elective surgical works as followed in certain countries, e.g. South Korea and Singapore.

Methods : The records of our hospital were reviewed to retrieve the number of daily COVID-19 patients hospitalized, those requiring surgical management and those discharged home

Results : During the period from March 25 to August 31, 2020, we have tested (RT-PCR) 892 admitted patients, out of them eighteen came positive (~ 2%): three patients were admitted in emergency basis, rest were for elective surgeries. Except one surgical resident, no HCW of our department was COVID positive during this period.

Conclusion : From our experiences, during the said period, we came into conclusion that in no way elective surgeries should be avoided. It will ensure the best care for the non-COVID surgical patients, helps to ease future load and save many lives from denial death. If we maintain simple precautions,then elective surgical services can easily run without special equipment and theatre.

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***Key words* : SARS CoV-2 virus, COVID-19 outbreak, surgical practices, Lockdown, Postponement.**

SARS CoV-2 virus is a novel RNA virus, and many of its characters and behaviors are yet to be explored. COVID-19 or Coronavirus Disease 2019 has got variable impact over different geographical location of the world. WHO (World Health organization) declared a pandemic on 11th of March, 2020[1].

During this COVID-19 pandemic, there are inundation of recommendations and guidelines[2-4]. Most of the recommendations have advised postponement of non-essential elective surgery. Moreover, the impact of COVID-19 pandemic and total "Lockdown" in India[5,6] on surgical practice is widespread ranging from patient mobility due to lack of transport, workforce and staffing issues.

We continued our emergency and elective surgical works as pre-pandemic days as followed in certain countries, eg, South Korea and Singapore, who have continued their elective surgery throughout the COVID-19 outbreak[2-4].

This article is based on sharing information about experiences of the authors from the general surgical departments at Institute of Post Graduate Medical Education & Research, Kolkata which is a teaching, tertiary care hospital during this virus pandemic and "Lockdown".

Usage of Surgical Facilities at Our Institution During Total Lockdown and Unlock :

Government of India (GOI) had declared complete nationwide "Lockdown" from March 25 2020; initially it was for fourteen days, but gradually it was extended to May 31 2020 in a phase wise manner (Table 1). Complete lockdown severely affected all sectors especially healthcare facilities by limiting the movement of the entire country population, assumed to control the spread of pandemic; it was declared when the confirmed COVID-19 cases was 500 approximately[5,6].

Most of the teaching hospitals across India immediately stopped admitting elective surgical cases and operations as per advisory of GOI; as per Indian Council of Medical Research (ICMR) and GOI, "the medical infrastructure in the country needs to be prepared for any possible influx of patients on account of COVID-19. In this context, the following interventions are proposed up to 31st March 2020. They will be reviewed as per the evolving situation. *Non-essential elective surgeries should be postponed"* [7].

From the beginning of Lockdown, as our hospital was designated as non-COVID-19 hospital and we continued to offer surgical services to the people. All emergent and scheduled operations were going on. But we noticed that there was a steep fall in numbers; both in emergent and scheduled operations. Due to total Lockdown there was inaccessibility to transport, people were unable to reach the healthcare facility and moreover fear of getting infected.

Editor's Comment :

- Avoiding elective surgeries not only increased the tremendous future load, but it also increased the morbidity and mortality of the sufferers due to non-COVID ailments.
- It hampered the training opportunity of Resident doctors.If we maintain simple precautions, then elective surgical services can easily run without special equipment and theatre.

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As we reviewed our database, we have noticed that the numbers of patients attending for surgeries were increasing slowly after Unlock started from June 1, 2020 but not reaching to the pre-Lockdown stage. This might be due to non-availability of full public transport, containment zones and moreover less bed availability as the bed numbers were reduced due to rearrangements of beds like allotting some beds in transitional area.

Table 1[5,6]:

Date :

Nationwide lockdown

Phase 1: 25 March 2020 – 14 April 2020 (21 days)

Phase 2: 15 April 2020 – 3 May 2020 (19 days)

Phase 3: 4 May 2020 – 17 May 2020 (14 days)

Phase 4: 18 May 2020 – 31 May 2020 (14 days)

Unlock

Unlock 1.0: 1 June 2020 – 30 June 2020 (30 days)

Unlock 2.0: 1 July 2020 – 31 July 2020 (31 days)

Unlock 3.0: 1 August 2020 – 31 August 2020 (31‘ days)

Unlock 4.0: 1 September – 30 September 2020 (30 days)

Location India

Caused by COVID-19 pandemic in India

Goals To control the spread of coronavirus outbreak in India.

Methods :

- Ban on people from stepping out of their homes
- All services and shops closed except pharmacies, hospitals, banks, grocery shops and other essential services
- Closure of commercial and private establishments (only work-from-home allowed)
- Suspension of all educational, training, research institutions
- Closure of all places of worship
- Suspension of all non-essential public and private transport
- Prohibition of all social, political, sports, entertainment, academic, cultural, religious activities

Status Partially Lifted

Strategical Patterns followed in Our Institution :

Outpatient Department (OPD) Management :

As per Centers for Disease Control and Prevention, *"most hospitals have to cancel or reduce nonurgent outpatient visits as part of their COVID-19 containment strategy. Surgeons should prioritize urgent or emergency visits and procedures. Elective and nonurgent admissions should be rescheduled"*[8].

But we continued our usual OPD services as before but we only allowed asymptomatic, afebrile patients in our OPDs. Any suspected patient was referred to the designated "fever clinic".

Maintaining the six feet social distancing, we were running the OPD with surgical masks and gloves only; except for most essential close clinical examination we use full personal protective equipment (PPE).

Apart from the routine disease-related queries, we mandatorily asked questions about recent travel and contact histories (both patients and the family) with people especially from containment zones; this is unique for COVID-19 that even some asymptomatic or mild symptomatic patients can be highly contagious[9].

Inpatient Department (IPD) Management:

Patients with no history of close contact with confirmed or suspected COVID-19 patients and with no fever or respiratory symptoms were admitted for elective surgeries in a designated transitional area. If they were tested (RT-PCR) negative, they were shifted to the main surgical wards; protocols for emergency patients were also same but no emergent procedures were delayed for RT-PCR test results. All emergency and trauma patients were suspected as potentially infectious and they were managed with full PPE.

As surgeons and other HCWs of the department are at high risk of being infected and limited supply of PPE and N95 masks in our institution, we judiciously used them according to risk level.

1. For daily rounds and activities at surgical wards with asymptomatic, RT-PCR negative patients; we strictly took primary protection with disposable surgical mask, cap, latex gloves and surgical gowns.
2. Full PPE with N95 mask was required for airway care, collecting airway samples or intubation of trachea and Ryle's tube introduction.
3. The transitional area where waiting for results of RT-PCR reports, all activities were done with full PPE.

Emergency Surgeries :

1. We admitted all kinds of critical and trauma patients who need emergent surgical care even they might have so called COVID symptoms and signs; we managed them with full PPE and did immediate surgical interventions, if needed. During this pandemic, need for emergency surgery should be considered as a priority for admission.
2. All patients who needed emergency surgery had to complete pharyngeal swab sampling before surgery (if possible), or it was done later. No routine X-ray or CT scan of chest was done. Patients were placed in the transitional area; all HCW wore full PPE who would manage the emergency patients in the transitional wards, during transport and in theaters [10].
3. After the operation, the patients were returned to the original transitional ward. After the test results came negative, they were transferred to main wards.

Elective Surgeries :

1. The American College of Surgeons (ACS) advises to postpone nonurgent surgeries during the beginning of the pandemic of COVID-19. They have classified surgeries into various tiers according to the urgency of surgery. Up to Tier 2b (most elective surgeries like hernia), they are advising postponing of surgery. For Tier 3a and 3b, where most cancer surgeries will fall, ACS is not advising postponement at the moment though it may change[4].

According to guidelines from the Indian Council of Medical Research, all high-risk patients undergoing elective surgery should undergo RT-PCR test for COVID-19 before surgery[7].

2. No special measures were taken in our operating theaters as per literature:

Laminar air flow should be used, and air supply should be closed after operation. Peracetic acid air is used for fumigation. The operating theater should be cleaned and disinfected and high-efficiency filter changed. Cleansing should be done using detergent and water followed by use of with 1000 ppm bleach solution for all hard surfaces in the operating theater. The disinfection time should be longer than 30 min. The operating theater should be closed for at least 2 h, and the next operation should be performed after laminar flow and ventilation being turned on[10].

3. No special system was installed in our operating rooms for scheduled operations. We did not develop a dedicated COVID-19 operating space. If any patient found to be positive after operation, we used to sterilize the area as usual; it happened in three of our cases after emergency surgical interventions.

4. We admit asymptomatic patients with no history of contact/ travel for elective surgeries in transitional area. When they were tested negative, they were shifted to main surgical wards and we treat them as normal patients as before. We had not followed tertiary protection measures for anesthesia and surgical procedures for elective procedures.

Postoperative Management :

Apart from standard postoperative care, we closely monitored their oxygen saturation and look for symptoms, suspicious for Covid-19. Patients who developed cough with fever after surgery, HRCT chest and repeat RT PCR test was performed and assessed accordingly.

Materials and Methods

• It was an institution based, retrospective observational study conducted in General Surgery department of Institute of Post Graduate Medical Education & Research, Kolkata.

• The records of our hospital were reviewed to retrieve the number of daily admissions, those requiring surgical management and those discharged home.

• Furthermore, all the records of surgical procedures performed during study period were reviewed.

• Surgical team members who acquired COVID-19 infections within 14 days of surgery was only included in the study.

Study Period :

• The period of study was 25th march,2020 (Beginning of 1st lockdown) to 31st August,2020(end of Unlock 3.0)

Aim of the Study :

• To studyTrends of cases during lockdown and Unlock period in Covid-19 pandemics and compare with the previous year data(2019).

• To study risk of exposure to Health Care worker while handling surgical Patients.

• Sharing experiences of the authors from the general surgical departments at tertiary care hospital during this virus pandemic and "Lockdown".

Results

	25.3-31.3.2020	1.4-30.4.2020	1.5-31.5.2020
Patients admitted (n)			
OPD	21	83	70
Emergency	25	85	69
Total	46	168	139
Elective Surgeries	**39**	**80**	**69**
Emergent Surgeries			
	05	67	40
Total surgeries	44	147	109

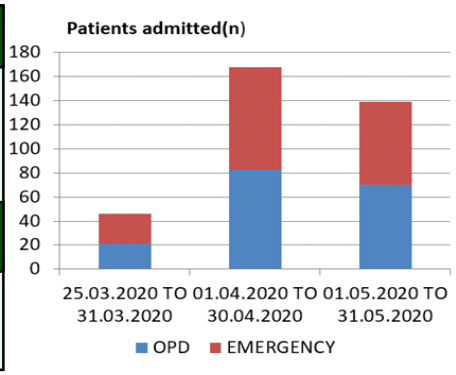


Table 2(A) : Details of operations performed during Lockdown (25.03.2020 – 31.05.2020)

	25.3-31.3.2019	1.4-30.4.2019	1.5-31.5.2019
Patients admitted (n)			
OPD	52	273	241
Emergency	46	125	167
Total	98	398	408
Elective Surgeries	**46**	**208**	**217**
Emergent Surgeries			
	32	102	122
Total surgeries	78	310	339

Table 2(B) : Details of Operation performed previous Year(2019)

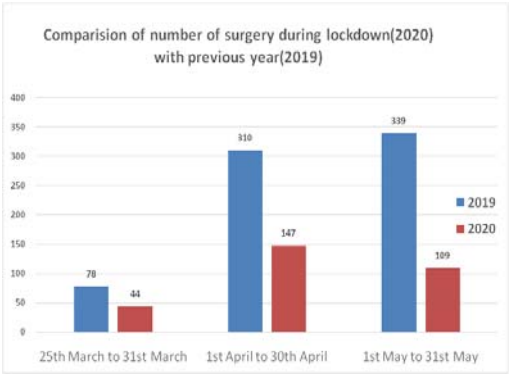


Table 3(A) : Details of operations performed during Unlock (01.06.2020 – 31.08.2020)

	1.6-30.6.2020	1.7-31.7.2020	1.8-31.8.2020
	Patients admitted (n)		
OPD	144	174	123
Emergency	82	80	154
Total	226	252	275
	Elective Surgeries		
	136	**179**	**169**
	Emergent Surgeries		
	49	69	67
Total surgeries	185	248	236

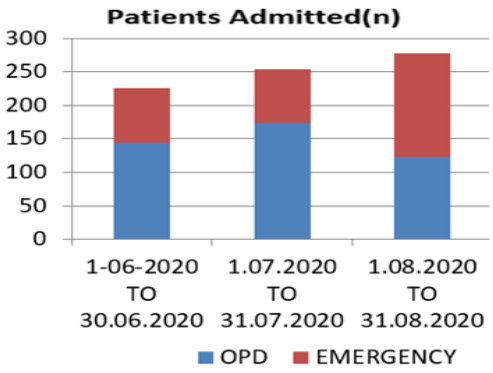


Table 3(B) : Details of Operation performed previous Year (2019)

	1.6-30.6.2019	1.7-31.7.2019	1.8-31.8.2019
	Patients admitted (n)		
OPD	245	275	253
Emergency	126	112	136
Total	371	387	390
	Elective Surgeries		
	214	**252**	**225**
	Emergent Surgeries		
	109	103	119
Total surgeries	323	355	344

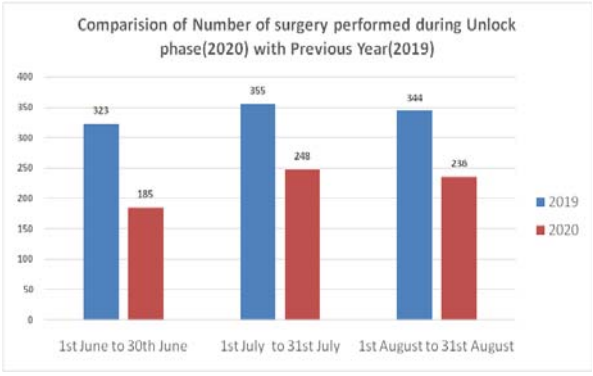
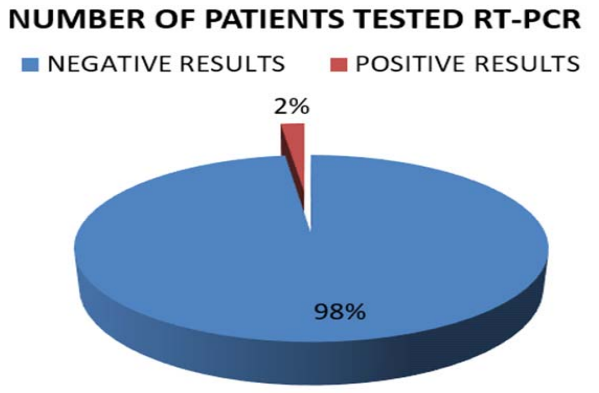


Table 4 : (From 25 March to 31 August, 2020)

Total patients admitted	No of patients tested RT-PCR	Positive results	Percentage
896	892	18	~2%



Discussion

Most of the recommendations have advised postponement of non-essential elective surgery. Most of the recommendations are based on case series of trivial numbers, case reports based on personal accounts or adept opinions[2].

We were facing a very critical times during pandemic and avoiding elective surgeries not only increased the tremendous future load, but it also increased the morbidity and mortality of the sufferers due to non-COVID ailments.

In India estimated 505,936 non-emergency surgeries, 51,100 cancer surgeries, and 27,700 obstetric surgeries could have been delayed across India during the twelve-week (48728 total elective surgeries per week) period before and after the peak of the viral outbreak. Worldwide data best estimated to be 28404603 operations would be cancelled or postponed during the peak 12 weeks of disruption due to COVID 19 pandemic (2367050 operations per week)[11].

Moreover, the impact on surgical training during these unprecedented times: the cancellation of elective surgery will adversely impact on training opportunities, particularly for elective workload[12].

We observed that during the total Lockdown days, the numbers of patients (both elective as well as emergency;) attending our hospital were very less as compared with pre-pandemic times (Table 2). This might be of fewer access to transport and fear of getting COVID-19 infection.

Everywhere in the world except in few countries, elective surgeries were avoided assuming that COVID-19 respiratory complications might occur postoperatively, viral transmission risk intraoperatively especially with laparoscopic surgeries. In our experiences, this was unjustified and irrational. We agree that some asymptomatic COVID patients are there and if proper precautions and right use of PPE is maintained the risk of transmission from hospital is very much avoidable (Table 4).

Recommendations also suggest to avoid laparoscopic surgeries and surgeries of long durations. Out of six hundred and seventy-two elective surgeries in our series, we have done more than hundred cases of laparoscopic surgeries and long duration operations like Whipple procedures, total thyroidectomy with bilateral neck dissections D2 gastrectomies. We did not feel that it increases

the risk of transmission of COVID as no postoperative elective case was positive in our series. We acknowledged that in the beginning of pandemic and Lockdown, we also avoided laparoscopic surgeries and surgeries of long hours; but from May, 2020 onwards we were doing all kind surgeries.

During the period from March 25 to August 31, 2020 (Data analyzed), we have tested (RT-PCR) eight hundred and ninety-two admitted patients, out of them eighteen came positive (~ 2%): three patients were admitted in emergency basis, rest were for elective surgeries. Except one surgical resident, no HCW of our department was COVID positive during this period (Table 4). That unfortunate event had occurred during a lifesaving resuscitation procedure of a trauma patient, who later tested RT-PCR positive. The resident, in hurry got no time to wear PPE as he remembered.

Conclusion

From our experiences and data collected during the said period, we came into conclusion that in no way elective surgeries should be avoided. It will ensure the best care for the non-COVID surgical patients, helps to ease future load and save many lives from denial death.

The percentage of COVID positivity in asymptomatic surgical patients is around two percent. If we maintain simple precautions carefully and properly, then elective surgical services can easily run without special equipment and theaters.

The running of elective surgical services also has a good impact on surgical training and education. The segregation of emergency and elective surgical care helps to protect training for surgeons.

If COVID-19 is likely to become endemic, all the current surgical guidelines need to be revised critically with the focus of resuming all the surgeries. These new guidelines need to be evidence-based and should provide cost effective solutions for effectively preventing disease transmission and cross infection, without excessively escalating the cost of treatment.[13].

Acknowledgements

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Review Article

Hypokalaemic Periodic Paralysis — A Diagnostic and Therapeutic Challenge

Sarmishtha Mukhopadhyay[1], Abhijeet Sharan[2], Bhaskar Ghosh[3]

Hypokalemic periodic paralysis is characterized by episodic acute onset flaccid paresis associated with hypokalemia. Classically it is a hereditary disorder with autosomal dominant inheritance causing intracellular shift of serum potassium provoked by carbohydrate or sodium load, rest after execise or certain drugs. Apart from classical hypokalaemic periodic paralysis due to inherited channelopathy, several other causes of hypokalaemia due to intracellular shift of potassium, renal or gastrointestinal loss may lead to periodic paralysis. An in-depth knowledge, thorough history and appropriate investigations are needed for underlying aetiological disorder. In this review, various aetologies, clinical features and management of hypokalemic periodic paralysis have been described with particular focus to its aetiological diagnosis.

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Key words **: Familial hypokalemic periodic paralysis, Thyrotoxic periodic paralysis, Primary hyperaldosteronism, Barter's syndrome, Gitelman's syndrome.**

Periodic paralysis (PP) is a group of rare neuromuscular disorder characterized by episodic painless acute onset flaccid muscle paresis due to muscle channelopathies. PP is classified as hypokalemic periodic paralysis (HPP) when paretic episodes are associated with low serum potassium (K^+) level. Classically HPP is a hereditary disorder with autosomal dominant inheritance pattern known as familial hypokalemic periodic paralysis (FHPP), but various other congenital and acquired causes of hypokalemia may produce similar illness manifested by episodic muscle weakness of varying frequency and intensity.

Bouts of mild to severe muscle weakness may last for hours and even days. Typically, the weakness recovers when serum K^+normalizes. Despite complete reversibility hypokalemic periodic paralysis is a medical emergency as sometimes it may cause life threatening complications like cardiac arrhythmias and respiratory muscle paralysis.Prompt and accurate etiological diagnosis is mandatory to start early interventions and to prevent the devastating outcome.FHPP is indeed the commonest etiology, but several other secondary causes of hypokalaemia should also be considered as they can also cause episodic weakness.Normal serum K^+ level in between attacks is an important feature differentiating FHPP from secondary HPP.[1]

Editor's Comment :

- Hypokalemic periodic paralysis is characterized by episodic acute onset flaccid paresis associated with hypokalemia. Classically it is a hereditary disorder with autosomal dominant inheritance causing intracellular shift of serum potassium provoked by carbohydrate or sodium load, rest after exercise or certain drugs.
- Classical hypokalaemic periodic paralysis is due to inherited channelopathy in which voltage gated calcium or sodium channels are mutated leading to intracellular shift of potassium. Apart from that, there are several other causes of hypokalaemia due to intracellular shift, renal or gastrointestinal loss of potassium.
- Thyrotoxic periodic paralysis is the second most common cause of intracellular potassium shift leading to periodic paralysis next to familial hypokalaemic periodic paralysis.
- Renal loss of potassium leading to episodic paralysis include primary hyperaldosteronism, renal tubular acidosis, Bartter's syndrome, Gitelman's syndrome, Liddle's syndrome, licorice and toluene abuse.
- Thorough history and appropriate investigations are needed for diagnosing underlying aetiological disorder. Management is based on oral potassium chloride and intravenous potassium therapy is reserved only for patients with arrythmias or respiratory muscle paralysis. Specific treatment may be required for underlying disorder.

Aetiology : Hypokalemic periodic paralysis may be classified as :

(A) Intracellular K^+shift

1. Familial hypokalemic periodic paralysis (FHPP)
2. Thyrotoxic periodic paralysis (TPP)
3. Sporadic periodic paralysis (SPP)
4. Hypothyroid periodic paralysis (HyPP)
5. Hypernatremic hypokalemic paralysis (HHP)

(B) Renal K^+ loss

1. Primary hyperaldosteroism (PH)
2. Renal tubular acidosis (RTA)
3. Barter's syndrome (BS)
4. Gitelman's syndrome (GS)
5. Liddle's syndrome (LS)

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6. Licorice ingestion
7. Toluene abuse

C. Extra-renal K^+ loss

1. Gastroenteritis
2. Zollinger Ellison syndrome
3. Fistulas

History and epidemiology :

PP was first described in 1727 by Musgrave.[2] HPP being the commonest form of PP has been described all over the world as isolated case reports as well as case series.

In a study from Taiwan by Lin et al, 97 cases with hypokalemia (serum potassium level < 3.0 meq/L) and profound muscle weaknesswere studied.[3] It was a retrospective study in Asian males over a period of 10 years. In this study, only those patients were classified as HPP who had muscle paresis due to hypokalemia as a result of intracellular shift of potassium without any acid-base disorder.Based on this criterion, seventy three out of 97 patients had HPP of which 39 had TPP, 29 had SPP, 3 had HHP and 2 had FHPP. On the other hand, 24 patients had paresis associated with hypokalemia due to kaliuresis. All of them had acid base disorder either in the form of metabolic alkalosis (PH 6, BS or GS 6, diuretic induced 3) or hyperchloremic acidosis (distal RTA 6 and toluene abuse 3).

Several case series from different parts of India were reported which implicates that HPP is not that uncommon as it is thought, rather it is under-reported. Most of the studies were done over several years. Agarwal et al described 40 cases of HPP over a period of 23 years.[4] In another series 22 cases of HPP were reported over 30 years.[5] Relatively more number of patients have been observed in a short span of 6 years in a study from south India.[6] From 1995 to 2001, 31 patients presented with HPP of which 13 had RTA, 13 had PH, 2 had TPP, 2 had sporadic HPP and 1 had GS. A study from western Odisha reported 50 cases of HPP consisting of 11 TPP, 3 hypothyroid PP, 6 SPP, 1 hypernatremic hypokalemic PP, 3 FPP, 5 distal RTA, 4 GS, 4 unidentified and 13 due to non-renal potassium loss.[7] A prospective study from North-east India reported 30 cases in 3 years.[8] A study in north-east India reported 56 patients of HPP which included 27 SPP, 5 FHPP, 4 distal RTA (d RTA),4 GS, 3 TPP, 2 HyPP.[9]

The largest study so far observed is an observational study from Midnapore, West Bengal, where among 200 cases, 56 GS, 44 d RTA 40 BS, 38 HPP, 6 TPP, 4 diuretic induced, 4 PH, 2 LS and 6 undiagnosed cases were found.[10]In this study, FHPP was associated with more frequent and recurrent episodes of periodic paralysis in comparison to HPP secondary to other causes.Recovery time was also less in FHPP compared to others.

Studies show HPP is more prevalent in summer months from April to June with dip in winter months, particularly in eastern part of India. The cause behind it is unclear. Probably, dehydration and more consumption of sweetened drink precipitates the attack.[10]

(A) HPP due to intracellular K^+ shift : HPP due to intracellular K^+ shift is typically characterized by normal acid base balance and low urinary K^+ irrespective of aetiology.

(1) Familial hypokalemic periodic paralysis (FHPP) — It is the most common HPP with a prevalence of 1 in 100,000.[11]It has autosomal dominant inheritance with incomplete penetration in females. It is 3 to 4 times more common in males than in females.FHPP is a channelopathy in which voltage-gated ion channels (typically calcium or sodium) are mutated resulting in persistent depolarization of muscle cell in presence of low potassium leading to abnormal sarcolemmal excitation and weakness. Majority of FHPP is due to mutations in either the *CACNA1S* or *SCN4A* genes, encoding the ion channels CaV1.1 (skeletal muscle L-type Ca2+ channel) and NaV1.4 (skeletal muscle voltage gated Na+ channel) respectively.[12]

Attacks typically begin in late childhood or teenage with varying frequency and duration.They may be provoked by excessive carbohydrate or sodium load in diet, rest after exercise and exposure to drugs like insulin, β2 agonists and steroids which promote shift of potassium into cells. Weakness usually involves proximal more than distal muscles and legs more than arms. Sensory, bladder and bowel involvement are usually absent. There is gross hyporeflexia or areflexia. Bulbar muscle involvement is rare.Respiratory muscles are usually spared, but rarely they may be involved to cause fatal outcome. In between attacks neurologic examination are mostly normal.

ECG findings are consistent with hypokalemia including ST segment depression, decreased amplitude of T wave and increased amplitude of U wave. Cardiac arrhythmias, such as, supraventricular tachycardia, atrial fibrillation and rarely life-threatening ventricular fibrillation may also occur due to hypokalemia.

(2) Thyrotoxic periodic paralysis (TPP) — It is a rare but well-known complication of thyrotoxicosis in Asian population including Chinese, Japanese, Vietnamese, Filipinos and Koreans. The overall incidence of TPP in Chinese and Japanese population is 1.8% and 1.9% respectively whereas its incidence is largely unknown in the West.Although thyrotoxicosis is predominantly a disease of females, TPP occurs mostly in males with a male to female ratio ranging from 17:1 to 70:1. Incidence of TPP among non-Asian hyperthyroid population, Asian hyperthyroid population and Asian hyperthyroid males are 0.1to 0.2%, 2% and 8.7 to 13% respectively.In a recent Indian study, among 244 cases of thyrotoxicosis, 15 were diagnosed as TPP. These 15 patients (14 male and 1 female) had 32 episodes of TPP. The mean age was 32± 6.2 years. Overt thyrotoxicosis was present in all cases except 1 who had subclinical hyperthyroidism.13 out of 15 patients were diagnosed as Graves' disease and the remaining 2 were subacute thyroiditis and gestational thyrotoxicosis.[13]

Unlike FHPP which occurs in younger age group (usually <20 years) and has autosomal dominant inheritance, TPP occurs at relatively later age (20-40 years) with sporadic occurrence. Pathology is not well understood but it may be due to over activation of Na^+/K^+ ATPase pump on skeletal muscle membrane due to excess thyroid hormones.Enhanced tissue responsiveness to beta

adrenergic stimulation caused by excess thyroid hormone further increases Na^+/K^+ ATPase activity.[14] In addition to enhanced adrenergic response patients having TPP have exaggerated insulin response to carbohydrate load in comparison to thyrotoxicosis patients without TPP. Insulin response sequences are present in the upstream region of Na^+/K^+ ATPase gene thus playing permissive role for intracellular K^+ shift. Often it is associated with single nucleotide polymorphism of $Ca_v1.1$ (-476A3→ G, intron 2 nt 57G→ A, intron26 nt 67A→G). Mild to moderate hypophosphatamia and mild hypomagnesaemia may accompany hypokalaemia which are due to intracellular shift of phosphate and magnesium respectively and need no separate replacement therapy. Respiratory muscles are seldom involved but total paralysis of respiratory, bulbar, and ocular muscles have been reported in a severe attack.

(3) Sporadic periodic paralysis (SPP) — It is the second common cause of HPP in Asia and has a presentation very similar to FPP but there is no family history. Few of them have same genetic mutation as FPP (*CACNA1S and SCN4A*), but most of the do not have de novo mutation. In the study from Western Odisha, out of 50 HPP patients, 6 were SPP, all of them being male. The number of SPP in this study is double the number of FPP.[7] Similarly, in the study from North East India, the number of SPP patients outnumbered FPP (SPP 27, FPP 5) out of total 56 HPP patients.[2] In Taiwan study also, out of 97 patients, 29 had SPP whereas only 2 had FPP.[3] In another Taiwan study out of 60 SPP patients, only 4 had *CACNA1S and SCN4A* mutation. SPP patients with de novo mutation usually manifest phenotype similar to FPP but with later age of onset. SPP patients without mutation also have later age of onset, but fewer attacks and lack of definite precipitating factor.[15]

(4) Hypothyroid periodic paralysis (HyPP) — It is much less common than TPP although few cases and case series have been reported. In studies from Odisha and North eastIndia, the number of HyPP are 3 and 2 respectively. In one case report, it has been postulated that hypokalemia is developed during early period of thyroxine replacement. Thyroxine in pharmacological doses can cause increased potassium excretion and water diuresis in patients with myxedema, particularly in background of malnutrition and low total potassium store in body.[16]

(5) Hypernatremichypokalemic periodic paralysis (HHP) —In Taiwan study, one unique group of patients were found, 3 out of total 97 HPP, all male, who had severe degree of hypernatremia (plasma sodium concentration 167± 5.0 mmol/L)accompanying HPP.[3] Two of them had brain tumour and one had tuberculosis with involvement of hypothalamus.Exact cause of hypokalemia in these patients are not known. Hypothalamus is an area which controls osmoregulation including thirst as well as adrenergic activity. It has been speculated that involvement of this area of brain due to some infiltrative disease or tumour impair thirst and lead to hypernatremia. It also results in hypokalemia via hyperadrenergic state which activate Na^+ K^+ ATPase activity causing transcellular shift of K+ into cell. In addition, hypernatremia has been implicated to some extent for muscle paresis.

HPP due to renal K^+ loss — HPP due to renal K+ loss is always associated with acid base disorder, either metabolic alkalosis (PH, BS, GS, LS, diuretics and licorice ingestion) or hyperchloremic metabolic acidosis (RTA, toluene abuse).

Primary hyperaldosteronism (PH) — It is also called Conn's syndrome and is characterized by overproduction of mineralocorticoid hormone aldosterone by adrenal gland.Two most common causes of Conn's syndrome is adrenal adenoma and bilateral adrenal hyperplasia followed by adrenal carcinoma and glucocorticoid remediable aldosteroism. Plasma aldosterone is not only elevated, but also non-suppresible along with suppressed plasma renin activity. Excess aldosterone causes sodium and water retention in the body and excess potassium excretion through the kidney, leading to arterial hypertension and hypokalemia.Periodic paralysis due to Conn's syndrome is relatively rare. In studies from Taiwan, north-east India,Odisha and Midnapore, the number of PH cases were 6 out of 97, 1 out of 56, 0 out of 50 and 4 out of 200 respectively showing the rarity of the entity.[3,4,8,11]

Renal tubular acidosis (RTA) — It is metabolic disorder with evidence of hypercholremic acidosis that occurs in a patient of nonazotemic renal acidification defect. Two major type of RTA are proximal RTA (pRTA) and distal RTA (dRTA). pRTA is characterized by large excretion of bicarbonate in urine that leads of hyperchloremic metabolic acidosis and alkaline urine. There is proximal absorption defect that leads aminoaciduria, phosphaturia and glycosuria. dRTA is characterized by defect of distal nephron in its ability to excrete hydrogen ion primarily due to decreased H-ATPase activity.[17] It is characterized by hypokalemia, hypercalciuria, nephrocalcinosis, and/or nephrolithiasis. Principle finding that leads to strong suspicion of RTA is metabolic acidosis, normal blood urea nitrogen level and normal GFR, alkaline or neutral urine(pH > 5.9) and inability to acidify urine below pH 5.5 after ammonium chloride load along with typical electrolyte abnormality (hyperchloraemia, hypokalaemia and hypocalcaemia) with normal anion gap. HPP is more common in patients with dRTA, mostly reported in patients with primary or secondary Sjogren's syndrome The pathophysiology of RTA in Sjogren's syndrome is debated in literature. The most common histological renal lesion is interstitial nephritis, but it is unclear whether the renal tubular defects are direct results of interstitial inflammatory process or not. The cause of renal tubular defect may be lymphocytic and plasma call infiltrate surrounding renal tubule. Hypergammaglobulinaemia may also be the cause of renal tubular dysfunction.[18] HPP due to pRTA is very rare. One case of HPP has been reported due to pRTAassociated with membranoproliferative glomerulonephritis. Till now, 16 cases of RTA with respiratory paralysis have been reported.[19]

Bartter's syndrome (BS) — It is a rare disease (1 in 1,000,000)which result from mutation affecting transport protein in the thick ascending loop of Henle (NKCC2, ROMK,C1C-KB).[20,21] It most often presents in neonatal period or early childhood with polyuria, polydipsia, salt craving and growth retardation. It is a

hereditary condition transmitted as either autosomal recessive disorder (Bartter 1 to 4) or autosomal dominant disorder (Bartter 5). Metabolic abnormalities include hypokalemia, hypochloremic metabolic alkalosis, hypercalcuria with nephrocalcinosisand mild hypomagnesemia, hyperprostaglandinaemia E and increased urinary prostaglandin excretion. Hypokalemic periodic paralysis may occur in Bartter syndrome, but it is rare. In Odisha and North east Asia series single case of BS was not found.[8,10]In Taiwan series BS and GS were mentioned in single group and there were 6 such cases.[4] BS constituted the second largest group of HPP in Midnapore study next to GS although mutation analysis was not done.[11]

Gitelman's syndrome (GS) — It is another salt-losing tubulopathy due to mutations in thiazide sensitive Na-Cl co-transporter. It is more common than Bartter's syndrome (1 in 40,000) with milder clinical course and late age of presentation. In contrast to Bartter's syndrome, Gitelman syndrome is a molecularly homogenous disorder caused by loss of function mutation in SLC12A3 gene.[22] It is distinguished from most forms of Bartter's syndrome by the presence of severe form of hypomagnesemia and hypocalciuria.[22] Hypokalaemia and metabolic alkalosis are common to both. Usual presentation of this rare syndrome is tetany or hypokalaemic periodic paralysis. In Odisha series 4 out of 50 HPP cases were GS, all of them were males. One important clue to the etiological diagnosis was definitely tetany as it was present in all 4 cases. The possible cause of tetany was metabolic alkalosis and consequent low plasma calcium in presence of hypomagnesaemia.[7] 56 among 200 cases were diagnosed as GS in Midnapore study, highest amongst all causes and distinctly larger number than any other studies.[10] But confirmation of diagnosis by mutation analysis have not been done in most of the studies.

Liddle's syndrome (LS) — It is a rare autosomaldominant form of salt-sensitive hypertensiondue to activating mutation of epithelial sodium chanel(ENaC) of distal nephron. ENaC complex is composed of 3 subunits (α, β & γ) each encoded by specific gene (*SCNN1A, SCNN1B & SCNN1G*) and consisting of 2 trasmembrane regions, 1 large extracellular domain and cytoplasmic carboxyl amino acid termini. The majority of causative mutation alter or delete a proline-rich segment (PY motif) in the carboxyl cytoplasmic tail of žorãsubunit, responsible for negative regulation of the channel resulting into its overactivation.[23] They usually present with hypertension, hypokalemia and metabolic acidosis but with low level of renin and aldosterone level. Hypokalemic periodic paralysis is rarely reported in Liddle's syndrome although myopathy is more common**.**

Licorice ingestion — Licorice induced hypokalaemia is a rare disorder first described by Revers in 1946.It is a plant product consumed as candy, French alcoholic beverages *boisson de coco***,** chewing tobacco, chewing gum,some oriental herbal preparations and some medications like *p*-aminosalisylic acid and carbonexolone sodium. The active ingradient of licorice glycyrrhizic acid causes hypokalaemia by inhibition of renal enzyme 11β hydroxysteroid dehydrogenase which is responsible for local conversion of cortisol to locally inactive cortisone.This leads to activation of renal mineralocorticoid receptors by cortisol resulting in a state of apparent mineralocorticoid excess.[24] It is a reversible condition usually recovering within days but sometimes may be sustained for several weeks according to amount consumed and individual susceptibility.Regular dailyitake of 100 mg glycyrrhizic acid produces adverse effect in susceptible individual whereas more than 400 mgper day of same causes hypokalemia with hypertension in most patients. Increased salt intake potentiate the adverse effect of glycyrrhizic acid. Critical cases with periodic paralysis, rhabdomyolysis and ventricular fibrillation leding to death have been reported.

Toluene abuse — Toluene is the most widely abused inhaled volatile drug mostly present in industrial solvent. Its deliberate inhalation due to recreational purpose known as glue sniffing is not uncommon. Chronic Toluene abuse may cause distal RTA, Fanconi's syndrome, nephrolithiasis, glomerulonephritis and Goodpasteur's syndrome. Toluene interferes with the hydrogen ion gradient in distal renal tubules either due to structural damage or inhibition of intracellular process. More precisely metabolic acidosis is caused by high rate of production of organic acids like hippuric acid and benzoic acid, the metabolites of Toluene.[25] The exact cause of hypokalemia is not known. One of the possible explanations are mineralocorticoid excess due to volume contration as a result of increased osmotic load of Hippurate and increased urine flow. Another possible mechanism iskaleuresis due to presence of poorly reabsorbed anions and low urinary chloride concentrations. Periodic paralysis may be apresentation of chrinc toluene abuse. Commonest presentation of acute toluene intoxication is also hypokalemic periodic paralysis.It is not that uncommon as it was thought previously and has high mortality rate.

HPP due to Extra-renal K^+ Loss :

This is not an uncommon entity. In western Odissa series 13 cases out of 50 were due to extra-renal K^+loss which consisted of 4diarrhoea, 5 vomiting and 4 excessive sweating.In North East India series, 2 patients had post-gastroenteritis HPP.

Approach to a Patient with HPP :

As soon as hypokalemia is detected in a patient with acute onset flaccid paresis, an attempt for etiological diagnosis is always needed by careful history and examination. The following history is helpful to diagnose the cause:

- History of similar attack before
- Family history of similar attack
- Provocating factors- heavy carbohydrate or salt load, execise followed by rest, recent stress
- History of young onset hypertension
- History of thyroid disorder
- History of recent diarrhea, vomiting, exceesive sweating
- History of offending drug- insulin, ž2 agonist, steroid, diuretics

- History of addiction or abuse- licorice, toluene
- History of nephrocalcinosis
- History of tetany

Investigations :

- Serum electrolytes- to establish hypokalemia
- ECG- to corroborate hypokalemic changes
- 24 hours urinary potassium: > 15 mmol/day is suggestive of renal loss of K^+
- Transtubular potassium gradient (TTKG): TTKG=(urine K/ plasma K) x (plasma osmolality/ urine osmolality)> 4 is suggestive of renal loss of K^+
- Arterial blood gas analysis(ABG)

- Normal acid-base balance
- HPP due to intracellular shift

Metabolic acidisis- RTA, toluene abuse

Metabolic alkalosis- PH, BS, GS, LS, diuretics, licorice

- Thyroid function test- to rule out or establish diagnosis TPP
- Plasma aldosterone/renin raio- to rule out or establish diagnosis of PH in hypertensives
- Serum calcium- hypocalcaemia in RTA, BS
- Serum magnesium- hypomagnesaemia in GS
- 24 hours urinary calcium- hypercalciuria in BS, hypocalciuria in GS
- 24 hours urinary magnesium-hypermagnesuria in GS, occasionally in BS
- Genetic tests- for FHPP, BS, GS, LS, RTA

Management :

Management consideration in hypokaaemic periodic paralysis include accurate diagnosis, proper dosage of potassium supplement in acute attacks, correct choice of diuretic for prophylaxis, maintenance therapy and identification of triggering factors. Oral potassium chloride supplementation is the preferred method of replacement. 1500 mg of potassium chloride (powder or tablet) is equivalent to 20 meq of potassium. 40-60 meq of potassium raises plasma potassium concentration by 1 to 1.5 meq/l and 135 to 160 meq of it raises the level by 2.5 to 3.5 meq/l. A suggested protocolis potassium chloride 30 meq orally every 30 minutes until serum potassium normalizes.[26]

Intravenous potassium is to be avoided whenever possible except for arrhythmias, airway compromise due to ictal dysphagia or accessory respiratory muscle paralysis. Mannitol should be used as solvent rather than dextrose or saline which are potential triggers of attacks. Caution should be taken not to use more than 10 meq at a time with a time gap of 20 to 60 minutes to avoid overshoot hyperkalaemia.[26]

Rare patients with respiratory muscle involvement need assisted ventilatory support.

For maintenance therapy, a potassium sparing diuretic is usually favoured. Commonly used aldosterone antagonists are spironolactone (100 mg daily) and eplerenone, the latter having less incidence of gynaecomastia.[26] Carbonic anhydrase inhibitor (acetazolamide 250 mg twice daily) is a suitable alternative and sometimes combination of the two is effective.[38] The patients should be counselled for avoidance of triggering factors.

Thyrotoxic periodic paralysis also requires potassium replacement, but along with that definitive therapy for thyrotoxicosis (antithyroid drugs/ radio-iodine therapy / surgery) is mandatory. Non-selective b-blocker propranolol has been reported to help in some cases.[27] Definitive therapy in Conn's syndrome is surgery for aldosterone producing adenoma and aldosterone antagonist for bilateral adrenal hyperplasia. Renal tubular acidosis is treated by potassium citrate or bicarbonate to combat hypokalaemia and metabolic acidosis at the same time. Bartter syndrome is treated with prostaglandin synthetase inhibitor indomethacin as an adjunct to potassium replacement.[28]Gitelmansyndrme primarily needs lifelong magnesium replacement and may need potassium replacement also if hypokalaemia remains uncorrected.

Limitations :

The article reviews mainly the large studies of recent past in India and other countries. The ongoing review may add some other studies in future which may contribute to better understanding and management of hypokalaemic periodic paralysis.

Conclusion

Management of HPP is really a diagnostic and therapeutic challenge. Early establishment of diagnosis and exclusion of secondary causes is important because once it is diagnosed and managed properly, it is not only fully reversible, but also helps toprevent further attack. Further long term prospective studies are needed in future to look for the efficacy of maintainance therapy.

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Case Report

Mesh Migration into the Urinary Bladder with Calculi Formation and a Vesico-cutaneous Fistula after Inguinal Hernia repair — A Rare Case Report

Rajeshkumar Parshuram Shrivastava[1], Jigar Ramesh Desai[2], Samir Bagasrawala[3]

Inguinal hernias are the most common type of hernia. Inguinal hernia repair is a widely performed surgical procedure. A tensionless repair with meshplasty is usually employed in the treatment of these hernias with good outcomes worldwide. The use of a polypropylene mesh has reduced recurrence rates to less than 2%. 2 Complications with mesh repair include infection of mesh, sinus tract formation, abscess, visceral adhesions, and fistulas. Mesh migration into the Urinary Bladder along with calculi formation following Inguinal hernia repair is an uncommon complication. Here we report the rare occurrence of mesh migration into the urinary bladder following inguinal herniaplasty along with bladder calculi formation and a vesico-cutaneous fistula.

[*J Indian Med Assoc* 2021; **119(3):** 42-3]

Key words **: Mesh Migration, Urinary Bladder Calculi, Inguinal Hernia.**

Inguinal hernias are the most common type of hernia. Inguinal hernia repair is a widely performed surgical procedure.A tensionless repair with meshplasty is usually employed in the treatment of these hernias with good outcomes worldwide.[1,2] The use of a polypropylene mesh has reduced recurrence rates to less than 2 %.[2] Complications with mesh repair include infection of mesh, sinus tract formation, abscess, visceral adhesions, and fistulas.[3] Mesh migration into the Urinary Bladder along with calculi formation following Inguinal hernia repair is an uncommon complication.[4] Here we report the rare occurrence of mesh migration into the urinary bladder following inguinal herniaplasty along with bladder calculi formation and a vesico-cutaneous fistula.

Case Report

We present the case of a 55 year old, gentleman, who presented with a discharging sinus over the suprapubic region since 6 months. There were associated symptoms of urgency of micturation, hematuria and suprapubic burning sensation since one month that had recently aggravated his condition. Abdominal examination was greatly unremarkable, save for a discharging sinus being present in the suprapubic region along with a "thread like" foreign body emanating from the discharging sinus. There was a background history of a right inguinal hernia repair being done in 2011 which was followed by suprapubic cystolithotomy being done for multiple badder calculi in 2013.

Ultrasonological examination was suggestive of an irregular urinary bladder wall with increased thickness of 10 mm along with 3.8 cm vesicle calculus. There was evidence of 13mm x 10mm and 12mm x 9mm sized mixed echogenic lesion in the right iliac fossa which was suggestive of a stitch granuloma. Bilateral Enlarged inguinal lymph nodes were also noted.

Surgical management was planned and a Pfannnenstiel incision was taken following which the fistulous tract was traced upto the bladder. The fistulous tract contained the prolene Mesh which was traced upto the bladder. On entering the bladder a complex mass of a large calculus with an entangled mesh was encountered. The bladder calculus and mesh were excised and the bladder was repaired. The post operative recovery was uneventful (Figs 1-5).

Editor's Comment :

- **Mesh erosion and migration is a rare complication that can occur following Inguinal hernia repair with meshplasty.**
- **A high degree of suspicion is required in patients that present following inguinal hernia repair with urinary tract symptoms.**
- **A thorough Examination and Investigative evaluation aid in formulating a diagnosis as well as an early intervention reduces the morbidity of the patient.**

Discussion

Mesh migration after Inguinal Hernia repair with meshplasty is unpredictable and not well elucidated. The complications related to hernia mesh repair include infections, contractions, rejections, and, rarely mesh migration.[5] Mesh migration can occur as an early or late complication after hernioplasty. Although, mesh migration into the urinary bladder is the most commonly reported mesh migration in the literature it is still an extremely rare phenomenon.[6]

There are various theories postulated regarding mesh migration and erosion where the sharp edges of the mesh may injure the viscera and induces inflammatory response which causes erosion,[7]and primary mesh migrations caused by inadequate fixation of the mesh along with secondary migrations which are due to the slow and gradual movement induced by foreign body reactions.[5]The Secondary migrations appear to be more befitting our case considering the late migration that has occurred in our case.

Patients presenting with mesh migration after hernia repair may present with hematuria, recurrent urinary tract infections, bladder stones or a vesico-cutaneous fistula. Management of such patients include a thorough History and examination which should direct the suspect towards a diagnosis for mesh migration. Radialogical Investigstions aid in the diagnosis. Urine routine and microscopy with culture would show evidence of a urinary

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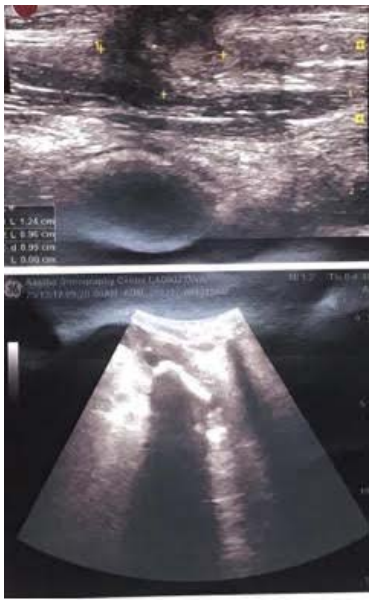
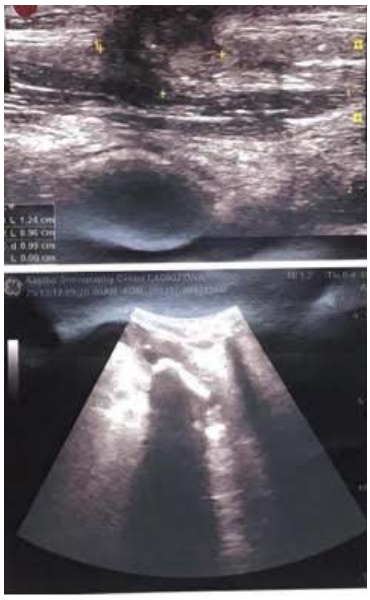


Fig 1



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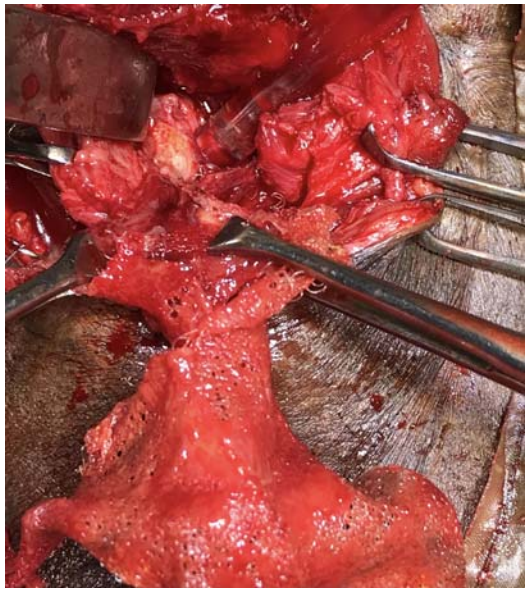

Fig 3

tract infection. Cystoscopic examinations would be able to directly visualise the eroded mesh.[8] Long-term foreign body stimulation may lead to malignant change of the bladder mucosa, thus making it necessary to exclude bladder tumour, particularly in long standing cases of mesh extrusion and migration.[9,10]

Surgical management of the patient could include either an open approach or a Laparoscopic approach for excision of the foreign body along with any calculi that may have formed along with badder closure. Periurethral extraction of the mesh has also been described.[5,7,9]In our case we chose an open method for excision of the mesh and bladder stone along with excision of the vesico-cutaneous fistula.

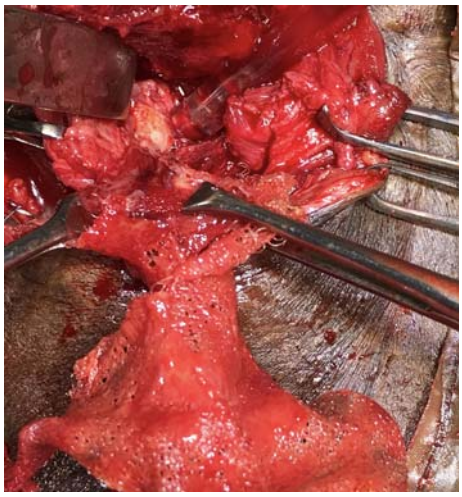

Fig 4

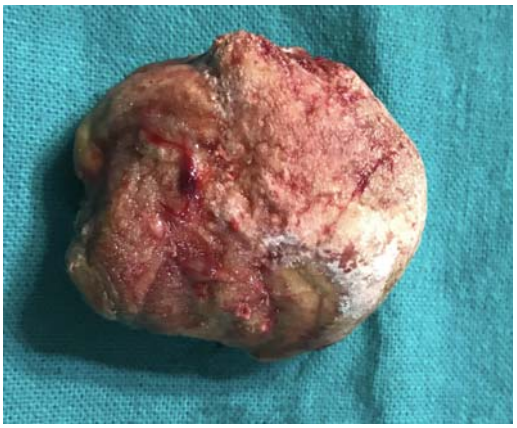

Fig 5

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Voice of the Expert

Participation of Private Sector in COVID-19 vaccination

Almost after 100 years World is facing Pandemic. Already 117 million people infected and 2.6 million died worldwide. But this is tip of iceberg. India is vulnerable having 139 crore population , highly congested living condition, overcrowded transport , vast migrant labour and but accepted the challenge.

To rid over pandemic development of herd Immunity must. Herd immunity can develop by natural infection or by Vaccination. To wait to develop Herd Immunity by natural immunity is costly , as it will take many lives. So mass Vaccination should be the real answer.

Govt of India successfully launched vaccination programme. First the Health care workers, then Frontline workers , now people aged more than 60 years and between age 45 -59 having comorbidities. But this is a huge task.

The Government of India plans to vaccinate 300 million Indians by August 2021. This ambitious initial goal to distribute the COVID-19 vaccine comes as more than 10 million people have been exposed to COVID-19, and more than 1,55,000 people have died after contracting the virus .

Today the government sector is able to vaccinate nearly 80 lac persons in a month. At this rate it will take 10 years to vaccinate the entire 130 crore population.

Even to achieve herd immunity we need to vaccinate 70% of population which comes to 91 crore persons. Here lies the need of involvement of Private sector hand to hand with Govt sector to make it faster. In India the private health sector provides services to nearly 70% population.

In other vaccination drives egpolio,private sector has been actively participating. Like Childhood Immunization Programme, To make COVID vaccination program effective and successful in a vast country like India involvement of private sector is essential.

Dr Ravi Wankhedkar
Past National President, IMA
Treasurer, World Medical Association

Even the vaccine is developed by private sector firms can be sold privately as of now.

Serum institute has 10 crore doses lying idle with a production capacity of 10 crore per month.

In such a situation the policy of government trying to do everything and keeping all in its control is contradictory to what our Hon PM said in parliament about involving the robust private sector in all areas.

IMA has already written to PM & GOI it's willingness to help in vaccination drive.

Hence it is high time to actively engage the private health sector in vaccination drive to make mass vaccination timely and effective.

Dr Wankhedkar, thank you for the valuable insight into Vaccine Development of COVID-19.

Voice of the Expert

What Should be the Future of Medical Practice in India ?

How Medical Practice has Evolved in India in Last 5000 Years ?

Modern Medicine had progressed and had got out of the superstitions and established scientific basis, starting with Hippocrates and steadily progressed with countless pioneers. They all procured inspiration and tips from ancient systems of India, China, Persia and Greece. Slowly technological revolutions started coming in and started replacing clinical methods with laboratory techniques, and the people who wanted to sell technology, marketed them vigorously in such a way that, people and doctors were made to believe that use of technology alone is science. Or only those who used a modern technique, or used the most novel medicine, or investigations based on genes were considered modern, and others were slowly ignored and thrusted to the background.

As an outfall of this trend, organ based specialisation made the entry, and the quick fame, quick money, and support from all sources, especially from the business lobby, which happily pushed it forward, all made the doctors leave general practice and even general medicine. Slowly, the most needed family doctors, who would have worked for wellness and cost effective diagnosis and treatment, became unimportant in the eyes of the ignorant public. In countries like India this trend went to the extent of almost total elimination of family doctors, and a total disintegration of genuine scientific modern medicine.

Dr P K Sasidharan (PKS)
Professor of Medicine & Former HOD, Govt. Medical College, Kozhikode
Former Dean Faculty of Medicine, University of Calicut

This disintegration and over-dependence on technology rocketed the cost of Medicare sky-high, made modern medicine unpopular among a section of society, and gave ample opportunities for the quacks and alternative systems for a comeback. The only scientific alternative is to solve the problems in modern medicine, because it evolved from all the traditional systems. If that is the case, why should we go back to the dark age of superstitions and false beliefs.

We need to talk about integration in modern medicine, with policy changes to develop a strong base for medical practice with family doctors, referral system and avoid its disintegration by making doctors hesitate to identify themselves with one organ. Doctors are doctors only when you manage a person as a representee of the society, with all its problems ad priorities. A reoriented modern medical practice is the only alternative for the future.

Scientific research is the key for progress of modern medicine. As such there is no replacement of clinical examinations though technological revolutions and laboratory techniques help in delivering modern medicine.

What Changes we have Observed in Medical Practice before Independence and after Independence?

Before Independence it was very bad and still continuing like that in some places.

What are the Impact of Medical Practice in Post-liberalisation Era ?

It has gone from bad to worse.

Should India give Emphasis on Preventive Health or a Curative Health Care?

This question is very relevant because India is ignoring social health, wellness and all the social determinants of health and we are literally manufacturing diseases. With the result that we have ended up as the country with highest disease burden in the world. To address the heavy disease burden we focus on increasing the number of medical colleges and PG seats to bring out more single system specialist doctors, with the objective to make available treatment for all. That too with a health system which is largely controlled by private agencies and corporate bodies whose main objective was profit. The focus on treatment of diseases thus has become oriented towards tertiary care, when in fact India needs an army of trained family doctors working under government guidelines. Without adequate numbers of family doctors the treatment system anywhere in the world cannot sustain and it is bound to collapse. In India the AYUSH and even quackery is growing in the huge vacuum created by the missing of family doctors. Only the family doctors will have an outlook for blending curative services and preventive care that too working in a community setting living in close association with families and persons. They are certain to work for health and wellness, that too only if they are working under the government without any profit motives. But if family practice is also promoted in the corporate sector as it has already started, it will only be worse than the USA model which is still a NON-SYSTEM.

Abolishment of family doctors & overdependence on technology including organ based specialization is making healthcare inaccessible to a large section of population. Commercialisation of healthcare is another challenge.

What will be the Future Threat in India- Communicable or Non-communicable Disease ?

Future is very bleak in India if we continue like this. If we do not change, the human species itself would be wiped out in another 100-200 years and it would happen at a faster rate in India. When India is going ahead with double burden in diseases, other countries too are catching up with more non-communicable disease, which are increasing all over the world. India with highest number of people with poor nutrition, will be impacted more adversely by the consumerism and the consequent surge of non-communicable diseases. We have been witnessing early onset of all the non-communicable diseases like hypertension, diabetes, cancers and autoimmune disorders. The profit hungry consumerist lobby is still happily fishing in troubled waters. Strong health policy to be drafted by visionary social health workers is the need of the hour.

Growth of pharmaceutical companies definitely needed for economic health of the country but there is a perception that pharmaceutical growth have impacted medical practice negatively. Do you feel so? Pharmaceutical growth with the main objective of profit is the issue we need to rectify. This kind of growth is impacting medical practice as they are given an opportunity to influence the medical practitioners. Why do we allow them to manufacture lifesaving medicines in different brand names? Only the nutritional supplements and vitamin tablets be allowed to be manufactured in different names. Let us make all the pharma companies manufacture all essential lifesaving medicines in generic names only, rather than asking doctors to prescribe in the generic names

Research in India from government, non-government agencies and from pharmaceutical companies are not

optimistic. Also medical practitioners are reluctant to hold medical research in India. Do you feel there is a need for change in attitude and what are the steps that are needed to be taken for India to become a world leader in medical research in future? Research in medical profession is now done only for developing a new medicine or a new technique and always it has an eye on profit. Research in medical field is now guided on the lines of drug trials only and there is no true research on genuine issues that we face.

Availability of life-saving drugs to all people & integration in modern medicine is very much required. Government needs more focus on medical research.

Do you Feel Medical Practice should be Insurance based like USA?

NO- it should never be like USA at all, it is the worst model in the world, it is NON-SYSTEM. What India needs is universal insurance cover under the government controls as in Canada and the Scandinavian countries with the entire health system controlled directly by the government. Even if the hospitals are owned by private persons, we can evolve a system on the lines of these socialist countries. In USA 50 million people are unable to get treatments in spite of being the richest nation. The rich persons are not getting the best treatment in USA due to wrongs in the system. Every person should have equal rights in getting access to the social determinants of health and treatment facilities, that alone should come up and that alone will ensure sustainable health care.

Do you Feel there is a Need for Change in Medical Education Policy at Present which Mostly Concentrate on Individualistic and Technological Aspects of Modern Medicine ?

YES, very much- we need to change the MBBS curriculum with the main objective of bringing out large numbers of family doctors. Majority of the MBBS doctors (70-80%) should be made to choose family practice as a career option, not by pressure, but by incentives.

Thank you Dr P K Sasidharan (PKS) for your answers. We appreciate the time taken by you and we are sure that our readers will be benefited immensely.

Pictorial CME

Young Stroke of Indeterminate Cause

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

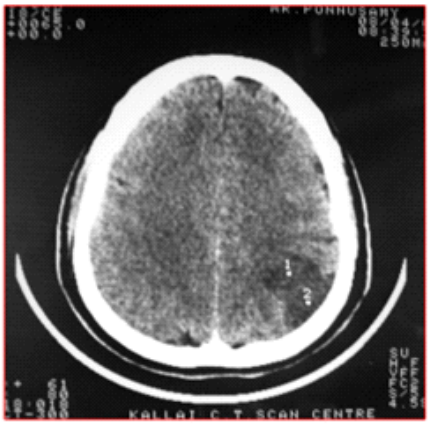
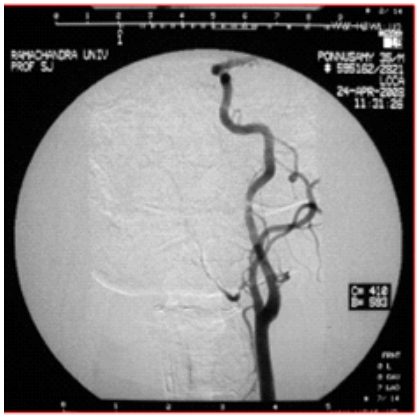
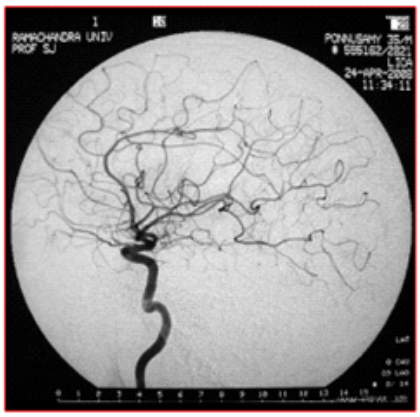


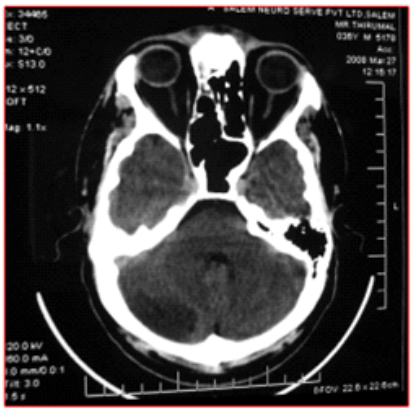
Fig 1 — CT brain showing left parieto occipital infarct

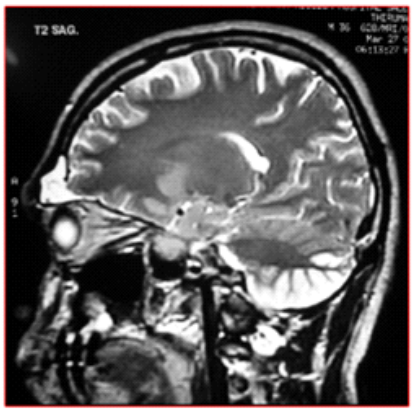




Figs 2 & 3 — DSA showing AP view of left CCA and lateral view of left ICA and its branches respectively

Stroke in young accounts for an increasingly large proportion of overall stroke cases. Thorough investigations do not reveal an etiology in 30% of cases. We report some cases of stroke in young with indeterminate cause after extensive investigations. Our aim is to highlight strokes of indeterminate cause fitting into a particular syndrome and to hypothesize about possible causes in them.





Figs 4 & 5 — CT and MRI brain revealing right PICA infarct

Case 1 — 35 yrs old smoker ,occasional alcoholic presented with features of dizziness and difficulty in seeing in lower half of visual field. MRI Brain showed left parietooccipital infarct (Figs 1, 2 & 3).

Case 2 — 38 yrs old smoker presented with giddiness .MRI Brain Imaging showed a right PICA infarct (Figs 4 & 5).

Case 3 — 28 yrs old male presented with vertigo and vomiting.MRI BRAIN showed right SCA infarct.After 15 days the patient developed left AICA infarct.

Investigations included evaluation for metabolic syndrome,vasculitis work up, prothrombotic state evaluation, VDRL, HIV, Hemogram,peripheral smear evaluation and relevant biochemical investigations, CT brain and MRI Brain with contrast,ECG,Trans esophageal echocardiography(TEE) and a arch + 4 vessel DSA.

Discussion

Stroke in young forms a significant proportion of stroke cases in

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a neurology practice. A significantly large number of these do not reveal any etiology inspite of extensive investigations. Smoking has been a common factor in these cases. We did detailed angiographic analysis of both intracranial and extracranial cerebral vessels trying to look for any atherothrombotic/stenotic pathology. This analysis did not yield any cause with the angiographies including arch aortography being normal. A detailed cardiac analysis including Transthoracic and Trans esophageal echocardiography did not reveal any potential causes of an embolic stroke. Biochemical investigations including evaluation for vasculitic and prothrombotic states were normal.

We present this series to focus attention on a unique syndrome of stroke. The features of this syndrome are

(1) Young males predominantly between 20 to 40 years of age.

(2) Predominantly smokers.

(3) Large anterior/posterior circulation infarcts suggesting involvement of prominent pial vessels.

(4) Clinical and imaging features ruling out lacunar syndromes.

(5) No evidence of any vascular pathology on detailed angiographic analysis.

(6) No evidence of any cardio embolic cause.

(7) All other investigations not suggestive of any particular cause.

A normal cerebral angiography in pial vessel infarcts suggests an embolic pathology, either arterio or cardioembolic.But in our patients,we were unable to find out an aetiology inspite of detailed cardiac and large vessel imaging. The only possible explanation that we can think of is a transient cardiac arrythmia,probably a transient atrial fibrillation,causing a clot to form and subsequently embolize. In none of our cases was there a history suggestive of syncope,palpitations,black outs or anything else to suspect an arrythmia. Neither did a rhythm strip ECG show any abnormality. 24 hour Holter monitoring was not done in our patients.

We present these cases and possible syndrome to generate discussion on possible etiologies, prognosis, cost effectiveness of investigations and management of this problem. In our opinion,such cases need a detailed cardiac electrophysiology studies. We also believe that cessation of smoking may prevent a recurrence as noted in our patients,though a long term follow up is needed. Prognosis of these patients and the need for antiplatelets/ anticoagulants etc need to be studied further.

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Case Discussion in Surgery

Acute Abdomen — Case Based Approach For Clinicians

Deborshi Sharma[1], Sanjay Meena[2], Gautam Anand[3]

Acute abdomen refers to the condition where patient experiences sudden onset severe abdominal pain lasting for ≤5 days. It is one of the most common complaints that drives patient to emergency (Approx. 4-5% of total casualty visits). Initial approach directed to rule out most emergency conditions by focused evaluation along with ongoing resuscitation to prevent fatalities is necessary. Ultrasound which is regarded as an extension of clinical examination is an invaluable investigation along with an Abdominal and Chest x-ray, all of which together and clinical examination provides the diagnosis in more than 90% cases. Operative cases need to be identified and conditions requiring conservative management, a further diagnostic / staging workup and management protocol can be followed afterward.

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Key Words : Acute abdomen, Cholecystitis, Pancreatitis, Appendicities, Peritonitis, Acute Intestinal obstruction.

Case Scenario 1 :

A 35 year old lady, presented in surgical emergency with complaints of pain abdomen associated with vomiting for the last 3 days. The pain was acute in onset, dull aching, moderate to severe intensity, radiating to back, it gets aggravated on lying supine and somewhat relieves on sitting and leaning forward. She also has complaints of nausea and multiple episodes of non-bilious, non-projectile, non-blood staining vomiting during the last 3 days. On examination she was conscious, co-operative and oriented. She was dehydrated having pulse rate of 108 beats per minutes and BP of 96/60 mm of Hg. On per abdominal examination guarding and rigidity was present along with rebound tenderness predominantly in central abdomen. Investigations revealed TC 18000 and Serum Amylase 1100 and Lipase 800 while her other blood parameters were normal. Plain abdomen x-ray revealed dilated bowel loop with colon cut-of sign. Ultrasonography showed multiple calculi in the gallbladder with normal biliary tract. A diagnosis of acute gallstone induced pancreatitis made and patient was managed with intravenous fluid, analgesics and antibiotic. She improved well and after a span of 1 month an elective laparoscopic cholecystectomy was performed,she had an uneventful post-operative period and was discharged on POD[1].

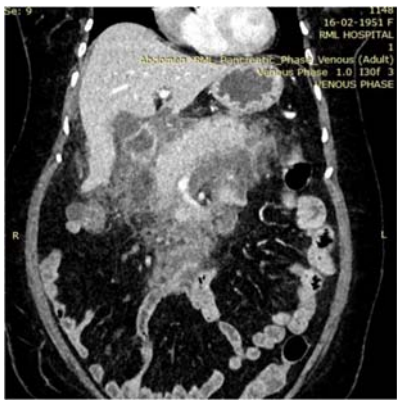

Fig 1 — Coronal Image of Oedematous pancreatitis

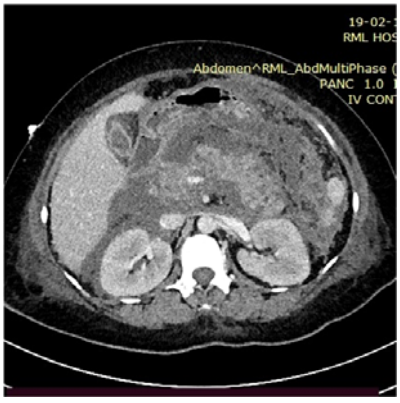

Fig 2 — Axial CECT image showing Haemorrhagic pancreatitis with necrosis

Case Scenario 2 :

A 22 years old gentleman, presented to emergency with complaints of pain abdomen for the last 2 days associated with fever and nausea. The pain was acute in onset, colicky character, moderated to severe intensity, initially in periumbilical region which migrated to right iliac fossa. The fever was high grade and associated with chills but not rigor, not associated with rash, body ache. He has no other significant history and no addictions. On examination patient looked anxious while hydration was adequate &had tachycardia (104/min) and BP of 106/70 mm of Hg. Total leucocyte count was raised 15000 with predominantly high neutrophil count. Other blood investigation were normal. Chest X-Ray and abdomen x-rays were grossly normal. Ultrasonography suggested features of acute appendicitis. Diagnosis of acute appendicitis was made and patient was taken for appendectomy after resuscitation and informed consent. Intraoperatively appendix was inflamed at tip and base was normal. Appendectomy was performed and patient shifted to ward. Post op was uneventful and discharged on POD[2] and sutures removed on POD[8].

History Taking in Acute Abdominal Pain:

Thorough and meticulous history is crucial to diagnose the causes of the overlying pathology. Age, sex, occupation, residence and social status should also be taken into consideration to appropriately localise the cause.

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Symptom Analysis for Acute Abdominal Pain :

Original site of pain — Ask patient to localise by fingertip the site of origin of pain, e.g., hepatitis, acute cholecystitis or pleurisy in the right upper quadrant, peptic ulcer disease or angina in epigastric region, pancreatitis in central abdomen, acute appendicitis periumbilical in origin but migrate to localise in right iliac fossa, diverticulitis in left lower quadrant, renal colic in flanks, cystitis or PID in supra pubic region etc.

Mode of onset — Sudden onset pain may indicate acute pancreatitis, acute appendicitis, rupture of aneurysm, perforation etc.

Character of Pain :

Colicky pain — Sharp intermitted gripping pain which comes suddenly and disappears suddenly often associated with vomiting and sweating, eg, ureteric colic, biliary colic, intestinal colic and appendicular colic.

Constant burning pain — Burning sensation eg, perforation, peptic ulcer disease.

Stabbing pain — Sudden, severe, sharp and short-lived pain eg, acute perforation of peptic ulcer.

Severe agonising pain — eg, acute pancreatitis or torsion

Throbbing pain — throbbing sensation eg, pyogenic abscesses.

Scalding pain — type of burning sensation felt particularly during micturition, eg, cystitis, acute pyelonephritis or urethritis.

Twisting pain — sensation of something twisting inside the body.e.g.,volvulus of intestine, torsion of testis or ovarian cyst.

Change in character of the pain — colicky become constant burning type may indicate strangulation. Pain may become less intense in spite of ongoing disease eg, 2nd stage of peptic perforation due to dilution of gastric contents by peritoneal exudate.

Effect of pressure on pain — colicky pain decreases while inflammatory pain aggravates.

Relation of the pain to jolting, walking, respiration and micturition — ureteric colic gets worse on jolting. Pain during act of micturition or 'strangury' may suggest ureteric colic, vesical calculi, pelvic appendicitis, pelvic abscess. In diaphragmatic pleurisy pain is aggravated during deep inspiration.

Radiating pain — extension to another site whilst the original site persists at its site eg, acute pancreatitis and duodenal ulcer penetrating posteriorly radiates back. This pain is of same character.

Referred pain — Pain felt at a distant site from its source while no pain at the site of disease. eg, irritation of diaphragm in cases of hepatitis, acute cholecystitis may cause referred pain at right shoulder tip.

Migrating or shifting pain — pain felt at one site at beginning and then shifted to another site with no pain at initial site e.g., acute appendicitis pain migrates from umbilical region to right iliac fossa.

Special time of occurrence — acute appendicitis on waking up in the morning, duodenal ulcer at 4 pm in the afternoon and in the early morning at about 2 to 3 a.m. 'hunger pain'.

Aggravating and relieving factors — hunger aggravates duodenal ulcer while food aggravates gastric ulcer, fatty meal aggravates acute cholecystitis. In peritonitis lying down still may reduce pain while rolling about aggravates the pain, forward leaning patient may get some relief in pancreatitis. Vomiting usually relieves peptic ulcer.

Vomiting :

Character — projectile ie, involuntary forceful ejection of a large quantity in high intestinal obstruction, toxic enteritis etc. In case of peritonitis non projectile is seen.

Vomitus — non bilious when obstruction is proximal to D2, bilious when obstruction is distal to D2, more distal obstruction may cause feculent vomiting

Frequency — multiple, profuse, constant in intestinal obstruction and acute pancreatitis. In appendicitis nausea is more prominent.

Relation with pain — pain precedes vomiting e.g., acute appendicitis, acute pancreatitis, peptic ulcer, biliary and renal colics. In high intestine obstruction pain appears almost with vomiting.

Bowel habits — absolute obstipation in intestinal obstruction. In children passage of mucus and blood per annum may suggest intussusception. Diarrhoea is seen in ulcerative colitis, ileitis&acute enteritis.

EXAMINATION :

Meticulous examination is of paramount importance to identify red flag signs and to localise the possible etiology and streamline the essential investigations.

General Physical Examination :

- Appearance: Often the patient with acute abdomen present with anxious look and dehydrated state with alter higher mental function. From local signs of dehydration to typical 'facies Hippocratica'(terminal stage of peritonitis) can be observed.
- In condition like acute pancreatitis patient may be in leaning forward position. In peritonitis patient may lie still avoiding movements or in renal colic placing hand over the flanks.
- Pallor may be present in haemorrhagic conditions like aortic aneurysm rupture, haemorrhagic pancreatitis, bleeding varices, peptic ulcer eroding vessels, ruptured ectopic gestation etc.
- Patient may be icteric in conditions like cholangitis, hepatitis, acute pancreatitis
- Febrile in cases of inflammatory conditions. (eg, liver abscess, lower lobe pneumonia, cholangitis)
- Tachycardia in cases of febrile illness, dehydrated state, haemorrhagic conditions.
- Tachypnoea with decreased abdominal movement and avoiding deep inspiration in cases of peritonitis. Also observed in chest pathologies.

Per Abdomen Examination :

Inspection :

Shape — Distension of abdomen is seen in acute intestinal obstruction (central in small bowel obstruction whereas peripheral in large bowel obstruction), ascites secondary to perforation, severe complicated pancreatitis, chronic liver disease etc.However,shape is normal in acute appendicitis, acute cholecystistis, renal or biliary colic.

Abdominal Movement with respiration — restricted /absent in diffuse peritonitis (perforation), haemorrhage into peritoneal cavity (ruptured ectopic gestation). Localised restriction of movement in cases of acute cholecystitis, liver abscess, appendicitis etc.

Umbilicus — everted in ascites, displaced from central position in cases of abdominal distension (supra pubic distension may cause umbilicus shifted upward)

Skin — visualised skin may have signs of inflammation like in abdominal wall cellulitis, abscess (parietal or intraabdominal seeping through abdominal wall). Discolouration in flanks (Grey Turner sign) or bluish hue around umbilicus(Cullen's sign) in cases of acute haemorrhagic pancreatitis

Dilated/engorged veins — portal hypertension or IVC thrombosis

Peristaltic movements — step ladder pattern in small bowel obstruction, from left to right over upper abdomen in cases of gastric outlet obstruction and opposite direction in colonic obstruction.

Hernial site with expansile cough impulse should be inspected

Palpation :

Temperature — Rise in local temperature in inflammatory conditions.

Hyperaesthesia — Cutaneous hypersensitivity in presence of underlying inflamed abdominal organ (e.g., sherren's triangle in case of acute appendicitis, Boas's sign in acute cholecystitis)

Tenderness — There may be localised tenderness (eg, just below the tip of 9th costal cartilage on lateral border of right rectus in acute cholecystitis, tenderness at 1 inch to the right of midline in transpyloric plane (duodenal point) in duodenal ulcer, right iliac fossa tenderness in acute appendicitis also on palpation on left iliac fossa tenderness can be elicited on right iliac fossa suggestive of acute appendicitis (Rovsing'sign) or generalised tenderness (eg, peritonitis, pancreatitis etc.)

Rigidity — Protective mechanism in parietal peritonitis, can be involuntary (underlying parietal peritonitis) and voluntary (guarding: abdominal muscle contraction by patient himself due to fear of being hurt). Board like rigidity in end stage of peritonitis.

Lump — Appendicular lump in appendicitis, sausage shaped lump in intussusception in epigastric or left lumbar region associated with empty right iliac fossa (Sign-de-dance), cold abscess, phlegmon, interstitial hernia.

All hernial sites should also be palpated.

Percussion :

Shifting dullness to look for presence of free fluid (Perforation, acute pancreatitis, ruptured ectopic gestation)

Fluid thrill large amount of fluid in abdominal cavity. Eg, Gross Ascites

Obliteration of liver dullness by resonant sound in cases of free gas under diaphragm (perforation).

Auscultation :

Silent abdomen in diffuse peritonitis whereas noisy abdomen in acute intestinal obstruction later become silent.

Digital rectal examination should be done in all cases (Red currant jelly in intussusception, fresh blood staining and clots in lower GI bleed, black colored foul smelling staining in upper GI bleed).

Vaginal examination in suspicion of PID.

INVESTIGATIONS :

Laboratory :

- **Complete hemogram**
  Anaemic in haemorrhagic conditions
  Leucocytosis indicates inflammatory conditions
  Platelets may be decreased in severe sepsis.
- Liver function test, kidney function test, Serum electrolytes
  Deranged ALT/AST in hepatitis
  Increased ALP with bilirubin level in biliary obstruction (eg, cholangitis, pancreatitis), hypocalcemia in pancreatitis
- Serum amylase / lipase
  Increased in acute pancreatitis (lipase is more specific)
- Arterial blood gas analysis to assess base excess, lactate level, saturation, metabolic abnormalities etc.
- Coagulation profile
- Tridot
- ESR/CRP as sepsis marker
- Urinalysis (dealing with urinary tract pathology)
- Urine Pregnancy Test (in reproductive age group of female)
- Serum glucose
- Trop-T (to rule out MI)

Radiologic Investigations :

- ECG (to rule out cardiac cause)
- Chest x-ray (pneumothorax, hydro/hemothorax, pneumohemothorax, pleural effusion, consolidation in basal pneumonia, raised hemidiaphragm in case of subphrenic abscess or liver abscess, free gas under right hemidiaphragm & as a work up for surgery)
- Abdomen x-ray erect and supine (dilated bowel loops, air fluid levels, colon cut-of sign, volvulus, calculi etc)
- Ultrasound abdomen (to look for free fluid in the peritoneal cavity (perforation, SBP, ascites), look for signs of cholecystitis, dilated biliary tract, pancreatitis, appendicitis, liver abscess, pyonephrosis.
- NCCT KUB (urinary tract calculi)
- CECT abdomen & pelvis in cases of diagnostic dilemma or complications.
- CECT angiography as diagnostic approach for uncontrolled bleeding (eg, Lower GI Bleed)
- Endoscopy: GI Bleed

Exploratory laparotomy in case of acute abdomen and patient not improving and diagnosis not confirmed.

Red flags for Abdominal Pain:

- Acute onset abdominal pain
- Hematemesis, hematochezia
- Jaundice

- Bilious / feculent vomiting
- Guarding/rigidity
- Rebound tenderness
- Absent bowel sounds
- Absolute constipation
- Gross abdominal distension
- Intolerance to feed
- Presence of other co-morbidities and old age
- Previous history of abdominal surgery

Management :

- Triage to rule out most emergency conditions, which require urgent intervention.
- ABCDE
- Intravenous fluid replacement and then maintenance
- Intravenous analgesics and antibiotics
- Ryles tubes placement to decompress the GI tract in cases of obstruction, recurrent vomiting, ileus, perforation, etc.
- Foley catheterization to monitor urine output.
- Vital charting and blood sugar charting as needed

Intervention as per the Disease Requirement :

Pigtail/needle aspiration — Liver abscess, localised collection (appendicular abscess, subphrenic abscess, splenic abscess, pyonephrosis etc.)

Conditions Requiring Emergency Surgeries :

Perforated peptic ulcer, typhoid perforation peritonitis, tuberculous perforation, acute complicated appendicitis, GB perforation, ishaemic bowel disease, irreducible/obstructed/strangulated hernias, ruptured liver abscess, torsion testes, complicated diverticulitis, acute intestinal obstruction, ruptured aortic aneurysm, etc.

Diffuse Pain Abdomen :

- Peritonitis
- Bowel ischemia
- Obstruction
- Pancreatitis
- Aortic aneurysm

RUQ Pain :

- Biliary: cholecystitis, cholangitis
- Colonic: colitis, diverticulitis
- Hepatic: abscess, hepatitis, mass
- Pulmonary: pneumonia
- Renal: calculi, pyelonephritis

Epigastric Pain :

- Cholecystitis, cholangitis
- MI, angina
- Gastritis, PUD
- Pancreatitis

LUQ Pain :

- Gastric: PUD, gastritis
- Cardiac: angina, MI
- Spleen: abscess, infection
- Renal: calculi, pyelonephritis
- Pancreas: pancreatitis
- Pulmonary: pneumonia

RLQ Pain :

- AppendicItis, Colitis, Diverticulitis, IBD, IBS
- Ectopic Pregnancy, Ovarian Cyst, Torsion, PID
- Nephrolithiasis, Pyelonephritis

Suprapubic Pain :

- Appendicitis
- Colitis, Diverticulitis, IBD, IBS
- Ectopic pregnancy, Ovarian cyst
- Cystitis, pyelonephritis

LLQ Pain :

- Diverticulitis, Colitis, IBD, IBS
- Ectopic pregnancy, ovarian cyst, torsion
- Nephrolithiasis, pyelonephritis

Ultrasonography :

- Cholecystitis, liver abscess, biliary tract calculi and dilatation, pancreatitis
- Intra-abdominal collection, splenic abscess, pyonephrosis, renal calculi,
- Acute appendicitis, appendicular lump, typhilitis, ovarian cyst and torsion, PID, testicular torsion
- Obstruction, hernial defect its content and vascularity, aortic aneurysm

Chest X-ray PA View & Abdominal X-ray (erect & supine) :

Thoracic causes : Opacities(pneumonia)
Abdominal causes :

- free gas under right hemidiaphragm (perforation),
- elevated hemidiaphragm (subphrenic abscess, liver abscess)
- Urinary tract calculi
- Colon cut of in pancreatitis
- Multiple air fluid level (intestinal obstruction)
- Coffee bean sign (sigmoid volvulus)
- Ground glass appearance (ascites)

Approach to Acute Abdomen :

- ABCDE
- History and examination
- Resuscitation: I/V fluids, analgesics, antibiotics
- Laboratory investigations: hemogram, LFT, KFT, Serum electrolytes, amylase, lipase, CRP/ESR, PT/INR, viral markers, UPT, HCG, Trop-T
- Electrocardiogram

In cases of diagnostic dilemma and complications, CECT (abdomen+pelvis) should be done provided Kidney functions are normal.

In certain situations of acute abdomen exploratory laparotomy may be required where investigations fails to delineate the cause.

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Special Correspondence

[We are publishing this Special Correspondence to commemotare World TB Day on 24th March]

National Tuberculosis Elimination Programme : New Guidelines for Management of Drug Sensitive TB

Swapnendu Misra[1], Papia Mondal[2], Jaydip Deb[3], Rama Saha[4]

India has largest number of tuberculosis patients in the world. India accounts for 27% of global TB burden[1]. India has highest burden of both TB and MDR TB and second highest of HIV associated TB[2]. 2.69 million incident TB cases emerged in India in 2018. Incidence of HIV TB and pediatric TB was 92000 and 342000 respectively. MDR TB incidence was 130000 contributing to 24% of global MDR TB burden. Moreover any drug resistance among new patients is 22.54%, among previously treated patients is 36.82% and among all patients 28.02% . This is a very alarming situation. TB kills more adults in India than any other infectious disease.In India every day more than 6000 develop TB disease, more than 600 people die of TB (ie, 2 deaths every 5 minutes).

Revised national tuberculosis control programme (RNTCP) was launched in India in 1993. In 2006 entire country was covered by RNTCP. World health organization (WHO) started stop TB strategy in 2006. WHO adopted End TB Strategy in 2020.Vision is a world free of TB and zero death, disease, suffering due to TB. Goal is to end the global TB epidemic. Government of India preponed END TB Strategy by 2025, 5 years ahead of global target. Indian target by 2025 is to reduce TB incidence, prevalence and mortality per lakh population to 44, 65 and 3 respectively. It is to be ensured that no family should suffer catastrophic costs due to TB. In this scenario National Strategic Plan 2017-2025 has been implemented and it is built on 4 pillars '**DETECT-TREAT-PREVENT-BUILD**'. Activities under the plan are :

- Active TB case finding
- Latent TB infection (LTBI) management in high risk population
- Newer and shorter regimen
- Private sector engagement
- Preventive and awareness measures
- Financial/Nutritional support to patients
- IT enabled surveillance

Now the new goal is not to control TB but to eliminate TB. In this context Revised National TB Control Programme (**RNTCP**) nomenclature has been changed to National TB Elimination Programme (**NTEP**) from January 2020.

Nodal point of NTEP is tuberculosis unit(TU). It is situated at sub district level. In urban areas 1 TU per 2,00,000 population.TU will have one designated microscopy centre (DMC) for every 1 lakh population (50,000 in tribal, desert, remote and hilly region).Microscopy centres are also located in medicalcolleges, corporate hospitals, ESI, railways, NGOs, private hospitals.

Presumptive pulmonary TB is defined as any patient with cough for more 2 weeks, fever for more 2 weeks , significant weight loss, hemoptysis or any abnormality in chest radiograph. Contacts of microbiologically confirmed TB patients, patients living with HIV AIDS (PLHIV), diabetics, malnourished, cancer patients, patients on immune suppressants or steroids should be regularly screened for signs and symptoms of TB. Presumptive extra pulmonary TB is defined as organ specific symptoms and signs like swelling of lymph node, pain and swelling in joints, neck stiffness, disorientation and constitutional symptoms like significant weight loss, persistent fever for more than 2 weeks, night sweats. Presumptive pediatric TB is defined as persistent fever more than 2 weeks or cough more than 2 weeks or loss of weight / no weight gain and history of contact with infectious TB case. Loss of weight is defined as loss of more than 5% body weight as compared to highest weight recorded in last 3 months.

Microbiologically confirmed TB caseis defined as biological specimen positive for AFB or positive for Mycobacterium tuberculosis on culture or positive for tuberculosis through quality assured rapid diagnostic molecular test. Clinically diagnosed TB case is defined as presumptive TB patients who is not microbiologically confirmed but diagnosed with a active TB by a clinician on the basis of X-ray abnormalities, histopathology or clinical signs with a decision to treat the patient with a full course of anti tubercular drugs (ATD). There are some changes in nomenclature of cases. Previously patients defined as relapse now defined as recurrent TB cases. Similarly previously called failure cases now called treatment after failure (Figs 1&2).

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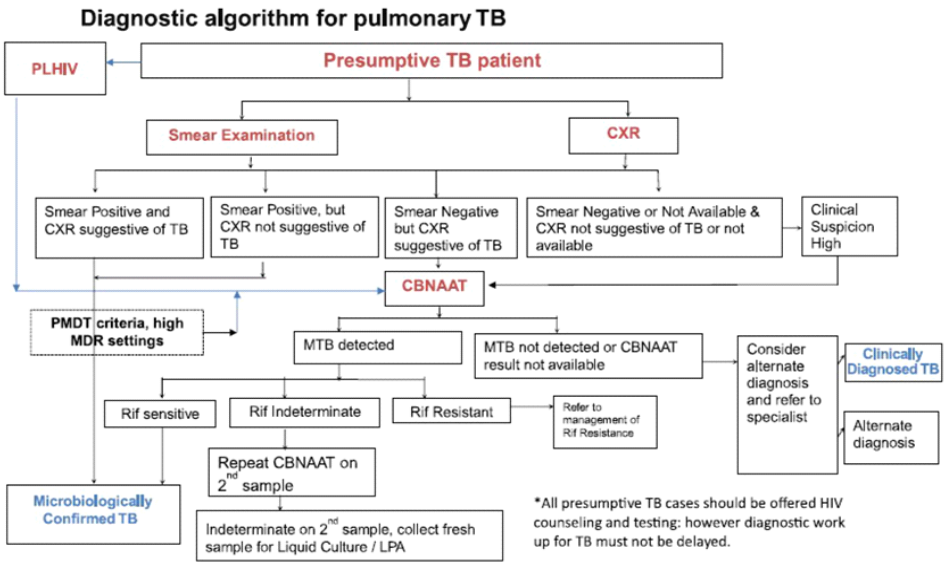

Fig 1 — Diagnostic algorithm for Pulmonary TB

In the diagnosis more emphasis has been given on microbiological confirmation of cases with universal drug sensitivity test (U-DST). NTEP is committed to provide UDST for all notified TB patients (bacteriologically confirmed and clinically diagnosed).DST to be done for at least Rifampicin through rapid molecular test.DST for Isoniazide offered through first line line probe assay (LPA). Cascading DST for fluroquinolone and second line injectable are offered through second line LPA.

Diagnostic tools for microbiolocal confirmation are sputum smear microscopy (ZN stain, Fluroscent stain), culture (solid LJ media, liquid culture system) and rapid molecular diagnostic tests (CBNAAT, Tru NAAT, Ultra NAAT). For culture at present liquid culture like mycobacterium growth indicatorTube (MGIT) is commonly used. Facility of liquid culture now available through NTEP lab network and other accredited laboratories.Under current universal DST strategy specimens like induced sputum, gastric aspirate, bronchoalveolar lavage fluid may be used for upfront rapid molecular tests or for liquid culture if rapid molecular tests are negative.

Among rapid molecular tests, ultra NAAT has lower detection limit (16 bacilli per ml sputum) as compared to 131 per ml for CBNAAT.It isspecially useful for paucibacillary disease, children andforHIV TB-coinfection.Ultra NAAT may replace CBNAAT in near future (Fig 3).

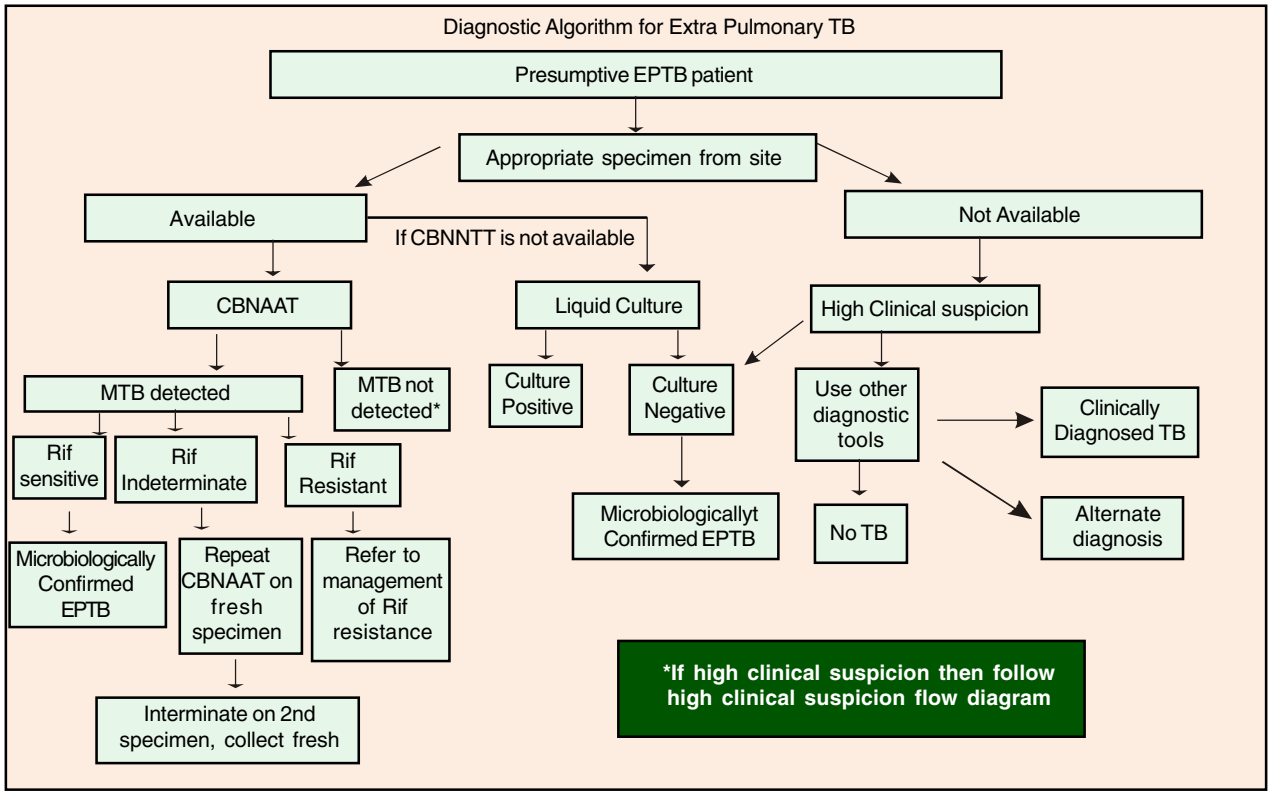

Fig 2 — Diagnostic algorithm for Extra Pulmonary TB

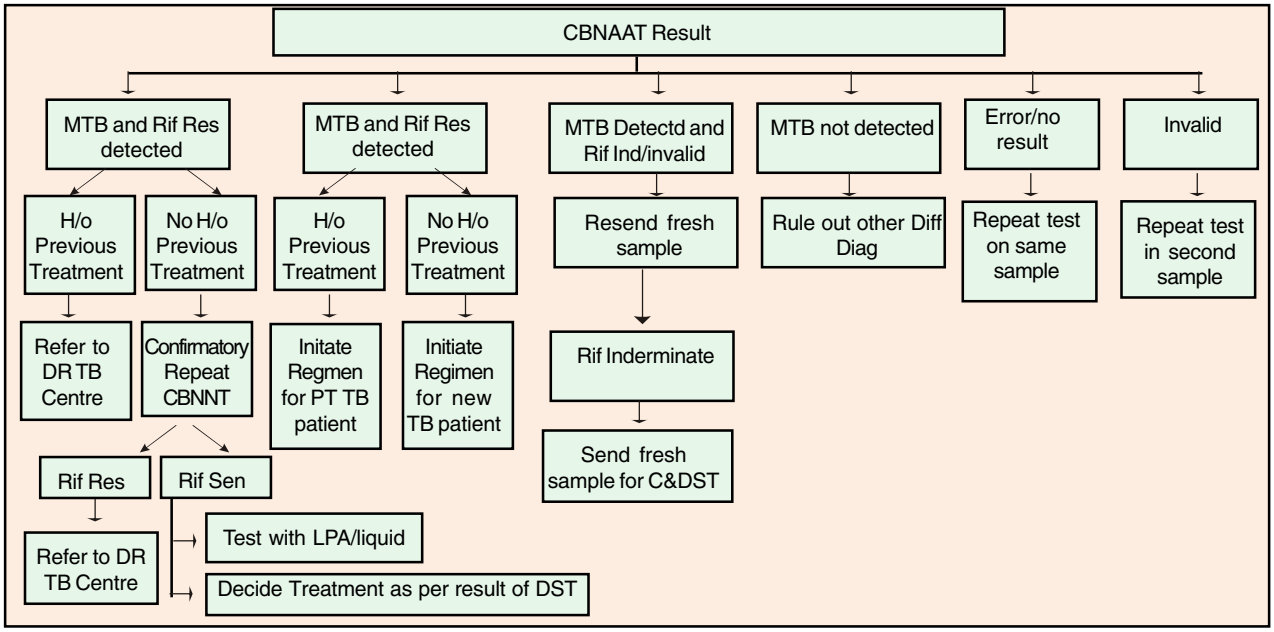

Fig 3 — CBNAAT result algorithm

Two newer diagnostic tools have been developed. Lateral flow urine lipoarabinomannan (LF-LAM) assayused for diagnosis of TB in HIV positive patients with signs and symptoms of TB(pulmonary and/or extra-pulmonary) who have a CD4 cell count less than or equal to 100 cells/μL. C-TB is a next-generation skin test with high specificity. It contains the same antigens used in IGRA ie, ESTA 6 & CFP 10. It is unaffected by BCG vaccination status and very useful for latent TB diagnosis.

In pediatric patients also every effort should be made for microbiological diagnosis. As per NTEP guidelines, diagnosis of non tubercular mycobacteria (NTM) should be done using a mix of diagnostic technologies.

Goals and objectives of treatment are render patient non-infectious, break the chain of transmission, decrease pool of infection, decrease case fatality and morbidity, ensuring relapse free cure, minimize and prevent development of drug resistance.The principal of treatment of drug sensitive tuberculosis (other than DR-TB) is with daily regimen with daily fixed dose combination of first line antitubercular drugs in appropriate weight bands. Changes from past guideline are:

- Daily regimen.
- Fixed dose combination drugs (FDC).
- New weight band.
- Ethambutol in Cat-I continuation phase (CP).
- No extension of intensive phase (IP).
- No Cat-II regimen.

Intermittent regimen changed to daily regimen because relapse rate with intermittent regimen is as high as 8.8%[3] and 12.3%[4] as evidenced by two separate studies whereas internationally acceptable relapse rate is less than 5%. FDC drugs are given because of simplicity of treatment, increased patient acceptance (fewer tablets to swallow, prevents concealed irregularity), increased health worker compliance (fewer tablets to handle),easier drug management, reduced use of monotherapy and lower risk of emergence of drug resistance.

In India pre treatment INH resistance is high[5]. Pre-treatment INH resistance lead to amplification of acquired rifampicin resistance, leading tomulti drug resistance (MDR). Ethambutol now included in CP because it will protect Rifampicin and prevent emergence of MDR TB.

In previous weight band dose of ATD for weight band 30 to 40 kg was inappropriately high. It was leading to drug toxicity and default. In NTEP guidelines weight band has been revised into 5 weight categories.

The revised weight band for standard first line regimen for TB in adults (Fig 4).

Weight Category	Number of tablets (FDCs)	
	Intensive phase HRZE	Continuation phase HRE
25-34 kg	75/150/400/275 2	75/150/275 2
35-49 kg	3	3
50-64 kg	4	4
65-75 kg	5	5
>75 kg	6	6

Fig 4 — The revised weight band for standard first line regimen for TB in adults

To initiate treatment, new and previously treated drug sensitive TB will be given "Regimen for new patients"-2 months intensive phase with Isoniazide, Rifampicin, Ethambutol, Pyrazinamide and 4 months continuation phase with Isoniazide, Rifampicin, Ehambutol. For new and previously treated drug resistant TB regimen will be based on DST pattern. Systemicsteroids given as adjunctive therapy in TB Pericarditis & Meningeal TB. For CNS TB, skeletal TB, disseminated TB continuation phase may be extended by 12 to 24 weeks.

Follow up of treatment should be both clinical and laboratory follow up. At the end of 2 months if sputum smear is positive, there is no provision of extension of intensive phase. Sample to be sent for rapid molecular test or liquid culture and regimen will be based on DST pattern. Long term follow up is a new inclusion in guideline. After completion of treatment, patients should be followed up at the end of 6,12,18 and 24 months. It will help to detect recurrence of TB at the earliest. Pyridoxine is not required for all TB patients. To prevent INH related neuropathy it should be given in persons at high risk of Vitamin B6 deficiency like alcoholics, malnourished persons,pregnant and lactating women,patients with conditions such as chronic renal failure, diabetes and HIV infection.

In HIV infected patients, active case finding to be done. Treatment of TB and HIV should be done from a single window.

INH preventive therapyto be given to children less than 6 years who are close contacts of drug sensitive TB patient irrespective of BCG vaccination/nutritional status. Active TB must be excluded. Dose is 10mg per kg body weight for 6 months. Additional indications for IPT are HIV infected children known exposure to infectious TB case or TST positive (≥5mm induration) ,all TST positive children receiving immunosuppressive therapy (eg, Childrenwith nephrotic syndrome, acute leukaemia, etc), children born to mother diagnosed with TB in pregnancy (Give BCG at birth) and adults & adolescents living with HIV.

Latent TB is defined as presence of mycobacterium tuberculosis in the body without signs and symptoms or radiographic or bacteriologic evidence of tuberculosis disease. It is considered as a state of persistent immune response to stimulation by M. tuberculosis antigens. In India 35 to 40% population have latent TB. Latent TB patients has 10% lifetime risk of active TB. Risk is 16 to 21 times higher in HIV infected persons.As it is not possible to treat all patients with latent TB, eligible patients who should receive latent TB treatment are people living with HIV, infants less than 12 months in contact with active TB, household contacts of pulmonary TB, children/adult on immunosuppressive therapy (Fig 5).

99 DOTS has been implemented in the new guideline for accurate treatment monitoring at very low cost. Patients take medicines based on weight band and calls a toll free number.

Recommended dosages of Drugs for the Treatment of LTBI

Drug Regimen	Dose per kg body weight	Maximum dose
Isoniazed alone, daily for 6 or 9 months	Adults, 5 mg Children, 10 mg (range, 7-15 mg)	300 mg
Daily rifampicin alone for 3-4 months	**Adults, 10 mg Children, 15 mg (range, 10-20 mg)**	**600 mg**
Daily isoniazid plus rifampicin for 3-4 months	Isoniazid : Adults, 5 mg Children, 10 mg (range, 7-15 mg) Children, 15 mg (range, 10-20 mg)	Isoinazid, 300 mg Rifampicin, 600 mg
Weekly rifapentine plus isoniazid for 3 months (12 doses)	Individuals aged 12 years; Isoniazid : 15 mg Individuals aged : 2-11 years: Isoniazid : 25 mg Rifapentine: 10.0-14.0 kg = 300 mg 14.1-25.0 kg = 450 mg 25.1-32.0 kg = 600 mg 32.1-50.0 kg = 750 mg >50 kg = 900 mg	Isoniazid, 900 mg Rifapentine, 900 mg

Fig 5 — Recommended dosages of drugs for the treatment of LTBI

Benefits are focused and more efficient care and accurate reporting.

Nikshay is an Integrated ICT(Information Communication Technology) system for TB patient management and care in India.It is real-time, case-based, web-based surveillance tool. Nikshayaushadhi which is a software for supply chain management of ATD and laboratory consumables has been launched recently.NikshayPoshan Yojana provides nutritional support through direct benefit transfer of 500 INR per month. It is given for all patients on TBtreatment throughout duration of treatment.

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Image in Medicine

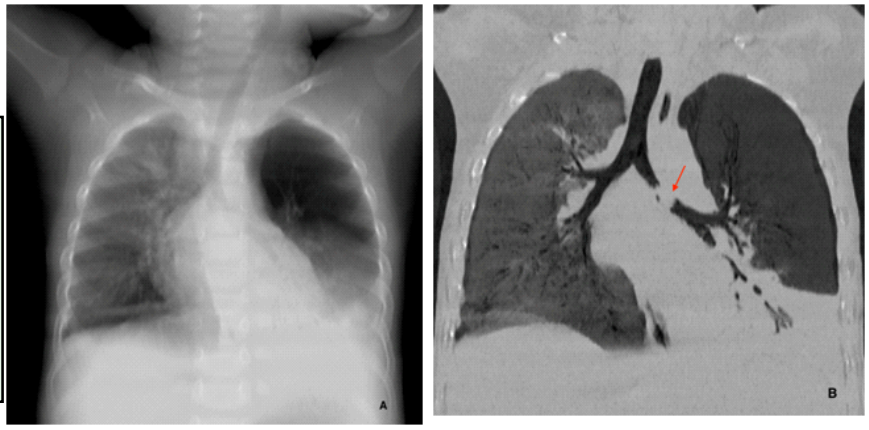
Bhoomi Angirish[1], Bhavin Jankharia[2]

Quiz 1

2 years old presented with sudden onset of breathlessness and cough since 1 day.

Questions :

(1) What is the diagnosis?
(2) What are the common causes of unilateral hyperlucent hemithorax in children?
(3) What is the role of MinIP CT scan algorithm in such cases?



Answers :

(1) Hyperinflation and air trapping is seen in left upper lobe with consolidation in left lower lobe. CT scan of chest was performed which showed a foreign body in left main bronchus (arrow).

(2) There are many factors responsible for unilateral hyperlucent hemithorax in children . Common causes include – airway obstruction (endobronchial foreign body or extrinsic compression), bronchial atresia, congenital lobar emphysema, congenital pulmonary airway malformation, Swyer-James syndrome, pneumothorax, pulmonary agenesis, Scimitar syndrome, poland syndrome.

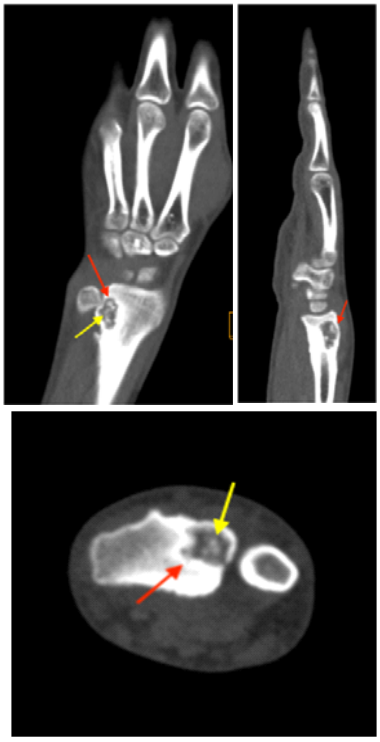
(3) Minimun intensity projection (MinIP) (Figure B) is a data visualisation algorithm that enables detection of low-density structures. It is optimal reformation technique for airways. It is also helpful for detection of ground-glass opacities and in mosaic attenuation.

Quiz 2

20 year old female presented with swelling over distal forearm since 2 months.

Questions:

(1) What is the diagnosis?
(2) What are the common locations of this lesion?
(3) What are the common differential diagnosis?



Answers :

(1) Well defined expansile osteolytic lesion (red arrow) with rim of reactive sclerosis and internal nidus of calcification (yellow arrow) is seen in distal metaphysis of radius. These imaging findings are in favour of osteoblastoma, which was subsequently confirmed on biopsy .

(2) The common locations of osteoblastoma are posterior elements of spine and metaphysis of long bones.

(3) The most common differential diagnosis is osteoid osteoma, which are usually less than 1.5-2 cm in size, whereas osteoblastomas are larger than 2cm in size.

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Student's Corner

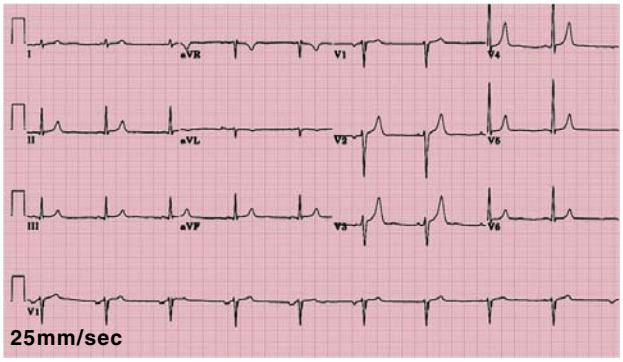
Become a Sherlock Holmes in ECG

M Chenniappan[1]

Series 3 :

"Roaming but not Running"

Routine ECG of 55 years old diabetic and hypertensive



ECG of 55 years old diabetic and hypertensive

Questions :

1. **Describe ECG changes**
2. **Why is this clue?**
3. **What are practical implications?**

ECG Changes :

ECG shows Borderline bradycardia with varying P waves in Rhythm strip. The R-R interval shows slight variation. There are 3 different types of P waves indicating, the atrial pacemaker is shifting from one area to the other (Fig 1, arrows). In this situation, there are 2 differential diagnosis.

1. Wandering Atrial pacemaker
2. Multifocal atrial tachycardia.

In both of these situations, 3 different configuration of P waves have to be demonstrated as in our ECG. The only difference is the atrial rate. If the atrial rate is more than 100/mt. with at least 3 different configuration of P waves, it is Multifocal Atrial Tachycardia (MAT). If the HR is less than 100 with 3 different configuration of P waves it is called Wandering Atrial Pacemaker (WAP). The difference between MAT and WAP is shown in (Table 1)

- Wandering pacemaker is usually caused by varying vagal tone. With increased vagal tone the SA Node slows, allowing a pacemaker in the atria or AV Nodal area, which may briefly become slightly faster. After vagal tone decreases, the SA Node assumes its natural pace.
- A wandering atrial pacemaker, also termed multifocal atrial rhythm, is present when there are three or more ectopic foci within the atrial myocardium that serve as the dominant pacemaker.
- Since they discharge in random fashion, the pacemaker location is continuously shifting and may be located anywhere in the atrial myocardium. As a result, there is a changing vector of atrial activation that causes a changing P wave morphology and PR interval duration.
- A dominant P wave (sinus or atrial) cannot be identified.
- The rate is less than 100 beats per minute.

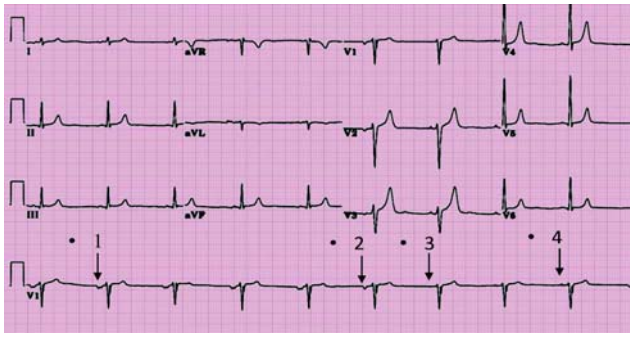


Fig 1 — ECG showing 4 different types of P waves with HR of about 60/mt

Table 1 — *Differences between WAP and MAT*

WAP	MAT
HR <100/min	HR>100/min
Vagal tone	Increased irritability
Mostly normal	Abnormal
No organic HT disease	Non cardiac diseases (COPD)
No TMT (Increase SR)	Amiodarone ; non DHP Ca. Blockers

The Clue :

Because atrial depolarization (P) is roaming or wandering inside atrium (WAP) and not running (not >100/mt.) like MAT the clue of "Roaming but not Running" is given.

Practical Implications :

- A Benign condition generally has no clinical significance.
- It is often an expression of high vagal tone.
- Usually transient.
- Can be unmasked by beta or calcium blockers.
- Severe forms of wandering pace maker can be a marker of sinus node dysfunction and wouldneed further evaluation
- In the coronary care units, it is associated with infero-posterior MI when the vagal fibers are insulted.
- This attractive and descriptive ECG entity is largely insignificant in clinical cardiology.
- It should not be confused with more dangerous cardiac arrhythmia like sinus pauses and arrest and treated wrongly.

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Medical History

Epistemological Principles of Medicine in India — A Historical Overview

Indranil Sen[1]

Medicine is said to be a miniature history of any civilization in the world. In fact, each and every form of human intellectual pursuit over the long journey of mankind, be it in the field of Philosophy, Art, Literature, Science, Politics or Trade and Commerce, can epistemologically be linked to the contemporary development of Medicine and its prevalent theories. The present development of Surgery would not have taken place, had there not been the Barber surgeons in the battlefield inventing the different methods of successful repair of wounds or the safer methods of limb amputations while treating the soldiers. Neither the development of Pharmacology would have taken place, had there not been the ancient merchants transporting the different herbs and medicinal products from one continent to the other, sailing their ships across the turbulent seas or driving their caravans across the deadly deserts for centuries together. On the other hand, medicine in this 21st century would not have attained the status of a scientific discipline and would have remained a slave serving under the authority of religion, had there not been the pathfinders like Bacon and Descartes shaping the minds of the medical thinkers of Medieval Europe in particular and those of the World forever.

Indian Medicine is no exception to this rule. For time immemorial, our intelligent ancestors have devoted their life in finding out the way to alleviate the suffering of mankind from Disease, Infirmity and Death and the way to achieve the salvation towards Immortality, both from the spiritual as well as from the practical point of view. The first effort has resulted in the enormous treasure of Indian Philosophy and the emergence of the legendary personalities like Kapil, Kanada, Gautama, Patanjali and Buddha and the second effort has resulted in the emergence of the rich treasure of Ayurveda and personalities like Caraka, Sushruta, Vagbhata Madhava and Cakrapani. As far as the institutionalization of medical education is concerned, it was Taxilla where the first medical institution in India was known to function under the auspices of Atreya Punarvasu in c. 5th century BC.[1,2]

In the present article, effort has been made to delineate a historiographic account of the epistemological developments of Indian Medicine over the ages.

[1] **Empirical Stage** — As far as our knowledge go, Man arrived in this world about 80,000 – 100,000 years ago. Unfortunately, the first 95,000 years of this period is devoid of any written history, and there exist considerable lack of continuity is the intellectual achievements of mankind.[4] The rudimentary sources of history of medicine in this period include the cave paintings, palaentological specimens, and the timeless oral traditions of numerous tribes all over the world and the age old practices and rituals of the tribal folk, in particular, their birth, fertility and death rituals.

Approximately 10-12 thousand years ago, Man discovered the marvel of agriculture which gave him the freedom from the nomadic life of the hunter-gatherer and ensured the constant and adequate supply of food for his primitive community. At the same time, there came important changes in the social life of Man. This was because of the concept of the 'Division of labor' and the 'Right over the Land.

Important changes came into the medical practice of the community. So long, everybody of the clan was conversant about the identification and usage of the natural sources of medicine like the herbs and the minerals. But, due the increasing pre-occupation of the members of the society with the agricultural and the ancillary activities, the job of medical service to the community was entrusted to a few, having an aptitude for the same and in this way the birth of the primitive 'Medical Men' took place.[3]

At this stage, the medical knowledge was empirical in character and limited in volume. This is the first stage of medicine and may be called the **'Stage of Empirical Medicine'** in the historical context. This is still a living tradition even in this 21st century and prevalent among the common people all over the world, irrespective of their origin, education, culture and the scientific development of the country.

The training of the Doctors were marked by the empirical methods of learning about the natural healthcare among the numerous indigenous communities spread over a large area, from time immemorial. This is, indeed, a living tradition among the tribal population of the country and serves a large section of our population as far as their healthcare needs are concerned.

[2] **Religious stage (Stage of immature rationality)** — Gradually, with the advent of time, the village based primitive community entered into the era of surplus production and the resultant trade exchanges gave rise to urbanization and the establishment of towns, cities and trade-centers. The increasing communication among people resulted in the enormous increase in the volume of knowledge in every sphere of life, including medicine and gradually, the corpus of knowledge became unmanageable. With the discovery of the written language, the problem of record and documentation could be solved to a large extent, but the enormous amount of

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discreet information made the affairs extremely complicated and confusing, thereby necessitating an epistemological methodology for dealing with this ever-increasing huge corpus of information. To start with, this necessity of rationalization was provided by the prevalent religious schools of the society. There are ample evidences in every system of medicine in different civilizations starting from the Egyptians in 6000 BC down to this 21st century when Gods and Deities are worshipped and prayers are chanted to ward off the outbreak of diseases. In our country, one can find such references in the texts of 'Atharva Veda'.[4] This is the second stage of medicine known as the **'Stage of Religious Medicine'**.

[3] **Philosophical stage (Stage of mature rationality)** — As the civilization progressed, the rational mind of the intelligent men tried to get rid of the clutches of the religion and forwarded secular theories for the explanation of the natural events. Thus the era of 'Philosophy' began.

In India, 'Theories of knowledge' as a whole reached a fantastic height with the rich culture of the different schools of classical 'Philosophy' like Samkhya, Nyaya, Vaisheshika, Yoga, Mimangsha, Vedanta and atheists like the Buddhism and the Jainism.[3] As a result of this, medical information gathered so far, started getting systematized and around 1000-600 BC, the system of medicine called 'Ayurveda' could attain the status of an organized system The practice of 'Ayurveda' and its potential reached new height during the Buddhist period. It was during this period, that the famous compilation of medical texts, the 'Charaka Samhita' and the 'Sushruta Samhita' saw the light of the day for the first time. The theories and methodologies of 'Ayurveda' were strictly confined within the philosophical premises of the prevalent period and it took the shape of a 'Holistic discipline' under the auspices of legendary scholars like Jivaka Komaravachcha, Brddha Sushruta and the masters of the schools like 'Charakas' and the 'Sushrutas'. When compared to the contemporary systems of medicine in Europe like the Greek, Roman or the Jewish Medicine, the 'Ayurveda' appears to be quite advanced and mature in its theory as well as in its approach.[1] This stage may aptly be designated as the **'Stage of Philosophical Medicine'.**

In the later period, the development of the material sciences came to a standstill in India due to the prevailing social system and the casteism. This area has been extensively dealt by Acharya P. C. Ray in his book titled 'History of Hindu Chemistry' and little is left to any further comment.

Since c1500 BC down to the present days, the traditional schools of the indigenous medical systems of the country eg, Ayurveda, Unani & Tibbi, Siddha etc. followed the classical 'Gurukul' system of medical education which has been replaced by the western model of institutional education only in the recent past to a considerable extent. However, there are a large number of indigenous medical schools and 'Ashramas' in the country who are following the traditional methods of medical education for the young learners of the 'Indigenous Medical systems'.

Comparing with Europe, after the fall of the Roman Empire, the 'Dark period' prevailed for about fourteen hundred years, after which, the darkness of the medieval barbarianism passed off and the sun of the 'Renaissance' made its appearance. During the period of darkness, it was the Arabian world, which kindled the light of rational spirit of knowledge in its cradle and made invaluable contributions in the field of various intellectual pursuits, including the 'Art of Medicine'.[7] In fact, the modern civilization owes the concept of 'Modern hospital' to the Arabic medical scholars.[6]

[4] **Scientific stage** — With the advent of 'Renaissance' in Europe, the spirit of 'Scientific enquiry', as it was in the ancient Greek Civilization, within the European sense of its meaning, achieved the supreme position in any sort of intellectual pursuit and stark 'Objectivity' became the sole criteria for evaluating any intellectual endeavor before it claims any worth for consideration.[7] Medicine was no exception to this rule. Gradually, the Human face of medicine disappeared and it increasingly aligned itself with the material sciences like the Physics and Chemistry. According to Dr. Bernard Lown, the co-recipient of Nobel Peace Prize (1985) -"the practice of medicine has in increasingly shifted to a scientific paradigm and the patient transformed into a biomedical model…… a sick person is merely a repository of malfunctioning organs or deranged regulatory systems that respond to some technical fix."[8] Medicine, in this way entered into the fourth stage of development called **'The Stage of Scientific Medicine'.**

DIFFERENT STAGES OF EVOLUTION OF MEDICINE
■ Collection of Empirical Information - Clans & Tribes in the Rural level
■ Compilation- With the advent of Trade & Urbanization
■ Immature Rationalization- In relation with Religion & Traditional Causality
■ Mature Rationalization- Approach by the different schools of Philosophy
■ Scientific Rationalization- Introduction of Physics & Chemistry with Modern Technology
■ Stage of Holistic Idealism…. Yet to arrive!

Advent of Western Medicine in India — The advent of western medical healthcare delivery system and the related education in India during the colonial rule should be viewed in the light of the practical compulsion of the foreign rulers. It is evident from the literature that they were actually concerned with the health of their soldiers and officers lest they should fall ill and eventually

die in discharging the duties of the unpleasant compulsion of ruling the God-forsaken land of India, full of malaria, cholera, kala-azar and various kinds of known and unknown pestilences. The native subjects of the land were entirely dependant on the age-old traditional systems of medicine.

The credit of introduction of the western medicine in India does not go to the British, but it was the Portuguese rulers of Goa who made an appeal to their superiors abroad for establishment of a hospital for the treatment of their people as early as in 1687 AD. As a result of this, a hospital was built in Panveilim, Goa and in 1703 AD it was converted to a medical school for imparting medical education to the Indian and the Anglo-Indian students. In 1801 AD, Miranda and Almeida, two renowned teachers of the school, started a regular 3 years course which was extended to 4 years in 1821 Ad. The Goa medical school was founded in 1842 AD in Panjim and the 5 years regular course was started in the year of 1847 AD.[9]

In the eastern part of India, the British rulers were compelled to establish a system of training the Anglo-Indian boys in the Sub-medical service as early as in 15th June, 1812 AD. But, this arrangement was not sufficient considering the load of the patients and the demand of the society. On the 9th may, 1822 the Government order was passed for the establishment of an appropriate board of studies for the purpose of training the native doctors. Finally, on 21st June, 1822 AD, 20 Indian students were admitted to the 'Native Medical Institution' [NMI] under Surgeon Jamieson as its first Superintendent. After the death of Jamieson, in June 1823 AD, The famous Dr. Bretton took the charge of the institution.[10] This is an important phase, often overlooked by the historians, characterized by the systematic and synthetic approach to formulate an 'Integrated' system of healthcare and medical education, taking into consideration the huge treasure of the traditional indigenous systems of medicine in India and the European medical systems on the other side, for this part of the globe. This phase can be identified as the '**Intermediary phase'.** The 'Native Medical School', established by the British rulers and the pioneering efforts of Jamieson, Bretton and Tytler in this direction, marked the beginning of a new concept in the medical education of India but unfortunately, their efforts faced a premature death due to the active and well-contrived interference of Macaulay and Trevelyan.[10.11] The experiment initiated by Bretton and Tytler has remained a long-cherished desideratum of the medical education in India, even in this 21st century. The strong sentiment of the people of India about the indigenous systems of medicine has been amply reflected in the 5 Year plans since independence and even in the recent 11th plan. Provisions have been made for the indigenous systems under the aegis of 'AYUSH'. Moreover, the increasing interest of the medical- scientific community of the world in these indigenous systems and their acceptability in the healthcare programs have made the situation almost imperative for the Indian medical community to consider the whole affair with due seriousness and a scientific, rational attitude.

The most important problem of imparting 'Medical education' to the Indian students at that time was the acute dearth of medical text books. Moreover, the knowledge of English was so rudimentary among the Indian youths at that time that it was not possible for them to comprehend the western medical texts in original. Dr. Bretton took the initiative and translated a large number of medical and scientific text books in vernacular. He also insisted that the students of the NMI should be proficient in the general education and therefore, the students were sent to the Sanskrit College and the Calcutta Madrassa. Pandit Madhusudan Gupta, the famous pioneer of 'Anatomical dissection' in India, translated Hooper's Anatomy for this purpose. The students used to receive their clinical training in the Native Hospital and the total duration of the course was 3 years. Dr. Bretton breathed his last in Calcutta in the year 1830 AD. He was succeeded by another famous teacher and pioneer in the medical education in India in that nascent stage, Dr. Tytler who strived a lot to give it a definite shape. Both of these pioneers, Dr. Bretton and Dr. Tytler suggested that medical teaching be given in vernacular. They also forwarded their logic to develop the system of western medicine in India side by side with the enforcement of the traditional systems of medicine of this land. In fact, they were the pioneers who tried to organize a truly synthetic system of healthcare and medical education in India taking materials from both the European and the Indian systems of medicine.[10.11]

In 1833 AD, Governor General Lord Bentinck made a commission to assess the functions of the NMI and they made adverse comments about the standard of students and the standard of education imparted in NMI in their report on 20th October, 1834 AD. This is a landmark report in the history of medical education in India as it marked the clear watershed between the synthetic, integrated system of medical tradition which was envisaged by Bretton and Tytler for the Indian people and the imperial, European system of medicine which was awaiting its hurried entry into the newly found native market in India with an immense potential for the European economy. There are ample historical evidences to support that the advent of western medicine in India was more an economic compulsion of the imperial Europe than an endeavor of pure philanthropic benevolence. The indigenous systems of medicine in India had to be sacrificed to the altar of the imperial, colonial interests of Europe. In this connection, the role of the Anglicists like Macaulay and Sir Charles Trevelyan was instrumental.[12]

At last, by the General Order no. 28 dated 28th January, 1835 AD, the NMI was abolished along with the study of medicine in the Sanskrit College and Calcutta Madrassah, and the 'Medical College, Bengal' started its journey with an immense potential for the future and as the pioneer institution for the advent of western medical education in India. Surgeon Major Bramley became the first superintendent of the college. Within a short time, three more renowned teachers, namely, Assistant Surgeon Dr. H.H. Goodeve, Dr. William O' Shaughnessy and Pandit Madhusudan Gupta joined the college. The college started functioning on 20th February, 1835 AD. Initially, the course was for three years duration which was converted to a full 5 years course in 1845 AD. The recognition of

the students were given by the college itself by conferring 'Diploma' till the year 1857 AD, when, after the establishment of the Calcutta University, the onus of awarding the students with the diploma (LMS- Licentiate in Medicine and Surgery) and the degree (MB) was entrusted to the University. Later on, the degree was renamed as MBBS.[9]

Presently, since 2004, the newly founded W.B. University of Health Sciences has been discharging the responsibilities.

MEDICAL COLLEGE, BENGAL (Record of Facts)	
28th January, 1835	General Order No. 28 was passed
20th February 1835	College started functioning
10th January 1836	First Anatomical dissection took place, headed by Pandit Madhusudan Gupta
1845	Five years course was started
1857	Recognition of the diploma by University of Calcutta

After the establishment of Medical College, Bengal, the necessity was felt for similar institutions in the Madras and the Bombay Presidency by the British rulers. As a result of these, the Madras Medical School (1835), which was later elevated to a college in1850 and the Grant Medical College, Bombay (1843) was established.

GRANT MEDICAL COLLEGE (Record of Facts)	
3rd January, 1843	Foundation of J. J. Hospital was laid down
30th March, 1843	Foundation of Medical College was laid down
15th May, 1845	J. J. Hospital was opened
October, 1845	Grant Medical College building completed
3rd November, 1845	GM College opened by Sir George Arthur
1860	Affiliated to Bombay University

MADRAS MEDICAL COLLEGE (Record of Facts)	
13th February, 1835	General order passed by Governor General Fredrick Adams as 'Madras Medical School'
July, 1835	Classes were started in the college
1850	Converted to 'Madras Medical College'
1863	Degree was recognized by Madras University
11th October, 1875	Ladies were admitted for the first time as students

Gradually, more and more medical teaching institutions came into existence in the different parts of the country. The 'Lahore Medical School' was established by Sir John Lawrence in 1837 AD in Lahore and another medical college was established in Lucknow by the initiative of Raja Rasul Khan in 1905 AD. These two institutions were later named as King Edward Medical College (1910) after Prince Edward VIII and the King Georges Medical College (1912) after King George V, respectively, as they visited India during that period.

LAHORE & LUCKNOW MEDICAL COLLEGE (Record of Facts)	
1837	Started as Lahore Medical School
1905	Raja Rasul Khan proposed for the Medical College, Lucknow after the visit of King George V
26th November, 1905	Foundation stone was laid down for the Lucknow Medical College
1910	Lahore Medical School was named after King Edward Medical College
25th January, 1912	King Georges Medical College, Lucknow was opened

By 1914 AD, apart from the five medical colleges, there were fourteen medical schools functioning in the different parts of the country. These were in Calcutta (Campbell), Cuttack, Rangoon, Lahore, Agra, Dibrugarh, Poona, Hyderabad (Sind), Ahmedabad, Tanjore, Royapuram, Vizag and Ludhiana. They were gradually upgraded to the status of Medical Colleges within a few decades.[10]

The standard of the medical education imparted in these institutions and the subsequent recognition of the medical degrees awarded by the different universities in India remained a persistent issue for concern to the rulers. Since 1843 AD, the three Medical Colleges of India namely, Medical College, Bengal, Grant Medical College, Mumbai and the Madras Medical College, Chennai were recognized by the Royal College of Surgeons in England. After the establishment of the General Medical Council [GMC] of Great Britain in 1858 AD, it accorded recognition to the 3 (three) Medical Colleges in India. In 1921 AD, the GMC expressed its dissatisfaction over the training of the students in India in Midwifery. They intended to visit the examination process in India which the University of Calcutta did not permit. As a result of this, GMC decided to de-recognize the medical degrees awarded by the Indian universities. Desperate attempt of salvage was undertaken by the Calcutta University by inviting Col. Needham from London as the inspector for the MBBS examination of the university with a view to retain the recognition. But the authorities in London were reluctant to consider. In the mean time, since 1835, the number of medical teaching institutions in India had greatly increased in number and it became increasingly difficult for the authorities in London to look after the huge set of affairs across thousands of miles from the headquarters. Moreover, the recognition of GMC accorded to the Indian degrees was valid for only six months. Finally, GMC resolved to withdraw themselves from the Medical Education in India in 1925 AD. As in effect, the Indian Medical degrees faced a challenge of loosing their recognition in the world from 1930 onwards.

The sternness exhibited by GMC, probably, had a different reason altogether, behind the curtain. It is not difficult to assume, the upsurge of the Nationalist Movements for Freedom that started in the later part of the 19th Century onwards and the subsequent socio-political developments in India had a catalyzing effect that led to this drastic decision by the authorities of GMC, creating a sudden and unexpected void and uncertainty in the future of the almost a century-old tradition of the western medical education in the country. Reactions among the medical fraternity in India were instantaneous and fierce, as expected, and the upsurge ultimately led to the formation of the 'Medical Council of India' in 1933 AD as the sole authority for the maintenance of the standards of medical education in the country.

Medical Council of India [MCI] :

The need for the establishment of a single, uniform, standard of medical practice in the whole country was felt as early as in 1890 AD when the first attempt of registration of the Doctors was made. Subsequently, in December, 1894 AD, Surgeon General Harvey raised the issue in the Indian Medical Congress for the first time. In the mean time, a number of autonomous societies e.g. Calcutta Medical School (1886 AD), College of Physicians & Surgeons of Bengal (1897-98 AD) were formed were formed and they started training the aspiring students and issued certificates and diplomas allowing them to practice medicine openly in the society. There was no control of the Government authority over these societies about the standards of teaching and infrastructure and the whole affair of healthcare of the community was in perpetual confusion and jeopardy. As a result, the need for the establishment of an authority to ensure a uniform standard of medical training was strongly felt by the medical fraternity of the country and the Government. The process progressed further with the establishment of the Bombay Medical Act in 1911 AD and Bengal Medical Act in 1914 AD.[13]

Further consolidation of these attempts took place when Sir Pardey Lukis proposed for a national act at the Imperial Legislature Council held in Shimla on 22nd September, 1916 AD.

The de-recognition of the Indian medical degrees by the GMC in 1925 AD onwards, which was effected from 1930 AD, made the affairs serious and imperative for the medical fraternity in India amidst widespread confusion, disappointment and frustration. The senior stalwarts of the fraternity were extremely agitated and the zeal of nationalism was mounting up for a permanent and effective solution to the problem.

At the last, all these uproars came to a closure with the establishment of the famous act known as the 'Indian Medical Council Act' in 1933 AD by the Indian Government and this led to the formation of the famous 'Medical Council of India' with Maj. Gen. C. A. Sprawson as its 1st President. The act has since been amended more than once with the introduction of the 5 years course in 1935 AD and the duration of the clinical training to 3 years in 1937 AD and so on.[13] The 1st inspection of MCI was held in October, 1934 AD in the Patna University.

In the later part of the 19th Century, national leaders of our freedom movement felt the need of independence and self-confidence in the field of healthcare and medical education in the country. This may be identified as the 'Nationalist phase'. It is difficult to pin-point the exact beginning of the 'Nationalist phase' of Education in India. However, a section of the historians are of the opinion that the movement of the 'Young Bengals' inspired by the ideologies of Derozio, can be accepted as an watershed in the history of education in India when the Indian mind tried to create an alternative model of education different from that set by the British rulers on the recommendations of Macaulay and Trevelyan.[14] Since the Nationalist Freedom Movement gained momentum in the last part of the 19th century, the feeling for the need of a parallel system of healthcare and medical education in India grew stronger among the leaders of the freedom movement and the intellectual section of the society, doctors in particular, as many of them were actively involved in the movement. As a result of it, a number of schools and societies were formed by them in order to address the burning health problems of the society, mostly 'Public Health' in nature like Malaria and Kala-azar. They were also eager to form an indigenous

system of medical education in India in the western model and as a result of it, institutions like the Belgachia Medical College (1916 AD), which was later renamed as the R. G. Kar Medical College in 1948 AD and the National Medical Institute (1921 AD) later named as Calcutta National Medical College in 1948 AD, were established. [15] In this connection, it will not be irrelevant to mention that apart from the medical institutions, ancillary research and pharmaceutical establishments like the 'Bengal Immunity Co.' (1919 AD) and the 'Bengal Chemical Laboratory'(1901 AD) were also founded by the 'Nationalist' medical and scientific community of this country during this period. There was an attempt to modify the system of medical education and the curriculum different from that which was practiced in the so called 'Imperial' medical institutions, mostly in line of the 'Public Health' oriented education in these 'National' institutions instead of the 'European model of approach' of the former ones. These attempts, though transient, had a far reaching impact on the future planning of the 'Healthcare & Medical Education policies' in India and this period should be marked as the 'Nationalist phase' of Medical education in India. This upsurge of these activities merged later with the more prominent 'Socialistic phase' of healthcare and medical education in independent India.

Socialistic Phase — The British rulers in India were concerned about the miserable status of the public health in India since they decided to rule this country in the 18th century. But the principal focus of that concern was to protect the British officers and their staff in India from the innumerable pestilences that prevailed in the country. Therefore, the principal area of the attention was the sanitation and the prevention of the epidemics. Later on, with the actual magnitude of the huge public health problems understood, there were attempts of various reforms as well as decentralization of the health administration and management. However, some of the important steps like the establishment of the birth and death registration and promulgation of some of the important health related acts like the 'Vaccination act', the 'Epidemic diseases act', the 'Central Malaria bureau' etc. were undertaken in British India.

The efforts in the direction of socialized form of health care in India was actually epitomized in the famous report of the celebrated 'Bhore Committee' (1943-46) which reviewed the health of the nation under (a) Public health, (b) Medical relief, (c) Professional education, (d) Medical research and (e) International health. The committee recommended a short term and a long term program for the attainment of reasonable health services based on the concept of modern health practice.

In the independent India, under the leadership of Pandit Nehru envisaged a developed nation, on the principles laid down in the Constitution of India to develop an 'Welfare State'. The 'Bhore committee' report became an important cornerstone in framing the plans and measures adopted by the national government. The building of the newly founded Nation, further inspired by the model of the erstwhile Russia, adopted a 'Socialistic model of development' with overwhelming control of the State in every sphere of the national life, as evident from the drafts of the 1st and the 2nd five year plans in 1951-55 and 1956-61 respectively.[18,19] In fact, the healthcare problems in the newly independent India was keenly alike those in Russia in the contemporary period, where the re-organization of the public health services, the change in the direction of the training of doctors, as well as a sharp increase in the number of students made it imperative the necessity of changing the organizational structure of medical educational institutions. [18] In the same line, the plan for the development of Medical Education in India included the reorganization of the Medical Institutions and laid a strong emphasis on the development of 'Preventive & Social Medicine' in the 1st plan (Para 74-85) [18] and the establishment of a separate department for the 'Preventive & Social Medicine' in the 2nd plan (Para 9-11)[17] ,more commonly known as the 'Mahalanabis Plan' after the name of the pioneer statistician of India Prof. P. C. Mahalanabis. Since then, a number of experiments have taken place in order to organize the healthcare and medical education of the country in the direction of 'Socialistic ideals'. Inspired by the 'Feldshers' system of USSR and the 'Bare-foot Doctors' of the Peoples Republic of China, the introduction of the ROME (Re-orientation of Medical Education) program and revamping of the 'Licentiate course' were attempted in India.[21] In fact, the history of medical education in India till the 90's remained centered around the idea of 'Socialized Rural Health Care for all'.

The present stage of the healthcare and medical education in India may be designated as the ' Globalization phase'. The political, social and economic changes over the globe since 1990 did not spare India. The economic liberalization, increased influence of the market economy on the social sectors, resulted in the fundamental changes in the healthcare sector as well as in the medical education of the country. In this stage of globalization, the difference in the philosophy of the social governance between a developed country like USA and a developing nation like India has been narrow and in both of the countries a public service like health has been transferred into a for-profit enterprise in which physicians are 'health-care providers', patients are viewed as consumers and both of them sub-serve the corporate interests.[8] This shift in attitude has led to an alarming rise in the incidences of medical malpractices and there has been a paradigm shift in the mindset of the medical world to a variable extent towards increasing violence instead of benevolence.[20] A large number of private medical institutions came into existence over the last two decades and many are coming up every day, particularly in the southern and the western provinces of India. The trend may be compared to the status of the medical education in USA in the first part of the 20th century. Maintenance of the standard became a great problem and it was discussed in details in the celebrated 'Flexner report' in 1910.[21] Newer concepts like the 'Corporate health-care', 'Health tourism', "Intellectual property rights' and in particular, the large scale involvements of the multi-nationals in the drug and pharmaceutical sectors of the country are shaping the face of the healthcare and the medical education of the country in the 21st century in a new direction. The emerging scenario is not very clear, even to the most knowledgeable ones and as a

result, a lot of confusion, as well as apprehension prevail among the different sections of the society. The problem has been duly identified by the 'National Knowledge Commission' in their report and they said - "Medical education is a part of the whole system of education which is in crisis mode today and we are paying a very heavy price for inadequately investing in balanced growth for the social sector, i.e. Health and Education, and in permitting moral degradation to set into these areas while building an industrial and technological capacity."[22] The downward shift of healthcare from the status of a 'Noble profession' to the 'Health services' and then towards the 'Customer care' may not be a welcome change for the Indian society which is traditionally accustomed to visualize the 'Doctor' in the light of a 'Messiah'. None could have even dreamt of a situation that the 'Doctors' could have been booked under the CPA in India, even quarter of a century ago.

Conclusion

Historically, the guiding Philosophical principles of the system of healthcare as well as medical education in India have passed through a number of phases over the centuries. The most striking point is that the different phases did not come in a linear pattern, that is, one after another. Rather, they continued to emerge like newer petals of a flower over-riding the older ones. As a result of which, all of these stages actually co-exist in the contemporary India, although, to a variable extent. If one searches seriously, it is not difficult to find that the traditional system of 'Gurukul' method of teaching peacefully co-exists just by the side of a modern medical research institution, at times, often inside it! A definite attempt of balance has been tried by the Union Government in the planning of the healthcare and medical education in the country in the 21st century as evident from the layout of the 11th Five-year plan of the Government of India [23]. The question is to what extent the Government will be able to formulate a perfectly integrated and balanced system of health-care and medical education for the country in future taking into consideration the complex aspects of the different systems of medicine prevalent in the country, each having its unique role in the Indian society?

Health is said to be the 'Mirror of the society' and so is the system of healthcare and medical education in any society I history. It is the same set of values and foresight that operate behind both of these essential constituents of a social system. Faculty development is an important component in medical education. It is necessary to organize faculty development in a systematic manner. Prudence and insight is necessary at various levels, as the stakeholders are many, viz., the policy makers, the Government of India, Medical Council of India, teachers, students and private and government college managements.[24]

India lies at an important crossroad in the field of the healthcare and medical education in the 21st century and has a difficult task ahead to formulate the suitable mode of action that should fit the pauper as well as the millionaire at the same time.

A fine act of balance indeed!

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Mediquiz - 03 / 2021

Hematology

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1. One unit of RDP increases platelet count in an adult by :

a) 5000 b) 10000
c) 15000 d) 20000

2. Which of the following is true about von Willebrand Factor (vWF) ?

a) It cross links platelets to each other.
b) It is non-functional in large multimeric form.
c) Plasma vWF is derived from platelets.
d) It carries Factor VIII.

3. Which of the following can be given safely in pregnancy for prolonged period ?

a) Warfarin.
b) Unfractionated heparin (UFH).
c) Low Molecular Weight Heparin (LMWH).
d) Acenocoumarol .

4. Which of the following matching is incorrect ?

a) Pencil cel (ovalocyte) – Iron Deficiency Anemia.
b) Spurr cell (Acanthocyte) – Acute Kidney Injury.
c) Burr cell (Echinocyte)–Chronic Kidney Disease.
d) Tear drop cell (Dacrocyte) – Myelofibrosis.

5. The earliest sign if Iron Deficiency Anemia is :

a) Decreased TIBC.
b) Decreased serum iron.
c) Decreased serum Ferritin.
d) Decreased % saturation of iron.

6. What is true about oral iron therapy ?

a) It should be coadministered with vitamin C.
b) Maxium dosage is 300 mg of elemental iron per day.
c) Maximum iron absorption occurs in terminal ileum.
d) Best given one hour before meal.

7. All of the following is true about Thalassemia Major except :

a) Splenomegaly. b) Increased RDW.
c) Presence of target cells in peripheral smear.
d) Most common cause of mortality severe extra-vascular hemolysis.

8. Which of the following states habe most number of cases of HbE disease ?

a) Punjab b) Tamil Nadu
c) West Bengal d) Bihar.

9. Which of following situation will lead to intravascular hemolysis ?

a) Group 'O' RBC transfused to Group A recipient.
b) Group 'O' RBC transfused to Group AB recipient.
c) Rh (+ve) RBC transfused to Rh (-ve) recipient.
d) Group A RBC transfused to Group 'O' recipient.

10. What is true about concentrated RBC (Packed Cell) unit ?

a) It should be brought to normal room temperature before transfusion.
b) It should be used within 30 minutes after removal from cold storage.
c) It should be preserved at 4°C temperature if not used within two hours.
d) The approximate volume required (ml) = Target rise of Hb (g/dl) x Body weight (kg) x 1.75

11. Immune destruction of platelets is seen in all, *except* :

a. CLL b. SLE
c. Hepatitis C
d. DIC (Disseminated Intravascular Coagulation).

12. Eosinophilia is defined as absolute Eosinophil Count :

a. >400 /cmm b. >500/cmm
c. >600/cmm d. >700/cmm

13. Which of the following is true about Neutropenia ?

a. Neutrophil count <1000 /cmm in Aplastic anemia.
b. Rarely associated with vitamin B12 deficiency.
c. May be drug induced in Hyperthyroid patients.
d. Acute Myocardial Infarction may precipitate it.

14. Which is *not* associated with Fanconi's anemia ?

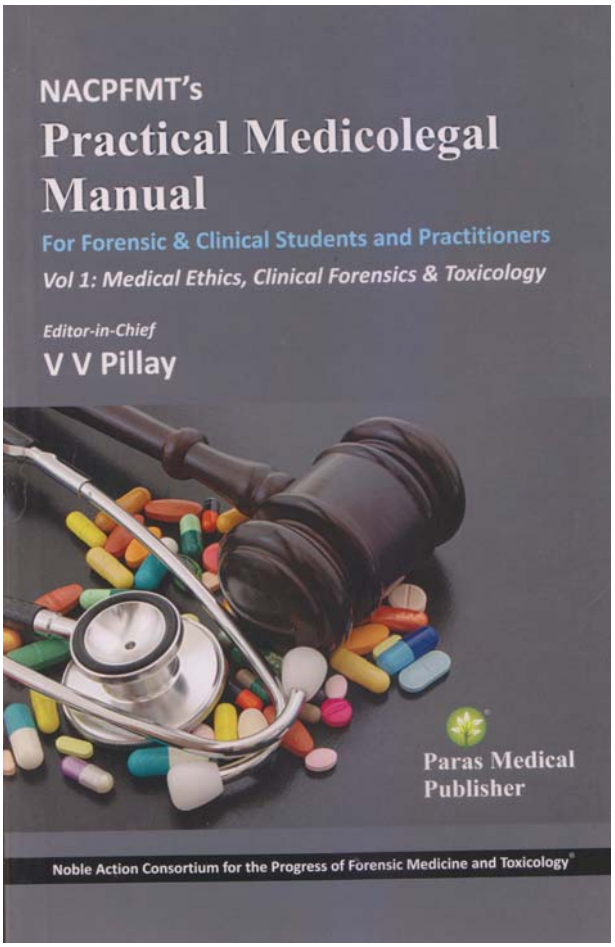
a. Hypopigmented patches on skin.
b. Short stature.
c. Upper limb abnormality.
d. Hypogonadism.

15. All of the following may cause Megaloblastic anemia except ?

a. Valproic acid. b. Methotexate.
c. Rifampicin. d. Phenytoin.

(Answer Page 69)

Book Reviews



"NACPFT's Practical Medicolegal Manual" by Prof V V Pillay, 1st Edition, 2019, Published by Paras Medical Publisher, 5-1-475, First Floor, Putlibowli, Hyderabad 500095, Telangana, India, pp 1-499. 14cm x 21.5cm, Rs550.00.

The book entitled "Practical Medicolegal Manual" Edited by Prof. V V Pillay is compiled in two volumes. Volume 1 contains chapters on Medical ethics, Clinical forensics and Toxicology. The multi authored handbook aims to guide the basic doctors, non forensic specialists and clinicians during their day to day practice of medicine.

As it is a practical manual hence it is quite obvious that indepth theoretical discussion will not be the priority. Selection of the chapters have been done keeping in mind the needs of clinical practice and the problems faced by the doctors. Basic knowledge about the legal and ethical aspects of medical practice is the need of the hour. The issues addressed in the chapters of "Gender Sensitization for Doctors", "Ethics and Law in Relation to LGBT Issues" and "Religious Issues in Medical Practice" are new ideas and deserve special mention.

In the Clinical Forensic Medicine section stress has been laid on the practical aspects of dealing with injury, asphyxia deaths and burn cases which is quite justified. However the format for reporting or certification of injuries or wounds projected in the book is an ideal one where as in reality the format varies in different states of the country, especially the ones used by the doctors in the emergency department. However the concepts of injury reporting reflected in the book would be a useful guide for the clinicians. The chapter dealing with "Dead on Arrival" is another innovative idea to present a topic of clinical relevance and is well appreciated.

Section 3 deals with "Medical Toxicology" which is no doubt one of the most important sections of the book. The current patterns of poisoning in the country and their management in acute cases have been dealt nicely. The antidotes of different poisons as listed in this section would be very helpful for the Emergency Medical officers. The chapter on "Basics of Paediatric Toxicology" is another unique idea reflected in the book. The final chapter of the book dealing with "Basics of Analytical Toxicology" is a bit off the track keeping in mind the primary readers of the book. The clinicians and basic doctors managing cases in semi urban and rural areas have limited access to the analytical techniques discussed in this section. None the less it would be beneficial for the postgraduate trainees in Forensic Medicine to enrich their knowledge.

Finally the hard glossy cover of the book with coloured figures and illustrations add to the quality of the book. The font, text size and the flow of language are also soothing for reading.

Overall the book definitely achieved what it intended to present to the readers. There is no spec of doubt that the book would be beneficial and very helpful for the non forensic specialists and fresh graduates to deal effectively with various critical issues in course of their practice. To sum up the authors and the editors efforts are truly worth appreciating.

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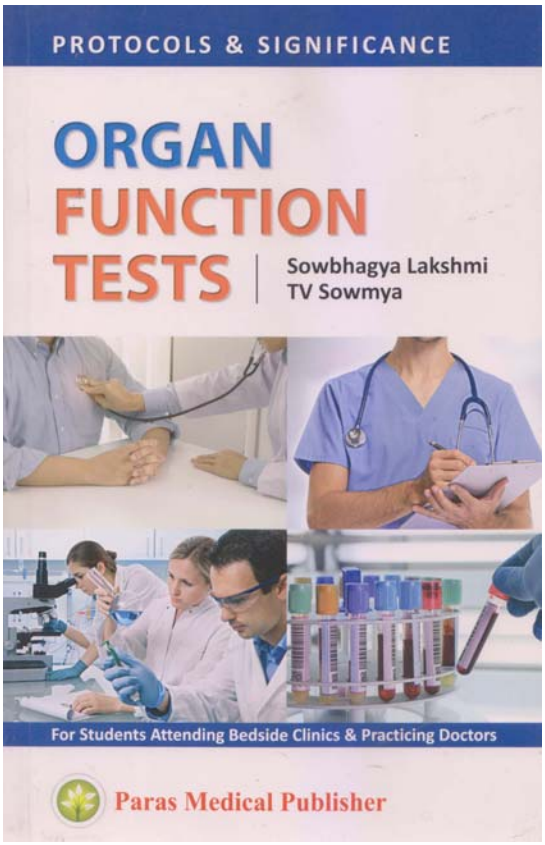

"Organ Function Tests" by Sowbhagya Lakshmi, TV Sowmya, 1st Edition, 2019, Published by Paras Medical Publisher, 5-1-475, First Floor, Putlibowli, Hyderabad 500095, Telangana, India, pp 1-275. 14cm x 21.5cm, Rs295.00.

"Organ Function Tests" by Sowbhagya Lakshmi, TV Sowmya is of great relevance to both undergraduate and post-graduate students of Biochemistry. The authors have done very well to balance the unavoidable technical terminology of the discipline of Biochemistry with lucid language that makes it easy to follow the discussion. Each topic starts with introduction of basic anatomy of the organ involved then going in detail about the different tests involved. The reference values of different biochemical parameters are given along with their interpretations in different pathological conditions. The liver function tests & Renal function tests need special mention as they are described elaborately with adequate examples, the various metabolic pathways are also touched upon which the students will find very easy to understand and correlate well with different disease conditions. The MCQs & case studies at the end of each chapter are carefully designed to enhance the reader's own involvement in the penetrating reflection that the book is intended to introduce him/her to. Newer tests should be given special emphasis which will evoke further interest. I recommend it highly for students of the discipline of Biochemistry & also convey my best wishes to the authors for upcoming editions.

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(Answer : Mediquiz 03/2021)

Answer keys :

(1) a, (2) d, (3) c,

(4) b, (5) c, (6) d,

(7) d, (8) c, (9) d,

(10) b, 11 (d), 12 (c),

13 (c), 14 (a), 15 (c).

Letters to the Editor

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

Global Hunger Index

Sir, — After the outbreak of pandemic Covid-19, and the great lockdown, the world as well as India faces the greatest crisis of shortage of purchasing capacity of food and a famine like condition pervasive. It is another famine - which is not visible, and being carefully covered - but which is spreading like wildfire.

On Friday, October 16, 2020, the results of a study published by "Concern Worldwide and Wealthungerhlife" ie, - World Hunger Index. It is published every year. This year, India ranks 94th out of 107 countries in the world in terms of global hunger index. For a country like India, the results have been disappointing and embarrassing, even though it has been a few steps up since last year. There are tears of hunger all over the country - not reaching the ears of the country's directors. No matter how dazzling the eyes may be on top, no matter how many boastful stories of development may be haunted, the tears in the chest can never be suppressed.

The report of the World Organization shows the deteriorating situation in India. India's position in the last few years according to the hunger index—

2011-67	**2015-80**
2012-66	**2016-97**
2013-63	**2017-100**
2014-55	**2018-102**

As much as there has been discussion of building up India's economy and improving expectations for everyday comforts, the more all discussion of improvement, the more the cry of hunger grows; Appetite is also increasing. Proving how stupid the development story is. More directly demonstrates the neglect in the preservation of our national child health, resulting in the deterioration of child health. This is because the World Hunger Index is based on a number of essential components of child health.

What are those elements ?

Malnutrition :

First, the rate of malnutrition. What percentage of Indian children are suffering from malnutrition. The survey says 14 percent. Although in reality the rate of malnutrition is much higher, many scientists believe.

Child Wasting :

Second is the calculation of whether the children are underweight according to their height. In English it is called Child Wasting Rate. In India, the child wasting rate is 17.3 percent.

Child Stunting :

Thirdly, where the height and growth of children is less than the age. Child stunting rate in India, is very high at 37.4 percent. This is a reflection of malnutrition and low birth weight.

Child Mortality :

Fourthly, the under-five mortality rate in India has come down slightly. Respiratory infections, infections, pneumonia, diarrhea have been reduced at birth, but on the other hand for low birth weight, premature infant mortality has increased.

Judging by these four criteria, India ranks 94th in the world hunger index in 2020, even below Pakistan. Ranks of some neighboring countries: Pakistan 88, Nepal 73, Bangladesh 74, Sri Lanka 64, Myanmar 78, and even 24 African countries are ahead of India. The report says the situation in India is serious.

In a country where only 2% of GDP is spent on health, child health is neglected; the situation in that country will be serious –without any doubt!

In this country on the one hand the grain is wasted in the warehouse and on the other hand the children are crying with hunger, which is suppressed. Child malnutrition is a major obstacle for the overall development of a nation.

In 2020, according to Human developmental index, India is lagging behind, 131st out of 189 countries, even behind Bangladesh. As mentioned earlier, infant mortality rates have declined somewhat. The state health minister has claimed that the infant mortality rate in West Bengal is lower than other states. But the survival of a sick, infirm, disabled child who is suffering from anemia, who is underweight, who is underweight in proportion to his age, increasing the burden of society - the ability to lead a successful life will remain elusive for all those children - and if the child suffers from such malnutrition, his talent and intellect will not be able to develop.

This cry of hunger is not of today – It was started a long time ago. In the context of globalization, it was said - the tears will decrease, will go away - but instead it has increased - it is increasing day by day. Pandemic Covid-19 has boost up it further. A private survey in West Bengal found that more than 18 per cent of people go to bed with hunger, while 44 per cent are forced to borrow money to buy two handfuls of food. Getting nutritious food is a far cry.

Past Associate Editor, JIMA **Dr. Amitabha Bhattacharya**

Are We Marching away from Safety

JIMA, Volume 119, Number 1, January 2021

Sir, — Today a patient was referred for fistula in ano . He had consulted an Ayush doctor for fistula in ano two years back , who tied a kshar sutra and has been treating from two years with worsening of symptoms. At present there is anal stenosis, persistent fistula but cannot do per rectal examination because of tight anal stenosis.

Who is responsible? No one blames the Ayush doctors for the negligence.

Second case : a patient came with sloughing of anal area in shock, giving history of sclerosant injection in haemorrhoids, we had to perform colostomy to heal the anal area. Again who is liable? These are some examples who come to surgeons all over the country. These are the few procedures which Ayush doctors perform freely without thinking about the morbidity and mortality of the patients.

In the editorial above the editor has brought up the current issue of allowing Ayush doctors to perform Surgery. Especially the remark in the last paragraph "we all know that MS stands for Master of Surgery in modern Medical education in Indian Medical education system. In this vast country it is next to impossible to identify/distinguish somebody who designates himself as only MS."

If they are allowed other procedures without any liability it will increase the morbidity of patients. Already patients come with advanced stage of malignancy as they were promised by Ayush doctors of treatment. In India illiteracy and ignorance leads the patient to an easily available option or fooled by middleman to be treated.

Ayush doctors do not face the violence against doctors and are not held responsible for procedure they do.

Government should look at the consequences and instead of giving Guns to amateurs provide facilities at already existing surgical centres.

Hope government understands these things and puts the Ayush doctors too under some law and answerable to patients.

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