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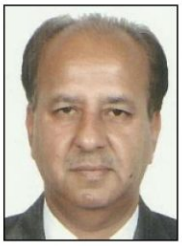

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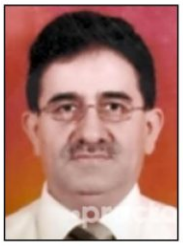

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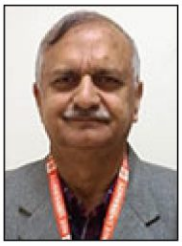

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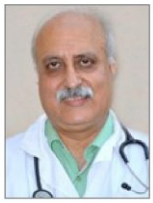

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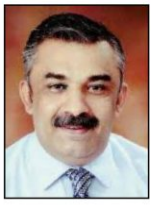

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Editorial

Congenital Hypothyroidism : Need for National Health Policy

Congenital Hypothyroidism (CH) is caused due to insufficient production of thyroid hormone at birth[1]. It is one of the most common treatable causes of mental and growth retardation[2]. Neurodevelopmental outcome is normal if CH is diagnosed and managed within two weeks of birth. If left untreated, it may cause lifelong suffering as a result of mental retardation and growth deficiency. Clinical presentation of CH is usually subtle and most newborns with CH appear normal at birth because some amount of thyroid hormone is transferred from mother to baby during pregnancy. Maternal thyroid hormone provides protective effect and masks clinical features of CH in newborns. Common forms of CH also have some functioning residual thyroid tissue, making it more difficult to diagnose at birth. Within few weeks of birth, clinical signs and symptoms of CH become evident due to deficiency of thyroid hormone production. Delay in diagnosis and management of CH causes permanent neurologic damage[3]. There is an inverse relationship between age at clinical diagnosis of CH and Intelligent Quotient (IQ) score[4,5].

Newborn screening for CH is the most feasible and cost-effective way to detect CH at birth and to begin treatment immediately. It is one of the cornerstones of preventive medicine having proven benefits. Introduction of universal newborn screeninghas eliminated CH as a cause of mental retardation in developed nations[6]. However, it remains a problem in developing nations such as India where universal screening programs for detecting CH in newborns are not routinely implemented[2].

Epidemiology :

Globally, incidence of CH usually varies between 1 in 3000 to 1 in 4000 live births. Females are more likely to have CH than males. Infants with Down Syndrome are at increased risk of being born with CH[3]. Incidence rates vary due to differences in geography and ethnicity, iodine deficiency or type of screening methods used[2]. In India, the first newborn screening for CH was conducted in 1982 using cord blood Thyroid Stimulating Hormone (TSH) and then in 1984 using postnatal dried blood spot (DBS) T4. Prevalence was 1:2481 and 1:2804 respectively[7]. Studies also showed state-wise incidence to be 1:1985, 2.1:1000, 1.6:1000, 1:1700, and 1:1221in Hyderabad, Kochi, Chennai, Andhra Pradesh, and Uttar Pradesh, respectively[8].

Recent assessment by ICMR revealed a much higher incidence of congenital hypothyroidism all over India at 1 in 1172, particularly in south Indian population (1 in 727)[9].

Etiology :

CH may be primary due to thyroid gland dysfunction or secondary due to pituitary gland dysfunction. In primary hypothyroidism, there is deficiency of thyroid hormone at birth caused by abnormal thyroid gland development (thyroid dysgenesis) or disorder of thyroid hormone synthesis (thyroid dyshormonogenesis)[1]. Thyroid dysgenesis accounts for 85% of cases while thyroid dyshormonogenesis accounts for 15% of cases[3]. Secondary or central hypothyroidism at birth results from deficiency of thyroid stimulating hormone. It is usually associated with congenital hypopituitarism[1,3].

CH is further classified into permanent and transient CH. In permanent CH, there is permanent deficiency of thyroid hormone which requires life-long management. On the other hand, transient CH is characterized by temporary deficiency of thyroid hormone at birth, which slowly resolves with time[1].

Clinical Features :

CH goes undetected in many newborns because clinical features are not apparent at birth. Symptoms appear slowly and are often non-specific. This indicates the importance of universal newborn screening programs to ensure diagnosis and prompt management. Presence of goiter, prolonged jaundice, birth weight more than 90th percentile, delayed development, poor growth, poor feeding, hypothermia, bradycardia, large fontanelles, macroglossia and umbilical hernia are some symptoms of CH[1,3,6].

CH is associated with an increased risk of other congenital abnormalities or malformations, the commonest being cardiac defects. Other abnormalities may include hearing loss, genitourinary anomalies, interstitial lung disease, cleft palate, bifid epiglottis, spiky hair, neonatal diabetes, congenital glaucoma, and liver and kidney disorders[6].

Diagnosis : Universal Newborn Screening

Universal newborn screening is the most effective method for detecting CH at birth. This is followed in most of the developing world, which has helped reduce incidence of CH in these countries. In absence of newborn screening, diagnosis is delayed which causes poor prognosis. Complete diagnostic evaluation should include detection of CH by newborn screening, confirmation by repeat thyroid function test, and determination of underlying etiology by diagnostic studies[1,2].

Newborn screening is usually carried out between two and five days of life, before discharge from hospital. Specimens collected before 48 hours of life may give false positive results. On the other hand, screening very sick newborns or screening after blood transfusion may give false negative results. Blood sample from heel prick or cord blood sample is collected on filter paper and sent to central laboratory for initial TSH or initial T4 test, with a follow-up TSH test[3,6].

Diagnostic Criteria :

According to the Indian Society for Pediatric and Adolescent Endocrinology (ISPAE)[10],

- Every newborn should be screened using heel prick method ideally within 48 to 72 hours of birth.
- Newborns with TSH < 20 mIU/L for >48hours of birth or TSH <34 for sample taken between 24-48 hours of birth should be treated as normal.
- Newborns with TSH > 20 mIU/L at > 48 hours of birth or TSH >34 mIU/L for samples taken between 24 to 48 hours of age should be recalled for confirmation within 1 week (by 7-10 days of life).
- For screen TSH > 40 mIU/L, immediate recall for confirmatory venous T4/FT4 and TSH, and for milder elevation of screen TSH, a second screening TSH at 7 to 10 days of age, should be taken.
- Sick babies should be screened at least by 7 days of age.

Management :

According to Indian Academy of Pediatrics (IAP) standard treatment guideline 2022[11],

- As soon as diagnosis is made, treatment with levothyroxine should be started within first 2 weeks of life. Initial thyroxine dose is 10–15 μg/kg/day.
- Treatment is recommended for newborns with FT4 < 1.17 ng/dl or T4 < 10 μg/dl with the same dose.

- Newborns with high TSH > 20 at less than 2 weeks and TSH >10 at more than 2 weeks are to be treated.
- Newborns with low FT4 (1.1 ng/dl) or T4 (<8 µg/dl) with normal TSH and those with normal FT4/T4 with high TSH (>10 beyond 3 weeks) are to be treated.
- A single morning dose at the same time is to be taken every day on empty stomach by crushing with a spoon and mixing with few ml of breast milk.

Prognosis :

Timely diagnosis and management are essential for preventing long-term adverse outcomes due to CH. Universal newborn screening, along with repeated screening of high-risk infants, and diagnostic tests are required for appropriate diagnosis and management. Treatment with levothyroxine should be started within first two weeks of life to ensure normal thyroid function. Prognosis is excellent for newborns with CH when properly managed[6].

Conclusion :

Newborn screening program for CH must be established at national level in India in order to reduce morbidity by preventing mental retardation and physical disabilities. CH is easy to detect, and inexpensive to treat. Newborn screening programs should be aimed at detecting all cases as early as possible, with an acceptable cost-benefit ratio.

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Original Article

Association of Dietary Protein on Level of Anti Mullerian Hormone (AMH) and Antral Follicle Count (AFC) in Patients of Infertility

Poonam Singh[1], Radhika Anand[2]

Background : "Infertility is defined as the inability to conceive within a year with normal frequency of sexual intercourse and no contraceptives." Relatively little is known about the effect of nutritional content on fertility.

Objective : To study the correlation of level of AMH and AFC with dietary habits especially protein intake in patients of infertility.

Material and Methods : It is hospital based study.

Design of study : Cross sectional study.

Place of study : Teerthankar Mahaveer Medical College & Research Centre, Moradabad, India .

Number of Patients : 95 patients of infertility included in the study .Patients were between 30 and 45 years.

Time Period : 18 months from January 2020-July 2021.

Method : All cases underwent full history taking; clinical examination and all completed a questionnaire consisting of demographic characteristics, FFQ (Food Frequency Questionnaire).

Main Outcome Measures : Moderate to high protein intake in diet corresponds to those having met their more than 20% calorie intake by protein had a higher mean AMH as well as had a higher mean AFC.

Result : Based on the results of the current study the effects of higher protein intake was found to be significant on the level of ovarian reserve .

Conclusion : This study suggests that good and healthy Nutrition, rich in proteins , in fertility treatment is required for better outcome and also helps in limiting the financial burden.

[*J Indian Med Assoc* 2022; **120(12):** 15-9]

Key words **: Antral Follicle Count, Anti Mullerian Hormone, In Vitro Fertilization, Body Mass Index**

On a global basis, roughly 15% of eligible couples experience infertility, which translates to about 60-80 million couples[2]. Infertility rates may differ by area[3]. According to the World Health Organization (WHO), prevalence of primary infertility in India ranges between 3.9 percent to16.8 percent. Lifestyle, diet, sexual health, substance abuse and psychosocial factors all have an impact not only on the outcome of fertility treatment but also on pregnancy health, which is essential in pre-conception care[4-6]. While it is well accepted that diet and modifiable lifestyle variables affect female[7-11] as well as male fertility[12-14], knowledge in this area is sparse, which make planning of pregnancy limited with few evidence-based resources to aid with pre-conceptional nutrition and lifestyle advice. Relatively little is known about the effect of nutritional content on fertility .

The Antral Follicle Count (AFC) and serum Anti Mullerian Hormone (AMH) are the most relevant indicators of ovarian reserve[16]. AMH and AFC have shown to be more accurate predictors of the number of ovarian primordial follicles

Editor's Comment :

- Females with poor health due to unhealthy and unbalanced diet have poor fertility as is seen in many infertile ladies. A good and healthy Nutrition, rich in proteins is required for better fertility and also helps in limiting the financial burden.

Although it is widely assumed that lifestyle variables have a detrimental influence on ovarian reserve and AMH levels[17-20], not all research agree[19] and the majority of studies do not examine the response of other contributing factors.

The purpose of this study is to examine the probable influence of dietary factors (proteins) in determining the level of both the mentioned markers of ovarian reserve in infertile patients.

As limited number of studies are available in India of regarding impact of dietary and lifestyle factors in patients of infertility. Therefore, this study would aim at studying the correlation of level of AMH and AMC with dietary habits.

Aims :

To Study the association of dietary proteins on level

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of Anti Mullerian Hormone (AMH) and Antral Follicle Count (AFC) in patients of infertility.

Review of Litrature :

(Rich-Edwards JW, *et al*)[28] Unbalanced meals high in carbs, fat, proteins constituents and other micronutrients negatively influence ovulation (Chavarro JE, *et al*)[29]. in their study "Diet and lifestyle in the prevention of ovulatory disorder infertility" concluded that in an otherwise healthy women, following a "fertility diet" plan may help them conceive.

(Chavarro JE, *et al*)[29], researchers at Harvard Medical School, found that carbohydrates influences ovulation and fertility in healthy women because it affects the metabolism of glucose and demand of insulin and its sensitivity (PCOD).

(Hohos NM, *et al*)[32] stated that diet with high fat has ill effect on female fertility, having possible impacts ovulation. Similar findings were seen in a research done by (KaboodMehri R, *et al*)[33] studied the correlation between Anti Müllerian Hormone (AMH) levels and food consumption in Iranian females. Additionally, some have discovered diet rich in fat exacerbates atresia of follicles[34,35].

Materials and Methods

Study Design : A cross sectional study

Study Setting : The Department of Obstetrics and Gynaecology, Teerthanker Mahaveer Medical College & Research Centre.

Study Population : Women attending the Department of Obstetrics and Gynaecology with Diagnosis of Primary or Secondary Infertility.

Study Duration : 18 Months

Sample Size : 95

To calculate sample size based on the prevalence we can use the following formula :

Sample Size = $(Z^2 PQ)/ E^2$

Z = Standard Normal Variate

P = Prevalence of infertility

E = absolute error (5-10%) acceptable

Q= (100-P)

Z =2.58 at 1% type 1 error

Here

Z^2 = 2.58 at 1% type 1 error

P=3.7%

E=5%

n = [(2.58)2 X 3.7X (100-3.7)]/ (5^2) =94.86 =95

Inclusion Criteria :

- Women attending the Department of Obstetrics and Gynaecology with diagnosis of primary or secondary infertility.
- Women between ages of 30-45 years, married for at least 1 year and sexually active.
- Patients with both ovaries intact
- Patients ready to give consent to participate in the study

Exclusion Criteria :

- Patients <30 years and >45 years
- Patients with immune infertility
- Patients with male factors of infertility
- Patients with sexually transmitted infection
- Traumatic or congenital malformation in the genital systems.
- Endometrial cause of infertility
- Patients of primary amenorrhea

23040 number of patients attended the Gynaecology OPD during the duration of 18 months, 691 number of patients were patients of primary or secondary infertility anxious to concieve out of which 389 belonged to the age group of 30-45 years. After applying inclusion and exclusion criteria, we enrolled 95 patients in our study. All the participants were assesed on the basis of the prevalidated questionnaire to assess their protein intake .

Calculation of Antral Follicle Counts Using Ultrasound Techniques :

Each participant in the study underwent a standard infertility evaluation, that included determination of the AFC using the Siemens ACCUSON S2000 ultrasound machine on third day of an unstimulated menstruation or on third day of bleeding after progesterone withdrawal. One examiner performed all transvaginal ultrasounds. AFC was done on 1st visit of each patient in OPD, before starting any treatment so as to avoid any bias.

AMH Assessment :

A sample for AMH obtained for all subjects under aseptic precaution on the 1st visit of patient to OPD. The sample sent to Biochemistry Department.

AMH values differentiated according the normal value depending upon age group[41].

Value of Normal Range of AMH According to Age Groups

Age	ng/ml	pmol/L
Under 33 years old	2.1-6.8	15.0-48
33-37 years old	1.7-3.5	12.14-32.13
38-40 years old	1.1-3.0	7.8-21.42
41 + years old	0.5-2.5	3.57-17.85

Statistical analysis : Data so collected was tabulated in an excel sheet, under the guidance of statistician. The means and standard deviations of the measurements per group were used for statistical

analysis (SPSS 22.00 for windows; SPSS inc, Chicago, USA). For each assessment point, data were statistically analyzed using one way ANOVA. Difference between two groups was determined using student t-test and the level of significance was set at $p \leq 0.05$.

Observation and Results

Table 1 — *Co-relation of Age to AMH*

Age	Group					
	Frequency	Percent	Mean	STD Deviation	F value	p value
Under 33	63	66.3	4.66	1.11	4.93	0.021*
37-40	2	2.1	1.53	1.40		
33-37	21	22.1	4.25	1.18		
>41	9	9.5	1.43	1.41		

Table 2 — *Co-relation of AFC to Age*

Age	Group					
	Frequency	Percent	Mean	STD Deviation	F value	p value
Under 33	63	66.3	4.44	1.75	3.08	0.042*
37-40	2	2.1	2.50	0.71		
33-37	21	22.1	4.33	1.76		
>40	9	9.5	4.78	1.59		

The subject were classified according to their age corrected AMH groups.We found that a total of 31 subjects that amounts to about 32.6% had low AMH values while 24.3% had high AMH values while the rest 41% which was the majority belonged to the nomal range of AMH (Table 3).

We found that a total of 27 subjects that amounts to about 28.4% had low AFC values while 13% had high AFC values ie >10 while the rest 55% which was the majority belonged to the normal range of AFC ie 3-8 in each ovary (Table 4).

The majority of the participants 57.9% preffered mixed diet while 42.1 % prefered vegetarian diet. It was found that the mean AMH was higher in the patients

Table 3 — Level of AMH

AMH	Frequency (n)	Percent (%)
Low	31	32.6
Normal	41	43.2
High	23	24.2

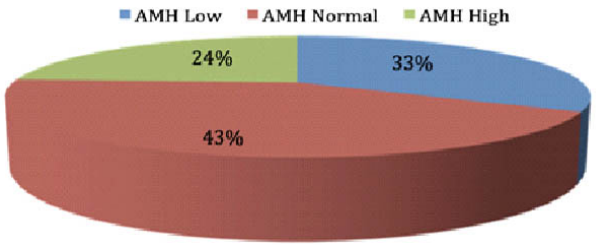
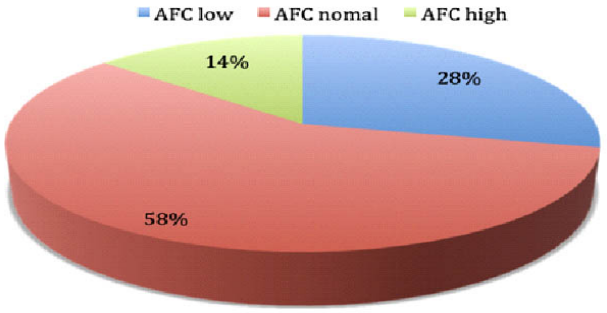


Table 4 — Level of AFC

AMH	Frequency (n)	Percent (%)
Low	27	28.4
Normal	55	57.9
High	13	13.7



that were vegetarian as compared to the ones who prefered mixed diet but the p value was 0.653 so the relationship was not significant (Table 5).

Majority of the patients 69.5% had moderate protein intake that is about 20-35% of their calorie intake was from the protein. The relationship of moderate to high protein intake in their diet that corresponds to those having met their more than 20% calorie intake by protein had a significant relation with the level of AMH and had a higher mean AMH (Table 6).

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Discussion

Our study found a strong association between a high ovarian reserve and AMH and AFC in patients on a moderate protein diet, defined as individuals consuming between 20% and 35% of calories from protein. Patients on this diet had a higher ovarian reserve in both AMH and AFC. The link between carbohydrate and fat consumption and ovarian reserve, on the other hand, was determined to be statistically negligible. There have been few studies examining the link between the calorie percentage from various macronutrients and the degree of ovarian research such as AMH and AFC. Souter I, *et al*[1] according to their findings, total protein intake (as a percentage of total calories) was not associated with AFC in 264 women. The researchers identified a negative connection between protein derived from dairy products consumption and Antral follicular count when they looked at protein from other dietary sources

independently of dairy protein consumption. There were no associations found between protein derived from non-dairy diet or protein derived to vegetable components and AFC in the research.

Conclusion

- Based on the results of the current study the effects higher protein intake was found to be significant on the level of ovarian reserve.
- This study suggests that inculcation of Nutrition and lifestyle modification Counseling into fertility treatment is required for better outcome and also help in limiting the financial burden.

Limitations of the study included :

Data acquired was self-reported via questionnaires administered to research participants for many lifestyle variables. For example, it is widely established that participants tend to underreport non-socially desirable activities such as alcohol consumption and smoking, which may result in some persons being misclassified.

Additionally, the very small sample size, in particular, may create some statistical power issues. This may be represented in the fact that some of the results are statistically insignificant, while others indicate substantial and steady trends.

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Contributions : PS contributed to the design and drafting of the manuscript. PS contributed to the formal analysis, statistical analysis and editing of the manuscript. RA contributed to the methodology and experimental test. The authors have read and approved the final manuscript.

Conflicts of Interest : There is no conflict of interests

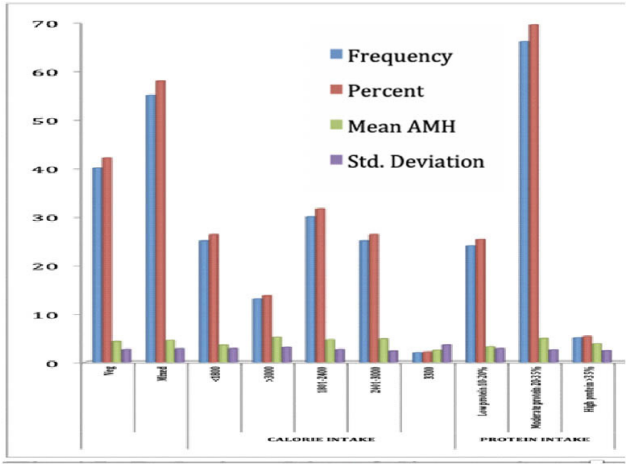
Table 5 — *Relationship of protein intake and level of AMH*

	Frequency(n)	Percent%	Mean	Std. Deviation(SD)	t value	p value
Veg	40	42.1	4.44	4.81	0.45	0.653
Mixed	55	57.9	4.02	3.83		
CALORIE INTAKE						
<1800	25	26.3	4.57	3.04	1.807	0.134
1801-2400	13	13.7	6.79	9.20		
2401-3000	30	31.6	3.48	2.45		
3000-3300	25	26.3	3.31	2.54		
>3300	2	2.1	4.50	2.12		
PROTEIN INTAKE						
Low protein 10-20%	24	25.3	1.92	1.03	8.11	0.002*
Moderate protein 20-35%	66	69.5	4.49	1.31		
High protein >35%	5	5.3	4.26	1.26		

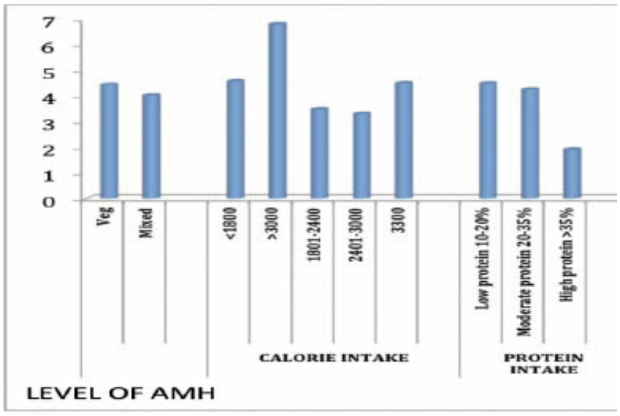
Table 6 — *Relationship of dietary intake and level of AFC*

	Frequency(n)	Percent%	Mean	Std. Deviation(SD)	t value	p value
Veg	40	42.1	4.28	2.63	-.419	0.676
Mixed	55	57.9	4.51	2.77		
CALORIE INTAKE						
<1800	25	26.3	3.52	2.82	1.380	.247
1801-2400	13	13.7	5.15	3.08		
2401-3000	30	31.6	4.63	2.63		
3000-3300	25	26.3	4.80	2.31		
>3300	2	2.1	2.50	3.54		
PROTEIN INTAKE						
Low protein 10-20%	24	25.3	3.21	2.81	3.77	0.02*
Moderate protein 20-35%	66	69.5	4.89	2.57		
High protein >35%	5	5.3	3.80	2.39		

Relationship of Protein Intake and Level of AMH



Relationship Protein Intake and Level of AMH



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Original Article

A Clinical Correlation of EEG Changes in Relation to Ischaemic Stroke on its Prognosis as per Location

Amit Mukherjee[1], Paramita Bhattacharya[2], Sujoy Sarkar[3], Arkadeb Maity[1], Mrinal Kanti Roy[4], Salil kumar Pal[5]

Background : Stroke is a common, potentially devastating disease with potential high morbidity and mortality. EEG (Electro-encephalogram), functional representation of electrical activity of brain, changes are closely tied to CBF (Cerebral Blood Flow). Thus EEG is useful to establish the location of Ischaemic CVA (Cerebro-vascular accident). It can also prognosticate Ischaemic stroke.

Aims & Objectives : (1) To assess the grade and severity of clinical manifestations in acute ischaemic stroke patients by clinical scoring following admission. (2) To obtain EEG findings of ischaemic stroke patients following admission and after 1 month. (3) To assess the morbidity of ischaemic stroke patients by Modified Rankin Scale after 1 month. (4) To correlate EEG changes according to the clinical outcome and according to the site of involvement of ischaemic stroke.

Materials and Methods : 90 Patients were selected during the study period as per the inclusion and exclusion criteria. Clinical scoring was done by NIHSS (National Institute of Health Scoring System). CT (Computed Tomography) scan of brain and MRI (Magnetic Resonance Imaging) Brain with DWI (Diffusion Weighted Image) extension was done. EEG findings on admission of morbidity was done by Modified Rankin Score on follow up after 1 month was noted. EEG findings after 1 month was noted on follow up. Assessment Clinical correlation was compared with EEG changes. All the data were collected and analysed by statistical software SPSS version 20.

Results : The mean MRS (Modified Rankin Score) after 1 month for abnormal EEG on admission was 4.50 in comparison to score of 3.36 in case of normal EEG. The p value of this association was 0.003 and was considered significant.

Conclusions : Normal EEG and focal slowing of EEG was mostly noted in MCA (Middle Cerebral Artery) and PCA (Posterior Cerebral Artery) infarcts involving the cortical region. Those with normal EEG findings had good clinical outcome in comparison to those with abnormal findings in EEG.

[*J Indian Med Assoc* 2022; **120(12):** 20-2]

Key words **: Stroke, EEG, NIHSS, MRS.**

Stroke is a common disease with potential high morbidity and mortality, requiring accurate diagnosis rapidly. EEG, representation of electrical activity of neuronal network of brain, is closely related to changes in Cerebral Blood Flow. Thus EEG is closely related to changes in Cerebral Blood Flow. Thus EEG is important in establishing the site and prognostication of Ischaemic CVA.

Aims and Objectives

Our aims and objectives were grading the severity of clinical manifestations in acute ischaemic stroke patients by clinical scoring and to obtain EEG findings following admission. Then to assess the morbidity by Modified Rankin Scale (MRS) and obtain EEG of them after 1 month. Lastly to correlate EEG changes according to the clinical outcome and according to the site of involvement of ischaemic stroke.

Editor's Comment :

- CVA is a major cause of mortality and morbidity.
- EEG is a simple test that can predict the severity of the disease.
- It can help in prognostication of the patient and thus help in proper care and rehabilitation of the patient.

Materials and Methods

It was an institution based descriptive study done at Medicine Ward at CNMCH, Kolkata for a period of 18 months. 90 haemodynamically stable patients, without existing neurological diseases and metabolic encephalopathy, from the age group of 18-95 years with signs of ischaemic stroke, NIHSS>4 and supportive neuro-imaging were selected. EEG findings of these patients were noted during admission and during follow up after 1 month. During follow up

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morbidity was assessed by MRS. All the data were collected and tabulated. Categorical variables are expressed as Number of patients and percentage of patients and compared across the groups using Pearson's Chi Square test for Independence of Attributes/ Fisher's Exact Test as appropriate. Continuous variables are expressed as Mean, Median and Standard Deviation and compared across the groups using Mann Whitney U test/Kruskal Wallis Test as appropriate. The statistical software SPSS version 20 has been used for the analysis. An alpha level of 5% has been taken, ie, if any p value is less than 0.05 it has been considered as significant.

Analysis and Results

In our study most of the patients were in the age group of 61-70 years (45.6%), followed by the 51-60 years age group. Range of age was 51-85 years. Females were 44.4% and Males were 55.6% of the study-population. MRI of Brain with DWI extension revealed - 63.3%, 14.4%, 4.4% of the cases had MCA territory infarction, Multi-infarct state, ACA territory involvement respectively. On admission, 58.9%, 18.9%, 14.4%, 7.8% of the cases showed Normal EEG, Focal, Diffuse slowing and Multifocal slowing respectively. During follow up at 1 month, 91.8% of the cases showed Normal EEG, Focal and Diffuse slowing was noted in 4.1% cases each. The mean MRS after 1 month for abnormal and normal EEG on admission was 4.30 and 3.68 respectively, p value being 0.024 (significant). Among the abnormal EEG on admission the mean values of MRS were 3.29±0.59 and 5.77±0.44 in cases with focal slowing and diffuse slowing respectively, with p value of <0.001 (significant). The mean values of MRS were 3.36±0.8, 4.0±0, 5.0±0 in cases with normal EEG, focal slowing and diffuse slowing of EEG on follow up, with the p value of 0.006 (significant). In our study all Normal EEG on admission were focal lesions. Among abnormal EEG findings 64.86% and 35.14% were with focal lesions and Multi-infarct state respectively with p value being <0.001 (significant). During follow up all of the normal EEG was of patients with Focal lesions and abnormal EEG findings were equal among focal lesions and multi-infarct state with p value of <0.001 (significant). Our study shows 73.58% and rest of normal EEG on admission were with Subcortical lesions and Unifocal lesions respectively. Among the abnormal EEG 66.67%, 4.17% and rest were of unifocal, subcortical and multifocal lesions respectively, with p value <0.001 (significant). Our study showed 96.43% of cases with MCA territory infarct had normal EEG after 1 month in comparison to 68.42% on admission, which was statistically significant. Also 3.57% of cases with MCA infarct showed EEG with focal slowing after 1 month against 19.3% on admission, which was also considered significant. Significant improvement was also found in case of multifocal slowing of EEG in MCA territory infarct. 90.0% of PCA territory infarct showed normal EEG after 1 month against 54.55% on admission, with a significant p value. 10% of them had focal slowing after 1 month in comparison to 45.45% on admission, which was statistically significant. 91.67% of cortical lesions showed normal EEG after 1 month in comparison to 37.84% on admission with p value of <0.001 (significant). 8.33% of them showed focal slowing after 1 month in comparison to 43.24% on admission, which was statistically significant. Significant improvement change in multifocal slowing of EEG in them was also found. This study showed good clinical outcome in patients with ACA, MCA and PCA infarct. Whereas, Pontine infarct and those with Multi-infarct state showed very poor clinical outcome with high mortality. The p value of this correlation was found significant. The mean MRS after 1 month for ACA, MCA, PCA, Multi-infarct and pontine infarct respectively were 3±0, 3.44±0.91, 3.73±1.19, 5.77±0.44, 6±0. Multi-infarct state was associated with high mortality rate, whereas, cortical or subcortical lesion showed good clinical outcome according to MRS after 1 month which for cortical, subcortical and multi-infarct state respectively were 3.54±0.77, 3.7±1.34, 5.77±0.44. The p value of this study was also significant (Tables 1 & 2).

Discussion

The patients in our study was between 44 to 85 years of age, with maximum patients in the group of 61-70 years (45.6% of the patients). In our study there were 55.6% males and 44.4% females. A previous study[1] showed prevalence of stroke for individuals older than 80 years is more than that of individuals of 60-79 years of age. Other studies[2,3] showed that stroke is commoner in men and most common age group was 61-70 years. In our study MCA territory infarct was commonest followed by Multi-infarct state, PCA infarct and Pontine infarct. Previous studies[4,5] revealed MCA territory was most frequently involved. On admission normal EEG was commonest finding followed by focal slowing and diffuse slowing. But in previous studies[6,7], the most common EEG finding was focal slowing (43.5%). 91.8% cases showed normal EEG on follow up, similar to a previous study[8]. In our study Abnormal EEG findings significantly decreased from 41.1% on admission

Table 1 — *Comparison of EEG findings on admission and after 1 month according to site of infarct*

		NORMAL EEG			FOCAL SLOWING			DIFFUSE SLOWING			MULTIFOCAL SLOWING		
		On Admission	After 1 month	p Value	On Admission	After 1 month	p Value	On Admission	After 1 month	p Value	On Admission	After 1 month	p Value
MRI FINDINGS	ACA INFARCT	3(75)	4(100)	0.248	1(25)	0(0)	0.248	0(0)	0(0)	NA	0(0)	0(0)	NA
	MCA INFARCT	39(68.42)	54(96.43)	<0.001	11(19.3)	2(3.57)	0.007	0(0)	0(0)	NA	7(12.28)	0(0)	0.005
	PCA INFARCT	6(54.55)	9(90)	0.046	5(45.45)	1(10)	0.046	0(0)	0(0)	NA	0(0)	0(0)	NA
	MULTI-INFARCT	0(0)	0(0)	NA	0(0)	0(0)	NA	13(100)	3(100)	1.000	0(0)	0(0)	NA
	PONTINE INFARCT	5(100)	0(0)	NA	0(0)	0(0)	NA	0(0)	0(0)	NA	0(0)	0(0)	NA

Table 2 — *Comparison of EEG findings on admission and after 1 month according to site of lesion*

		NORMAL EEG			FOCAL SLOWING			DIFFUSE SLOWING			MULTIFOCAL SLOWING		
		On Admission	After 1 month	p Value	On Admission	After 1 month	p Value	On Admission	After 1 month	p Value	On Admission	After 1 month	p Value
Lesions/ Site	Cortical	14(37.84)	33(91.67)	<0.001	16(43.24)	3(8.33)	<0.001	0(0)	0(0)	NA	7(18.92)	0(0)	0.003
	Subcortical	39(97.5)	34(100)	0.311	1(2.5)	0(0)	0.311	0(0)	0(0)	NA	0(0)	0(0)	NA
	Multiinfarct	0(0)	0(0)	NA	0(0)	0(0)	NA	13(100)	3(100)	1.000	0(0)	0(0)	NA

to 8.2% after 1 month Among all the cases discharged, 17 patients died before follow-up. The mean MRS after 1 month for abnormal EEG on admission was 4.50 that is significantly more than a score of 3.36 in normal EEG. There was significant improvement in EEG findings on follow up in comparison to that on admission in cases with MCA and PCA territory infarct. Cortical lesions also showed significant improvement in EEG findings after 1 month. Clinical outcome determined by MRS after 1 month also showed significant correlation with territory and site of infarct corroborating EEG findings. Patients with ACA, MCA and PCA infarct showed better prognosis than those with Pontine infarct and with Multi-infarct state. Simple EEG study can give an idea about the site of Simple EEG study can give an idea about the site of infarct as well as the clinical outcome. Though neuroimaging have taken an important place in determination of site of ischaemia, EEG can be used as a contemporary measure to diagnose and prognosticate this. Neuroimaging needs expensive apparatus and infrastructure whereas EEG can be done with portable machines in the remotest corners in our country. With proper training reporting can also be done locally or with the help of Telemedicine. Thus we can prognosticate cerebral infarct in a cost effective way in a resource poor country like ours.

Conclusion

Patients with normal EEG had better clinical outcome. Normal EEG and focal slowing of EEG was mostly noted in MCA and PCA infarcts involving the cortical region. Hence an idea about the site and vascular territory of the lesion can be determined.

Limitations of the study : As the study used small population group, it may not simulate other studies. Simple EEG recordings were done instead of Continuous EEG or Quantitative EEG. As the study was done in a tertiary care centre it may not represent the community, as mainly patients with poorer condition presents here.

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Original Article

Benign Retrovesical Pelvic Mass in Men : Diagnostic and Management Dilemma

Rama Kishan Saran[1], Kiran Mirdha[2], Sanya Saran[3], Irshad[4], Aishwarya[4]

Aim : To identify the diagnostic difficulties and management issues of benign pelvic masses in males and high light the diagnostic protocol for these rare pelvic masses.

Methods : A prospective single center study over a period of six years and three months. History, physical examination, operative findings and histopathological (HPE) diagnosis were recorded.

Results : A total of 20 male patients presented with retrovesical mass, aged 17 to 65 years old (mean age 36.7 years) were evaluated. masses were found to be of prostatic origin in seven cases (5 prostatic utricle cyst and 2 prostatic abscess), connective tissue in seven, seminal vesicle origin in four, mullerian duct remnant in one case, and embryonic urogenital vestigial remnants in one case. Of these 20 patients, 19 presented with acute or chronic lower urinary tract symptoms and in one case, the mass was asymptomatic and found incidentally. Ultrasound showed cystic lesions in 17 patients and solid masses in three. Nine cases underwent exploratory laparotomy. Further biopsies of specimen demonstrated tissue of origin in all cases (8/9) except one. HPE report confirmed the same clinical and operative diagnosis in six cases.

Conclusion : Benign retrovesical mass presents with lower tract obstructive symptoms, palpable pelvic mass and retention of urine. Needle or open biopsy is required in most cases to establish a histopathological diagnosis. Benign retrovesical mass is rare, we faces difficulty in diagnosis and management. Hence, diagnostic protocols can be helpful to manage retrovesical pelvic masses.

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Key words **: Diagnostic protocol, Seminal vesicle, Prostate, Histopathology.**

Retrovesical pelvic mass are often inflammatory, neoplastic or congenital. Benign pelvic masses in males apart from benign prostatic hypertrophy and bladder or prostate cancer may be a rare entity and pose problems in diagnosis and management[1]. Rare retrovesical masses can be classified as cystic includes mullerian duct cyst, prostatic utricle cysts, congenital or acquired vesicle cysts and dermoid cysts or solid includes teratomas.

These retrovesical masses can be presented with varying clinical features and signs, which may mimic various other common diseases of the lower tract. There are often numerous differential diagnoses for a retrovesical mass which must be narrowed down to a histologically confirmed or biopsy-proven diagnosis. A series of diagnostic tests are available including USG, CECT or MRI and vasography etc. Hence a diagnostic protocol for suspected pelvic masses needs to be made clear. Inspite of many new diagnostic modalities still present a diagnostic dilemma. We are here with presenting a case series of the following rare benign pelvic masses in male patients, their presenting features, diagnosis, and management aspects. The aimed is to identify the diagnostic difficulties and management issues of benign pelvic masses in males and high light the diagnostic protocol for these rare pelvic masses.

Editor's Comment :

- Diagnosis and management of retrovesical pelvic (RVP) masses pose problems in men.
- This study identified the diagnostic difficulties and management issues of RVP masses.
- Radiological investigations showed cystic extra prostatic mass with no specific features.
- The surgical approach of CSVC can be challenging and associated with many complications.
- Therefore, there is a need of accurate treatment whenever symptoms are present.

Materials and Methods

A prospective study conducted at the Department of Surgery, Dr S N Medical College, Jodhpur, Rajasthan, India between September 2013 and December 2019. This study protocol was reviewed and

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approved by Institutional Ethics Committee. All male patients diagnosed with pelvic mass with age between 17 and 65 years were included. A total of 20 male patients presented with retrovesical mass, aged 17 to 65 years old (mean age 36.7 years) were evaluated. We were analyzed our data with regard to history, physical examination obtained with special attention to age, clinical presentation, diagnostic tests-haemogram, renal function test, X-KUB and USG, individualized investigations-CT scan, vasography, TRUS, MRI abdomen and pelvis, type of operation, operative findings, and histopathological diagnosis. Exclusion criteria-Common pelvic masses such as bladder diverticula, BPH, or malignant bladder or prostatic masses were excluded.

Results

Table 1 summarizes the clinical findings, details of diagnosis and management of 20 patients with rare benign pelvic masses. These masses were found to be of prostatic origin in seven cases (5 prostatic utricle cyst and 2 prostatic abscess), connective tissue in seven, seminal vesicle origin in four, mullerian duct remnant in one case and embryonic urogenital vestigial remnants in one case.

Clinical presentation : Of these 20 patients, 19 presented with acute or chronic lower urinary tract symptoms and in one case, the mass was asymptomatic and found incidentally. Two patients presented with acute inflammatory symptoms, such as fever with or without flank pain and nine patients had non-inflammatory, such as urinary retention. In contrast, six patients had chronic symptoms, such as perineal pain, frequency, hemi- scrotal pain and urinary incontinence. Two patients had primary infertility and perineal pain.

On Abdominal, Digital Rectal and Bimanual Examination : Large suprapubic cystic mass was palpable in two cases, in the same two patients on Digital Rectal Examination (DRE), huge bimanually palpable cystic mass was found, prostate could not be felt separately and upper limit was not reachable. In addition, DRE revealed a large hard, non-tender, non-pulsatile, smooth surface, felt anterior to rectum just above the anal verge, upper limit not reachable, prostate can felt separately likely connective tissue masses in three patients, while four patients revealed soft, non-tender, non-pulsatile, smooth surface, felt anterior to rectum just above the prostate, upper limit not reachable, likely connective or adipose tissue

Table 1 — *Clinical findings, details of diagnosis and management of 20 patients with rare benign pelvic masses*

Sl No	Age	Presenting complaints	Digital rectal examination	USG Findings	CECT/MRI Abdomen	Other Investigations	Diagnosis	Treatment
01	60	Supra pubic lump, Recurrent retention of urine	Bi manually palpable cystic mass	5x8cm cystic mass pushing bladder to right side and upwards	-	Vasography HPE-mullarian duct cyst with cystadenoma	Mullarian duct cyst with cystadeno-ma	Exploratory laparotomy
02	17	ROU and painless lump in lower abdomen	large cystic mass was palpable arising from the left posterolateral side. 31	-	-	HPE- cyst wall predominantly made of smooth muscles alongwithfibrocol lagenous, adipose and nervous tissue.	Embryonicurogenital vestigial remants? presacralmeningo c-ele	Exploratory laparotomy
03	36	Pain in right hemiscrotum, burning micturation	7x6 cm soft cystic non-tender, mass felt anterior to rectum, 3 cm above the anal verge.	-	-	FNAC-anucleated epithelial cells having abundant pale stained eosinophilic cytoplasma.	Epidermoid or dermoid cyst	Excision
04	23	Anejaculation, Primary infertility Chronic perineal pain	3x2 cm sized, midline,cystic, nontender,swelling felt just above the prostate, and 4 cm above anal verge.	normal	7.8 x 7 mm cyst noted in prostate in midline (prostatic utricle cyst) Both seminal vesicles are dilated and show water density (seminal vesicles cysts)	TRUS-Showed Multiple anechoic lesion just above the prostate in mid line	Prostatic utricle cyst	Trans urethral resection of ejaculatory duct
05	18	Bleeding per rectum LUTS Limp in gait Retention of urine	A large hard, non-tender, smooth surface, felt anerior to rectum just above the anal verge.	Large mix enchogenic mass of size 10x9x8cm posterior to urinary bladder? Haematoma, collection	Large lession with solid, cystic &haemarrhagic component, seen in pelvis, posterior to bladder.Differentialdignosis were 1. Teratoma? 2. Rhabdomyosarcoma? 3. Hematoma?	HPE- Teratoma	Teratoma	Exploratory Laparotomy
06	25	Pain Retention of urine	A smooth non tender anterior bulge noted.	-	Cystic lesion is noted in the pelvis anterior to bladder locatedslightly more toward the left side. It measures 5 x 4.5 x 3.6 cm The lesion is in adipose layer, without intramuscular/ intrapelvic extension.	HPE-Inclusion cyst	Inclusion cyst	Excision
07	33	Infertility	A cystic non-tender swelling felt above prostate.	-	Cystic lesion is seen in the midline (prostatic utricle)	TRUS-Multiple anechoic lesion in midline.	Prostatic utricle cyst.	Trans urethral unroofing of cyst

(Contd.....)

Sl No	Age	Presenting complaints	Digital rectal examination	USG Findings	CECT/MRI Abdomen	Other Investigations	Diagnosis	Treatment
08	38	Pain in left hemiscrotum	Approximately 6 × 8 cm cystic mass with smooth surface is felt anterior to rectum.	-	large cystic mass of size 63 × 82mm is noted in pelvis posterior to bladder.	-	Dermoid cyst	Excision
09	24	LUTS	A smooth nontender cystic mass felt anterior to rectum towards the right side.	-	Bilateral small undescended inguinal testes. Hemorrhagic right seminal vesical cyst associated with right renal agenesis (Zinner syndrome)	-	Right Seminal vesical cyst	Trans urethral resection of vesicle
10	40	Bleeding per rectum LUTS	A large, non-tender, smooth surface mass felt anerior to rectum just above the anal verge.	-	a circumscribed benign-appearing cystic lesion in posterior to bladder.	HPE-Teratoma	Teratoma	Exploratory laparotomy
11	40	LUTS	A smooth non-tender anterior bulge in the midline above the prostate of size approximately 5 × 8cm.	Normal	circumscribed benign multilocular cystic lesion in midline.	TRUS -Anechoic areas noted in the pelvis.	Prostatic utricle cyst	Trans urethral lay open of cyst
12	23	LUTS	Approximately4 × 5cm Smooth cystic non-tender mass felt anterior to rectum.	-	large thin-walled pelvic cystic massof size46 × 52mm is noted in the pelvis. Diferentials are left seminal vesical cyst/postratic utricle.	-	Left seminal vesical cyst.	Trans urethral resection of vesicle
13	18	Retention of urine	Smooth non-tender anterior bulge noted.	-	large cystic mass of size 44 × 34mm is noted in pelvis posterior to bladder.	HPE-dermoid cyst	Dermoid cyst	Excision
14	38	LUTS	2x2 cm sized, midline,cystic, nontender,swelling felt above the prostate	Normal	Cyst noted in prostate in midline (prostatic utricle cyst	TRUS-Multiple anehoic lesion just above the prostate in mid line	Prostatic utricle cyst	Trans urethral unroofing of cyst
15	35	Flank pain LUTS	3x2 cm sized, midline,cystic, nontender,swelling anterior to rectum	Normal	Cyst noted in the right seminal vesical	TRUS-Anechoic cystic area in the right seminal vesical.	Right seminal vesical cyst	Trans urethral resection of vesicle
16	59	Fever, painful micturition	Tender, soft cystic mass felt anterior to rectum	Normal	-	TRUS-hypoechoic areas with internal echoes	Prostatic abscess	Unroofing and drainage
17	18	None	A hard-non-tender, smooth surface mass felt anterior to rectum	Mixechogenic mass of size 3x4x4cm posterior to urinary bladder? Hematoma, collection	MRI-lesion with solid, cystic and hemarrhagic component, seen in pelvis, posterior to bladder.Differential diagnosis were Teratoma? Hematoma??	HPE-Teratoma	Teratoma	Exploratory laparotomy
18	22	Chronic perineal pain	Midline, cystic, nontender, swelling felt above the prostate	-	circumscribed benign multilocular cystic lesion in midline.	TRUS -Anechoic areas noted in the pelvis.	Prostatic utricle cyst	Trans urethral unroofing
19	49	Fever, painful micturition	Tender, soft cystic mass felt anterior to rectum	Normal	-	TRUS-hypoechoic areas with internal echoes	Prostatic abscess	Unroofing and drainage
20	50	Flank pain LUTS	Midline, cystic, nontender swelling anterior to rectum	Bilateral seminal vesical cyst are seen largest measuring 15 × 11mm on left side	Multiple thin-walled pelvic cystic masses largest of size15 × 11mm is noted in the pelvis. Differentials are bilateral seminal vesical cyst/prostatic utricle.	TRUS-Anechoic cystic area in the bilateral seminal vesical.	Bilateral seminal vesical cyst	Trans urethral resection of cyst

masses. Intraprostatic lesions were noted in seven patients with a prostatic mass. Extra-prostatic masses were detected in four patients with a seminal vesicle mass.

Laboratory studies: All patients had haemoglobin, blood counts, urine examinations complete microscopic with culture, renal function tests. Urine examination showed pus cells 4-6 to full field per high power field in seven cases and *E. coli* was detected in urine culture of two cases. Urinalysis also demonstrated microhaematuria in all cases of prostatic and seminal vesicle masses. white blood count and Urine leukocytes were significantly higher in two patients (prostatic abscess) than for a simple prostatic utricle but renal function tests was within normal range for all cases.Two patients presented as primary infertility had normal testosterone, FSH, LSH, serum prolactin and azoospermia but one patient had an ejaculation with azoospermia in post-void urinary sample. In the other patient's laboratory studies revealed no pathological findings.

Ultrasound studies : Ultrasound showed cystic lesions in 17 patients and solid masses in three. Medial locations of a cystic retro-vesical mass were consistent with a prostatic utricle cyst (Fig 1) or abscess (Fig 2). Transrectal ultrasound was performed

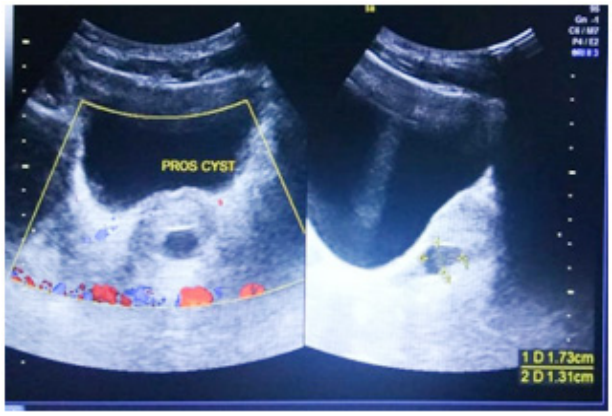

Fig 1 — USG images showed prostatic cyst

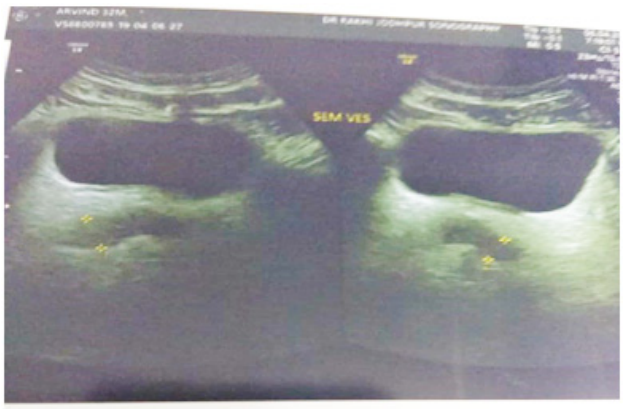

Fig 4 — USG images of seminal vesicle cyst

additionally in eight patients to confirm the intra-prostatic or extra-prostatic location of the cysts. Ultrasound revealed mixed echogenic masses in all the three patients with retro-vesical teratoma (Fig 3) which was difficult to differentiate from haematoma and four patients had cystic lesion contained hyperechoic material consistent with dermoid cyst but one letter on confirm on HPE was mullerian duct cyst with cystadenoma. A cystic extra-prostatic mass lateral to the bladder neck was demonstrated on ultrasound for all seminal vesicle (Fig 4).

IVU, CYSTOGRAM, AGP and Vasography : One patient reported large mass shadow seen in pelvis left side pushing bladder towards right and anteriorly with raised base of the bladder. Vasography -B/l vas and seminal vesicle normal, bladder base elevated and grade 1 reflex on left side (Fig 5) (mullerian duct cyst with cystadenoma). In Case-4 vasogram confirm the

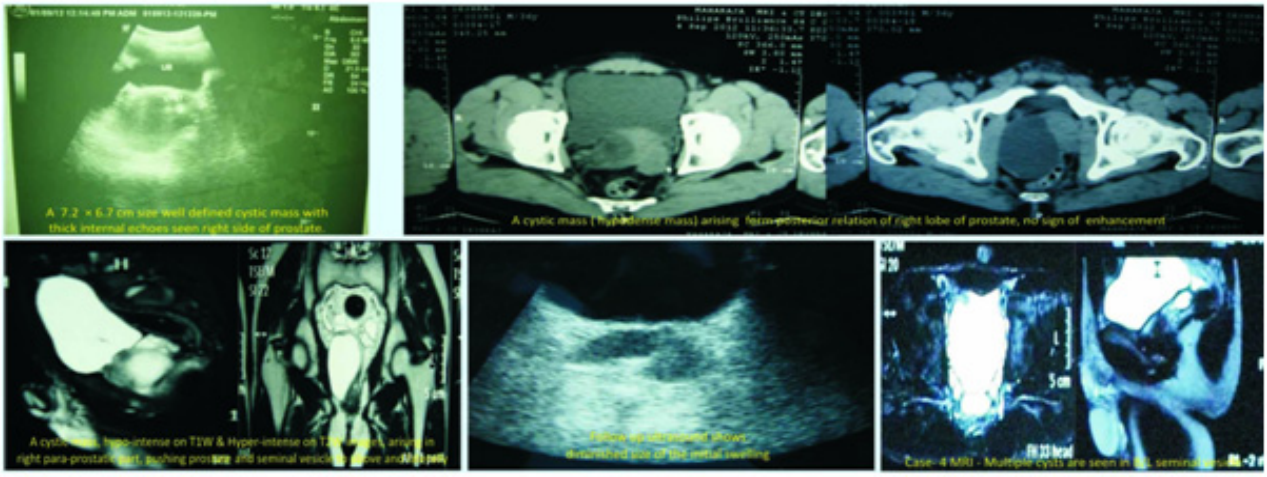

Fig 2 — Radiological pictures of Epidermoid cyst (case no 3) and Last MRI picture showed b/l seminal vesicle cyst (case no 4)

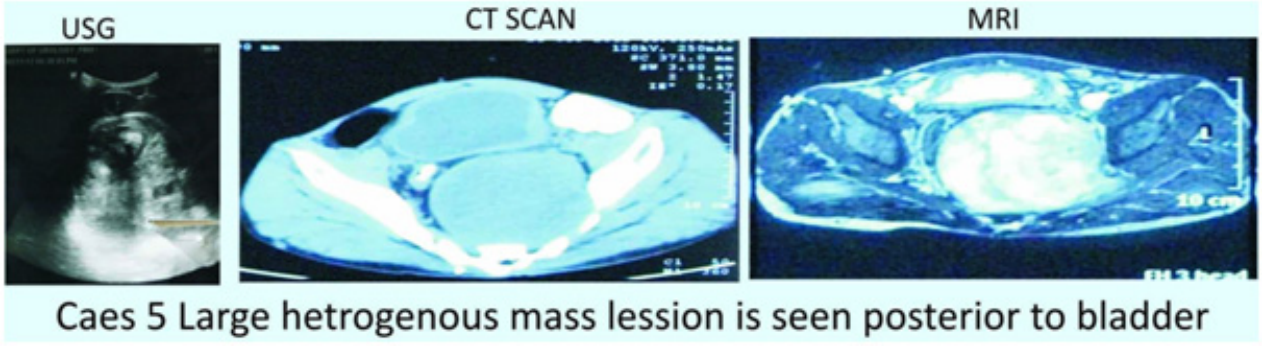

Fig 3 — Radiological images of Teratoma (case no 5)

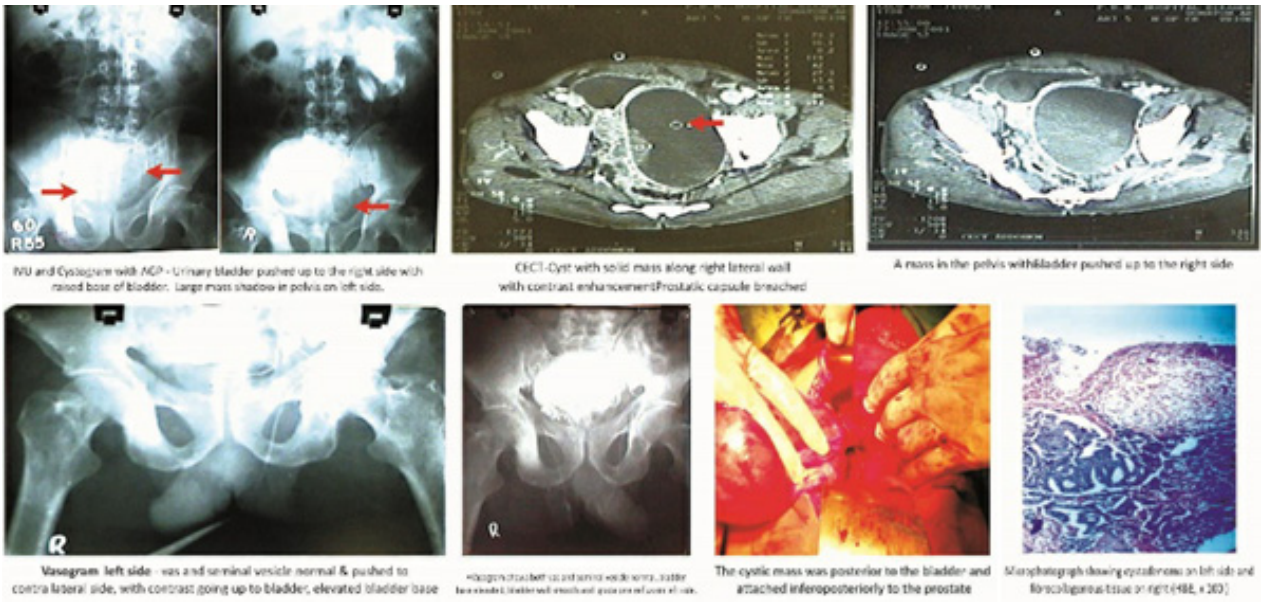

Fig 5 — Radiological and operative images of mullarian duct cyst with cystadenoma (case no 1)

diagnosis of ejaculatory duct cyst.

CT scan and/or MRI abdomen pelvis : CT Scan and/ or MRI abdomen pelvis was performed in 16 cases, both were accurately demonstrated the anatomical relationship of associated intra pelvic organs with surrounding fat and pelvic lymph nodes. CT Scan and/ or MRI abdomen pelvis clearly depicted prostatic utricle cysts in 3/3(100%) cases, intraprostatic abscess cavities in 2/2 (100%) cases, seminal vesicle cysts 2/ 2 (100%) and cystic connective tissue masses in 4/4 (100%). CT scan abdomen pelvis accurately demonstrated retro-vesical connective tissue solid masses in three cases. CT scan and/or MRI abdomen pelvis failed to differentiate accurate diagnosis in two cases (ejaculatory duct cyst and mullerian duct cyst with cystadenoma). However, MRI failed to differentiate between teratoma and haematoma. FNAC accurately demonstrates diagnosis in two cases of intraprostatic abscess (Fig 6).

Open Surgical and Endoscopic management: Nine cases underwent exploratory laparotomy ie, three cases solid masses cut surface finding suggestive mature teratoma, three cases semi solid cyst masses on cut suggestive dermoid cyst and 3 were cystic masses surgical specimen finding inconclusive to clench the diagnosis. All surgical specimen sent for histopathological examination to confirm the diagnosis of the pelvic mass. Prostatic utricle and seminal vesicle cysts and prostatic abscess were treated with transurethral route. Transurethral unroofing was done in prostatic utricle cyst (4 cases) and in seminal vesicle cysts (3 cases). Transurethral resection of the ejaculatory duct was performed in one case of ejaculatory duct cyst and was uneventful. Transurethral unroofing and drainage of the prostatic abscess was done in two cases and were uneventful. One case of bilateral seminal vesical cyst managed conservatively. Follow up period was unremarkable in all cases.

Histopathological examination : Biopsies of specimen demonstrated tissue of origin in all cases (8/9) except one. HPE report confirmed the same clinical and operative diagnosis in six cases (3 were

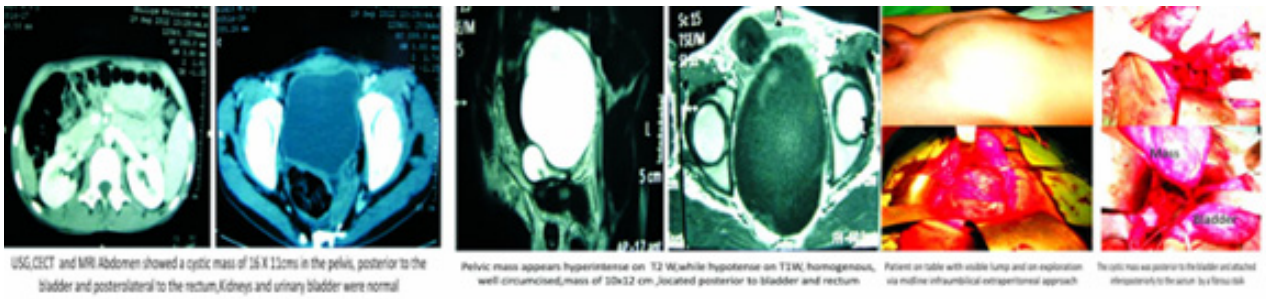

Fig 6 — Radiological and operative images of embryonic urogenital vestigeal remnant ??/ Presacral meningocele ??(case no 2)

mature teratoma and 3 were dermoid cysts). We were unable to clench the diagnosis in two cystic mass with our clinical and operative finding but confirm with HPE ie, Mullerian duct cyst with cystadenoma and inclusion cyst. Even after HPE report in one case of cystic mass suggestive diagnosis embryonic urogenital vestigial remnant? presacral meningocele but not confirmed.

Discussion

Retrovesical pelvic masses in males are uncommon and presented with varying features[1]. They can be congenital or acquired. The mesonephric duct and the ureteral bud join the urogenital sinus during embryogenesis[2]. The Wolffian duct differentiates into the genital duct system, forming the epididymis, vas deferens, seminal vesicles and ejaculatory ducts in males.

The appearance of Mullerian duct cyst was associated with the remnants of the Mullerian duct[3] and usually occur in the 3rd and 4th decades of life, maybe incidental[4]. If large enough, they can cause obstructive or irritative urinary symptoms, like haematuria, ejaculatory impairment or suprapubic or rectal pain. In this study, a 65 years old male patient presented with LUTS and a cystic supra pubic lump with MRI abdomen showing cystic mass pushing bladder to right side. Final diagnosis of Mullerian duct cystadenoma was made on HPE of the cyst excised. In 1942, Clyde, *et al* described a Mullerian duct cyst in 34-year-old male with LUTS where final diagnosis was made on histopathological examination[5].

Pre-sacral meningocele most frequently presenting as a presacral mass. It is an extension of the dura mater and arachnoid out of the sacral spinal canal into the retroperitoneal and intraperitoneal space through a congenital defect in the sacrum. Most of the patients presented with long standing constipation and urinary dysfunction. In case of constipation, the urinary dysfunction may be related to direct pressure on the bladder or may result from spinal cord tethering or sacral nerve root compression. Here we represent a 17-year-old male student with constipation for 5 years, episodes of ROU in the last one year & painless lump in the lower abdomen for 6 months. CECT and MRI abdomen showed a cystic mass in the pelvis, posterior to the bladder and posterolateral to rectum. On exploratory laparotomy confirm CECT finding with a fibrotic attachment to the posterior surface of the prostate. Mass was excised and sent for HPE. Biopsy of the specimen suggestive of embryonic urogenital vestigial remnants? Presacral meningocele? In 1971, Chovnick, *et al* reported a case of 50-year-old male patient with retention of urine and cystic mass, diagnosis of anterior sacral meningocele was confirmed by HPE.

Dermoid cysts of the presacral space are relatively common while dermoid cysts presented at the anterior to the rectum are not so common, and those which involve the bladder usually occur in women and are ovarian in origin and rare in men[6]. In the present study, three male patients diagnosed to have dermoid cyst in pelvis, where all of them presented with pain in the scrotum and burning micturition. Radiological investigations showed cystic extra prostatic mass with no specific features and confirm by FNAC . In one case, dermoid cyst was wrongly diagnosed to be ischiorectal abscess and incision drainage was done, which yielded whitish material. Wilson, *et al* in 1973, reported a case of dermoid cyst in a 51-year-old male, which was diagnosed to be a gluteal hernia on clinical examination, final diagnosis of dermoid cyst was made on HPE and fluid examination of the cyst after excision.

Prostatic utricle cysts are emerged at the extent of the verumontanum and most of the time found within the midline. Utricle cysts are usually smaller and are less likely to extend above the prostate. There is an association between utricle cysts and variety of genitourinary abnormalities[7].

Congenital Vesicle Cysts (CSVCs) related to anomalies of the ipsilateral upper urinary tract are uncommon. This condition has been reported as “Zinner syndrome”. In such patients onset was reported during second or third decade of life with high incidence of dysuria (37%), frequency (33%), perineal pain (29%), and epididymitis (27%)[8]. The diagnosis is mainly achieved in adult age but demanding in pediatric age . The surgical approach of CSVC can be challenging and associated with many complications. Therefore, there is a need of accurate treatment whenever symptoms are present. Livingston L and Larsen CR reported seminal vesical cyst in all five patients, two patients were examined for primary infertility. Four patients were seen because of a history of dysuria. Other clinical symptoms included hematuria; nocturia; urinary frequency; urgency; lower abdominal, perineal, and ejaculatory pain; and haematospermia. One patient was treated empirically for prostatitis and chronic recurrent epididymitis with antibiotic therapy during a 6-year interval[9].

Teratomas are congenital tumours that contain derivatives of all three germ layers. Retrovescical teratomas are rare entity of extragonadal tumour commonly observed in adults, especially in males. The

prevalence of retrovescical teratomas is more in various sites and organs. The majority of patients were asymptomatic with large neoplasm at the time of presentation which can cause urinary disturbance[10].

Prostatic abscess is rare in the era of antibiotics. Most of them presented with perineal pain, fever, urinary tract infection. In 1992, 25 patients with prostatic abscess were diagnosed mainly by TRUS and IVP. Treated with parenteral antibiotics and 22 underwent surgical drainage[11].

The present study proposed a diagnostic algorithm (Fig 7) for suspected pelvic masses, according to proposed diagnostic guideline. Every retro-vesical mass evaluated by history, general physical and local examination with findings on DRE followed by ultrasound allow reliable diagnosis of retro-vesical lesions whether cystic or solid mass but most of the times exact location, tissue origin, involvement of organs and lymph nodes cannot be confirmed. In such situation, most of the cases according to the present study diagnostic approach CT and MRI of abdomen and pelvis are needed. However, rare retro-vesical mass may require biopsy and exploratory laparotomy followed by histopathological examination to confirm the diagnosis.

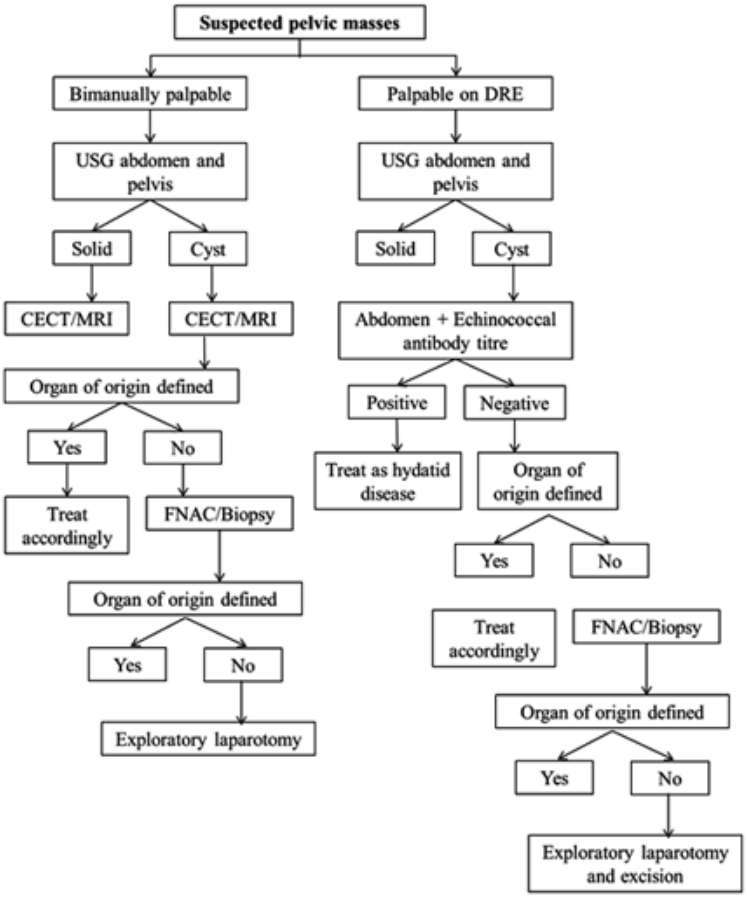

Fig 7 — Proposed diagnostic protocol flow chart

Conclusion

Benign retrovesical mass presents with lower tract obstructive symptoms, palpable pelvic mass and retention of urine. CT or MRI is useful for exact location, tissue of origin, the involvement of organs and lymph nodes. Needle or open biopsy is required in most cases to establish a histopathological diagnosis. Laparotomy and histopathological examination are the procedures of choice when other findings are equivocal. Excision of benign retrovesical mass is difficult because of deeply situated in pelvis. Benign retrovesical mass is rare, we faces difficulty in diagnosis and management. Hence, diagnostic protocols can be helpful to manage retrovesical pelvic masses.

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Conflict of interest : None to be declared
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Original Article

A Single Centre Experience of Spontaneous Bacterial Peritonitis in Ascites with Cirrhosis : A Record Based Observational Study

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Spontaneous Bacterial Peritonitis (SBP) is one of the complicated infections in patients with cirrhosis and ascites which can be fatal if not diagnosed and treated. This is a record based observational study using the data of all patients admitted with established cirrhosis of liver with ascites. Aim of the study was to find out the incidence of SBP in cirrhosis patients and also to study the clinical profile of SBP. Thirty nine patients' data were included in the study. Three patients had classic SBP, one patient had Culture Negative Neutrocytic Ascites (CNNA) and two had bacterascites. Patients were treated with injection cefotaxime (2 gm) 8hourly for 5 days and clinical and laboratory parameters were evaluated.

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Key words **: Ascites, Cirrhosis, Spontaneous Bacterial Peritonitis (SBP), Culture Negative Neutrocytic Ascites (CNNA), Bacterascites.**

Ascites or hydroperitoneum is the collection of fluid of more than 25 ml in the abdominal cavity .The word ascites was derived from a Greek word "Askos" meaning a bag or sack. The term was coined by an Irish Physician Triwsa. Cirrhosis of liver is the commonest cause of ascites but many other conditions like cardiac (congestive cardiac failure), infections (tuberculosis, chlamydia), hypoproteinemia, pancreatitis, renal (nephrotic syndrome), hypothyroidism and familial Mediterranean fever can cause Ascites[1]. Laennec coined the term "Cirrhosis" in 1826 and derived from a Greek word meaning 'Orange' or 'Twany'. Worldwide cirrhosis contributes to 1.1% of all deaths[2]. Causes of cirrhosis can be alcoholic or post necrotic or NAFLD. Spontaneous Bacterial Peritonitis (SBP) is the bacterial infection of peritoneum in the presence of ascites. SBP rarely occurs without ascites. It is potentially a reversible condition if treated early and can be fatal without diagnosis and treatment. With availability of newer antibiotics the mortality rates has been reduced from 100% to less than 20% with early diagnosis and treatment[3]. Clinical presentation of SBP may be varying. It could be starting from asymptomatic to minor symptoms to severe symptoms. Clinically SBP is classified into three variants —

Editor's Comment :

- Spontaneous bacterial peritonitis (SBP) needs early recognition in patients ofcirrhosis with ascites to prevent mortality.
- We had conducted a record based observational study including 39 patients.
- Of the 39 patients, 3 patients had classic SBP, one case was CNNA and two patients had bacterascites and rest had sterile ascites.
- Injection cefotaxime 2 gm 8 hourly for 5 days were used which was associated with zero mortality in our study.
- Small sample size of the study is an important limitation.

(1) Classic SBP- More than 250/mm^3 polymorpho-nuclear leucocytes in ascitic fluid and culture is positive

(2) Polymorpho-nuclear leucocytes >250/mm^3 but culture is negative

(3) Bacterascites- Culture is positive but polymorpho-nuclear leucocytes are less than 250/mm^3

Common clinical manifestations are fever, pain abdomen, altered GI motility, features of hepatic encephalopathy in severe cases[4]. Early diagnosis and proper treatment reduces the mortality rates. In this back ground this study was conducted to find out the incidence of SBP in ascitic patients and to study the clinical profile of patients with SBP.

Materials and Methods

This is a record based observational study done with patients admitted with history of ascites over a period of one year from May 2021 to April 2022. Ethics committee permission was obtained. Patients with history of abdominal paracentesis in the last three weeks, patients who had received antibiotics four weeks prior and patients with secondary causes of

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peritonitis were excluded from the study. Detailed history was taken and clinical examination was done. Patients underwent relevant investigations, were evaluated. Diagnosis of cirrhosis was confirmed by the report of ultrasound abdomen. After admission all patients 30 ml of ascitic fluid wad obtained immediately which was sent for cytological examination and biochemistry and 10 ml of fluid for culture. Ascitic fluid cell count was done under microscope. Ascitic fluid cultures were done as per standard culture methods.According to record based evaluation of all these documented data focusing on the ascitic fluid Polymorpho-Nuclear count (PMN), patients were grouped into-

(1) Sterile ascites

(2) Classic SBP- Culture positive and PMN count more than 250/mm^3

(3) Culture Negative Neutrocytic Ascites (CNNA)

(4) Bacterascites- PMN less than 250/mm^3 but culture positive

Results

We had included the data of 39 patients who were matching predefined inclusion and exclusion criterion.Among the study population,29 were male and 10 were female patients. The mean age was 49.1±9.6 and 47.3±12.05 in male and female patients respectively. Age range was 20-65 years. 25 patients had alcoholic cirrhosis, 4 had post necrotic (hepatitis B) and rest 10 had non-alcoholic fatty liver disease (NAFLD). Patients with SBP had Child-Turcotte-Pugh class C.

Of the 39 patients, 3 patients had classic SBP, one case was CNNA and two patients had bacterascites and rest had sterile ascites. Average age of the patients with classic SBP and bacterascites was less than 40 years and only case with CNNA age was more than 40 years. Majority patients with SBP had alcoholic cirrhosis and one patient had post necrotic cirrhosis. Jaundice was a common finding in all cases with SBP, two patients had fever as presenting symptom and two had abdominal pain and one patient had GI bleed and no one had encephalopathy. Of the 6 cases of SBP only one was female and had classic SBP.

Table 1 is showing the characteristics of patients SBP in the study.

Table 1 — *Characteristics of patients with SBP*

Parameter	Value
No of patients positive in all categories of SBP	6 (in number)
Total No of patients in study	39(in number)
Incidence of SBP	15.38%
Incidence of Classic SBP	7.69%
Age	47.12 ±10.6 (SD)
Sex Male/Female	5/1 (in number)
Jaundice	6 (in number)
Fever	2 (in number)
Pain abdomen	2 (in number)
GI bleed	1 (in number)
Total counts	12670 ± 6732 /uL
Hemoglobin	9.5 ± 2.1 gm/dl
Platelet count	124670 ± 51670 /uL
T Bilirubin in Classic SBP	6.23 ± 5.4 mg/dl
T Bilirubin in CNNA	2.8 mg/dl
Total protein	5.6 ± 1.1 gm/dl
Albumin	2.1 ± 0.31 gm/dl
Ascitic Fliud PMN counts	1500 ± 2897 /uL
Ascitic Fliud Protein	1.38 ± 0.89 gm/dl
Ascitic Fliud Sugars	88.65 ± 32 mg/dl
Ascitic Fliud Culture	5 positive
Ascitic Fliud Organism grown	*E coli*
Ascitic Fliud Response to treatment	All Recovered

Discussion

Spontaneous Bacterial Peritonitis (SBP) is almost all in cases with cirrhosis of Liver cases with few exceptions some case reports have shown SBP in cardiac ascites[5]. Incidence rates of SBP vary from study to study because of sample size in general in hospitalized patients it is around 10-30%[6]. In the present study overall incidence of SBP is 15.38% and classic SBP 7.69%, CNNA 2.56% and bacterascites is 5.12%. A study published by Amarapurkar, *et al* in 1992 showed the incidence of Classic SBP is 12.9% and CNNA 9.6%[7]. However a study by Runyon and Hoef JC showed higher incidence of SBP is 64.7% classic SBP and 35.3% CNNA[8]. Two patients had fever in the present study (3.33%). Incidence of fever in study done by Weinstein, *et al* in 1978 was 68%[9]. However some studies had shown that they had fever but had vague abdominal pain. Abdominal pain was seen two patients the present study which almost similar to the other published studies. Heapic encephalopathy was observed in many studies like Weinstein, *et al* and Amarpurkar, *et al* but none of our patients had encephalopathy. GI bleed was seen in one patient the present study. Asymptomatic cases are also common as seen in the study by Conn and Fessel, *et al*[10]. Abdominal paracentesis was a contraindication earlier because of coagulopathy, now the studies have shown that abdominal paracentesis is safe and doesnot increase the risk of bleeding. There are several independent risk predictors of SBP like CRP>13 mg/dl, Platelet count <82000/uL and advanced age[11]. The other factors that determine the severity of SBP are severity of liver dysfunction; risk is more with advanced liver disease. Fever, high serum bilirubin, ascitic fluid total protein level of <1 g/dl and deranged renal functions are important predictors for

development of SBP[2]. MELD score is another important predictors for development of SBP[12]. MELD scoring was not done in this study as it is record based study. All patients with positive cultures grew *E coli*. Several other studies also shows similar results. Other common organisms that cause SBP are klebsiella pneumoniae, salmonella, staphylococcus aureus, klebsiella oxytoca, citrobacter spp, corynebacterium spp, pseudomonas aeruginosa, enterobacter cloacae, serratia marcescens, acinetobacter spp, proteus mirabilis[13]. Possible mechanisms that involve in the development of SBP are increased colonization of gram negative bacteria in the upper gastrointestinal tract and bacterial overgrowth and failure of the gut to control the bacteria and immune system[3]. SBP is one of the common causes of infection in the setting of ascites. Early diagnosis and treatment are very important in reducing the mortality. Despite of advances in medication, the one month mortality is around 26-48%[14]. Cefotaxime is the most extensively studied antibiotic and, should be given at a dose of 2 gm 8 hourly for 5 days, it rapidly penetrates the ascitic fluid and exceeds the MIC of 90% of the isolated organisms by 20-fold[3]. In the present study all patients were treated with cefotaxime 2 gm 8 hourly for 5 days and patient showed significant improvement in terms of clinical features and along with the Lab parameters. Other commonly used other two antibiotics are amoxicillin-clavulanic acid are ofloxacin. Use of intravenous albumin in the dose of 1.5gm /kg on day one and 1 gm on day three also reduces short and intermediate term mortality.

Limitations : Small sample size is an important limitation of our study.Predictive parameters could not be used as it is a record based analysis. Prospective observational study with adequate sample size needs to be done for generalization of the study result which emphasizes the need of preparing registry in this regard.

Conclusion : Spontaneous bacterial peritonitis in one of the common infections in setting of ascites secondary to cirrhosis of liver. Without treatment the mortality rates are very high and hence early diagnosis and treatment are very important. Gram negative bacteria like *E coli* is the commonest microorganism responsible for SBP. Injection cefotaxime 2 gm 8 hourly for 5 days would reduce the mortality rates.

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Original Article

Immunity Status of Health Care Workers Post-Recovery from COVID-19: Natural Adaptive Immunity Persists at Nine Months Post-Infection : An Online Longitudinal Panel Survey

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Background : Various studies have pinned longevity of protective Immunoglobulin-G (IgG) titres at 2-5 months. The robustness and longevity of the IgG antibody response to COVID-19 infection has been gauged in a cohort of 214 single institutional health care workers by serial quantitative immunometric tests. Currently no separate guidelines exist for vaccination of COVID-survivors and this study provides data to fill this lacuna in knowledge.

Methodology : Prospective longitudinal panel survey administered to the same cohort of Health Care Workers (HCW) till such time they got vaccinated under Indian Government's free vaccination drive for HCW. Depending upon the date of contraction of infection the HCW could be longitudinally monitored for variable periods (2-9 months). The survey questionnaire comprising multiple-choice, dichotomous, matrix and Likert-scale questions was deployed to the respondents online via email/WhatsApp. Data was expressed as box-whisker plots, trendlines and trend areas. A p-value<0.05 was considered statistically significant. The composite index of 'Effective Immunity' was calculated.

Results : The mean IgG antibody titre was 11.13±8.6AU at 1-2m, 9.68±8.9AU at 3-4m, 8.35±5.9 AU at 6-7m and 7.87±4.4 AU at 8-9m after first symptom, respectively. The lowest titre at all time points was 0 while the highest titres were 46.8 AU, 56.5 AU, 23.4 AU and 17.4 AU at 1-2m, 3-4m, 6-7m and 8-9m, respectively.

Conclusion : Adaptive active immunity acquired through natural infection may last for at least 9 months post-initial exposure and lies in the moderate protection range in 77% HCW, which can be extrapolated to vaccination and immunity passports. Separate vaccination guidelines are required for COVID-survivors. The first shot of vaccine serves as a booster second exposure/booster dose in all COVID-survivors.HCW with low IgG-titre may suffer from a false sense of security. Periodic quantitative IgG-titre based serological tests can help guide timing of second shot of vaccination and predict likelihood of re-infection.

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Key words **: Antibody, COVID-19, Humoral immunity, Immunoglobulin-G.**

The corona virus disease (COVID-19) pandemic with associated lockdowns had mercilessly brought life to a grinding halt. People have now adjusted with remarkable resilience to the new normal of social distancing, repeated hand-washing, personal protective equipment and the concept of work/study from home. The latest official sero-survey (28000 sample size; Februry, 2021) results have divulged that 56% of Delhi inhabitants are seropositive[1]. Herd immunity development is the Holy grail of the COVID-pandemic and duration for which seropositivity lasts is an important determinant. The free, state-sponsored vaccination drive exclusively for HCW has started on a priority basis since 16th January, 2021 after emergency use authorization of two vaccines[2]. 214 Health Care Workers (HCW) of a premier tertiary-care onco-hospital who are COVID-survivors periodically got their IgG-titres tested. On follow-up of this cohort until

Editor's Comment :

- Immunity acquired through SARS-CoV-2 infection may last at least 9 months.
- IgG-titres are inmoderate protection range in 77% convalescent individuals.
- First vaccine shot serves as a second exposure/booster dose in all COVID-survivors.
- Periodic quantitative IgG-based serological tests can guide spacing of second vaccination-shot and predict susceptibility to re-infection.
- Requirement of separate vaccination guidelines for COVID-survivors.

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the date they got vaccinated we could collect data for a maximum of 9 months from the date of symptom-onset (index/first case at our institution was diagnosed on 1st of May, 2020 and the last HCW in the survey was enrolled in December, 2020). It is important to gauge the existence, extent and duration of immunity in COVID-survivors, as this would be a predictor of the likely duration of protective effect conferred by the available vaccines and this is the research question we seek to answer. Our primary objective is to find out if IgG antibody levels decline with time and by what amount and the time duration for which they last.

Material and Method

Our prospective longitudinal panel survey was conducted after prior written informed consent from all HCW and approval from the Scientific Committee and Institutional Review Board. The survey was administered to the same cohort of HCW till such time they got vaccinated (15th January to 28th February, 2021) under Indian Government's free vaccination drive for HCW. Depending upon the date of getting infected the HCW could be longitudinally monitored for variable periods of time ranging from 2-9 months. The survey questionnaire comprising multiple-choice, dichotomous, matrix and Likert-scale questions was deployed to the respondents online via email/WhatsApp.

An online survey software (Google forms), was utilized to create the survey questions and get analyzed data on a dashboard which keeps updating real-time as respondents partake the online survey. Data presentation on this dashboard comprises charts and graphs for the ease of statistical analysis.

Initial three steps of the survey (defining the population and sample,deciding the type of survey, designing the survey-questionnaire) were completed before and the remaining three steps (distribution of survey and response-collection, survey-result analysis, penning the survey results) were conducted after ethics committee approval.

All HCW, employed at Rajiv Gandhi Cancer Institute and Research Centre (RGCIRC) with a history of being a laboratory confirmed COVID-positive patient and who underwent antibody tests were included in the study. Non-HCW and HCW without Reverse Transcription Polymerase Chain Reaction (RT-PCR)/Gene Xpert reports were excluded from the survey.

Antibodies binding to the receptor binding domain (RBD) of the surface glycoprotein/spike (S) protein of SARS-CoV-2 can neutralize the virus[3-5]. The antibody test kit utilized at RGCIRC (VITROS Immunodiagnostic Products Anti-SARS-CoV-2 IgG) is based on the high throughput automated Chemiluminescence Immunoassay (CLIA) technology and the antibodies tested are those produced against the S-protein of SARS-CoV-2. It is an immunometric test utilizing ECi/ECiQ, 3600, 5600/XT 7600 system with incubation time 37mins, time to first result 48mins and an intravenous serum sample of 20 µL tested at 37°C. Positive Percent Agreement to PCR of 90.0% and 100% clinical specificity (95% CI: 99.1–100.0%) are additional features[6].

It describes values<1AU as non-reactive, those between 1-1.46AU as providing low/inadequate levels of immunity, those between 1.46-18.45AU as moderate levels of protection and values above 18.45AU as providing high levels of protection.

Data was collected at three time points. T1, T2 and T3 at 1-2 months, 3-4 months and 6-7 months Post-development of first COVID-19 symptom/positive RTPCR test whichever was earlier, from the same cohort of HCW. IgG tests were repeated prior to vaccination at 8-9 months (T4) in the small subset of HCW who had contracted the disease in May/June 2020. The HCW then partook the nationwide free vaccination drive for HCW initiated on 15 January, 2021 (beginning 8.5 months after our index case) and their antibody levels could be tested for variable periods of time depending on the time elapsed from development of first symptom to first dose of vaccination.

Statistical Analysis : All **c**ontinuous/quantitative variables are expressed as mean ± Standard deviation while categorical/qualitative variables are expressed as numbers and percentage. Microsoft Excel 2010 (Microsoft Corp., Redmond, WA, USA) was utilized for Descriptive statistics and MedCalc software for Box-whisker plots, trendlines and trend-areas. P<0.05 was considered statistically significant.

Observations

Demographic parameters: Out of the 214 respondents,164 (76.64%) belonged to 20-40 years age group, 45(21.03%) in the 40-60 years age bracket, 3 (1.40%) in more than 60y bracket and 2 (0.94%) in <20 years bracket.129 (60.28%) of the COVID-19 infected HCW are females and 85 (39.72%) are male.

Mean IgG antibody titres with standard deviation at 4 time-points have been tabulated (Table 1).

We collected 304 readings from 214 HCW. 137 HCW had their titres measured at one time point only, 52 HCW had their titres examined at only 2 time points. 21 HCW underwent serological test at only 3 time points (18 HCW got their IgG titres measured at T1, T2 as well as T3 (Fig 1), another 3 HCW at T2, T3 and T4) and only 6 HCW had their IgG-titres tested four times in 9 months. None of the surveyed HCW had any symptoms suggestive of re-infection in the

Statistical Variable	T1	T2	T3	T4
Sample size	117	125	41	22
Lowest value	0.0000	0.0000	0.0000	0.0000
Highest value	46.8000	56.5000	23.4000	17.4000
Arithmetic mean	11.13	9.6797	8.35	7.87
95% CI for the mean	9.55 to 12.71	8.10 to 11.26	6.49 to 10.21	5.90 to 9.84
Median	9.19	6.6200	7.84	7.49
95% CI for the median	7.81 to 10.56	5.52 to 8.36	5.46 to 10.12	5.02 to 9.76
Variance	74.4090	79.4770	34.7668	19.7318
Standard deviation	8.6261	8.9150	5.8963	4.4421
Relative standard deviation	0.7748(77.48%)	0.9210(92.10%)	0.7062(70.62%)	0.5645(56.45%)
Standard error of the mean	0.7975	0.7974	0.9209	0.9470
Coefficient of Skewness	1.5793(P<0.0001)	1.9812(P<0.0001)	0.4493(P=0.2118)	0.3829(P=0.4132)
Coefficient of Kurtosis	3.6212(P=0.0001)	6.2236(P<0.0001)	-0.4191(P=0.6139)	-0.3718(P=0.8119)
Kolmogorov-Smirnov test for Normal distribution (with Lilliofer's correction)	D=0.1243 reject Normality (P=0.0001)	D=0.1571 reject Normality (P<0.0001)	D=0.0840 accept Normality (P>0.10)	D=0.1079 accept Normality (P>0.10)

Table 1 — Summary statistics for Health Care Workers at 4 time points
(CI=Confidence Interval; T1: 1-2 months; T2: 3-4 months; T3:6-7 months; T4:8-9 months)

entire study period.

117/214 HCW got their IgG antibody titre tested at 1-2m. 3 months had already elapsed since the institutional index case when the study commenced in August 2020 and hence, 97 HCW missed the T1 time slot of 1-2m. The mean IgG antibody titre was 11.13±8.6AU

125/214 HCW got their IgG tested at 3-4m.5HCW resigned and 85 HCW got vaccinated before they could complete 3-4 m. The mean IgG-titre was 9.68±8.9AU

41/214 HCW got their IgG antibody levels tested at 6-7m post infection. Another 2 HCW resigned between T2 and T3 (total 7 resignations out of 214 at 6-7m post infection) while 166 HCW got vaccinated before they could complete 6-7 months postinfection. The mean IgG-titre was 8.35±5.9 AU.

Only 22 HCW completed 8-9 months Post-Infection before they got vaccinated. Their antibody levels tested at 8-9m Post-Infection had a mean titre of 7.87±4.4 AU.

The lowest titre at all time points was 0 while the highest titres were 46.8 AU, 56.5 AU, 23.4AUand 17.4AU at 1-2m, 3-4m, 6-7m and 8-9m, respectively.

The box plots depict the median (middle line) and first and third quartiles (boxes), while the whiskers show 1.5 times the Inter Quartile Range above and below the box. There were 3 outside values/inner fences (values smaller than the lower quartile minus 1.5 times the interquartile range or larger than the upper quartile plus 1.5 times the interquartile range) at T1, one at T2 and none at T3 and T4. There was one far out value/ outer fence (value smaller than the lower quartile minus 3 times the interquartile range, or larger than the upper quartile plus 3 times the interquartile range) at both T1 and T2 but none at T3 and T4 (Fig 2).

The Standard Deviation at 1-2m and 3-4m was much higher (accompanied by skewed distribution and kurtosis)than that at 6-7m and 8-9m (bell-shaped Gaussian data-distribution).

Discussion

When time, resources and patient-compliance are of exponential essence, selecting the right medical diagnostic test is of utmost importance. Out of diverse antibody isotopes with differential neutralization capacity we chose to focus on IgG directed against RBD-spike protein because these are not just binding but also neutralizing in nature depending upon their plasma levels and a simple, reliable, quantitative immunometric test is available to gauge IgG-titres[7]. Although it is known that time to seroconversion ranges from 11-22 days depending on severity of illness and IgG-titres peak at 21-40 days post appearance of first symptom and thereafter decline[8,9], it is unknown for how long protective IgG-titres last. Long, *et al* have reported that the IgG levels in 93.3% of asymptomatic and 96.8% of symptomatic COVID-survivors declined during the early convalescent phase by 71.1% and 76.2% respectively compared to acute stage levels (3.4 and 20.5 units respectively) and that 40% of asymptomatic and 12.9% of symptomatic individuals became seronegative for IgG in the early convalescent phase[10]. Their study ends in the early convalescent phase (2months post first symptom) while we followed up our HCW (all of whom were symptomatic) for maximum 9 months into the convalescent phase. The

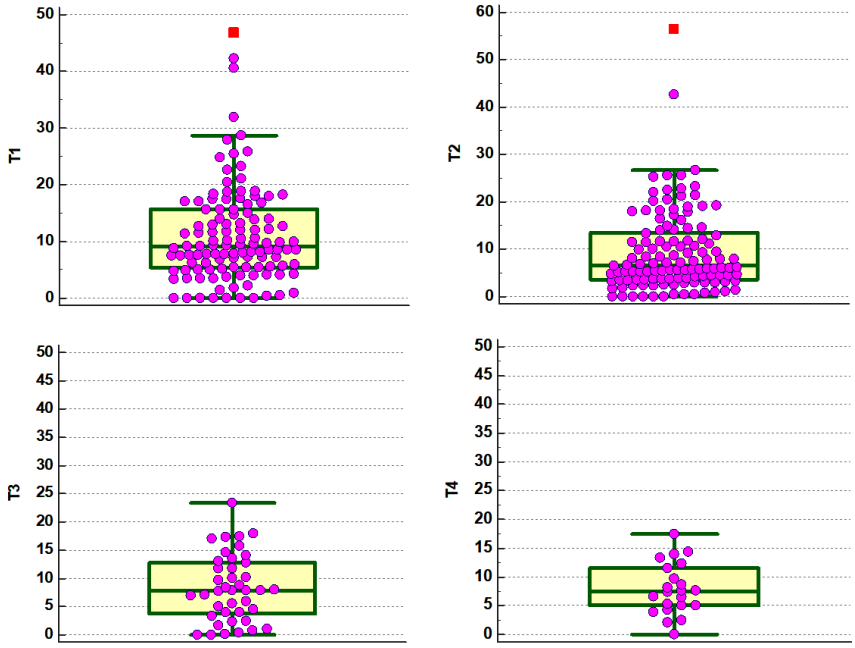

Fig 1 — Box-whisker plotsdepicting distribution of IgG-titres at four different time points

SIREN study, steered by Public Health England (PHE), reported that corona-survivors develop antibodies that provide 83% protection for at least five months duration[11]. Another two studies report detectable IgG-titres at 3 and 5 months post-exposure, respectively[12,13]. We have observed moderate IgG antibody titres in 17/22 (77.3%) HCW even after 9months of developing the first symptom/ positive RT-PCR test.

Immunity against SARS-CoV-2 is not binary, albeit it is graded. Although the mean IgG-titres progressively declined over 9 months (from 11.1 to 7.9AU) the values were still in the moderate immunity range (4.62-18AU) in our patients. On the face value,clinical implications of this decline for the concerned HCWs are insignificant as they still enjoy moderate levels of protection at the end of 9months. Of concern is the large Standard Deviation at T1 and T2, indicating that individual HCW have nil to low levels of protection (<4.62AU) making them vulnerable although the subset as a whole has moderate levels of protection. 20.5% HCW at 1-2months (IgG titre<1=10/171 HCW; IgG-titre 1-4.62 AU= 14/171 HCW), 34.7% of HCW at 3-4 months, 31.7%HCW at 6-7m(4/41 IgG-titre<1; 9/41 with IgG-titre 1-4.62 AU) and 22.73% HCW at 8-9m (IgG-titre<1=1/22; IgG-titre 1-4.62AU=4/22HCW) failed to develop protective levels of IgG.This underscores the importance of serological testing to discover and pinpoint those 1/3rd-1/5th patients with low IgG-titres who may suffer from antibody dependent enhancement[15] and concomitantly may lower their protective measures due to a false sense of security (Peltzman effect)[16].

The detailed sequential IgG-titres in 18 HCW have been plotted as trendlines (Fig 1).

5 HCW displayed a falling trend over the 3 time points with decay in IgG-titres as expected. But the fall in IgG-titres was too steep (18.2<5.52<4) and cannot be accounted for only by exponential decay and may be attributable to convalescent plasma donation by this HCW

4 HCW showed a rise at T2 followed by a fall at T3 (rhomboid pattern) attributable to a delayed IgG-peak at 3-4m instead of 1-2m.

7 HCW showed a fall at T2 followed by a rise at T3 (bowtie pattern). Fall at T2 is expected as per the exponential decay model. But the rise at T3 maybe explained by subclinical infection/anamnestic response

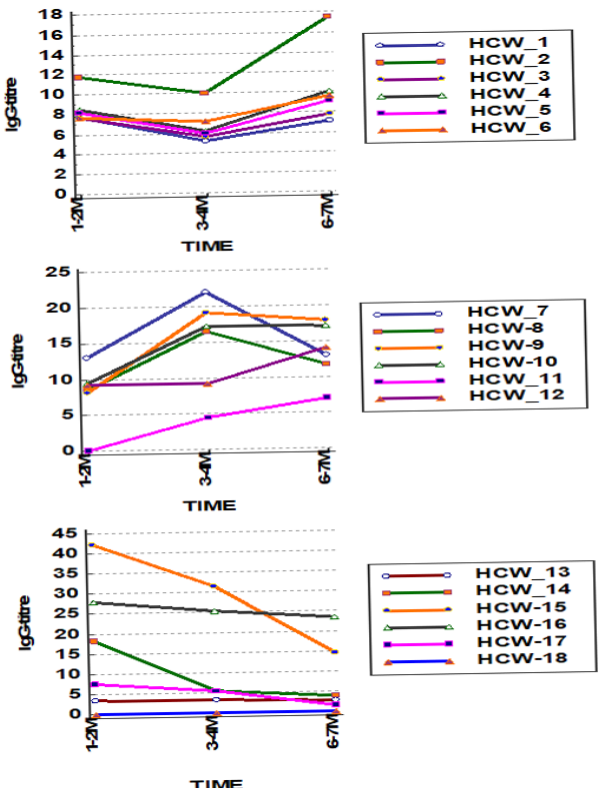

Fig 2 — Trendlines depicting IgG-titres over time

1 HCW failed to develop any antibodies at all three time points. This maybe due to a humoral immune system deficiency, accompanied by compensatory heightened T-cell immunity which enabled this individual to recover from COVID-19[17].

1 HCW showed a rising trend in antibodies at all three time points. Multiple subclinical exposures maybe responsible for this paradoxical rising IgG-titre trendline.

Declining IgG-titres in HCW signify the natural course of this disease. Rising/nearly constant IgG-titres at successive time-points can be explained by re-exposure to SARS-CoV-2 with subclinical infection, akin to a booster dose of vaccination.

An upslope between points T1 andT2 in one HCW may be countered by a downslope between points TI and T2 in another HCW. The vector sum of these individual undulating vectors may hence be a straight line. To demonstrate this we divided the 18 HCW into 3 strata, first strata was rhomboid (low-high-low IgG-titres at T1-T2-T3), the second was bow-shaped (high-low-high IgG-titres at T1-T2-T3) and the third was a right-angled triangle; hypotenuse sloping down from left to right; steadily declining IgG-titres). Stacking would give a false impression of antibody levels remaining fairly constant with elapsed time (Fig 3). Hence, the product of "IgG-titre numerical value" and the "time duration in months for which those titres lasted" is a superior measure of antibody levels in a particular HCW since it also takes into consideration the upslopes and down-slopes in the IgG-titre curves plotted against time. We shall denote this by the term "Effective Immunity" (EI) which is a composite figure facilitating comparisons between different individuals (Table 2).

The fact that 28/41 respondents still had moderate/high IgG-titres 6-7 months Post-Infection indicates that immunity triggered by natural infection to COVID-19 is more robust than imagined earlier. The fact that 22 out of these declined to take the free vaccines being provided to them and had their antibody titres tested at 8-9months indicates that they strongly believe that their IgG-titres would remain maintained at moderate levels in a gently undulating fashion till such time the pandemic lasts/herd immunity is produced. A wait and watch policy has been adopted by many HCW amidst apprehensions of adverse reactions to the vaccine. Some desire to derive full benefit from their pre-existing immunity till it lasts, as indicated by periodic IgG-titres and receive the vaccine shot once the titres fall below 4.62AU.

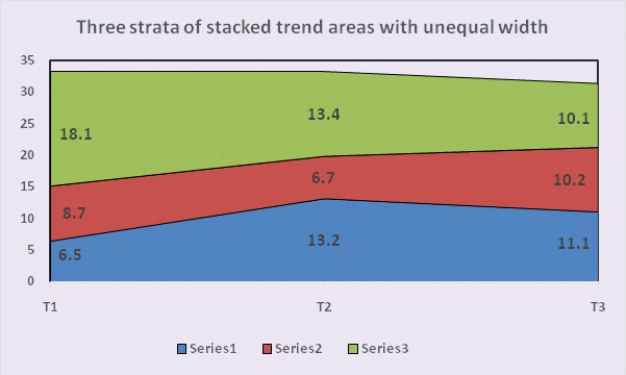

Fig 3 — Stacked area chart with IgG-titres clustered into three strata based on similar time-trends

No vaccination guidelines exist for COVID-survivors. We recommend that the initial dose/ first shot must be taken by all individuals irrespective of history of previous infection/ antibody status. It is unclear whether the second dose should be administered to HCW who have recovered from COVID-19. Their naturally acquired active immunity is at par or even more robust than the artificially acquired active immunity from the first dose of vaccination. The first dose of vaccination in COVID-survivors is akin to the second/booster dose of vaccination prescribed for exposure naïve people. Hence bimonthly serological tests gauging IgG directed at the RBD-antigen are required before the second dose to postpone it till a drop in IgG-titre corresponding to mild levels of protection is observed.

UK-based investigators utilized the Gamma Exponential Decay Model (GEDM) and gamma plateau model (GPM) for predicting longevity of antibody

HCW	IgG-1	IgG-2	IgG-3	Computation of EI	EI	IgG-4
1	0	4.42	7	0+13.26+14	27.26	Vac
2	13	22	13	26+66+26	118	Vac
3	9.19	9.15	14.1	18.38+27.45+28.2	74.03	13.9
4	7.73	5.23	7.12	15.46+15.69+14.24	45.39	4.29
5	11.8	9.98	17.5	23.6+29.94+35	88.54	Vac
6	8.5	16.5	11.7	17+49.5+23.4	89.9	14.3
7	7.69	5.69	7.82	15.38+17.07+15.64	48.09	Vac
8	3.46	3.28	2.91	6.92+9.84+5.82	22.58	2.13
9	8.5	6.2	10.1	17+18.6+20.2	55.8	8.2
10	9.41	17.2	17.1	18.82+51.6+34.2	104.62	Vac
11	8.1	19.1	17.9	16.2+57.3+35.8	109.3	Vac
12	8.2	5.97	8.77	16.4+17.91+17.54	51.85	7.68
13	18.2	5.52	4	36.4+16.56+8	42.76	Vac
14	0	0	0	0	0	0
15	7.77	7.17	9.65	15.54+21.51+19.3	56.35	Vac
16	42.2	31.4	14.6	84.4+94.2+29.2	207.8	Vac
17	27.9	25.4	23.4	55.8+76.2+46.8	178.8	Vac
18	7.53	5.45	1.63	15.06+16.35+3.26	34.67	Vac

Table 2 — Trends in IgG-titres over time and Effective Immunity (EI=Effective immunity; IgG-1=IgG-titre at 1-2months post first symptom; IgG-2= IgG-titre at 3-4months post first symptom; IgG-3= IgG-titre at 6-7months post first symptom; IgG-4= IgG-titre at 8-9 months post first symptom; Vac=Vaccinated)

response to SARS-CoV-2 and reported that the half-lives for the nucleoprotein, RBD and spike protein antibodies were 60 days, 102 days and 126 days, respectively under GEDM[18]. The half-life of RBD antibodies was 110 days while that of spike protein antibodies was projected as 364 days under the GPM, which assumes long-lived antibodies.This implies that at 126 days post infection the IgG-titres should have reduced to half the original values as per GEDM and halved at 364 days post infection as per the GPM. The results of our study demonstrate that at 274 days post first-symptom/RTPCR positive result, the mean IgG-titre was 7.87AU which falls in the moderate protection range. This is not half of the mean titres recorded at 1-2 months post infection (11.13AU) which implies that the GPM is a better predictor of IgG longevity while the GEDM under estimates the half-life of IgG.

The main strength of our survey is its conduction on HCW in a hospital setting who bear the brunt of SARS-CoV-2 exposure as an occupational hazard and would benefit from results and transmit the benefit to the society as a whole in terms of better-organized deployment of healthcare workforce in operation theatres, emergency wards and COVID-intensive care units based on their IgG-titres. Also, the results are reproducible since blood-samples have been preserved in the institutional biorepository for future reference. The main limitation of our study is that all HCW could not be followed for 6-7 months after first symptom as initially planned, owing to the nationwide vaccination drive.

Conclusion

Adaptive active immunity acquired through natural infection may last for at least 9 months postinitial exposure and lies in the moderate protection range in 77% HCW. Moderate levels of protection were observed by our immunometric test at 9 months which can be extrapolated to vaccination and immunity passports. Vaccine can be used as a booster dose/second exposure in all COVID-survivors especially those with low IgG-titre. Periodic quantitative IgG-titre based serological tests can help guide timing of second shot of vaccination.

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Original Article

Clinico-demographic Profile and Outcome of Scrub Typhus in North Eastern State of India

Soma Saha[1], Dipankar Prakas Bhaumik[2], Susmita Deb[3]

Scrub typhus is a form of bacterial Zoonosis caused by Orintia tsutsugamushi usually presents as Acute febrile illness with multiorgan involvement as a complication and is associated with significant mortality. This study aims to document the clinico-demographic profile, laboratory parameters and complication of Scrub Typhus in North Eastern Hilly State of Tripura with background of tropical climate.

This retrospective study was conducted at Tripura Medical College, including 42 patients admitted with acute febrile illness between June, 2020 to December, 2021 during the era of COVID-19 Pandemic. The diagnosis was established by Rapid card test, Lateral Flow Metry Assay (LFA) followed by confirmation through IgM, ELISA test and pathognomic Eschar where feasible. The clinlical, demographic and laboratory profile were documented and analysed.

Post rainy season and people from rural area with farming background were mostly affected population. Apart from Fever and Flu like symptom, respiratory and Gastrointestinal (GI) symptoms were more prominent feature. Pathognomic skin lesion eschar was found in maximum cases followed by shortness of breath, GI involvement and Renal failure. Acute Respiratory Distress Syndrome (ARDS), Acute Kidney Injury (AKI), Hepatic encephalopathy and meningitis were the serious complications.

While evaluating cases of acute febrile illness with multiorgan involvement clinician should have high index of suspicion for Scrub typhus specially resource poor areas of North Eastern (NE) state of India so that early detection and time bound intervention may help to reduce the mortality.

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Key words **: Febrile illness, Scrub Typhus, Zoonosis.**

Scrub typhus is a public health problem causing severe morbidity and mortality. It is caused by Orientia tsutasugamushi (O tsugtsugamushi) can result in severe multiorgan failure with a case fatality rate up to 70% without appropriate treatment[1]. It is the oldest vector born Zoonotic disease now re emerging with new trends worldwide specially in the endemic areas[2]. Antigenie heterogenicity of O tsugtsugamushi may be the reason behind the generic immunity which causes re-infection. Clinical picture consist of high grade fever, severe headache, apathy, myalgia and generalised lymphadenopathy. A maculopapular rash may appear first on the trunk and then on extremities. Eyelid edema and facial edema are also prominent feature. Black Eschar may be seen at the site of inoculation. Patients may develop complication like interstitial pneumonia, ARDS, HE, AKI, meningoencephalitis, and myocarditis[3-5]. Diagnostic approaches for Scrub Typhus are based on detection of antibody in the serum of patient suspected suffering from Scrub typhus. The mainstay in Scrub-Typhus diagnostics remains serology. The gold standard of diagnostic test is Indirect Immunofluorescent Antibody (IFA) test. Indirect immunoperoxidase (IIP) reduces cost of a fluorescent microscope by substituting peroxidase for fluorescein[6]. Weil- Felix OX-K agglutination reaction are the oldest test which lacks of specificity or sensitivity. Lateral flow assay, SD – Biolin rapid card test and detection of IgM antibody to Scrub Typhus by ELISA are also used in resource poor settings of difficult areas of India with high specificity and low sensitivity[18]. Early detection and treatment can reduce the burden of the disease. It is the general conception that in the state of Tripura Scrub Typhus is not seen, though the geo-topology, climate, humidity and vegetations are favorable for the growth of tick, the vector of the O

Editor's Comment :

- Scrub typhus is a bacterial zoonosis caused by Orintia tsutsugamushi presents as an acute febrile illness with multiorgan involvement and is associated with high mortality.
- A simple Rapid diagnostic test Lateral flow assay can assist in the early diagnosis of the disease especially in the resource-poor difficult areas of Northeastern states so that early initiation of treatment can prevent life-threatening complications and reduce mortality.

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tsugtsugamushi. As in the recent past we are encountering considerable number of patients being diagnosed as Scrub Typhus, we feel, it is relevant to study scientifically the characteristics of the patients. It will help to generate awareness among the health service providers hence forth of interest for the people of the beautiful state of Tripura.

Materials and Method

This is a retrospective observational study carried out in 2021 in the Department of General Medicine Tripura Medical College and Dr BRAM Teaching Hospital , Tripura. The case records of 42 Scrub Typhus antibody positive by rapid diagnostic test Lateral Flow Assay (LFA) subsequently confirmed by detection of IgM by ELISA admitted in the Department of General Medicine of TMC & Dr BRAM Hospital, in one and half year (1st June, 2020 to 31st December, 2021) were collected and analyzed. The demographic profile, Age, Sex. Gender, occupation and clinical features, examination findings, laboratory results, complications and outcome in the form of discharged or death were documented in pre-designed proforma.

Inclusion Criteria :

(1) Fever more than 3 days.
(2) Age more than 18 years.
(3) Positive serology for Scrub Typhus.
(4) With or without complication.

Exclusion criteria :

(1) Patient with other established causes of fever (Infectious or Non infectious)
(2) Negative serology for Scrub Typhus.

The study was conducted with due permission from the appropriate authority of Hospital and after Clarence from the Institutional Ethical Committee.

Result

Socio-demographic Profile :

The middle aged group of people between 31 to 50 years 60.05% (n=29) were mostly affected population in our study followed by young people below the age of 30, 21.43% (n=9) and older age group 9.52% (N=4). Male were affected more 61% compared to female population 31% (Table 1). The minimum and maximum age of the patient were 21years and 78 years respectively with a mean age of 43.6±12.2 years. The Male to female ratio was 2.23 : 1. Most of the affected people were from rural and hilly areas of Tripura with farming as occupation in the background. Maximum no cases were reported from South district of Tripura followed by Sepahijala and Gomti District the main harvesting areas of Tripura. Most of the cases were observed in Rainy season that is July to October (Table 1).

Clinical Profile :

All the study population (n=42) presented with fever with average duration of 5.52±2.07 days (Table 2). Maximum temperature noted was 104°F 23.08% (n=10)(Table 2). The most common symptom in our study were headache (81%) and respiratory symptom in the form of Cough (73.8%) and Breathlessness 16.7% followed by Body ache (64%), Arthralgia (64%) and GI symptom (64%). Only six (14.29%) patient had Central Nervous System (CNS) involvement in the form of altered sensorium of which two (33.33%) of them had seizure during their hospital stay (Fig 1). Among the six (14.3%) patient presented with Icterus two (33.33%) of them developed Hepatic Encephalopathy.

The most common clinical examination findings Eschar was observed in 26 (61.9%) patients in our study followed by Hepatomegaly 42.9% (n=18), Anemia 28.6% (n=12), Skin rash 19.5% (n=8), Eyelid edema 14.3% (n=6) and Jaundice14.3% (n=6). Four patient (66.67%) developed acute hepatitis, Two (33.33%) of them developed hepatic encephalopathy

Table 1 — *Showing Demographic profile (n = 42)*

Parameters	Number	Precentage (%)
Age group (in Years) :		
Group I (20-30 years)	4	9.52%
Group II (31-50 years)	29	69.05%
Group III (>50 years)	9	21.43%
Gender :		
Male	29	69.0%
Female	13	31.0%
Area of Distribution (District wise) :		
South District	13	31.0%
West District	10	23.8%
North District	0	-
Gomati	6	14.3%
Dhalai	1	2.4%
Sipahijala	5	11.9%
Khowai	6	14.3%
Unokoti	1	2.4%

Table 2 — *Showing pattern of fever (n = 42)*

Parameters		Number	Percentage (%)
Fever	Present	42	100%
	Absent	0	-
Temperature (in °F)	Average temperature – 102.57 ± 0.99 °F		
	101 °F	5	11.9%
	102 °F	18	42.9%
	103 °F	9	21.4%
	104 °F	10	23.8%
Duration of fever (in days)	Average duration of fever – 5.52±2.07		
	3-4 days	13	31.0%
	5-6 days	18	42.9%
	≥7 days	11	26.2%

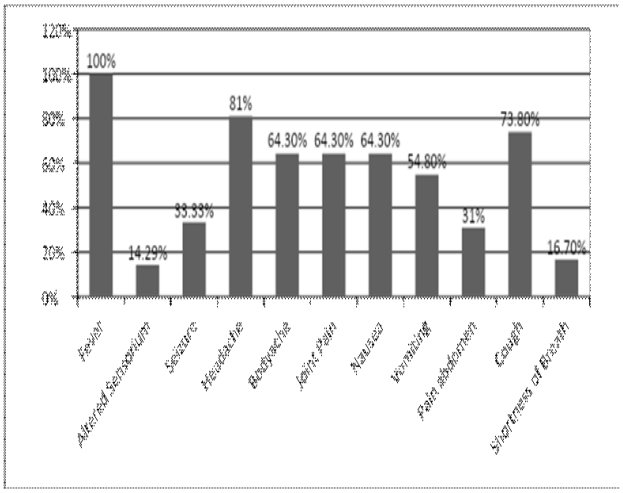

Fig 1 — Symptomatology of Scrub typhus

(Fig 2). Abdomainal Ultrasonography(USG) showed hepatomegaly in 23.81% (n=10), splenomegaly in 4.8% (n=2).There was no alteration of hepatic echotexture or obstructive features in USG except in two patients who showed periportal cuffing and increased echogenicity of liver. Chest radiography that is chest X-Ray postero anterior view done in all the cases (n=42), showed radio opacities in 64.41% (n=20), peribronchial thickening in 25.81% (n= 8) ARDS in 6.45% (n=2), pleural effusion in 3.22% (n=1) Lumber puncture were done in six patient who presented with altered sensorium. Amongst them only one (42.8%) had shown high protein and lymphocytic predominance in Cerebrospinal Fluid (CSF) examination. Computed Tomography with contrast were performed in six cases of suspected CNS involvement and was essentially normal study. Apart from sinus tachycardia no other significant abnormality

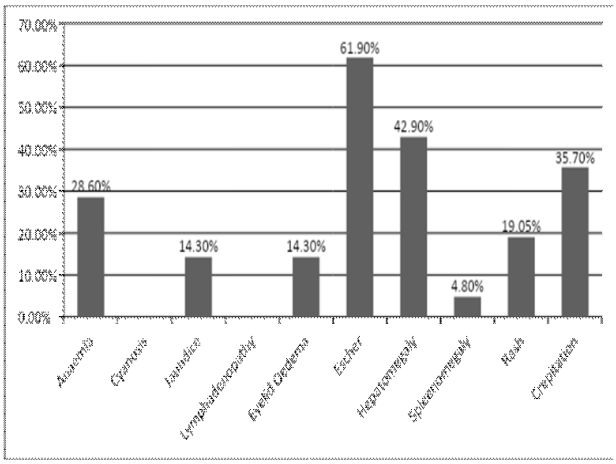

Fig 2 — Clinical signs of Scrub typhus

was found in Electrocardiography done in twenty patients. Urine routine and microscopic examination showed increased protein and Red blood cells in one case (2.38%)(Table 3).

Laboratory Parameter :

In laboratory parameter Anaemia was observed with mean of 10.83±1.54 followed by raised hepatic transamineses 99.996±8.96 for AST(Aspertate Aminotransferase) and 82.864±9.69 for ALT (Alanin aminotransferase). Total count ranges from 4100 to 18000 with mean of 8764.29±3095.85, with neutrophil predominance mean of 76.05±11.79. Alteration in kidney function also observed for urea mean 35.76±32.89 and creatinine 1.06±0.30. Electrolytes abnormality in the form of Hypontremia (n=4) 9.52% and hypokalemia also noted in our study (Table 3).

Discussion

Scrub Typhus is a Zoonotic disease caused by Orientia tsutsugamushi, has wide range of serotypal variability due to the antigenic protein -56Da, TSA in the genous Orienta[5]. The various type of clinical presentation, multiple organ involvement and case fatality may be duo to antigenic variability. The middle aged male were most affected group in our study like Varghese, *et al*, may be duo to outdoor activity in day time with an occupation of farming from the hilly areas of Tripura[6]. Maximum no of cases were observed in Rainy or extended Rainy season in the month of July to October due to the tropical climate of Tripura where rains continues even up to November[7]. This is the main

Table 3 — *showing Laboratory findings (n = 42)*

Parameters	Minimum	Maximum	Mean ± SD
Hemoglobin	5.80	13.00	10.83 ± 1.54
Total count	4100	18000	8764.29 ± 3095.85
Neutrofil	45	90	76.05 ± 11.79
Lymphocytes	10	50	19.79 ± 8.464
Eosinophil	0	5	1.07 ± 1.50
ESR	22	68	44.62 ± 10.92
CRP	0.0	58	21.68 ± 15.27
Billirubin	0.06	2.10	1.09 ± 0.43
SGPT	26	246	99.98 ± 68.69
SGOT	28	235	82.86 ± 49.69
ALP	130	242	175.26 ± 35.4
TP	5.6	7.7	6.86 ± 0.45
Albumin	2.1	6.8	3.54 ± 0.68
Urea	21	232	35.76 ± 32.89
Creatinine	0.70	2.00	1.06 ± 0.30
Urinary protein	0	1	0.31 ± 0.47
Urinary RBC	0	1	0.12 ± 0.32
Na^+	129	149	134.60 ± 4.41
K^+	2.9	4.8	3.6 ± 0.38
Mg^+	1.5	2.1	1.84 ± 0.15

[SD = Standard Deviation]

cultivating time for JOOM cultivations in the hills of Tripura. There are very few cases from the North Tripura probably due to lack of communication and difficult transport duo to the period of Lock down and Government regulation.

Eschar which is the pathognomic lesion for Scrub Typhus were found in 26 cases in our study corresponds with other Asian and Indian study[8]. The most commonest site of Eschar in the Inguinal, peri inguinal area followed by axilla and below the breast. It is very difficult to demonstrate Eschar in highly pigmented people because of its non itchy nature, so thorough clinical examination is required in suspected individuals in the endemic areas[9].

Almost all the cases presented with fever followed by headache, arthralgia, and myelgia which mimicked with other viral illness specially when the study was conducted during COVID-19 Pandemic period. Most prominent symptom was breathlessness in our study though less documented in other Asian study except in few North Indian study[5,11]. In the background of Pandemic it was difficult to differentiate the pulmonary involvement of Scrub Typhus from COVID 19. All the patient were admitted after screening through RT PCR and those developed respiratory complications were retested through RT PCR for COVID-19 on fifth day according to ICMR protocol. Interstitial pneumonia, bronchopneumonia and pleural effusion were the prominent respiratory findings which are similar to the other studies done in the sub Himalayan region[14]. Initial low oxygen saturation (SpO_2) may be due to mild pleural effusion and Pneumonia which resolved with treatment. Severe form of respiratory complication ARDS also found in our study which correlates with other North Indian studies[11].

Second commonest involvement is GI system in our observation in the form of elevated Liver enzymes and anicteric hepatitis, though jaundice was not a prominent feature but different study described Scrub typhus as a commonest cause for acute febrile jaundice in the sub Himalayan region[13].

Facial oedema and periorbital oedema were observed in few cases in our study is not very uncommon rather sizeable number of cases reported in other studies[10]. This oedema may be due to accumulation of fluid in the interstitial space after breeching of endothelial lining with perivasculitis[10]. Very few cases of Central Nervous System (CNS) involvement in the form of altered sensorium and seizure were noted, with a complication of meningitis in our study which is similar to other studies as well[15].

The important complications noted in our study were AKI (Acute Kidney Injury), ARDS, hepatic encephalopathy and Meningitis. Most of the complications were due to delayed presentation or treatment initiation. one patient developed AKI which resolved with treatment in the second week though some studies in adult showed AKI in 12% to 22%[16]. Two of our patient who developed hepatic encephalopathy during hospital stay had a history of chronic alcohol intake so may be preexisting liver disease worsen with acute injury, though hepatic complication mentioned in studies by Vikrant, *et al*[16].

Leucocytosis with neutrophilic preponderance observed in our study though different Indian studies showed lymphocytic preponderance with thrombocyopenia[17]. Some studies from China showed lower rates of Thrombocytopenia 4.6% to 48.9%[17]. Elevated CRP in our study may be attributed to systemic inflammation. Low albumin in few patient may be duo to acute on chronic Liver failure.

Dyselctrolytemia may be duo to Fever and Dehydration which is mentioned in other studies also.

The limitation of our study is that the study was based on first detection of Scrub Typhus by Lateral flow assay which has got high specificity and low sensitivity in the absence of Standard diagnostic test like Indirect immunofluroscence assay. All the cases subsequently confirmed by IgM positivity by ELISA. However, a positive correlation of 97% between IgM ELISA and SD BIOLINE rapid test was reported in India[18].

In conclusion Scrub Typhus should be one of the important differential diagnosis while evaluating a patient with Acute Febrile Illness and multiorgan involvement specially in the North Eastern Region of India where Malaria is endemic. Tropical rain forest is one of the main source of vector larval mite for Rickettsial disease. Varied clinical presentation and low case fatality of Scrub Typhus in NE Region may be due to antigenic variability of O tsutsugamushi and recurrent exposure to the organism. Primary care physician should have a high index of suspicion for Scrub Typhus especially in resource poor setting of difficult areas of NE States so that early diagnosis and treatment can prevent severe complications and also will help in reduction of mortality due to Scrub Typhus.

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Original Article

Preparedness of Phase 1 MBBS Students for Self-directed Learning Process

Soma Gupta[1], Alka Rawekar[2], Md Quazi Tajuddin[3]

Self-directed learning is important for MBBS students to prepare themselves as lifelong learner. But a "spoon-fed" school student needs to be sufficiently prepared to learn by SDL. In this study, the ability of the students to learn by SDL is measured along with evaluation of the reliability of as "Self-Directed Learning Instrument" (SDLI) as measuring tool. All willing students of the 1st phase MBBS curriculum (Batch 2020-21) were given a 20-item questionnaire known as "Self-directed Learning Instrument" (SDLI) to evaluate their learning abilities by SDL. A higher level of SDL is indicated by a higher score. A total of 247 students were included in the study. The result shows that students have poorest ability in Planning and Implementation domain (Mean: 3.9, variance: 0.26) whereas they are strongly motivated (Mean:4.3, variance: 0.37). SDLI score revealed that only 6 students need special care from faculties. Some (n = 81) needed observation and monitoring whereas majority of students (160, 64.8%) were supposed to be able to learn of their own. The method was found to be reliable as Cronbach's alpha for all domains were over 0.70. The students with poor ability to learn by themselves can be identified in the very beginning of the session who can be given special attention and facilitated to grow as lifelong learner.

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Key words **: Self-directed Learning (SDL), Self-directed Learning Instrument (SDLI), Domain wise assessment.**

The introduction of Competency-based Medical Education (CBME) Curriculum in India has endorsed many new concepts, one of which is Self-Directed Learning (SDL). In SDL the students are expected to take the initiative to diagnose their learning needs, formulate their learning goals, identify resources for learning and evaluate their learning outcomes[1]. Thus, SDL is primarily a higher order active learning technique where onus of learning lies with the students. Dedicated time has been allotted to SDL in CBME curriculum in each specialty. As SDL is a newly introduced method of learning, the implementation of SDL is facing some challenges. One of such problem is that medical students in Phase 1 of their MBBS curriculum are in the transition phase from their school life. They depend too much on teachers and expect some sort of "spoon feeding." A study by Sari D, *et al*[2] had reported that students are very much dependant on teachers. So, without active involvement of faculties, students can rarely develop the skills of becoming self-directed learner. Hence it is very much important to understand their preparedness to study by SDL.

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Editor's Comment :

- To implement self-directed learning successfully, the preparedness of MBBS students should be initially assessed by SDLI. The limitation of individual students, if identified and taken care of, then only they will be able to carry out their role as "Life long learner," as mentioned in CBME.

Garrison developed a model[3], where self- motivation, self - monitoring and self-management were demonstrated as components of SDL. In addition to these components, communication is an important learning process for the medical profession, which is also related to Self-directed learning process. The inner drive and external stimuli motivating a learner to learn and to take responsibility for own learning is known as learning motivation. The ability of setting learning objectives independently is called planning, Achievement of learning goals using appropriate learning strategies and resources is called implementation. The ability to evaluate one's learning process and outcome is self-monitoring. When learners interact with each other to promote their own learning, that is known as Interpersonal communication.

The measurement of ability of the students to learn by SDL is a challenge. Cadorin, *et al* compared several tools for the same and recommended superiority of "Self-Directed Learning Instrument" (SDLI) to evaluate SDL abilities[4]. SDLI was developed by Shen, *et al*[5] for mainland Chinese Nursing students. No such tool for

medical students is still available. So, the reliability of this tool in a Medical College set up needed to be established.

In this background, this study is conducted to assess the ability of the students to learn by SDL in a Government Medical College of West Bengal. The specific objective of the study is to find out whether the Phase 1 MBBS students are prepared to learn Biochemistry by self-directed learning activity. The reliability of measuring tool (SDLI) was also evaluated in the current study setting.

Materials and Methods

This cross-sectional study was conducted in a Government Medical College of West Bengal in December, 2021. All students of the 1st phase MBBS curriculum were asked to bring their own smartphone/ laptop with internet connection during one fixed date of Biochemistry class of one hour. They were introduced briefly to the objectives and the methodological workflow of the study by an interactive lecture. All willing students were included in the study. Those students, who were absent on that day were excluded for the study.

Then they were given a questionnaire prepared in google form. The first part consisted of questionnaire on personal data. In the next part, they were given 20 items of SDLI. The participants were asked to select their response from a Likert scale of 5-point rating: "strongly disagree," "disagree," "neutral," "agree," and "strongly agree." Estimated time to respond to the entire questionnaire was approximately 30 minutes. Research has been proved that Computer based methods are better than paper-based questions. It solves the problem of incomplete data or missing data by making the answer field mandatory. Retrieval of data in excel form is automatic and thus statistical analysis becomes easy. Electronic versions of questionnaires have shown consistent test-retest reliability of data. Due to all these reasons, though students were present physically, electronic version was used to gather survey data.

"Self-directed Learning Instrument (SDLI) is a validated tool composed of 20 items questionnaire, containing four domains. First domain is "learning motivation." which is defined as the inner drive of the learner as well as external stimuli motivating one to learn and to take responsibility for one's learning (first 6 questions state, I know what I need to learn; Regardless of the results or effectiveness of my learning, I still like learning; I strongly hope to constantly improve and excel in my learning; My successes and failures inspire me to continue learning; I enjoy finding answers to questions; I will not give up learning because I face some difficulties).

The next domain is "Planning and implementing" (Question No. 7 -12 stating I can proactively establish my learning goals; I know what learning strategies are appropriate for me in reaching my learning goals; I set the priorities of my learning; Whether in the clinical practicum, classroom or on my own, I am able to follow my own plan of learning; I am good at arranging and controlling my learning time; I know how to find resources for my learning). "Planning and implementing" is defined as the ability to independently set learning objectives, using appropriate learning strategies and resources in order to effectively achieve learning goals.

Third domain "self-monitoring," is defined as the ability to evaluate one's learning process and outcomes. It consists of Question No. 13 -16, stating I can connect new knowledge with my own personal experiences; I understand the strengths and weakness of my learning; I can monitor my learning progress; I can evaluate on my own my learning outcomes.

The fourth domain, "interpersonal communication" is defined as the ability of learners to interact with others to promote their own learning (Question No. 17-20 stating My interaction with others helps me plan for further learning; I would like to learn the language and culture of those whom I frequently interact with; I am able to express messages effectively in oral presentations; I am able to communicate messages effectively in writing).

All items of SDLI are positively stated. The respondent is asked to rate each item on a 5-point Likert scale ranging from 1 for "strongly disagree" to 5 for "strongly agree". Thus, the total possible score on the SDLI ranges from 20 to 100. A higher level of SDL is indicated by a higher score.

The summary statistics were presented using frequencies with percentage for all response. SDLI score was calculated. No cut off value of the score is available in existing literature. It is mentioned that higher the score, better is the ability to learn. We supposed if students have low score like 2 in all responses the score becomes 40. If all students give 3 in all responses the score becomes 60. This is considered as the cut off as students have no positive response. If students give 4 in all responses, the score is 80. Students scoring 80 or above are considered as good learner and the score within 60 to 79 is considered as borderline score.

The reliability of the score in the present setting was determined by calculating Cronbach's alpha co-efficient.

All data were analysed using SPSS software version 22.

The study was approved by Institutional Ethics Committee.

Results

Out of a total 252 students (Current academic year: 250 & Old academic year: 2), 247 students (156 male, 91 female) took part voluntarily in the study.

In SDLI, the participants were asked to select their response from a Likert scale of 5-point rating: "strongly disagree," "disagree," "neutral," "agree," and "strongly agree." The percentage of frequencies for all such responses are presented in Fig 1.

Mean score of each item of SDLI is presented in Table 1. Only 2% students had strongly disagreed (Response 1) with the statements and 3% only disagreed (Response 2). 14% of the students remained neutral (Response 3). Majority agreed with the statement (Response 4, 46%) and rest strongly agreed (Response 5, 35%). From item mean, it seemed that students have poorest ability in Planning and Implementation domain (Mean: 3.9, variance: 0.26) whereas they are strongly motivated (Mean:4.3, variance: 0.37).

Distribution of study population according to SDLI score is presented in Table 2. Though the cut off value was considered as 40, only 1 student was found below that score. 5 students were between 40 and 59. These 6 students need special care from faculties. A total of 81 students with score 60 to 79 need observation and monitoring. However, majority of students (160, 64.8%) scored above 80 and they are supposed to learn of their own. Table 3 shows Reliability statistics according to different domain expressed by Cronbach's alpha. Highest Cronbach's alpha was obtained for Planning and Implementation domain (0.852), followed by self-monitoring (0.807), self-motivation (0.786) and interpersonal communication (0.708).

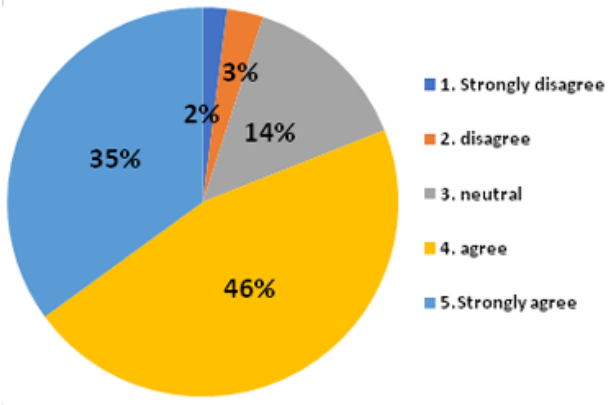

Fig 1 — Frequency distribution of response in percentage

Table 1 — *Mean score of each item of SDLI*

Item No	Statement	Mean score
Learning Motivation (LM)	**4.4**	
1	I know what I need to learn.	4.1
2	Regardless of the results or effectiveness of my learning, I still like learning.	4.2
3	I strongly hope to constantly improve and excel in my learning.	4.6
4	My successes and failures inspire me to continue learning.	4.44
5	I enjoy finding answers to questions	4.3
6	I will not give up learning because I face some difficulties	4.42
Planning and Implementing (PI)	**3.9**	
7	I can pro-actively establish my learning goals.	4.0
8	I know what learning strategies are appropriate for me in reaching my learning goals.	3.8
9	I set the priorities of my learning.	4.1
10	Whether in the clinical practicum, classroom or on my own, I am able to follow my own plan of learning.	3.9
11	I am good at arranging and controlling my learning time.	3.6
12	I know how to find resources for my learning.	3.8
Self-Monitoring (SM)	**4.06**	
13	I can connect new knowledge with my own personal experiences.	4.1
14	I understand the strengths and weakness of my learning.	4.2
15	I can monitor my learning progress.	4
16	I can evaluate on my own my learning outcomes.	3.9
Interpersonal Communication (IC)	**4.07**	
17	My interaction with others helps me plan for further learning.	4.3
18	I would like to learn the language and culture of those whom I frequently interact with.	4.3
19	I am able to express messages effectively in oral presentations.	3.6
20	I am able to communicate messages effectively in writing	4.1

Discussion

CBME has emphasized that from teacher Centric Learning Process must be replaced by Student Centric Learning process. One of such approaches is Self-directed learning, which is supposed to help the medical students to become lifelong learner and fulfil one of the goals of an Indian Medical Graduate[3]. But there are certain pre-requisites to learn successfully by Self-directed learning process. Students need to be focused and self-motivated. They should be able to assess themselves and thus monitor own learning process. They should plan according to their need and implement various methods of learning to achieve their goal. They need to communicate facilitators and other resource persons or their peers or seniors for necessary help. Medical students in first year are too young to have all these qualities.

Table 2 — *Distribution of study population according to SDLI score*

Total score of SDLI	Male	Female	No of students	Percentage	Remarks
Below 40	1	0	1	0.4%	Needs special care
40 - 59	4	1	5	2%	
60 -79	44	37	81	32.8%	Needs to observe and monitor
80 and above	107	53	160	64.8%	Can learn of their own
Total	156	91	247	100%	

In this study, the maximum score in SDLI was for item 3 (Mean score: 4.6), that states, "I strongly hope to constantly improve and excel in my learning, which is similar to the study by Bhandari, *et al* (Score:4.7)[6]. The minimum score of 3.6 was given to item 11 and 19. Item 11 states that "I am good at arranging and controlling my learning time and Item 19 states that "I am able to express messages effectively in oral presentations." Bhandari, *et al* also reported that students are poor in time management[6]. Moreover, they need to develop their interpersonal communication skills and express themselves orally. High score was also found in Item 4, stating, "My successes and failures inspire me to continue learning' (Score: 4.44), and Item 6, stating "I will not give up learning because I face some difficulties." (Score: 4.42). Bhandari, *et al* also got high score in Item 4. In fact, domain wise highest mean score was observed in learning motivation domain (Table 1). Mean scores of all individual items were above 4.1. Domain wise, lowest mean score was observed in Planning and implementation domain. Except Item 7 and 9, mean score of all individual items were below 4.

Self-monitoring domain shows that, they are aware of their strengths and weaknesses for learning (mean 4.2), can connect new knowledge with their personal experiences (4.1), can monitor own learning progress (Mean score:4). Unlike Bhandari, *et al*, mean scores of the interpersonal communication domain is better in our study. The only difficult part for them was expressing themselves orally (Mean score:3.6).

From Table 2; it is obvious that 2.4% students with SDLI score definitely need special guidance to learn by SDL. Another 32.8% students, with SDLI score between 60 to 79 needs to be observed and monitored. Rest 64.8% students can study of their own.

In the current situation SDLI was found to be reliable as Cronbach's alpha for internal consistency of 4 domains were between .708 to .852, which is similar to Shen, *et al* (0.755 - 0.825)[5].

Table 3 — Reliability statistics according to different domain

Name of Domain	No of item	Cronbach alpha
Learning motivation	6	0.786
Planning and implementing	6	0.852
Self-monitoring	4	0.807
Interpersonal communication	4	0.708

Conclusion

This study shows that SDLI is a reliable tool to assess the ability of phase 1 MBBS student to learn by Self-directed learning process. In the study majority of the students (64.8%) were found to learn of their own. Rest of the students need either some special guidance (2.4%) or monitoring by faculties (32.8%). Domain wise assessment shows students are motivated but they lack in planning and implementation of their abilities. Self-monitoring domain and interpersonal communication domains are more or less acceptable. Limitation of this study is that the result solely depends on self-assessment of the students. We have no scope to verify whether it is correct or not. The outcome of the study is we can identify the students with poor ability to learn by themselves in the very beginning of the session. Special attention can be given to them to overcome their difficulties and facilitate them to grow as lifelong learner.

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Original Article

Online Classes Design and Delivery Based on Student Responses

Surya Prakasa Rao[1], Sivakumar Vijayaraghavalu[2]

Background : COVID-19 has made a series changes in all system of life especially in education. As a result, education has changed dramatically with the distinctive rise of e-learning. The present study was aim to examine the preference and perception of MBBS student on newly introduced online live video classes.

Methods: An online questionnaire survey consisting of closed and open-ended questions on nine different categories such as accessing online video content, previous experience with online learning, interaction with video lectures addressing the content, duration, visualize, timings and screen size, perceived learning experience, the online content learning assessment methods and the experience with the online learning management system.Two hundred and thirteen undergraduate medical students were participating in this study. And it was conducted by the large medical institution in Andhra Pradesh.

Results: The e-learning methods were encouraged and its gaining popularity among the medical students and faculty. Our analysis shown 97.7% students were highly satisfied and 2.3% were not satisfied with online classes on comparison to the traditional methods of learning.

Conclusions: The teaching method and teachers support are the pivotal elements which enable online learning experience with a mutual relationship. Furthermore, the usefulness and acceptability of e-learning among medical students as a part of their curriculum is still not fathomed in medical education.

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Key words **: Medical Education, Assessment, Video lectures, E-learning, Feedback, Questionnaire.**

Editor's Comment :

- Given the dynamics of online learning, it is common for students to feel distant and isolated during the course.
- One of the best ways to prevent medical students from feeling this way is by delivering personalized feedback.
- The teaching method and teachers support are the pivotal elements which enable online learning experience with a mutual relationship.

The e-learning courses and lectures provide medical students with learning opportunities[9]. While devising the e-learning classrooms, one should consider the various situational, institutional and dispositional reasons for which students do not perform well in online classes[1]. The reasons can range from such as administrative problems, degree of interactivity, prior academic preparedness, technical skills, motivation level, time and support for learning, and availability of technical assistance designed to troubleshoot[1,13]. Assessment is a fundamental and essential issue in non-traditional learning environments. Clear understanding and the strategies for assessment are critical for both teachers and students in creating online environments for more effective teaching and learning[22]. Teachers need to identify and implement assessment strategies and methods appropriate for online learning. Teachers also need to be familiar with the potential of a variety of technology tools for monitoring student learning and improving their teaching effectiveness[4]. From the students' perspective, good assessment practices can show them what is essential to learn and how they should encourage learning; hence, engaging them in goal-oriented and self-regulatory cognitions and behaviors.

There seems to be an urgent need to devise a dynamic design expected to lead to higher learning outcomes and more positive approaches toward learning[4]. The faculty engaged in online teaching should understand the concept of flexible pedagogy that takes into account the audience members, the set of appropriate instructional and technological tools and strategies, course cadence or pace, and creating and maintaining an online learning community, as well as valid and reliable assessment measures[20].This type of online learning can be designated as negotiated learning, relying on using gradual community-building strategies, prior personal knowledge, and effective communication. This also creates a flexible pedagogy that takes into account the audience members, the set of appropriate instructional and technological tools and strategies, course cadence or pace and creating and maintaining an online learning student community,

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as well as valid and reliable assessment measures[20].

The objective of this paper is to describe the methodology and measures undertaken to devise an effective, influential dynamic implementation of the online teaching and learning for medical students. The student involvement in this endeavour is engagement which is both structured/formal and unstructured/ informal following every week in the online environment.

The Learning Management System (LMS), Moodle, along with ZOOM video conferencing tools are used in this online teaching[2]. Students feedback is gathered through google docs/ questionnaire. Both sets of evidence of student engagement during the online lectures and feedback are used to help the researcher devise and adapt the course content and delivery methods to suit the varied needs and interests of students, as they emerge from the wide range of online communicative exchanges.

Online classes are assessed through a questionnaire designed under the following criteria

(A) Accessing the Online Content :

i) Instrument : Mobile/ Tablet/ PC/ Laptop

ii) Network : Poor/ Satisfactory/ Good/ Excellent

iii) Audio-Visual Clarity : Poor/ Fair/ Good/ Excellent

(B) Online Experience :

i) Whether underwent any online courses: Yes/ No. If Yes whether it is assessment or learning or both

ii) How long he/ she underwent the course:

(C) Lectures :

i) Content : Whether the content of the lecture is interesting to the participant? The content mainly consists of textual material in routine physical lectures; do the participants prefer the same format of Power Point slides? If yes, why? If no suggest

ii) Duration : What should be the duration of the lecture? Whether they prefer short lectures of 5-10-minute duration followed by immediate assessment or a lengthy say 45 minutes of single lecture? What should be the optimal duration of an online lecture? Do you prefer varying duration of lectures for different subjects?

iii) Visuality : Whether the same teachers should teach or do they prefer other college teachers/ guests to teach them? Whether they prefer a complete view of the teacher or only the portrait view? Whether classroom background is acceptable or any other background? Whether they prefer the participant video at the administrator screen? Does the participant feel isolated in listening to the class?

iv) Assessment : Whether before beginning and after completion of the lecture, some form of assessment is preferred? Whether they would accept immediate online question & answer session after the lecture? Do they mind asking questions specific to one or more participants (students)?

v) Timings : Whether participants are satisfied with the timings of the online (10.00 am to 12.30 noon)?Do you suggest any suitable timing? If yes suggest, if No

vi) Screen Size : Which screen size do you normally watch for lectures?

vii) **Experience with Online Lectures:**

a) Acceptability: Cultural/ parental/ Peer/

b) Adaptability: Personal/

c) Learning experience: Enjoyable/ Lost personal touch

d) Preferability: Personal/ Priority

e) Difficulty level: Personal/ Peer

f) Suggestions if any:

(D) Learning Platform:

a) Have you heard about this video-conferencing platform before: Yes/ No?

b) Are you conversant with the facilities available in this platform?

i) Asking questions/ Raising hand : Yes/ No

ii) Mute/ unmute : Yes/ No

iii) Video sharing/ file sharing : Yes/ No

Constructive feedback can transform a student's learning experience. It encourages them to reflect, deal with criticism, learn better and stay motivated.

However, providing feedback in an online course is not as straightforward. In fact, the lack of meaningful feedback happens to be one of the biggest challenges online learners face. In a traditional classroom setting, instructors get more facetime with students, and this allows them to gauge students and offer frequent feedback accordingly. The same cannot be said about online classes because the interaction is limited.

Students learning through online teaching require continuous assessment by the teachers. Unlike the physical classes, during online teaching, teacher is devoid of assessment of the students understanding of the VL. Hence, students are enquired about the preferred method of learning assessment.

Research Questions :

(1) How are students accessing the online video lecture content at their homes?

(2) To what extent are students' perceptions of online video lectures related to the content, duration, visuality, timings and screen size?

(3) What is their overall experience with the online video lectures specifically concerning the adaptability, acceptability, learning experience, preference and difficulty level?

(4) What would be their preference for learning assessment of online lecture?

(5) What is their experience with the online learning management platform?

Methods :

This mixed-method study employed an online questionnaire survey consisting of closed and open-ended questions on six categories. The methodology was chosen because the integration of qualitative and quantitative data would lead to having a better understanding of the research problem than either of each alone. Moreover, this mixed-method would allow better corroboration via triangulation and in-depth visualization of the research problem.

Participants :

The participant sample for this study was a purposeful selection of the I MBBS students who underwent the ten-day-long online video lectures during the COVID-19 lockdown period in Andhra Pradesh, India. The selection criteria included : (1) undergraduate students participated in the online video lectures on Anatomy, Physiology and Biochemistry during I MBBS. and (2) Medical teachers' approval to explore the design of the online courses. All participant students were instructed to answer the online questionnaire and submit it in the stipulated period. Their participation was mandatory. However, those who are unable to access online video lectures are excluded from this questionnaire survey. A total of 213 out of 227 undergraduate students responded to the survey questionnaire.

Data Collection :

Data was collected using an online questionnaire survey. The online consisted of 33 questions that focused on six main categories: accessing online video content, previous experience with online learning, interaction with Video lectures addressing the content, duration, visuality, timings and screen size, perceived learning experience, the online content learning assessment methods and the experience with the online Learning Management System (LMS). Data from the focus group was collected by researchers in the form of digital notes.

Data Analysis :

The data collected from an online survey had both quantitative and qualitative responses. Basic descriptive statistics and graphical analysis were performed with quantitative data using percentages. Frequency and percentage were calculated for most of the questions to summarize the data. Furthermore, some basic cross tabulations were performed in order to better understand the student's response and the relationship between the variables. Data analysis of the qualitative portion followed the three concurrent flows of activity suggested by Miles and Huberman (1994): data reduction, data display and drawing conclusions. The three components were constantly interacting among themselves and with other stages in the process. Conclusions were drawn, reviewed and discussed as the data analysis process was ongoing. There was a constant interaction between the processes of data reduction, displays and verification of conclusions until final results were achieved (Fig 1).

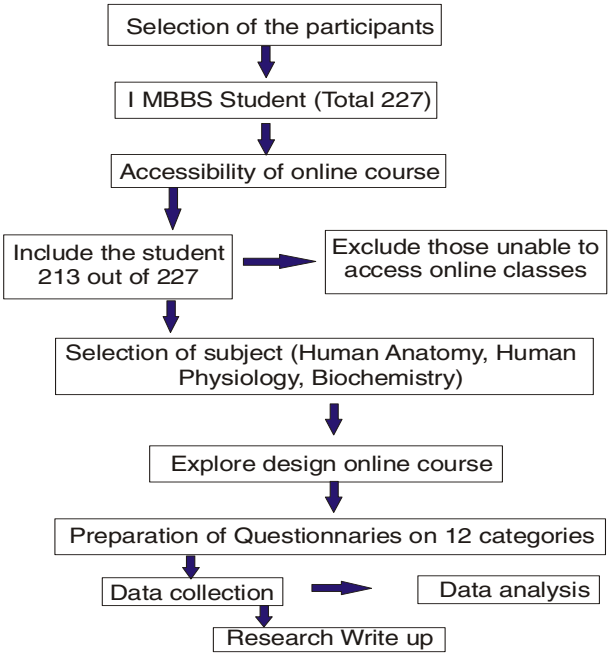

Fig 1 — Overview of Methodology

Results :

Quantitative Analysis —

The present data relate to I MBBS students' online lectures enrolling 250 students, offered during the compulsory home quarantine break as a part of COVID-19 control measures in a teaching and learning program at a large medical institution in Andhra Pradesh. Due to the suspension of physical attendance classes at medical colleges and to avoid large gathering of students, the institution offered online lectures. The teachers working at the institution developed their own teaching material for their online version of the lecture class while adapting the pedagogy to the specifics of Web-based teaching and learning. However, these teachers are a novice to online teaching. Hence, the author's research interest in the dynamics of online teaching, learning, and assessment

spurred the emphasis of this particular research area. Teachers are expected to teach a series of at least ten days entire lecture lessons to a whole class of students online. Students are prompted to attend the series of lectures between 10.00 am to 11.00 am and again 11.30 am to 12.30 noon everyday continuously for ten days. The students' attendance ranged from190 to 220 participants at the online conference lectures.

Students are requested to answer the questionnaire dealing with self-reporting on a variety of factors that could impact teaching effectiveness, such as planning for instruction; support and respect from peers, students, and parents; a student needs based on which to design effective learning opportunities; assessment of student learning; being supervised; and overall satisfaction, both for students and teachers. Teachers were questioned about the preparedness and the design of the online lectures and their preferences over the traditional, face-to-face version of the class lectures. The five-point Likert scale ranges from 1 being equated with "not being concerned at all" to 5 representing a serious preoccupation with the given factor is utilized.

There is a distinction between student feedback that emphasizes satisfaction with the quality of online class interactions and student responses that depend on engagement with peers during asynchronous and synchronous conversations (Table 1).

The background characteristics of the 213 participants who provided the feedback are described in Table 1a. Mobile is found to be commonest (86.4%) instrument used to access the video lecture content. Twenty-two students accessed through a laptop. The cellular network of the mobile is the preferred network utilised by the participants. Around half of the participants felt that the speed of the internet was felt to be good and excellent. When enquired, 46 students (22.0%) revealed to have had previous experience with online teaching and learning.

Table 2 depicts the distribution of students' perceptions concerning the characteristics of online video lectures. These characteristics are classified according to the content, duration of the session, visual preferences, the suitability of the timings and the picture size. Seventy-one (33.4%) clearly expressed that VL content is interesting. Rest 142 (68.6%) reserved their opinion. Among these, 113 (53.1%) said that the interest of the content depends on the subject/ topic and the teacher. Rest of the students, 29 (13.5%) indicated that the VL is not interesting. When enquired about the duration of the lecture and the method of assessment of their concentration/ attention/ learning, 89 (41.7%)

Table 1 — *Background characteristics of the online lecture users and their methods of accessibility of the online lectures*

Criteria	No (n=213)
Instrument/machine used to access the online content :	
Mobile	184 (86.4)
Ipad/ Tablet	5 (2.3)
Laptop	22 (10.3)
Desktop	2 (0.90)
Network used :	
Broadband/ Fiber network	37 (17.4)
Cellular	176 (82.6)
Satisfaction level with internet speed :	
Not at all satisfied	28 (13.1)
Average	79 (37.1)
Good	89 (41.8)
Excellent	17 (8.0)
Previous experience with online learning :	
Yes	46 (22.0)
No	167 (78.0)

Table 2 —*Distribution of Characteristics of Online lectures and the Students opinion*

No	Lecture Criteria	Student Response
1	Content:	
	a) Interesting	71 (33.4)
	Not interesting/ No opinion	29 (13.5)
	Depends on the Teacher/ topic/ subjectb)	113 (53.1)
	Should be same as traditional physical classroom lecture	
	Yes	154 (72.3)
	No	59 (27.7)
2	Duration of Lecture (minutes):	
	a) 5-10 followed by an immediate assessment	7 (3.2)
	b) 20-30 followed by an immediate assessment	89 (41.7)
	c) 45 NOT followed by an immediate assessment	93 (43.6)
	d) My personal preference	24 (11.2)
3	Preferred duration of lecture (minutes): (Median)	
	Anatomy	45
	Physiology	45
	Biochemistry	45
4a	Visuality Preferences: Speaker	
	Lecture by same Institute faculty	156(73.5)
	Reputed Guest Faculty/ Other institute faculty	24(11.2)
	Sharing other suggested video links of that topic	32(15.1)
4b	Visuality Preferences: Screen appearance	
	Only portrait/ Full view of the speaker	45(21.2)
	Toggle view/ Picture in Picture (PPT & Speaker)	167 (78.7)
4c	Visuality Preferences: Background of speaker	
	Classroom	160 (75.5)
	Customized	55(24.5)
4d	Visuality Preferences: Social Isolation	
	Social isolation unlike traditional classroom (Yes)	113 (53.3)
	Social isolation (No)	99(46.7)
5	Suitability of the lecture timings	
	10.00 am to 12.30 (Present timings)	193(91.0)
	Not suitable	19 (9.0)
6	Screen size preferred for watching	
	Smartphone (<10 inch)	148 (69.8)
	Tablet/ Ipad (>10 - <13 inch)	13 (6.1)
	Laptop/ Desktop (>13 – <15 inch)	41 (19.3)
	≥15 inch screen size	10 (4.7)

preferred 20-30 minutes of presentation, followed by an assessment of the content. However, 117(44.8%) preferred no such assessment of their learning following the VL. Only seven students opined that after every 5-10 minutes, there should be an assessment of the content. The preferred median duration of the lecture is 45 minutes for all the three subjects.

When enquired about the social isolation, 113 (53.3%) students replied affirmatively to social isolation during the VL. Unlike many reports where social isolation is being identified as a major hurdle for the online VL, 99 (46.7%) of students felt no social isolation while listening to online VL. The suitability of the online video lectures was approved by 193(91.0%) of the respondents. The timings of the VLs and that of the routine traditional lectures coincide.

The preferred instrument by the students to access the video lectures when enquired was found to be the smartphone (69.8%). The smartphone screen dimension was small (<10 inch) and is the most favoured screen size (Table 2).

The important aspect of the online VL is the assessment. It is necessary to monitor the student listening and assess the learning through vigilant assessment. The assessment frequency preferences by the students are depicted in Table 3. The speaker recapitulating the content delivered during the VL at frequent intervals during the lecture was preferred by 65 students (30.7%). Forty-eight students (22.6%) opined that questions based on the content delivered during the VL could be directed at the audience at the end to assess the learning of the students. Conducting once a week online tests on the respective subject content delivered during that week is the chosen assessment frequency by 84 (39.6%) of students. Routinely, weekly tests are organized during the traditional normal teaching course. Students are habituated to this method of weekly assessment (Table 3).

The distribution of perceived acceptability and the adaptability of the video online lectures by the students is shown in Table 4. When enquired about the cultural suitability of the VL in improving the learning process, 151 (71.2%) responded in agreement. The remaining 61 students (28.7%) responded negative and or unable to decide. When enquired about the adaptability of the students to the online video lectures as a teaching and learning medium, 81 (38.2%) expressed complete satisfaction and said that they are able to adapt to this online medium of instruction. Nearly 62.0% of students (172 out of 213) are unable to adapt to the online video lectures for their learning. Among these, 117 (54.9%) agreed that these they are able to adapt to these online VL somewhat partially.

The cognitive experience through online video watching and listening should be an enjoyable learning activity. Out of 213 students, 72 (34.0%) expressed this activity as an enjoyable learning experience. Out of the remaining students, 33 (15.6%) opined that there is no personal touch in the online VL. It is pertinent to note that 107 (50.4%) expressed that this online VL are either not interesting or boring. The difficulty level of this VL when questioned, only 31 students (14.6%) said that this online VL are easy to understand. Remaining 84.4% of students expressed reservations regarding the difficulty level in understanding. One hundred and eighteen Students (55.3%) suggested that online VL should be continued for further learning (Table 4).

Students' familiarity with the online platform (ZOOM) for video lectures was enquired, and the results are shown in Table 5. The advantages and the inbuilt facilities like raising the hand to ask a question, communicating through a chat room, video sharing and recording of the VL are known to 139 (65.2%) of students. Rest of the students (73 out of 213) are either not confident and/ unaware of these facilities. The

Table 3 — *Online Assessment for the video lectures Preferred by the Students*

Assessment schedule	Response
Questions at the end of each video lecture	48 (22.6)
Recapitulation at the end of every 5-10 minutes	65 (30.7)
At the beginning of each lecture on a topic covered before	15 (7.0)
Weekly online tests on topics covered in week	84 (39.6)

Table 4 — *Experience perception & acceptability of online Video Lectures*

Criteria	Response
VL is a culturally suitable way to improve your learning process :	
Yes	151 (71.2)
No	30 (14.1)
Don't Know	31 (14.6)
Perception of adaptability from classroom to online lectures :	
Yes Complete	81 (38.0)
Partially	117 (54.9)
No	11 (5.2)
Don't Know	4 (1.9)
The learning experience of listening and watching online lectures is	
Boring	10 (4.7)
Enjoyable & Good	72 (34.0)
Not so interesting	97 (45.7)
No personal touch	33(15.6)
The difficulty level of understanding VL :	
Easy to understand	31 (14.6)
Not so difficult	140 (66.0)
Difficult to comprehend	41 (19.3)
Do you suggest a continuation of the VL in future :	
Yes	118 (55.3)
No	71 (33.5)
Don't know	24 (11.3)

comfortability of sharing the video (switching on the self-video button) when inquired, 130 students (61.0%) declined to switch it on during the VL. Fifty-three students (25.0%) agreed to share their video and the remaining are unable to decide. The adaptation to Online VL is graded on a visual analogue scale of 1 to 5, in an ascending acceptability order. It is worthy to note that 172 (80.8%) accorded better adaptation of watching the VL and graded their adaptation between 3 and 5. The adaptation to online VL was perceived by the 41 students (19.2%) as poor denoted as less than two on a scale of 0 to 5 (Table 5).

Students were enquired about their preference of screen size for watching. Students who are regularly watching VL on their mobiles preferred the same mobile screen to watch (147 out of 184). In comparison,95.5% of students who watch VL on laptop preferred to continue watching them on a laptop screen. Though 86.4% of students are watching these VL online on mobile, only 80.0% preferred mobile screen to watch. In general, students prefer mobile to watch VL (Table 6).

The difficulty level of the online VL and its relationship with the instrument used for accessing these lectures is shown in Table 7. Thirty-one (14.6%) of students felt that these VL are easy to understand. Rest of the students 182 out of 213 felt that these lectures are not so difficult to understand and / difficult to understand. Among students who are connecting through a laptop, 31.8% felt that these lectures are easy to understand compared to 14.6% of those using mobile. Forty-one (19.2%) expressed that these VL are difficult to comprehend (Table 7).

It is proposed that the difficult level opined by the student might have had the influence of previous experience with online teaching and learning. Among those students who had previous experience of online learning, 17.4% felt video lectures are easy to understand. The difficulty levels felt are almost same among those who had experience and those who are a novice (17.4% and 19.8% respectively) (Table 8).

The various causes for the high difficulty level in understanding as perceived by the students suggest that the VL should be interesting and the concerned teacher/ topic also is responsible. Seventy (32.8%) students felt that the topics covered in VL are interesting. Majority of the students (53.5%) felt that the difficulty level of the VL depends on the topic covered and the teacher delivering the VL (Table 9).

Table 5 — *Familiarity with the Online Learning Video Conference Management Platform (ZOOM)*

Parameter	Response
Advantages & Facilities (lifting a hand to ask questions, Video sharing of you, recording)	
Yes	139 (65.2)
No	38 (17.8)
Not Sure	36 (17.0)
Comfortability of sharing the self-video during VL	
Yes	53 (24.9)
No	130 (61.0)
Undecided	30 (14.1)
Grading your adaptation to the VL	
1-2	41 (19.2)
3-4	162 (76.1)
5	10 (4.7)

Table 6 — *Present users and their preferences of Screen size to access VL*

The instrument to Access VL	No students who reported their preferred instrument to watch VL (%)				Total
	>15" including TV screen	Laptop (13-15")	Smart-phone	Tablet/ Ipad	
Desktop	0	1(50.0)	1(50.0)	0	2(1.0)
Ipad/Tablet	0	0	0	5(100.0)	5(2.3)
Laptop	1(4.5)	21(95.5)	0	0	22(10.3)
Mobile	9(4.9)	20(10.9)	147(79.9)	8(4.3)	184(86.4)
Total	10(4.7)	41(19.2)	149(70.0)	13(6.1)	213(100.0)

Table 7—*The difficulty level of VL perceived by the student and its relationship with the instrument used for accessing these lectures*

Instrument	Difficult to understand	Easy to understand	Not so difficult to understand	Total
Desktop	0	1(50.0)	1(50.0)	2 (1.0)
Ipad/tablet	0	2(40.0)	3(60.0)	5 (2.3)
Laptop	3(13.6)	7(31.8)	12(54.6)	22 (10.3)
Mobile	38(20.7)	21(11.4)	125(67.9)	184 (86.4)
Total	41(19.2)	31(14.6)	141(66.2)	213 (100.0)

Qualitative Analysis :

(1) Online Video Lecture —

a) Content : Students opined that these online

Table 8 — *The relationship of perceived difficulty levels of VL and the previous experience of online teaching and learning*

Attended Online Coaching before	Difficult to understand	Easy to understand	Not so difficult to understand	Total
No	33(19.8)	23(13.8)	111(66.4)	167(78.4)
Yes	8(17.4)	8(17.4)	30(65.2)	46(21.6)
Total	41(19.2)	31(14.6)	141(66.2)	213(100.0)

Table 9 — *The distribution of reasons for the perceived difficulty levels of VL among students*

Instrument	Difficult to understand	Easy to understand	Not so difficult to understand	Total
Depends on teacher/ topic/ subject	22(19.3)	13(11.4)	79(69.3)	114(53.5)
interesting	10(14.3)	16(22.9)	44(62.8)	70(32.8)
No opinion	6(25.0)	2(8.3)	16(66.7)	24(11.3)
not interesting at all	3(60.0)	0	2(40.0)	5(2.3)
Total	41(19.2)	31(14.6)	141(66.2)	213(100.0)

classes are helpful only for the subject revision but not for explaining new topics. Many students felt that these classes should incorporate more animations/ 3D pictures rather than simple text in the power points shown. They are also of the firm opinion that explanation of the topic on a blackboard is beneficial for clarity. Students also requested that the faculty should summarize the main points at the end of each online session. They also preferred more interactions with their fellow participants.

b) Assessment : Students requested that the faculty member should pose frequent questions in between to the participants by unmuting a specific participant.

c) Accessibility : The main hurdle expressed is the network connectivity at their respective home. The online lecture is a continuous one for nearly 45 minutes, and the students experienced automatic network disconnection after every 20 minutes. They also complained that the faculty voice not clear and even the video breaks in-between the session. These difficulties are mainly due to poor connectivity.

d) Others : Students who are regular in VL attendance, expressed that they could recall the subject taught in the previous class. However, they felt that the home environment is causing disturbances in concentration and experienced household interruptions at their home.

(2) VL Timings — Students felt that timings are acceptable and are suitable for them. Some students even suggested starting the VL sessions late in the morning and continuing beyond 1.00 pm. They also indicated an eagerness to attend the sessions even in the evening.

Discussion

The primary objective of this exploratory study was to examine the preference and perception of students regarding the newly introduced online live video lecture classes. Two hundred and thirteen undergraduate students' feedback was sought regarding the newly introduced online teaching sessions. These Online Video lectures replaced the traditional physical classroom teaching due to the COVID-19 pandemic. Students were instructed to leave the college campus and advised to stay at their respective homes. The online VL are accessed by these students through their mobile phone/ tablet/ desktop computer/ laptop. The present study revealed that 86.4% of students are routinely using their mobile phones to access the VL. Similar studies[19] also revealed that the majority of students (58.0%) are using a smartphone to access the online teaching. The internet is slow, and fifty percent of students expressed their dissatisfaction with the internet speed. As students are utilizing the mobile data, the speed is far below the required[19]. The habit of learning through online video lectures is a novice to the present student population, and 78.0% of them had no previous experience. Lack of familiarity and exposure to a different method of teaching, are causing conflicts in the habituated methods of learning among students. Hence 72.3% of students preferred online VL format and content to be similar to that of a traditional physical classroom lecture. Non-familiarity of this method of teaching might be influencing the students' perception of dissatisfaction with the current content delivery. On inquiry, students preferred this VL method should be complimentary and a blended system would be more interesting and effective[7,11,13,16]. Students reported that online lectures provide an additional educational value compared with "live" traditional lectures. In other words, blended learning would be more effective and should be continued further[11,16,21]. This method of online VL is also precipitating the feeling of social isolation among 53.3% of students. The habitual physical presence of their colleagues and appreciation of their friends' verbal and nonverbal reactionduring the traditional classroom atmosphere is conspicuously absent in the online method[1,2]. This is resulting in the perception of social isolation among them. It is known that students who receive personalized feedback have higher levels of course satisfaction and perform academically better than those students who receive only collective feedback[16,17,22]. Hence personalized feedback needs to be incorporated into the VL program. A simple act, like using the student's name while writing feedback, also helps in developing teacher's rapport with the student[17].

Seventy percent of the students preferred watching the VL on smartphone screen measuring less than 10 inches. The habitual use of the smartphone by students and non-availability of bigger screens are the underlying factors influencing the screen size preferences[19].

During the traditional classroom teaching, formative assessment is undertaken through weekly physical tests. Students, when inquired about preferred assessment method during online VL, only Forty percent opted weekly tests. 31.0% preferred recapitalization of the subject and assessment after every 5-10 minutes. Around 23.0% of students preferred assessment at the end of each VL. These findings affirm students' preference for the spot assessment to assess their understanding and learning. Due to this reason, the majority of the online course videos are of short duration, and at the end of 5-10-minute

VL, assessment is introduced.

Creating a conducive environment during online lectures is difficult but is necessary for online learning[1,2,20]. This would prevent the students from feeling isolated and also enhance the classroom ambience for better learning[1].

Seventy-one percent of students agreed that VL is a culturally suitable way to learn the subject. As the students are traditionally habituated to learn from the physical classroom teaching, nearly 58.0% of them expressed dis-comfort and inability to adjust with the online teaching. The same percentage of students expressed that online listening and watching is not such an interesting experience. The study finding that 66% of the students do not enjoy the online teaching requires introspection of the teaching methodology adopted for the online lectures. It is well known that the attention span decreases after 20 minutes in case of a physical lecture. This period might be much shorter for an online lecture[24]. Around 20.0% of students felt that it is difficult to comprehend the contents of the VL. All these factors emphasize that the faculty need to modify the way of teaching, assessment of learning and convert their teaching sessions into more interesting learning experiences[20]. Students would fully accept and appreciate online VL if they perceive that VLs would offer an advantage over traditional alternatives[16]. As the faculty is habituated to traditional teaching sessions, they require to modify their teaching and learning assessment methodology[20].

Interestingly, even after two sessions of training, 35.0% of students are not fully familiar with the facilities available in the online platform. Surprisingly, 75.0% of students refused to share their video online during the lecture. The use of the smart mobile phone has become universal and students are keen to access online content through their mobile phone devices only. The easy availability, portability and multiple uses are the reasons for their mobile phone preferences. When cross-tabulated, people who are accessing the VL through bigger screen devices (Ipad/ tablet/ laptop) find these lectures to be easy to understand. Bigger the screen, easy for them to visualise for a longer time and causes less eyestrain.

Conclusions

Based on the findings of the study, the following conclusions can be drawn:

The purpose of effective online lectures and learning is to provide learners with opportunities to engage in enhanced teacher supportive educational experiences. Such experiences are pillared by a triad of factors—student involvement, teachers support and teaching presence—that work in tandem. There are several areas of convergence that connect these components of educational experience, as follows: Not only the mere presence but listening and comprehending the audio-visual content, immediate clarification of concepts, visualizing whenever necessary at their own pace and convenience etc. would constitute the student involvement. The teaching presence and teachers support are pivotal in enabling this online learning experience into a mutual relationship. Teachers need to be aware that the controls are with the student. When the student is not interested, they can remotely switch off/ leave the VL without the knowledge of the teacher. Teachers involved in VL should change their style of teaching, encourage student involvement more frequently and deliberately to keep the interest. Unlike traditional physical class which is controlled by the teacher, VL is controlled by the student. The VL should appeal to the students. In order to design a better learning experience, continuous students' feedback is pivotal. Given the degree of interactivity in online classes, the need for the use of a constructive approach to teaching, learning, and assessment is crucial in helping students to co-construct knowledge by making meaning of their interactions with content, instructors, and peers, as well as the interface provided by the learning management system. Student responses and formative feedback connect supporting discourse, learning environment setting, and content selection in particular ways that are grounded in the context of the class where the research was conducted. In other words, formative assessment through feedback was an integral part of structuring student responses, thus creating a positive learning environment where communicative exchanges were student-centred. Formative course content assessment is as important as a dynamic VL course design to suit the student community requirements for meaningful enhanced educational experiences. The study findings support recommendations for future iterations of the flexible online lectures/ teaching & learning design procedures used, with a particular focus on the interplay among various considerations to be made when developing online teaching & learning effectively.

(1) Set Clear Expectations —

When you are designing an online discussion, take a moment to think about what you want the students to achieve. By setting clear expectations and giving specific instructions and training at the beginning, students will be familiarised with all the options available at the online learning platform and get a better idea of what is expected of them, and it saves both stakeholders time.

(2) Personalise It —

Given the dynamics of online learning, it is common for students to feel distant and isolated during the course. One of the best ways to prevent your students from feeling this way is by delivering personalised feedback. Knowing the social isolation, the assessments are devised in such a way that feedback is obtained from each and every student personally.

What is already known :

1) E-learning is gaining popularity among the medical faculty and students. The affordable video conferencing technology enabled some of the organisations to adopt and offer online e-learning to their students.

2) Many researchers documented the advantages of e-learning and its positive effect on learning among students.

3) Many students adopt e-learning for acquiring additional knowledge/ skills or as a means of intensified training method for competitive examinations.

4) However, the usefulness and acceptability of e-learning among medical students as a part of their curriculum is still not fathomed in medical education.

What this paper adds :

1) Information about the role of video lecture in students' overall online experience

2) Students' perception of VL based upon their accessibility, previous experience and their preferences.

3) Students perceptions and their acceptance of the video lectures and online assessment methods.

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Review Article

Executive Summary of the Recommendations on the Management of Asthma In Primary Care (2022) – New Updates

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Background : Asthma is a heterogenous disease defined by the history of respiratory symptoms (shortness of breath, wheezing, cough, and chest tightness) that vary over time and in intensity, along with variable expiratory airflow limitation**.** Despite an ever-increasing prevalence of asthma across all age groups, this condition remains poorly managed in India. Majority of the Indian patients remain undiagnosed or wrongly diagnosed in general clinical practice and even those who get diagnosed, remain poorly or inadequately treated[1,2]. Since the last published 2020 Indian Medical Association (IMA) recommendations on the management of asthma in primary care, noteworthy critical changes have been recommended in relation to the diagnosis/management of asthma in international guidelines. Hence, there was a need to update the existing IMA recommendations. For the same, an expert group meeting was organized with family physicians having clinical experience in managing patients with asthma along with chest physicians and pediatricians. Important updates related to asthma diagnosis and its management were discussed and the final recommendation decisions were derived from the joint group discussion. Some of the key points derived from the discussion are mentioned below in the executive summary.

For a detailed version of the new recommendations please click on the url.

[*J Indian Med Assoc* 2022; **120(12):** 57-60]

Key words **: Asthma, Stable Asthma, Exacerbations, Spirometry, Peak Expiratory Flow, Bronchodilator, Medication.**

New Updates in the IMA Recommendations 2022?

Diagnosing asthma in adults, adolescents, and children aged >5 Years :

- The diagnosis of asthma is based on the history of characteristic symptom patterns and evidence of variable expiratory airflow limitation[3].
- For general physicians (GPs), the peak expiratory flow (PEF) value (tested via a peak flow meter) can be a good diagnostic indicator for asthma if it shows

Executive Summary :

- Asthma is a clinical diagnosis; however, in cases where dilemma exists, refer to an expert. In clinical practice for general physicians, peak expiratory flow can be a good indicator for asthma diagnosis if it shows reversibility after bronchodilator therapy.
- In young children, asthma diagnosis is mainly based on recurrent symptom patterns, assessment of family history, physical findings (if the child is symptomatic), short-term corticosteroid trial therapy, and differential diagnosis.
- The optimal management of asthma includes the use of controller medications, which reduce the underlying inflammation and prevent the occurrence of symptoms, and reliever medications, which are used as required for quick symptom relief.
- Increased use of short-acting beta2-agonists is associated with adverse clinical outcomes.
- Low-dose inhaled corticosteroid plus fast-acting beta2-agonist, ie, budesonide-formoterol, is the preferred reliever in adults and adolescents, as it reduces the risk of severe exacerbations compared with regimens with short-acting beta 2-agonist alone as a reliever.

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reversibility after bronchodilator medication[3].

- Spirometry (forced expiratory volume in 1 second) should be considered more reliable than PEF. However, if spirometry is unavailable, bronchodilator reversibility may be assessed with a peak flow meter[3].

Diagnosing Asthma in Children Aged ≤5 Years :

- Based on the pattern of symptoms during and between viral respiratory infections, a probability-based approach may be useful for discussion with parents/carers[3].
- In children aged 5 years and younger, no specific tests can confirm the diagnosis of asthma, but there are a few useful adjuncts[3].

Updates about the Treatment of Asthma in Adults and Adolescents :

- The stepwise approach to the management of stable asthma in adults and adolescents has been updated with Inhaled Corticosteroid (ICS)-formoterol as the preferred reliever and short-acting beta2-agonist (SABA) as an alternative option.
- In Step 1 and Step 2 (Track 1), the recommendation for treatment is as-needed low-dose ICSFormoterol.
- For the alternate (Track 2), the following recommendations are made:
  Step 1: Low-dose ICS should be taken whenever SABA is taken.
  Step 2: Low-dose daily ICS should be taken for maintenance and as-needed SABA should be taken for relief.
- In Steps 3–5, maintenance and reliever therapy with budesonide-formoterol (preferred approach) or ICS-LABA as maintenance therapy plus SABA as reliever (alternate approach) is recommended.
- Newer recommendations for add-on long-acting muscarinic antagonist (LAMA) and introduction of anti-thymic stromal lymphopoietin (ATSL) as a new biologic agent have been included for severe asthma.
- Other controller options have been clarified and included in the treatment.

Updates about the Treatment of Asthma in Children 6-11 years :

- Step 1 includes low-dose ICS to be taken whenever SABA is taken.
- Steps 3 and 4 include maintenance and reliever therapy (MART) with very low-dose ICSformoterol and low-dose ICS-formoterol, respectively, to reduce exacerbations.

Preferred route for administering asthma medications :

- Inhalation therapy is the preferred route for the administration of medications in asthma management[4]. The inhalation route ensures the deposition of the optimum concentration of medication in the airways and rapid onset of action and causes fewer systemic adverse effects than oral delivery[3].
- The most commonly used inhalation devices include Pressurized Metered-dose Inhalers (pMDIs), Dry Powder Inhalers (DPIs), Breath-actuated Inhalers (BAIs) and Nebulizers[5].

Concerns with Prescribing SABAs alone for Asthma Management, including Mild Asthma :

- Large multicenter studies have demonstrated that increased use of SABA is associated with increased risks of exacerbation and mortality in asthmatics[6].
- Regular use of SABA, even for 1-2 weeks, is associated with adverse effects[7,8]:
  • Beta-receptor downregulation, decreased broncho protection, rebound hyperresponsiveness, and decreased bronchodilator response
  • Increased allergic response and increased eosinophilic airway inflammation

Hence, SABA should always be administered along with ICS3because ICS reduce the risk of asthma deaths, hospitalization, and exacerbations requiring oral corticosteroids[9,10].

The Emerging Concept of using an Anti-inflammatory Reliever in Asthmatics :

- Asthma is a chronic inflammatory disease. During an exacerbation, along with spasms of the smooth muscles, inflammation in the airways increases, which causes an increase in airway obstruction. Traditionally, SABA alone was recommended for quick symptom relief, which does not address the underlying inflammation and may eventually lead to a decline in lung function[3].
- The ideal constituents of reliever medication, thus, should be a fast-acting bronchodilator **used in combination with ICS** (popularly known as an **anti-inflammatory reliever**), thereby addressing both bronchoconstriction and inflammation[3].
- As per the new guideline, low-dose ICS-formoterol is the preferred anti-inflammatory reliever in adults and adolescents, as it significantly reduces the risk of severe exacerbations compared with SABA alone as a reliever[3].

Using SABA as a Reliever :

SABA can be used as reliever therapy in adults and adolescents in the following cases[3] :

- As an alternative to an ICS-formoterol reliever, in Step 1, SABA and low-dose ICS can be administered together for symptom relief, either with an ICS plus SABA combination inhaler or with ICS taken right after SABA[3].
- As an alternative to an ICS-formoterol reliever, in Steps 2–5, SABA can be administered as a reliever medication, in addition to a controller, to patients who are on controller therapy other than formoterol-budesonide[3].

Importance of correct inhalation technique :

- Though inhalation therapy is the cornerstone of asthma treatment, up to 94% of patients with asthma and chronic obstructive pulmonary disease do not use their inhalers correctly. It is important to reinforce the correct inhaler technique at every patient visit[11].
- Many people have difficulty using a pMDI, wherein the most common mistake is not being able to actuate and inhale the medication at the same time[12].
- Spacers are used as an add-on with pMDIs. They offer the advantages of easier use and improved deposition pattern of the inhaled drug, reduced side effects, and improved drug efficacy[13].
- DPIs have the advantages of being portable and compact and overcoming issues of coordination. In addition, they do not contain propellants. However, they require a minimum inspiratory flow for optimum delivery of the dose[5].
- BAIs have the advantage of overcoming the drawbacks of both DPIs and pMDIs. BAIs sense an inhalation effort through the actuator and mechanically actuate the dose in synchrony, resolving the issue of hand-breath coordination that is commonly seen with pMDIs[14].

Correct inhalation devices based on the age for the successful management of asthma

Selection of the correct inhalation device is crucial for successful asthma management (Table 1)[3].

Table 1 — *Selection of inhalation device based on age*

Age group	Preferred choice	Alternative
0–3 years	pMDI + spacer with face mask	Nebulizer with face mask
4–5 years	pMDI + spacer	pMDI + spacer with face mask
5 years and above	pMDI+ spacer/ DPI/BAI	Nebulizer

Role of the GP in Educating and Counseling Patients with Asthma :

Some pointers for GPs with respect to educating and counseling patients with asthma[15,16] :

- Adequate time should be invested in educating and counseling patients with asthma.
- It is also important to keep oneself updated about different inhalation devices so that the most appropriate inhalation device for patients can be prescribed.
- Train patients on correct inhalation technique and ensure technique at follow-up visits.
- Discuss the patient's treatment goals and guide the patient on an asthma self-management plan.
- Clarify queries during patient visits on a continual basis to improve compliance.
- Check for drug compliance and adherence to asthma treatment at every visit for ensuring optimal asthma control.

Guidance about Asthma and COVID-19 :

- It is advisable for patients with asthma having coronavirus disease (COVID-19) to continue taking their prescribed asthma medications, particularly ICS.
- COVID-19 vaccine is safe for people with asthma (follow the Government of India guidelines for more information).

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Review Article

Prevention Strategies to De-escalate Workplace Violence against Doctors...

Puja Bansal[1], Anirban Das[2]

Workplace violence is something we can discuss it, tolerating it but we can't prevent it even we can't accept it that it belongs to us, we are initiating it against people like us only. Nothing can solve violence, neither two wrong can make anything right. Though every sector is afflicted by it but healthcare sector is majorly affected by it because patients family is in great trauma of facing their people's death and no one have been able to do anything to stop it. Accepting loved ones especially death has always been painful to everyone. But blaming some sector and taking revenge is big NO NO. As we all know prevention is better than cure so via this paper I am trying to address some prevention Strategies that may be helpful to de-escalate this issue on ground level.

[*J Indian Med Assoc* 2022; **120(12):** 61-3]

Key words **: Workplace violence, Government laws, Standalone training, Prevention Strategies.**

Workplace violence has always been serious problem for doctors and healthcare workers as they have always been dealing with emotional breakdowns and loss of life on patients' family. However violence at workplace exists almost in everywhere and in every sector. This even exists in both developed and developing countries (Liu J*, et al*, 2019) and can be declared as top most occupational hazards.. there can't be universal formally accepted definition of workplace violence as this is subjective concept and everyone carries different opinions and beliefs (N Imran, *et al*, 2013).

The Occupation Health and Safety Act, 2019 defines workplace violence as "the exercise of physical force by a person against a worker, in a workplace, that causes or could cause physical injury to the worker; a statement or behaviour that it is reasonable for a worker to interpret as a threat to exercise physical force against the worker, in a workplace, that could cause physical injury to the worker (OSHA, 2019)".

This has always been serious issue to a sector who is engaging themselves in keeping nation healthy but failed to same themselves. According to report of IMA 75% of Doctors faced workplace violence atleast once in their career. Thousands of cases had been reported but no serious action has been taken till now. From Worldwide protest to hunger strike everything went in vein.

Now with this paper we as a author tried to point some basic strategies that can be adopted to prevent workplace violence before it goes extremely dangerous for doctors.

Editor's Comment :

- To de-escalate workplace violence, different strategies need to be taken such as standalone coaching, structured programme, multicomponent interventions, recordkeeping and program analysis. Apart from these, government should also take necessary steps like non-bailable offense with strict penalty.

These strategies are based on multiple studies includes Government role to de-escalate it.

Standalone Coaching :

The studies deals with the aggressive work place voilence that tend to done by nurse and hospital workers. Two studies were included in the research which assess the effectiveness of three to four hours of coaching on violence. Study also added the financial impact of workplace violence on the hospital. Other studies based on imapct of shorter coaching session that targeted violence managemnt and team work were also included. These studies concluded that intraction of nurses with their colleagues improved by the coaching and their level of comfort also increased during handling important conversations. Also, nurse replacement rate were also reduced due to standalone coaching. Study by Al Alietal, reported nurses were confidence enough to handle workplace violence once they have successful completed eight-hours of coaching session. There is no alteration of the basic safety issues in the coaching. It can be concluded the standalone coaching is definitely helpful however, it is effective at distinct parts of workplace violence. It fails

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to provide substantive impact on the violence faced by the nurses[1].

Structured Programme :

Structured teaching programs take issue from standalone coaching primarily in duration. These structured programs typically span weeks, permitting participants to absorb information info. The commonly seen perpetrators of this particular type of workplace violence are often seen as coworkers of victim, nurse managers or supervisors, and sometimes physicians. In two of the considered studies, how to deal with verbal aggression and psychological/emotional abuse were the primarily focus of the structured education program. In this, the common perpetrators were observed as patients and their relatives. Apart from having different prime focus points, the eleven studies adopt additionally used dissimiliar sorts of structured teaching programs in their interventions. for example, five of the included studies used or adopted a Cognitive Rehearsal Program (CRP).

CRP could be a technique whereby specific situations are role-played in an exceedingly structured method, expedited by trained professionals. Using CRP, nurses got the chance to firstly analyse and then apply what could be the most effective response to common violent behaviors. In keeping view the findings of the four major studies that had applied CRP as their intervention to workplace violence, it was shown as CRP enables nurses to build up their cope ability and hindrance skills against workplace adverse situations. It will facilitate improve participants' social bondings with each other and boost awareness regarding violence between nurses. So it can be concluded as CRP might play a handsome role in reducing nurse turnover[1].

Train-the-trainer programs are designed to coach bound 'champions' on the workplace supervisor, who learn and later on go onto their colleagues and train them. In simple words this system is meant to facilitate the unfold of specialist data in an economical, efficient manner. No of studies it was commonly observed train-the-trainer workshops pointed on controlling or solving lateral violence by giving strength to nurses' communication skills. Over the years of three, 203 workshops were conducted with 4,000 participants. The study showed that verbal abuse towards nurses attenuated from nineteenth to seventy six, and nurses' awareness of verbal abuse influencing their patient care accumulated from forty second to sixty three, following the implementation of workshops by trained facilitators[1].

Chipps and McRury two authors have evaluated the effectiveness of a three to four months of education program where they majorly focus on communication and conflict management skills to handle workplace bullying. This study discovered accumulated job satisfaction in participants.

Multicomponent Interventions :

This involves an action set up wherever multiple ways were enforced across 3 categories:

(1) Environmental that includes panic buttons, security locks.

(2) Administrative policies to deal with workplace violence hindrance, safety procedures.

(3) behavioural (staff coaching for workplace violence management).

Study by Arnetz, *et al* If this successfuly implemented in a unit that will surely results in reduction in workplace violence rates. Another study by Arnetz, *et al*. Where he used a three-staged intervention model, additionally that includes the involvement of relevant stakeholders too. It includes :

(1) Development of a formal and standardized reporting system for workplace violence

(2) application of a hazard risk matrix to spot most accumulated risk spots work units of workplace violence.

(3) Worksite walkthrough strategy.

This study shown a significant reduction in the rate of workplace violence within the intervention units as compared to manage units (IRR: 0.48, 95% CI 0.29e0.80) at six months and at twenty four months (IRR 0.37, 95% CI 0.17e0.83).

Similarly, in a new study a 3 pronged intervention model featuring:

(1) conferences with all shareholders and directors to revise and formulated workplace violence policies time to time.

(2) Walkthrough conferences with health care professionals for environmental changes if required.

(3) Education and coaching sessions for employees.

On the application of these steps, there might be a big cut in the rate of assaults and violent threats fully fledged by nurses collaborating within the study.

Two alternative studies additionally took a multicomponent approach, though they didn't feature the broad involvement of relevant stakeholders. Of these, study used a two-phase intervention:

(1) Implementation of alert system to spot risky patients upon admission

(2) Nursing employees coaching for hindrance of geographic point violence[6].

Record Keeping and Program Analysis :

Recordkeeping and analysis of the violence hindrance program must be done properly to see its overall effectiveness and to check any deficiencies or changes that ought to be created[2].

Proper recording system should be implemented of patients history where everything should be clearly written what kind of injury or illness patient was suffering from, what line of treatment was given, how about the progress, severity of problem and etc. that will surely help employers about the severity of problem and establish any developing trends or patterns above all locations, jobs or departments; measure ways of hazard control; establish coaching needs and develops solutions for an efficient program. And Records will be helpful to organizations and for members of a trade association that "pools" information[2].

As a part of their overall program, owners/ shareholders ought to measure their safety and security measures. prime management ought to analyse the program often and, with each and every situation so arise to evaluate its success and whom to accountable (including managers, supervisors and employees) ought to revise and reformulate policies and how to solve on a continuous basis to point problems and then how can it be corrected.

Management should share workplace violence prevention analysis reports regularly with whole of staff. Any changes within the program ought to be mentioned at regular conferences of the protection committee, union representatives or alternative worker teams.

What Government can Do :

The Government officials and the political leaders are the general public appearance up to for steering and solutions. they must set the example and shouldn't intend to do by force. they must condemn such acts instead of carry on them. there's a high time to implement formalized law to safeguard rights of doctors throughout the country. It needs to be included in Indian penal code with declaration of non bailable offense with strict penalization. An appeal against doctors by patients' family has to be deemed infructous if proof of violence is provided by hospital and even penalize for false complaint filling. The Government should pay attention towards filling of vacant post, additional security system to safeguard as well as Doctors. Some mishappening occurs due to shortage of sufficient infrastructure, medicines at Government hospitals that need to be solve by Government at their own level. thereby departure the doctors within the tertiary care centers to give more time and attention to cases that need masterful intervention from them.

a significant drawback is delay in reaching the hospital is too a major cause of death that can be solved by Government by opening primary and seconday hospitals, with better connectivity of roads, with transportation and ambulance facility. Paramedical coaching ought to run a lot of importance so cases of trauma may be may be and through transportation[3].

Conclusion :

From as a society to Government everyone needs to be involved in this process of saving Doctors. But what major role is to play by Government by implementing strict actions and laws against culprit. Passing law on central level, declaring it non bailable offense to include in rare of rarest case, everything has to be done immediately. Apart from it we as a human being has to accept this fact they can treat us neither of them can assure life. Life and death is in jands of destiny, no one has incharge of it so it is useless to harm some sector which is atleast trying to make people healthy always. Without them no one would ever be able to calculate death rate. So it's better to accept out responsibility towards them.

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Case Report

An Uncommon Presentation of a Common Etiology : Tubercular Cerebral Abscess in Pulmonary TB

Upoma Saha[1], Sriradha Chatterjee[2], Srijib Pal[3], Navoneel Debnath[4], Salil Kumar Pal[5]

A patient, recently diagnosed with Pulmonary Tuberculosis and on ATT for the last 1 month, was initially admitted in a primary care setup with severe headache and altered consciousness for 5 days and then referred to our institute for further management. Extensive investigations and imaging led to the conclusion that the patient had a massive Tubercular Brain Abscess (TBA) in the background of Pulmonary TB. [*J Indian Med Assoc* 2022; **120(12):** 64-6]

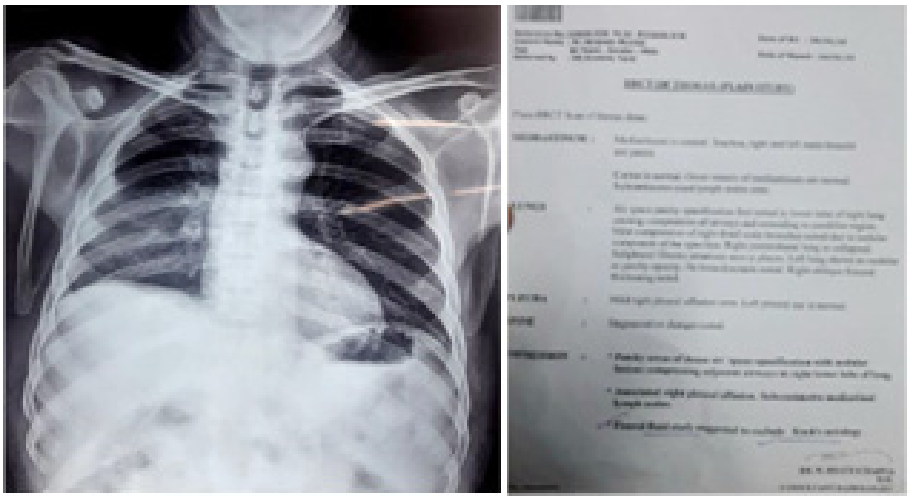
Key words **: Fever, Headache, Tubercular, Cerebral abscess, NCCT Brain, MRI Brain.**

Tuberculous Brain Abscess (TBA) is a rare presentation of Central Nervous System (CNS) tuberculosis. They often present with focal neurological signs, and are associated with a past history of tuberculosis. The following is a case report on one such patient encountered in our hospital setup.

Case Report

A 60-year-old male from Kultali, South 24 Parganas, West Bengal, presented with the chief complaint of fever, headache and altered sensorium for last 5 days and was admitted to a primary care setup from where he was referred to our hospital for further management. On admission, he was unconscious with a GCS of 8. There was history of high-grade fever for last 2 days, recorded as 102°F on a single occasion, not associated with chill and rigor and subsided temporarily with medication. There was no history of trauma, vomiting or any episode of seizures on presentation.

One month back, patient had presented with a history of low grade temperature for 2-3 weeks, night sweats along with loss of weight (undocumented), and right sided chest pain. Initial investigations including Chest X-ray and HRCT thorax were done which was reported as- pleural effusion and right lower lobe consolidation with subcentimetric mediastinal lymph nodes? Koch's etiology (Figs 1 & 2). Pleural fluid analysis was done and a diagnosis of 'microbiologically confirmed TB' was made based on which patient was started on ATD as per regimen (3 tabs 4 FDC) on 05.04.2022



Figs 1 & 2 — (1) Dig CXR showing Right lower lobe consolidation and (2) HRCT thorax report

He had been on regular medication till his condition started deteriorating 1 week back and he was unable to take oral feed properly.

There was a history of CVA with left sided hemiparesis 2 years back, with no residual paralysis. Patient was hypertensive, but on irregular medication for the same.

Editor's Comment :

- Tubercular Brain Abscess is a rare manifestation of CNS tuberculosis in adults, whose clinical presentation mimics that of pyogenic meningitis and poses a diagnostic challenge. It is rare even in a country like India where tuberculosis has a high prevalence and requires a high degree of clinical suspicion.
- Histological evidence may not always be available.
- ATT should be started as early as possible in all cases to limit the extent of complications before contemplating surgical intervention if TBA is considered as the diagnosis.

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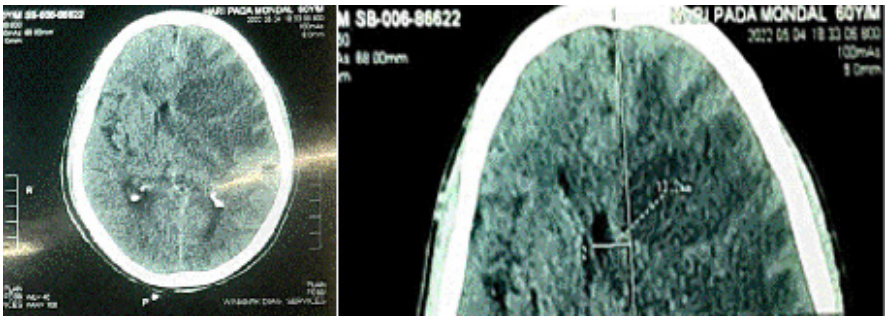
He had no known addictions, there was no history of high-risk behaviour. His family history was non-contributory as well.

Patient was unconscious at the time of admission and regained consciousness within a few hours after conservative management. Pulse rate was 100/min, respiratory rate 22/min, and BP recorded on admission was 120/80 mm Hg. $Sp0_2$ was 96% in room air. Temperature was 101 deg F.



Figs 3 & 4 — NCCT Brain – a large area of ? cavitation in the left fronto-parietal area with surrounding perilesional edema and midline shift

His higher mental function could not be assessed at the time of admission. Tone was reduced in all four limbs and plantar reflex was found to be extensor bilaterally. Signs of meningeal irritation were absent. Pupils were normal in size bilaterally and reacting sluggishly to light. When he regained consciousness, he was disoriented and restless.

An urgent NCCT Brain was done at admission which showed the following (Figs 3 & 4) : -

Immediate measures were taken to reduce the patient's intracerebral edema, ATT was continued and the patient slowly regained orientation over the next 24 hours. A Neuromedicine and Neurosurgical consult was sought and patient was advised MRI Brain (contrast) with a MR Spectroscopy.

Initial laboratory investigations showed low Haemoglobin (7 gm/dl), Total Leucocyte Count of 3800, Differential Leucocyte count – lymphocyte count of 400, neutrophil : 3200, Urea, Creatinine, Sodium, Potassium, Liver Function Tests within normal range. His ICTC report was non-reactive.

MRI Brain with contrast and MR Spectroscopy (Figs 4 & 5) was done, which revealed the following : -

"Large peripherally rim-enhancing irregular shaped cystic lesion about [(AP) 40.4 mm * (TR) 58.4 mm * (CC) 36.8 mm] showing incomplete internal septae, significant perilesional edema and mass effect at left fronto-parietal region showing MRS features-likely Tubercular Cerebral Abscess.

Microangiopathic chronic ischaemic changes in bilateral periventricular deep white matter, centrum semiovale, bilateral cerebral subcortical white matters.

Cerebrospinal Fluid (CSF) intensity chronic lacunar infarcts at bilateral basal ganglia and right paraventricular deep white matter regions."

Patient improved gradually over the next 48 hours with medical management. Spontaneous eye opening was present, he was responsive to verbal commands and oriented to time, place and person. Given the infrastructural constraints, we were not able to microbiologically prove the presence of AFB or M tuberculosis from a cerebral pus aspirate. However, taking into consideration the patient's background of pulmonary TB and the MRI Brain with MRS analysis, it was considered prudent to maintain him on ATT and steroids after due consultation with the Neurology department. The trajectory of the patient's hospital stay was satisfactory.

Discussion

Tuberculous Brain abscess (TBA) is a rarely reported form of CNS tuberculosis, occurring in 4-8% of non HIV patients. Despite the low frequency (only around 1% of extra-pulmonary tuberculosis cases)[2], it is given special importance because of the very high mortality associated with it. It is a focal collection of pus containing abundant Acid-fast Bacilli (AFB) surrounded by a dense capsule comprising vascular granulation tissue. The abscess is often single, sometimes multilocular and accompanied by greater perilesional oedema[3]. TBA is an uncommon clinical entity even in countries where TB is endemic[4].

TBA always poses a diagnostic dilemma as they are difficult to differentiate from pyogenic brain abscesses,

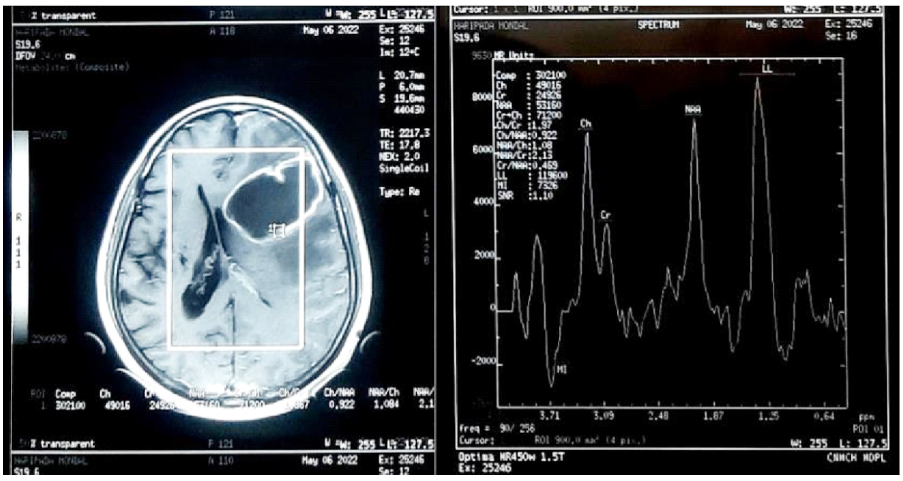


Fig 4 (B) — Choline Creatinine peak >2 , prominent lipid lactate peak

Tuberculous Meningitis and Tuberculoma on the basis of clinical, laboratory and roentgenographic information. They are more frequently encountered in patients who are immunocompromised. Patients with tuberculous abscess present non-specifically, with focal neurological deficits, seizures or signs and symptoms of raised intracranial pressure. These brain abscesses, like tuberculomas, are probably secondary to haematogenous dissemination from a primitive site, most often pulmonary[5].

Mycobacterium Tuberculosis can be isolated from the pus (ZN stain, AFB demonstration or PCR) which is sometimes unable to be isolated from Tuberculomas.

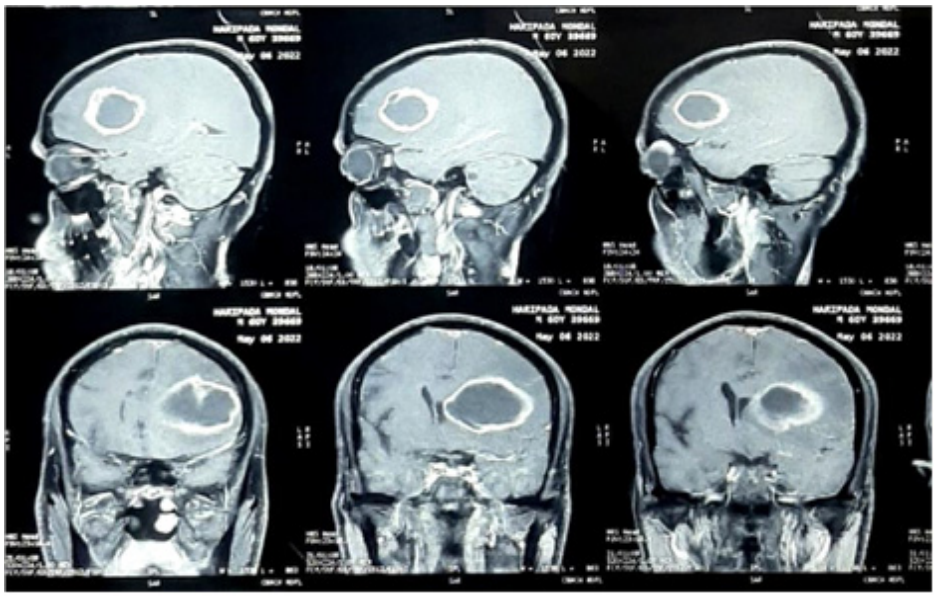


Fig 4 & 5 — Large peripherally rim-enhancing irregular shaped cystic lesion about [(AP) 40.4 mm * (TR) 58.4 mm * (CC) 36.8 mm] showing incomplete internal septae, significant perilesional edema and mass effect at left fronto-parietal region

Approach to management is medico-surgical. ATT along with corticosteroid therapy have been shown to improve mortality in multiple studies. Studies show that it reduces mortality and neurological sequelae in patients with a medium severity picture (confusion, focal signs) and also in comatose patients[6].

Surgical drainage is often curative and the mainstay of treatment for large abscesses, though associated with its own risks and sequelae. Progression under anti-tuberculosis treatment is not discriminatory diagnostic evidence. Several observations have reported the development of Tuberculous Abscesses under well-conducted specific treatment as was also seen in our patient[7,8].

Conclusion

TBA still remains a topic of concern and intrigue due to poor prognosis despite medical and surgical intervention. Despite best efforts and management under specialist care, outcomes in majority of patients have not thus far been as promising as hoped and expected. Given the rarity of the condition, even among the CNS TB manifestations, it remains an area of research and development. One of the reasons for the morbidity and mortality could be due to the late presentation seen in majority of patients and concomitant presence of an immunocompromised state.

Patient would need integrated approach with neurosurgical intervention and Neuromedicine consultation. The following was done from our end after management with ATT and steroids. Patient was ultimately lost to follow-up.

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Case Report

Mixed Germ Cell Ovarian Tumour in an 8-year-old Child — A Case Report

Bijan Kumar Saha[1], Richa Sharma[2]

In paediatric population occurrence of ovarian cancer is rare. In this study, an 8-year-old girl was diagnosed mixed malignant ovarian Germ Cell Tumuor (GCT), with predominantly Embryonal Carcinoma component (95%) and focal dysgerminoma component (5%). The patient presented with dull aching pain abdomen and mass in abdomen. On examination mass occupied whole of abdomen, hard in consistency, mobile and lower border per vaginally occupying right fornix. CECT abdomen was done which showed a well-defined solid cystic mass measuring 24.1x 18.7x 14.9 cm mass arising from the right adnexa causing suggestive of malignancy. Uterus, right ovary and rest of the peritoneal cavity was normal. CECT chest was normal. Tumour markers S. Beta-hCG was 27,601.44 mIU/mL, S. LDH was 1735 IU/mL, S. AFP was >400 ng/ mL and S.CA-125 was 114.5IU/mL. After multidisciplinary tumuor board discussion patient was planned for staging ovarian laparotomy (fertility preserving surgery). Intraoperatively ascites was present, right ovary was enlarged measuring about 25x15 cm occupying whole of abdomen, adherent to small bowel, fundus of uterus and right fallopian tube. Left ovary, Fallopian tube and Uterus was normal. Right pelvic and paraaortic lymph nodes was enlarged. Liver, bilateral diaphragm and rest of the peritoneal cavity normal. Procedure done was excision of right ovarian mass with right salpingectomy, bilateral pelvic lymph node dissection, retroperitoneal lymph node dissection, greater omentectomy and peritoneal biopsies. On histopathology right ovary was reported as poorly differentiated neoplasm. In retroperitoneal lymph nodes 1 out 15 lymph nodes showed tumour deposits measuring 0.2cm. Right fallopian tube, bilateral pelvic lymph nodes, greater omentum, peritoneal biopsies and ascitic fluid were free of tumour. On immunohistochemistry (IHC), right ovary tissue was positive for SALL4 and PLAP (germ cell tumour marker). CD30 (Embryonal carcinoma marker) was diffusely positive and CD117 (dysgerminoma marker) was focally positive. It was negative for Beta-hCG (choriocarcinoma marker), AFP (yolk sac tumour marker), EMA (epithelial marker), Calretinin (sex cord stromal tumour marker) and Inhibin (sex cord stromal tumuor marker). From above findings, diagnosis of FIGO stage III A1 (ii) (T1cN1aM0) mixed malignant GCT was made. Patient was advised adjuvant chemotherapy with Bleomycin, Etoposide and Cisplatin (BEP).

[*J Indian Med Assoc* 2022; **120(12):** 67-9]

Key words **: Mixed Germ Cell Tumuor, Ovary, Child.**

In paediatric population ovarian neoplasms are rarely seen. Annual incidence of ovarian cancer in paediatric population is about 2.2 cases per 1 lakh girls. 27% of all ovarian tumours in females less than 16 years are malignant[1]. Ovarian cancer represents 1.1% of all childhood malignancies[2]. In contrast to adults in whom epithelial carcinoma of ovary are common, whereas in paediatric population malignant Germ Tumours (GCTs)of ovary are more common[3]. The overall prognosis for patients with malignant Germ Cell Tumour is excellent[3]. Though understanding about etiology and pathogenesis of epithelial ovarian cancer has improved recently but understanding of etiopathogenesis of malignant ovarian GCTs has not improved[4]. Reporting a case of mixed malignant GCT diagnosed in an 8-year-old girl.

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Editor's Comment :

- Ovarian cancers are rare in paediatric age groups. Multidisciplinary team is required to treat the patients.
- Staging ovarian surgery is the standard of care.
- Fertility preservation surgery should be done whenever possible.
- Neoadjuvant chemotherapy should be used to decrease the tumour burden to increase the chance of fertility preservation.

Case Report

8-year-old girl with no significant family history presented with dull aching pain abdomen and mass in abdomen. On examination mass occupied whole of abdomen, hard in consistency, mobile and lower border per vaginally occupying right fornix. CECT abdomen was done which showed a well-defined solid cystic mass measuring 24.1x 18.7x 14.9 cm mass arising from the right adnexa causing right reflex hydrouteronephrosis suggestive of malignancy. Uterus, right ovary and rest of the peritoneal cavity was normal. CECT chest was normal. Tumour markers S. Beta-hCG was 27,601.44 mIU/mL, S. LDH was 1735 IU/mL, S. AFP was >400 ng/

mL and S.CA-125 was 114.5IU/mL. After multidisciplinary tumuor board discussion patient was planned for staging ovarian laparotomy (fertility preserving surgery). Intraoperatively ascites was present, right ovary was enlarged measuring about 25x15 cm occupying whole of abdomen, adherent to small bowel, fundus of uterus and right fallopian tube. Left ovary, Fallopian tube and Uterus was normal. Right pelvic and paraaortic lymph nodes was enlarged. Liver, bilateral diaphragm and rest of the peritoneal cavity normal. Procedure done was excision of right ovarian mass with right salpingectomy, bilateral pelvic lymph node dissection, retroperitoneal lymph node dissection, greater omentectomy and peritoneal biopsies. On histopathology right ovary was reported as poorly differentiated neoplasm with capsular breach. In retroperitoneal lymph nodes one out 15 lymph nodes showed tumour deposits measuring 0.2 cm. Right Fallopian tube, Bilateral pelvic lymph nodes, Greater omentum, Peritoneal biopsies and Ascitic fluid were free of tumour. OnIHC, right ovary tissue was positive for SALL4 and PLAP (germ cell tumour marker). CD30 (Embryonal carcinoma marker) was diffusely positive and CD117 (dysgerminoma marker) was focally positive. It was negative for Beta-hCG (choriocarcinoma marker), AFP (yolk sac tumour marker), EMA (epithelial marker), Calretinin (sex cord stromal tumour marker) and Inhibin (sex cord stromal tumuor marker). From above findings, diagnosis of FIGO stage III A1(ii) (T1cN1aM0) mixed malignant GCT was made[5]. Patient was advised adjuvant chemotherapy with Bleomycin, Etoposide and Cisplatin (BEP regimen)for 4 cycles which patient refused. Patient had no recurrence on 1 year follow up (Figs 1-4)..

Discussion

In children and adolescents, GCTs are the most common variety of ovarian tumours histologically and they are mostly benign[6,7]. In India most common type of GCT is dysgerminoma followed by teratoma[8]. Incidence of mixed malignant Germ Cell Tumour is extremely rare. In one study done by Khanna, *et al* most common combination of subtypes were Yolk Sac tumour and immature teratoma. Mature and immature teratoma combination was second most common followed by combination of Yolk Sac tumuor and embryonal carcinoma being third most common[9].

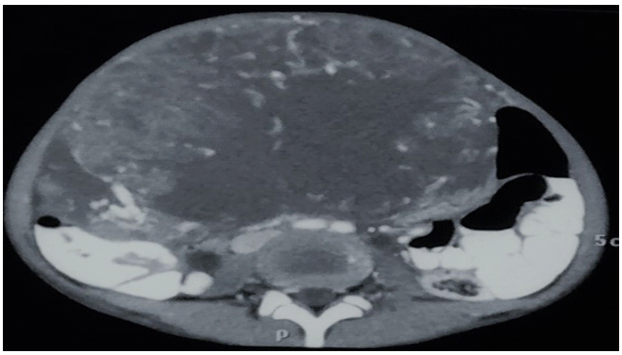

Fig 1 — CECT of abdomen and pelvis tumour arising from right ovary occupying whole of abdomen with ascites.

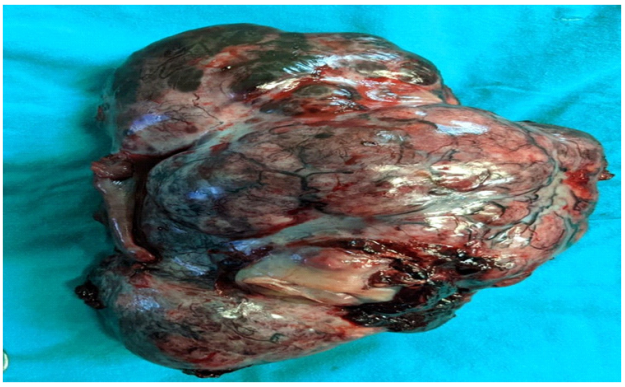

Fig 2 — Showing postoperative excised specimen of right ovary.

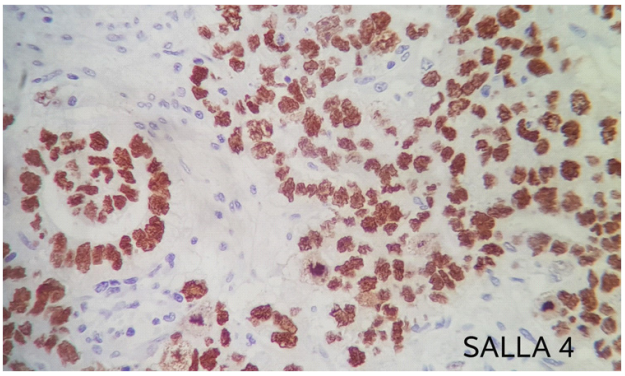

Fig 3 — Showing IHC on right ovary tumour was positive for SALL-4 (germ cell tumour marker).

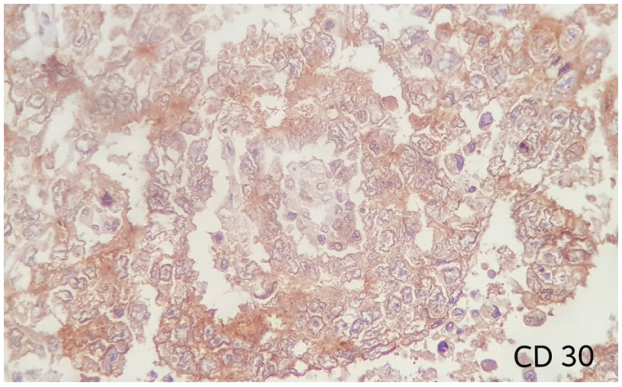

Fig 4 — Showing IHC on right ovary tumour was diffusely positive for CD 30 (Embryonal carcinoma marker).

World Health Organisation (WHO) classifies ovarian GCTs into many histological subtypes. Subtypes are : (1) Dysgerminoma, (2) Yolk Sac tumours, (3) Embryonal carcinoma, (4) Polyembryoma, (5) Choriocarcinoma, (7) Teratomas and (8) Mixed GCTs[10]. Dysgerminoma is most common followed by Yolk Sac tumuor also known endodermal sinus tumour[10]. In our patient, on histopathological examination and IHC revealed a combination two types tumours hence term as mixed GCT. 95% of tumour stained with IHC marker CD30 (Embryonal carcinoma marker) and 5% of tumour stained with CD117 (dysgerminoma marker). Most paediatric

patients with ovarian GCTs present between age 20-30 years[11]. Patients generally remain asymptomatic till ovarian mass grows to a large size causing abdomen pain adjacent organ compression. Less common presentations are vaginal bleeding, constipation and amenorrhoea. Sometimes they present as complication secondary to ovarian mass such as rupture of themass, infraction or torsion[1]. One-third of GCTs have extra-gonadal origin such as vagina, mediastinum, pineal gland, cervix, endometrium and sacrococcygeal area[12-14].

Surgery is main treatment of ovarian GCT. Fertility preservation surgery should be done whenever possible ie, preservation of uterus and opposite side ovary. When in doubt, opposite ovary biopsy should be taken before excision. Staging ovarian laparotomy is should be done to stage the disease[15]. Principles of staging surgery is defined by Children Oncology Group (1) Intact ovarian removal without rupture of the tumuor capsule. A salpingectomy must be performed if the fallopian tube is adherent. (2) Examination of the contralateral ovary with biopsy if a suspicious aspect is seen. (3) Inspection of the peritoneum, the liver and the omentum and resection of any abnormal tissue. (4) Inspection of aorto-caval and iliac lymph nodes and biopsy of suspicious ones. 5. Sampling of ascitic fluid for cytological examination. If ascites is absent, a washing is required[16,17]. Adjuvant chemotherapy should be used for tumours of FIGO any stage embryonal carcinoma and yolk sac tumour, stage II-IV dysgerminoma, Stage I with grade 2 or 3 and above immature teratoma[18]. BEP regimen is treatment of choice for treating ovarian GCTs[19]. Whenever extensive is disease is noted, neoadjuvant chemotherapy followed by surgery can be considered.In a study done by Rudaitis, *et al* showed that use neoadjuvant chemotherapy can significantly decrease the tumour size which minimizes the extent of surgery and thus helps in preserving fertility[20]. Overall prognosis of patients with ovarian GCT is excellent[3].

Conclusion

Ovarian tumours are rare in paediatric age group specially mixed ovarian Germ Cell Tumours. Multidisciplinary team is required to treat the patients. Coordination between paediatricians, surgical oncologist, medical oncologists, radiologists and pathologists is important for diagnosis and treatment. Surgery (staging ovarian laparotomy) is the standard of care. Fertility preservation surgery should be done whenever possible. Neoadjuvant chemotherapy should be used to decrease the tumour burden to enhance fertility preservation. Adjuvant chemotherapy should be used for tumours of FIGO any stage embryonal carcinoma and Yolk Sac tumour, stage II-IV dysgerminoma, Stage I with grade 2 or 3 and above immature teratoma.

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Case Report

The Rare Imitator : Pulmonary Nocardiosis Mimics Tuberculosis Reactivation

Ruchi Arora Sachdeva[1], Juhi Taneja[2], Litika Verma[3], Manas Kamal Sen[4], Kamran Chaudhary[5], Amrita Swati[6], Avinash Kumar[6]

Pulmonary Nocardiosis is a rare bacterial infection of lungs, caused by a filamentous bacterium. Immuno-compromised people are known to be at danger, but there are other new emerging risk factors to consider. The presentation and clinical course in such patients differ from the previous. Here the present case is aimed to underline the presentation and diagnosis in non-risk individual.

[*J Indian Med Assoc* 2022; **120(12):** 70-3]

Key words **: Nocardiosis, Filamentous Fungus, Immunocompromised, TMP-SMX.**

When Global economic expansion began in the 18th century, the Western World was still in its infancy and contagious diseases were rife among the populace. Koch and Pastuer, two of the greatest figures and Fathers of Microbiology, devised the germ theory of diseases, which paved the path for the discovery of disease-causing microbes. Edmond Nocard, a French Veterinarian and Microbiologist, was an assistant to Koch's adversary and Father of Bacteriology Louis Pasteur at the time when Koch discovered Tubercle Bacilli. He was fascinated by diseases that were passed from people to animals. His most significant contribution to medicine was isolating a filamentous fungus, that caused bovine farcy in economically important animals. The novel microbe was named Nocardia after him. He discovered that Nocardia can cause Nocardiosis in humans, which primarily affects the Central Nervous System (CNS) or immuno-compromised individuals. Nocard was also interested in the relation of tuberculosis in animals with that of humans, he published literature on bovine tuberculosis, tuberculin test in cattles, bovine pleuro pneumonia agent[14].

The finding of this bacteria by Edmond, who was working so closely with tuberculosis, couldn't have happened by mere chance.It has structural similarities to tubercule bacilli, is acid-fast, is a persistent illness comparable to tuberculosis, thus can occasionally be mistaken for tuberculosis. Nocardia genus is now classified under bacteria Actinomycetes and belong specifically to the family Mycobacteriaceae[15]. This account of Nocardia's discovery reveals a lot about the clinical acuity required for diagnosing Nocardia.

Editor's Comment :

- Nocardia can cause infection in both immunocompetent and immunocompromised hosts.
- Pulmonary Nocardiosis may mimic relapse of tuberculosis.
- Nocardiosis should always be thought as differential organism in patients with old treated Tuberculosis lung.

Nocardia species are gram-positive, filamentous bacilli belonging to the actinomycetes genus that are non-motile, catalase-positive, weakly acid-fast, aerobic and do not form spores[1,2,4]. These organisms are frequently found in the soil and also as saprophytes in fresh and salt water[8].

Tlymphocyte mediated immune response is significant in preventing Nocardia infection. Therefore, clinically, it manifests as a cutaneous, systemic, or disseminated infection mostly inimmuno-compromised hosts with autoimmune diseases, human immuno-deficiency virus, organ transplant recipients or patients on long-term steroid therapy[3,4,6-8].

The most common manifestation is pulmonary nocardiosis[3,5,8]. It may occur in patients suffering from chronic obstructive airway disease, asthma, bronchiectasis or chronic sarcoidosis[6,8]. Extra-pulmonary disease may involve the Skin, Brain, Kidneys and other Organs[1,3,5].

Because of being ubiquitous organisms, laboratory contamination or colonization without infection must

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be ruled out[8]. Clinical presentation is also important along with the laboratory diagnosis. The patient may present with cough, thick purulent sputum, fever, weight loss or malaise and with a sign for pre-existing medical condition[6,8].

We present a case of pulmonary nocardiosis in a patient who is a known case of old pulmonary tuberculosis, chronic obstructive airway disease and bronchiectasis.

Case Report

A 66-year-old male presented to the Emergency Department of our Hospital with difficulty in breathing for three weeks, cough with sputum for one week, localized left-sided chest pain three weeks back that lasted for three days and on and off fever for one week.

The patient was a known case of old Pulmonary Tuberculosis with Chronic Obstructive airway disease (COPD) with bronchiectasis with recent onset of bilateral pneumonia. The patient was not diabetic and had not received systemic steroid therapy.

He experienced weight loss in the past three months and also complained of loss of appetite.

He has a history of Pulmonary Tuberculosis 45 years back for which he took an extended course anti-tubercular treatment for three years.

He was on an anticholinergic inhaler and long-acting bronchodilator and corticosteroid inhaler medication for COPD for eight years.

Patient had a history of smoking 1 pack bidi per day for 11 years but left in the past 40 years. In the past, he worked in a factory that exposed him to cotton fibers for 24 years.

He was diagnosed with bilateral pneumonia elsewhere and was on treatment for the same. He was managed by Sulbactam-Cefoperazone and Clarithromycin for pneumonia.

On examination, his axillary temperature was 97.2 Fahrenheit, Blood Pressure 134/84mmHg, Pulse rate 100/min, oxygen saturation 92% on room air. The patient was dyspneic and general physical examination was within normal limits. Left eye aphakia and right eye pseudophakia present.

On Auscultation S1S2 heard. Bilateral air entry equal with bilateral crepitations and coarse crepitations in left infrascapular and scapular area.

Vital parameters, blood sugar and electrolytes were monitored and required corrections given. Patient was started on antibiotics, bronchodilators, and oxygen therapy.

HRCT chest was suggestive of multifocal patchy are as of consolidation in bilateral lungs.

Partial collapse with cystic bronchiectatic change and fibrotic parenchymal calcification was seen in the right upper lobe -sequel to old etiology (Figs 1&2).

RTPCR for COVID was negative.

Bronchoscopy showed bilateral infective secretions. Bilateral Bronchoalveolar Lavage (BAL) sample was collected and sent for investigations.

No fungal elements were seen on 10% KOH mount. Gram's stain and Ziehl–Neelsen modified stain of the BAL showed Gram positive bacilli and acid fast branching filaments, respectively (Fig 1). No atypical cells were seen on cytological evaluation.

Acid-fast filamentous branching bacilli resembling Nocardia were seen in bronchoalveolar lavage specimen on Modified Ziehl-Neelson stain (1000 x Magnification).

Culture grew colonies with a chalky white appearance after 48 hours of incubation on Blood agar. The isolate was identified as *N Otitidiscaviarum* by MALDIT-OF.

After microbiological confirmation, the patient was started on empirical triple therapy with Injectable Imipenem, Amikacin and Cotrimoxazole for suspected disseminated Nocardiosis. After CEMRI of brain showed normal study, the treatment was de-escalated to oral cotrimoxazole therapy and patient was discharged on the same. The patient showed significant symptomatic improvement in 1 week. A

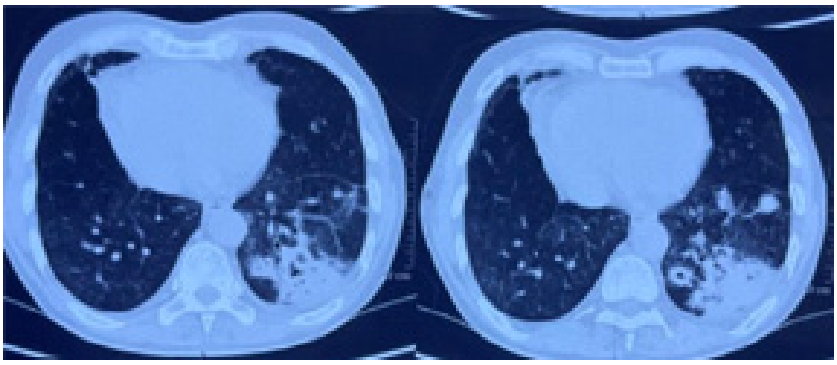

Fig 1 — CT chest

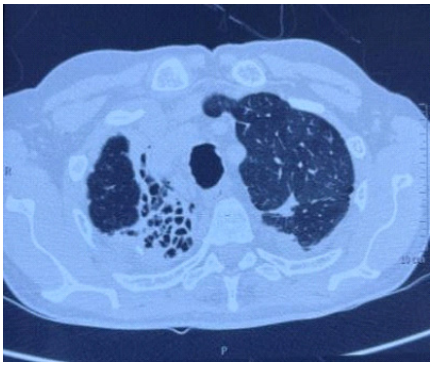

Fig 2 — CT chest

regular follow up and repeat chest X-ray after 2 months showed partial regression of pulmonary lesions.

Cardiac evaluation suggestive of trivial tricuspid regurgitation. The pulmonary function test revealed moderate obstructive with restrictive pattern (Figs 3&4).

Discussion

Nocardiosis, a tropical disease; primarily affects immuno-compromised people, but its diagnosis in an immunocompetent host is not an inconceivable entity. Despite the fact that it is a disseminated disease, it is shown to be confined in immunocompetent hosts[9], with pulmonary involvement being the most common.

As seen in the current report, such cases have been more frequently reported in patients with bronchiectasis or old tuberculosis, emphasising the need of considering this differential when traditional treatment options fail to relieve symptoms.Inhaled corticosteroid medication induced changes in local microbial flora and damage to airway and fibrosis-induced alteration in airway architecture may all be variables that pre-dispose to localised opportunistic infection and explain its incidence in these patients[10-12].

Treatment usually involves trimethoprim-sulfamethoxazole therapy, expect in instances of sulfa-drug allergy where minocycline has proven to be an effective alternative, while other would-be inhaled aminoglycosides, cephalosporins, carbapenems. Pulmonary Nocardiosis responds well on monotherapy

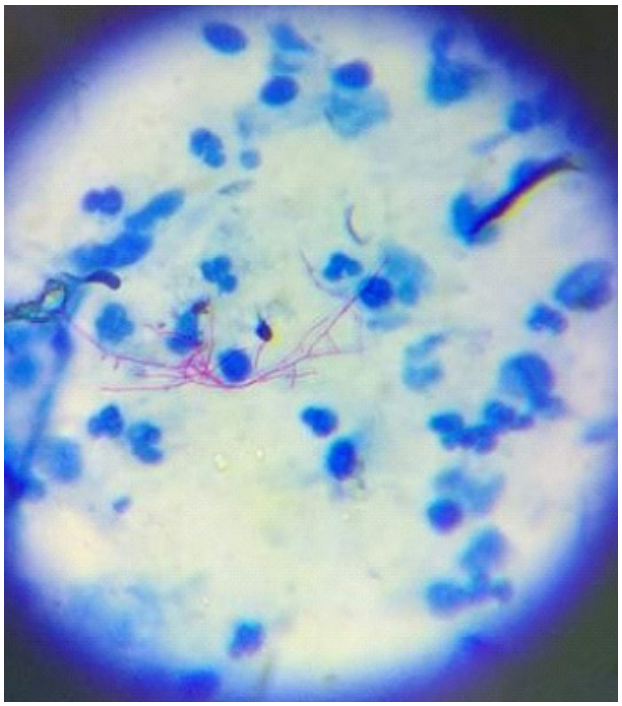

Fig 3 — Acid Fast filamentous bacteria in BAL specimen on Modified ZN Stain (1000x magnification)

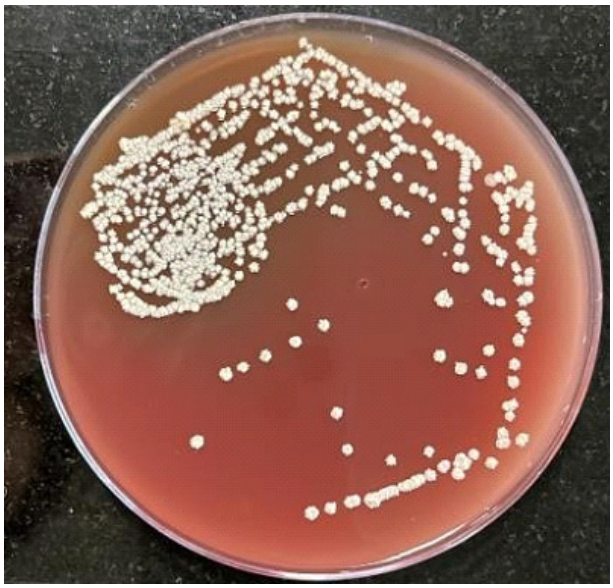

Fig 4 — Chalky white colonies of Nocardia on Blood agar

of 3 to 12 months[13]. Disseminated disease is treated with multi-drug therapy and partial treatment is associated with high mortality. Hence it is important to rule out brain or meningeal involvement by imaging or CSF studies in all cases and search for symptoms of dissemination other organs.

This report highlights the importance of differentiating such instances which are usually misdiagnosed as tuberculosis in an endemic zone like India. Doing a fungal culture more routinely in these newly defined high risk cases can help finding more such cases. Despite the relative rarity of these conditions, an awareness of the disease manifestations caused by these organisms is important because of their debilitating nature. In addition, outcomes are more favourable if they are diagnosed early and effective treatment is initiated in good time.

Nocardia, although rare in Indian scenario can present with unusual pulmonary lesion mimicking lung malignancy. Pulmonary infections due to *N Otitidiscaviarum* have been reported previously[16]. Species identification is important in deciding the clinical management and management of patients with nocardial disease. According to literature, isolates of *N Otitidiscaviarum* complex are usually resistant to betalactams, including most broad spectrum cephalosporins, ampicillin, amoxicillin clavulanic acid and imipenem but are usually susceptible to amikacin, the fluoroquinolones and sulphonamides[17]. However, sensitive isolates have also been reported[18].

Nocardiosis can present as acute or chronic disease. In acute presentation, it can lead to fatal disease when undiagnosed and untreated, especially

in TMP-SMX resistant cases. In chronic form it can get disseminate to other areas like Brain, Pleural, Abdomen[19].

Conclusion

Pulmonary Nocardiosis should always be kept in mind while treating old tuberculosis patients or COPD patients for exacerbation or recurrent infection. It responds well to treatment and significantly improves the outcome. Thorough microbiological investigations help in establishing the diagnosis and significantly improve the outcome.

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19 Fatal pulmonary nocardiosis in tmp-smx resistant cases.

Drug Corner

Assessment of Prescribing Practices in Overactive Bladder Pharmacotherapy across Different Specialties of India : A Prescription Trend Analysis

Vishavadia Krunal[1], Sandip Solanki[2], Sandesh Warudkar[3], Hiren Prajapati[4], Madhu Sharma[5]

Purpose : To assess the temporal prescription patterns of overactive bladder (OAB) pharmacotherapy based on the prescription trend analysis amongst Indian clinicians.

Methods : IQVIA (Quintiles and IMS Health) secondary sales audit (SSA) and prescription audit for antimuscarinics and beta-3 adrenoceptor agonist (mirabegron) from 2014 to 2022, were analyzed. Prescribers overlap analysis for solifenacin and mirabegron among Indian urologists was also analyzed.

Results : Urologists' prescription rates of OAB drugs were 65% in 2016 and 52% in 2022. The rate of OAB medication prescription by non-urologists was highest among surgeons (17%), followed by consultant physicians (9%) and gynecologists (8%) in 2022. In addition, among OAB medication prescription rates for antimuscarinics were 100% in 2016 and 56% in 2022 whereas for mirabegron, it was 0% in 2016 and 44% in 2022. The proportion of prescribers of OAB medication among urologists was 38% in 2016 and 33% in 2022. Exclusive prescribers of solifenacin were 748 in 2018 and 715 in 2022 at the urologist, whereas for mirabegron, it was 961 in 2018 and 1475 in 2022.

Conclusions : Urologists remained a top prescribing specialty for OAB drugs, although prescription share increased among surgeons and consultant physicians. OAB medicines prescriptions by urologists are shifting from solifenacin to mirabegron. The results of this study could further help clinicians, to design the optimum treatment approach in OAB patients according to their need, which can help to lower antimuscarinic side effects, improves treatment adherence, and improves patient's QoL.

[*J Indian Med Assoc* 2022; **120(12):** 74-9]

Key words **: Overactive bladder; Prescription analysis; IQVIA database; Antimuscarinics, Mirabegron.**

There are a variety of symptoms associated with an Overactive Bladder (OAB), which include urgency, frequency, and nocturia, with or without Urge Urinary Incontinence (UUI)[1]. OAB is also associated with decreased quality of life and a high economic cost to society[2].

International Continence Society (ICS) estimates that 12.8% of women and 10.8% of men suffer from OAB; the prevalence of frequency, urgency, and Urge Incontinence (UI) rises with age[3,4]. In Men, UUI was significantly lower than in women. The reported prevalence of OAB in India is 10-42%, with a progressive increase in prevalence from the third to seventh decade of life[5].

Behavioural and self-control training methods are regarded as first-line options for reducing urine incontinence in patients. Antimuscarinics or â3 adrenoceptor agonists are popular treatments for OAB if behavioural changes fail to alleviate symptoms[6]. In India,the most commonly prescribed OAB medications are solifenacin, oxybutynin, tolterodine, darifenacin, trospium, and mirabegron[7] (Table 1).

Antimuscarinics prevent the contraction of the smooth muscle wall around the bladder. Stimulation of the acetylcholine muscarinic M3 receptors in the detrusor muscle wall usually results in micturition. Solifenacin and darifenacin are muscarinic receptor antagonists that only affect the M3 receptor. Oxybutynin and tolterodine are non-selective antimuscarinics that affect all muscarinic receptors, which causes dry mouth[9]. As a beta-3 agonist, mirabegron relaxes the detrusor muscles and enhances bladder storage capacity without affecting voiding contractions. As a result, mirabegron can assist in alleviating the symptoms of OAB[10]. According

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Table 1 — *Treatment of Non-Neurogenic Overactive Bladder (OAB) in adults*[1,8]

First-Line Treatments	Behavioral Therapies	Bladder training Bladder control strategies Pelvic floor muscle training Fluid management
Second-Line Treatments	Pharmacologic Management	Antimuscarinic Solifenacin Oxybutynin Tolterodine Darifenacin Trospium Propiverine Fesoterodine Beta-3 adrenoceptor agonists Mirabegron Vibegron Serotonin noradrenaline reuptake inhibitor Duloxetine
Third-Line Treatments	PTNS and Neuro-modulation	Intradetrus oronabotulinumtoxinA (100U) Peripheral tibial nerve stimulation (PTNS) Sacral neuromodulation (SNS)
Fourth-Line Treatments	Augmentation Cystoplasty and Urinary Diversion	Augmentation cystoplasty or urinary diversion for severe, refractory, complicated OAB

to a report by the Urological Society of India, OAB is most commonly treated with antimuscarinic or beta-3 adrenoceptor agonists[5].

The objective of the present study is to assess the prescription patternof OAB pharmacotherapy especially antimuscarinic and beta-3 adrenoceptor agonists, based on the prescription trend analysis among Indian clinicians.

Materials and Methods

Data Source and Setting :

From August 2016 to August 2022, we have been using IQVIA Medical Audit Data (formerly IMS Health) to track the urological preparation prescription rates for primary care physicians in India who work in the private sector[11]. In more than 100 countries, IQVIA collects market intelligence and disseminates it. Medical audit data monitor prescriptions written by allopathic doctors in private practices. Data were gathered from a random sample of 4600 healthcare practitioners from 23 metropolitan areas of India (over 1 million population), 128 Class 1 cities (population over 100,000), and 1A cities (population fewer than 100,000). A national sample of prescriptions written by doctors in cities with populations greater than one million was drawn from the original data[12].

The data use the European Pharmaceutical Market Research Association's (EphMRA) Anatomical Therapeutic Classification (ATC).The data does not include prescriptions written in the public sector, thereby analysis only includes outpatient prescriptions from the private sector. Last but not least, IQVIA makes the data available to us in aggregate form, processed, and extrapolated to reflect national prescription practices.

Outcome Measure :

The study focused on the antimuscarinics (solifenacin, oxybutynin, tolterodine, darifenacin, and trospium) and mirabegron prescribed each year as a primary outcome measure. In addition, a study estimated and reported prescriptions by specialty and molecule.

Statistical Analysis :

The study used the International Statistical Classification of Diseases and Related Health Problems, 10th Revision, to code prescription diagnosis data from an IQVIA medical audit (ICD-10 classification; version: 2016)[12]. Anatomic Therapeutic Chemical (ATC) classification of antimuscarinics and beta-3 adrenoceptor agonists recommended for the related diagnosis have been coded to the 3rd level of WHOCC's proposed drug statistics methodology (ATC index-2016)[13]. Based on the diagnostic information provided, medical audit data was used to code the ICD 10 at the smallest level possible.

The annual prescription data of IQVIA medical audit for urological preparations, including antimuscarinics and beta-3 adrenoceptor agonists, were analyzed. The medicines prescribed were categorized into these subgroups: solifenacin, darifenacin, tolterodine, oxybutynin, trospium & mirabegron. We used software Microsoft Excel 2013 to perform statistical analysis.

Ethics Considerations :

The data used had no identifiers for the patients. So current study does not require Ethical Committee approval.

Results

Prescription and prescriber data of various antimuscarinics and beta-3 adrenoceptor agonists were analyzed for 7 Moving Annual Total (MAT) periods starting from MAT Aug'16 to MAT Aug '22.

In 2016, for OAB treatment, 84% of prescriptions were generated by the top 4 specialties, ie, urologist, consultant physician, gynecologist& general surgeon, which further increased to 86% in 2022. In MAT 2022, the urologist is the leading specialty prescribing OAB

drugs, with a 52% prescription share. General surgeon contributes 17%, while consultant physician and gynecologisthave a 9% & 8% prescription share, respectively (Fig 1A).

In 2016, 38% of urologists contributed 65% of prescriptions in the OAB drug market, which reduces to 33% and 52% in 2022, prescriber contribution and prescription contribution, respectively. At consultant physicians, prescriber contribution increases from 11% to 17%. Still, at the same time, prescription contribution did not grow at the same pace (6% to 9%), mainly because of low prescription per doctor per month (PDM). 8% of surgeons contributed around 5% of prescriptions in 2016, which increased to 17% in 2022 due to a positive change in the number of prescriptions per doctor (Fig 1B).

Antimuscarinics and beta-3 adrenoceptor agonist, mirabegron are the preferred drugs for the medical management of overactive bladder in India. Prescription share for antimuscarinics were 100% in 2017 & 56% in 2022 whereas for mirabegron, it was 0% in 2017 & 44% in 2022. Prescriber share data also reflect a similar trend, antimuscarinics were 100% in 2017 & 64% in 2022 whereas, for mirabegron, it was 0% in 2017 & 36% in 2022 (Fig 2).

Before the launch of Mirabegron in the Indian market, solifenacin was the most preferred drug for the treatment of OAB, with a prescription share of 37% in 2017. Mirabegron was approved in India by Central Drugs Standard Control Organisation (CDSCO) in June 2017 & marketed by Nov 2017[14]. The majority of Antimuscarinics lost their prescription share to mirabegron, as in 2022, mirabegron gained 44% prescription share in the OAB market (Table 2).

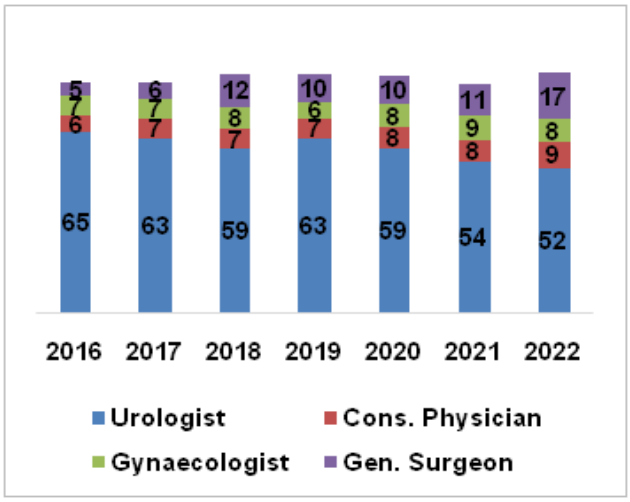
Solifenacin prescription share reduced from 36% to 30%, during 2016-2022. Major loss in prescription share for antimuscarinics was, oxybutynin (19% - 8%), tolterodine (18% - 9%), and darifenacin (25% - 9%). MAT 2020 period experienced COVID-19 impact in terms of loss in prescription, applicable to all the molecules. Greater relative prescription loss at antimuscarinics indicates the change in molecular preference in OAB management.

Among different specialties, urologists were the major specialty prescribing overactive bladder drugs & solifenacin was the most preferred molecule (38% prescriber share) in India before the launch of mirabegron. Tolterodine was the second preferred drug (29% prescriber share) for OAB by urologists in 2016, but in 2022, the prescriber share was reduced to 12%. Darifenacin also lost the prescriber share from 18% to 4% (Fig 3).

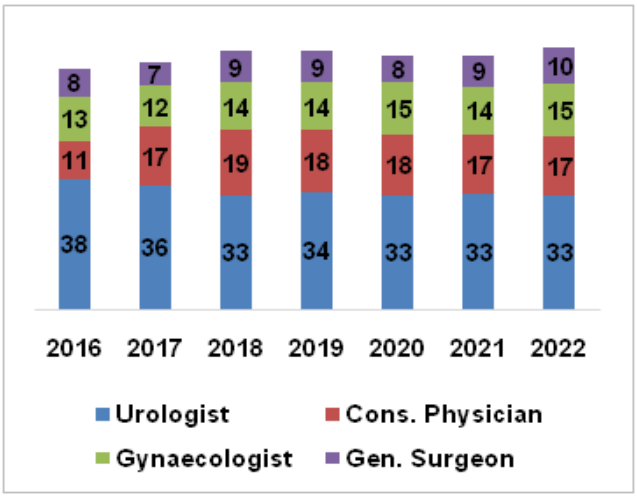
OAB medication preferences by urologists are shifting from antimuscarinics to mirabegron. Other specialties continue to prescribe antimuscarinics as a preferred drug for OAB (Fig 4).

Solifenacin and mirabegron are the most prescribed molecules across specialties and also by urologists. An exclusive prescriber (urologist) based analysis was done to understand the molecular shift at the prescriber level.

In India, before the launch of mirabegron, solifenacin dominated the OAB market. But after the launch of mirabegron, a considerable decline was observed in solifenacin prescribers and a significant gain in mirabegron prescribers. The decline in solifenacin exclusive prescribers and gain in mirabegron exclusive prescribers show the molecular shift at the urologist level from solifenacin to mirabegron.

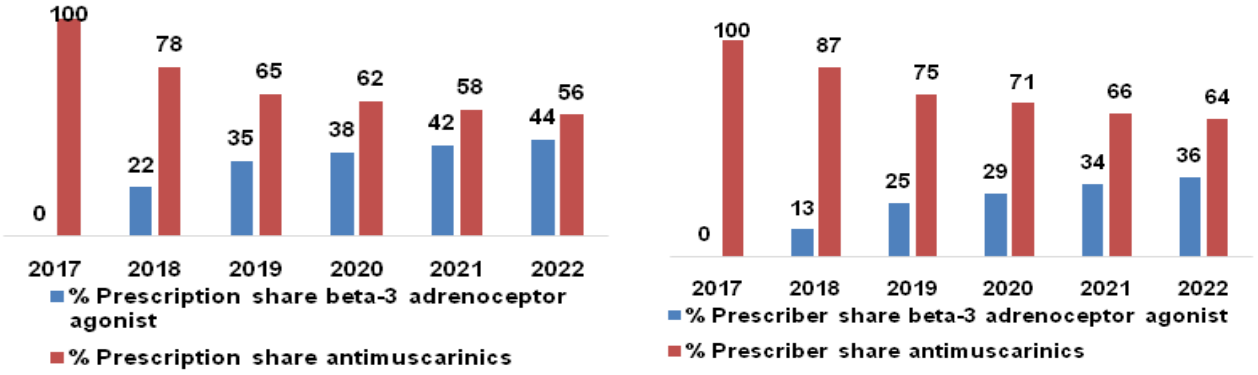


[A]



[B]

Fig 1 — Speciality-wise contribution for OAB drugs in India (2016-2022) : [A] Prescription share; [B] Prescriber contribution



[A] Prescription share [B] Prescriber share

Fig 2 — % Prescription and Prescriber share of beta-3 adrenoceptor agonist and antimuscarinics (2017-2022)

Table 2 — *Molecule-wise % prescription share of OAB drugs in India (2016-2022)*

Drugs for OAB	2016	2017	2018	2019	2020	2021	2022
Mirabegron	0	0	22	35	38	42	44
Solifenacin	36	37	28	31	33	33	30
Oxybutynin	19	20	17	12	10	7	8
Tolterodine	18	19	15	9	10	9	9
Darifenacin	25	21	17	13	9	9	9
Trospium	2	2	1	1	0	0	0

Discussion

The urology drug market contributes almost 1.6% to the Indian pharmaceutical market. Drugs for OAB contribute 7.3% of the total urology market. Although the prevalence of OAB in India ranges from 10 - 42%[15], the market size is minuscule, just 0.1% in the Indian pharmaceutical market[15].

Among Indian urologists, solifenacin (46.7%) is the most commonly prescribed drug for UUI, according to a survey conducted by the Urological Society of India (November 2017). In the two months following the launch of mirabegron in India, a 4.5% preference for mirabegron was recorded[16].

The efficacy and tolerability data unveil the reason behind shifting the molecular preference of Indian clinicians within the antimuscarinics or antimuscarinics to mirabegron. Many studies have compared the efficacy and tolerability of antimuscarinics/solifenacin vs. mirabegron. The majority of studies concluded antimuscarinics/solifenacin are comparable with mirabegron in efficacy, but mirabegron scores more on tolerability and thereby therapy adherence[17-19].

Solifenacin 5 mg/day was found to be as effective as other common antimuscarinics across the spectrum of OAB symptoms and more effective than tolterodine 4 mg/day in reducing incontinence and UUI episodes, according to a systematic review and meta-analysis. When compared to other solifenacin doses, such as 10 mg/day, darifenacin 15 mg/day, tolterodine IR 4 mg/day, fesoterodine 8 mg/day, propiverine 20 mg/day, and oxybutynin (IR 9-15 mg/day or ER 10-mg-daily), solifenacin 5 mg/day had a lower incidence of dry mouth[20].

Mirabegron is an oral adrenoceptor agonist that provides an alternative to antimuscarinics for patients with OAB, as phase III trials of mirabegron versus placebo found significant improvements in key efficacy measures (eg, urinary incontinence and frequency of urination)[17]. Researchers compared antimuscarinics and mirabegron 50mg in patients with OAB by conducting a systematic literature review and network meta-analysis based on peer-reviewed articles published between 2000 and 2013. Mirabegron 50 mg was as effective as antimuscarinics (excluding solifenacin 10 mg) for urinary frequency, incontinence, and UUI episodes, according to 44 RCTs involving 27,309 patients[21]. Also, mirabegron was found to be better tolerated in terms of dry mouth, constipation, and urinary retention than antimuscarinics.

Better symptomatic relief with patient satisfaction is the primary objective behind any medical treatment.

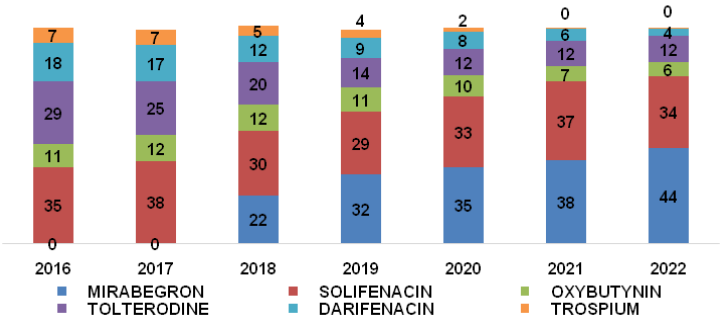
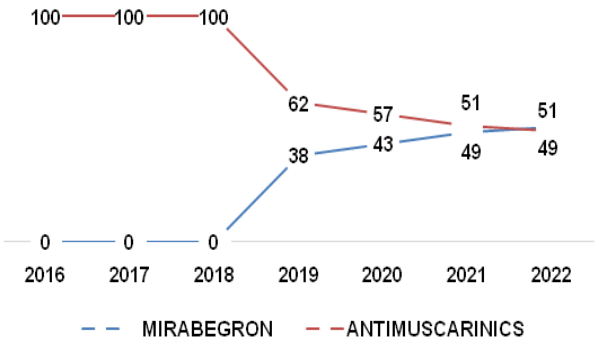
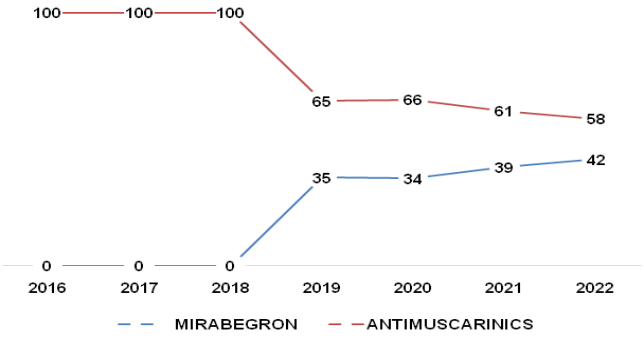


Fig 3 — Prescriber share of OAB drugs at Urologist specialty (2016-2022)



[A] %Prescription Share (Urologist)



[B] %Prescription Share (Other specialities)

Fig 4 — % Prescription share of antimuscarinics and mirabegron at urologists and other specialties (2016-2022)

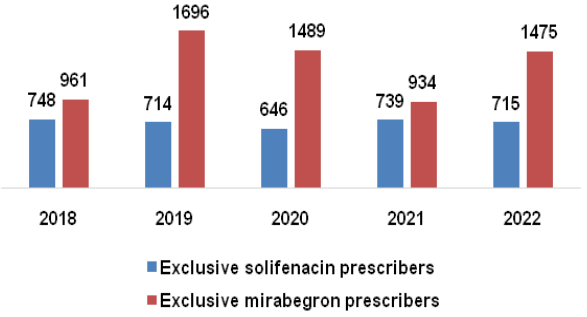


Fig 5 — Exclusive prescriber (urologist) analysis for Solifenacin and Mirabegron

Antimuscarinicfulfil the first requirement and provide better symptom relief, but patient satisfaction is less due to undesirable side effects. Patients switching from antimuscarinics to mirabegron for OAB have better outcomes if their baseline OAB symptom scores are higher, such as the OAB-SS and IPSS-S[22]. According to a retrospective cohort study, Mirabegron may reduce the antimuscarinic drug's dosage and thus improve NDO treatment's long-term efficacy[23]. High therapy adherence, comparable efficacy, and lower side effects could be why clinicians shift their preference from solifenacin to mirabegron.

Recently CDSCO has approved a fixed-dose combination of solifenacin and mirabegron[24]. The randomized, multicentre SYNERGY trial studied the long-term safety and efficacy of the combination of mirabegron and solifenacin in patients with overactive bladder compared to monotherapy. The study concluded that the treatment with a combination of solifenacin and mirabegron was better tolerated and found to be effective than solifenacin monotherapy[25]. In the Indian market, the mirabegron/solifenacin combi pack was introduced in late 2019, whereas the fixed-dose combination was approved in 2021[26].

OAB is a common disease that causes serious problems such as UTIs, skin infections, bladder stones, falling/fractures in the elderly, sleep disturbances, adverse effects on quality of life, and depression[27]. OAB is often accompanied by chronic diseases such as hypertension and diabetes. It is common for elderly incontinence patients to be managed by a non-urologist, especially in rural areas[28]. Urologists were most likely to prescribe mirabegron whereas non-urologists were found to prescribe older-generation antimuscarinics like oxybutynin and darifenacin; rather than a newer class of OAB drug, mirabegron[29].

Limitation :

Our study is not deprived of limitations. The IQVIA database did not offer detailed, patient-level data on OAB management; only limited OAB data could be included in this study, representing a source of bias. Moreover, IQVIA data were extrapolated to a population of Indian physicians using inverse proportional weight. In doing this, it is assumed that the stable panel generally represents other practices, pharmacies, and hospitals for which IQVIA did not have reliable data. Minor difference in the stable panel creates significant differences in the final data output. Also, the current study only evaluates prescriptions and prescriber trends of two major classes of drugs, ie, antimuscarinics and beta-3 adrenoceptor agonists used for the treatments of OAB. No other pharmacotherapy has been evaluated. Despite limitations, our study comprehensively evaluated the change in practicing trends of OAB management.

Conclusion :

Urologists remained a top prescribing specialty for OAB drugs, although prescription share increased among surgeons and consultant physicians. OAB medication preferences by urologists are shifting from solifenacin to mirabegron. Other non-urologist specialties continue to prescribe antimuscarinics as a preferred drug for OAB. Antimuscarinics' prescription

share shows a downtrend due to the risk of side effects and lowers therapy adherence compared with mirabegron, which is comparatively better tolerated & equally effective in OAB management. Across Indian specialties, mirabegron emerges as a promising treatment option for overactive bladder. Recently approved fixed-dose combination of antimuscarinic, solifenacin, and beta-3 adrenoceptor agonist mirabegron is the newer approach for refractory OAB management in India. Results of this study could further help clinicians, to design the optimum treatment approach in OAB patients according to their need, which can help to lower antimuscarinic side effects, improves treatment adherence, and improves patient's quality of life.

Ethics approval and consent to participate : The data we used had no identifiers for the patients. We, therefore, did not require ethical approval for our study.

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Competing interests : The authors have declared that no competing interests exist.

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Drug Corner

Expert Opinion on Novel Fixed Drug Combination of Metformin Sustained Release and Vildagliptin Immediate Release for Type 2 Diabetes Mellitus Management in India

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Type 2 Diabetes Mellitus (T2DM) is a highly prevalent cardiometabolic disorder in India and is further projected to rise (10.4% by 2030). In newly diagnosed patients, maintaining HbA1c 6.5-7.0% and minimizing glycaemic exposure, particularly during the first year following diagnosis, may be crucial for preventing complications. Early treatment initiation with a synergistic combination of vildagliptin and metformin is one of the many possible combinations to manage type 2 diabetes mellitus. In view of emerging clinical evidence on early initiation of combination therapy than monotherapy with metformin, there is a need for expert consensus on the use of the current approved Fixed Dose Combination (FDC) of Metformin SR + Vildagliptin IR in newly diagnosed diabetic patients. Experts framed final consensus statements based on available scientiûc evidence, experience and collective clinical judgment from practical experience this FDC.

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Key words **: Type 2 diabetes mellitus, Fixed-dose combination, Metformin, Vildagliptin**

Introduction

Current Indian Scenario :

The age-adjusted prevalence of diabetes in India as per the Diabetes Atlas 2021 released by the International Diabetes Federation (IDF) is 9.6% (projected to increase by 10.4 by 2030)[1]. In a recent 2020 Indian study, the average HbA_{1C} in a newly diagnosed diabetic patient was reported to be 9.1 ± 2.3%, whereas the average HbA_{1C} was 8.3 ± 2.4% in a diabetic patient diagnosed during screening[2]. This suboptimal disease awareness and high average HbA1C at diagnosis, in addition to the fact that the onset of diabetes among Indians is about a decade earlier than the Western counterparts, highlights that diagnosis is delayed or missed in Indians.Indians have a higher overall disease burden with a longer duration spent in pre-detection, hence a longer untreated period than the Western population[3].

Early *versus* Late Intensification of Diabetic Therapy :

A 1% increase in HbA_{1c} concentration was associated with about a 30% increase in all-cause mortality and a 40% increase in cardiovascular mortality[4]. Risk of hospitalization for heart failure increases 8-32% per 1% unit increase in HbA_{1c}[5]. Hence, optimal glycemic control is one of the most important treatment goals.

For most patients with HbA1c 8.0-8.5% at diagnosis, metformin monotherapy does not lower HbA1c sufficiently to achieve target levels[6,7]. Delayed

- Early combination therapy could potentially alter the course T2DM, thereby providing longer periods with stable HbA_{1c} levels, delaying the need for therapy intensification, and reducing the risk of chronic complications.Initial combination therapy with Metformin Sustained Release (SR) and Vildagliptin Immediate Release (IR) Fixed Drug Combination (FDC) should be considered in:
  - Patients presenting with A1C levels 1.5-2.0% above target,
  - Patients with any one of the below comorbidities:
    - # Patients with diabetic end-organ damage manifestations
    - # Patients with Cardiac or renal risk factors.
    - # Elderly patient
    - # Obese patients and patients in whom weight gain is undesirable.

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treatment intensification after monotherapy failure, seen in real-world settings, results in more time spent in avoidable hyperglycemia, raising a crucial barrier to optimized care[8].

The INITIAL study demonstrated that vildagliptin and metformin combination therapy was associated with significant and clinically relevant HbA1c reduction in relatively young drug-naïve Asian patients with T2DM[9]. In newly diagnosed patients, maintaining HbA1c 6.5-7.0% and minimizing glycaemic exposure, particularly during the first year following diagnosis, may be crucial for preventing complications[10,11].

The VERIFY (Vildagliptin Efficacy in combination with Metformin for Early Treatment of Type 2 Diabetes) Trial :

The five year long VERIFY trial demonstrated that initial combination therapy is superior to sequential addition of medications for extending primary and secondary treatment failure. Newly diagnosed T2DM patients that received early combination therapy had a significant reduction in the relative risk for time to initial treatment failure compared to initial metformin monotherapy (HR 0.51, p<0.0001). Compared to initial metformin monotherapy, at 5 years, more than twice as many patients had an extended time with good glycaemic control after early combination therapy. The median time to loss of glycaemic control was almost doubled in patients that received early combination therapy compared to patients that received initial metformin monotherapy (61.9 months *versus* 36.1 months). Thus, extending the need to intensify treatment by more than 2 years. Furthermore, patients receiving early combination therapy had consistently lower glycaemic exposure for the entire study duration, compared with those on initial metformin monotherapy, with a greater proportion of patients attaining HbA1c target levels of <7%, <6.5%, or <6.0%[12]. Both groups showed similar safety and tolerability profiles, with no new safety findings, low rates of hypoglycaemic events, and comparable changes in body weight, despite the concurrent use of two OHAs in the combination treatment arm.

Besides delaying the time to primary treatment failure, early combination therapy also reduced the risk of time to secondary treatment failure by 26% (HR 0.74, p<0.0001). This suggests a 'legacy effect' in which only the early normalization of blood glucose can help to reduce diabetes progression[11,13].

Early treatment initiation with a synergistic combination of vildagliptin and metformin is one of the many possible combinations to manage T2DM. Results from the ongoing GRADE study comparing the durability of different agents in combination with metformin will add evidence to the proposed early combination treatment strategy[14].

Current Treatment Guidelines on Combination Therapy for Diabetes :

(1) Global Guidelines :

The American Diabetes Association (ADA) 2021 states that more intensive early treatment has some clinical benefits, and it should be evaluated as part of a collaborative decision-making process with patients. Furthermore, since the absolute effectiveness of most oral hypoglycemic agents (OHAs) rarely exceeds 1%, initial combination therapy should be considered in patients with HbA_{1C} levels 1.5- 2.0% above the target. Treatment intensification recommendations for patients not meeting treatment goals should not be delayed. The choice of OHA added to metformin is based on the patient's clinical condition[3].

The American Association of Clinical Endocrinology (AACE) 2020 guidelines recommend dual combination therapy when HbA1c is ≥7.5% at diagnosis15.

(2) Indian Guidelines :

The latest Research Society for the Study of Diabetes in India (RSSDI) guidelines 2020 recommends initiating combination therapy early if the HbA1c >1.5% above the target[16].

Rationality of Metformin SR + Vildagliptin IR Fixed Drug Combination (FDC) :

The Metformin SR + Vildagliptin IR FDC consists of antidiabetic with complementary modes of action. Metformin helps with insulin sensitization and Vildagliptin with glucose-dependent beta-cell stimulation. Furthermore, both drugs reduce hepatic glucose production[17].

A survey showed that patients and providers both cited gastrointestinal side effects as the primary barrier to metformin use[18]. The once-daily metformin (Met-XR) formulation allows a more gradual release of metformin in the upper gastrointestinal tract compared to the immediate release of metformin (Met-IR)[19]. An open-label, prospective 24-week study showed that patients who switched to metformin XR observed the same clinical and metabolic benefits as for standard metformin but with fewer gastrointestinal side effects, reduced dosage, and a greater sense of well-being and satisfaction on medication[20].

Benefits of metformin hydrochloride sustained release (SR) and vildagliptin immediate release (IR) combination therapy have been summarised in Fig 1[19,20].

Need for Expert Opinion

In view of emerging clinical evidence on early

Assessment of key criterias of Metformin XR + Vildagliptin IR

HbA_{1c} control	Yes
Risk of hypoglycemia	No
Convenient to use	Yes
Risk of weight gain	No
Side effects (diarrhea, nausea, vomiting and abdominal pain)	Reduced compared to Met-IR
Ease of dose titration	Yes
Reduced pill burden	Yes
Usage in T2D patients at high CV risk	Safe
Better adherence and compliance	Yes

Fig 1 — Assessment of Treatment Satisfaction Criterion
CV: Cardiovascular; HbA_{1c}: Glycated haemoglobin; IR: Immediate release; XR: Extended release; T2D: Type 2 diabetes.

initiation of combination therapy than monotherapy with metformin, we need expert opinion on the use of the current approved FDC of Metformin SR + Vildagliptin IR in newly diagnosed diabetic patients.

Methodology

110 diabetologists from India convened for 10 advisory board meetings between June 2021 to August 2021 to discuss the use of Metformin SR + Vildagliptin IR in current practice. All meetings were conducted on a virtual platform. The experienced endocrinologists were selected based on their seniority (over at least 10 years of experience in field of diabetes management).Experts framed statements based on available scientific evidence, experience and collective clinical judgment from practical experience with this combination. Objectives and specific topics relating to metformin and vildagliptin combination were discussed, and each expert shared their views, which led to group discussions. The consensus was formed if the agreement to the statement was more than 80% within the group.

Consensus statements introduced for panel discussion :

- In India, diagnosis of type 2 diabetes is delayed.
- In India, the average HbA_{1C} at the time of diagnosis is higher than the west.
- In practice, treatment should be individualised for patients including shared decision making for early initiation of combination therapy early in newly diagnosed diabetics.
- In practice, Metformin sustained release (SR) has better tolerance than Metformin immediate release (IR).
- It is important to identify patient profiles who could benefit from Metformin SR + Vildagliptin IR combination therapy.

Expert Opinion

In the light of the above information, a panel of experts discussed the following topics to help arrive at final expert consensus statements.

Diagnosis of Type 2 Diabetes is Delayed in India

All experts agreed that only 50% of the patients with diabetes are diagnosed and only 50% of the diagnosed patients are on treatment. There is suboptimal disease awareness and limited accessibility to regular health care.

The average HbA_{1C} at the time of diagnosis is higher in India compared to the West

Most of the experts reported that the average HbA_{1C} at the time of diagnosis in their practice ranges between 8-10%.

Monotherapy has Limitations when used for the Treatment of T2DM Patients

Metformin monotherapy, which primarily controls fasting plasma glucose, is preferred, especially when the HbA1C is 7.5-8% at the time of diagnosis. Treatment failure to Metformin monotherapy is usually noticed at an average of 3 months. A trial with monotherapy is done for a maximum of 8-12 weeks before switching to combination therapy based on Hb1AC values at follow-up. Usually, a maximum dose of Metformin Monotherapy is needed to achieve an average of 1% drop in HbA1C. Monotherapy does not provide long-term stable glycaemic control, requiring up-titration of dose or initiation of combination therapy.

In Clinical Practice, Shared Decision-making should be for Early Initiation of Combination Therapy in Newly Diagnosed Diabetics

Experts believe that considering the unique challenges faced by Indian patients, the “Hit it hard” strategy is necessary. Early combination therapy using OHAs with complementary mechanisms of action can alter the course of the disease, allowing for more extended periods of stable HbA1c levels, delaying the need for treatment intensification, and lowering the risk of chronic complications.

Patients with high HbA1c (9-10%) at diagnosis need dual therapy or a Fixed-dose Combination (FDC). Experts also report that it is better to switch to combination therapy rather than increasing the drug dose used in the initial monotherapy. Dual therapy with two different classes of medication provides the benefit

of complementary action. FDCs are known to increase adherence to therapy and reduce pill burden. Patients also achieve glycemic control at lower doses of individual components of the combination. One of the drawbacks of combination therapy is the higher cost to the patient, therefore shared decision-making is critical. To facilitate shared decision-making in India, where the time spent with each patient is limited.It is helpful to have an algorithm (Fig 2) to help facilitate discussion.

Identify Patient Profiles who could benefit from Metformin SR + Vildagliptin IR Combination Therapy

Most experts agreed that Metformin SR + Vildagliptin FDC therapy benefits patients with baseline HbA1c 1.5-2.0% above target with any of the following comorbidities: (a) diabetic end-organ manifestations, (b) cardiac or renal risk factors, (c) elderly patients d) obesity or undesirable weight gain. The experts also agreed that patients with T2DM who practice fasting during Ramadan or Navratra would benefit from this combination therapy. Patients with T2DM at high risk of hypoglycemia or intolerant to Metformin IR formulations can be given this combination therapy, according to experts. Finally, the experts agreed that patients with T2DM on Metformin and Vildagliptin combination therapy can also be switched to Metformin SR + Vildagliptin IR FDC therapy.

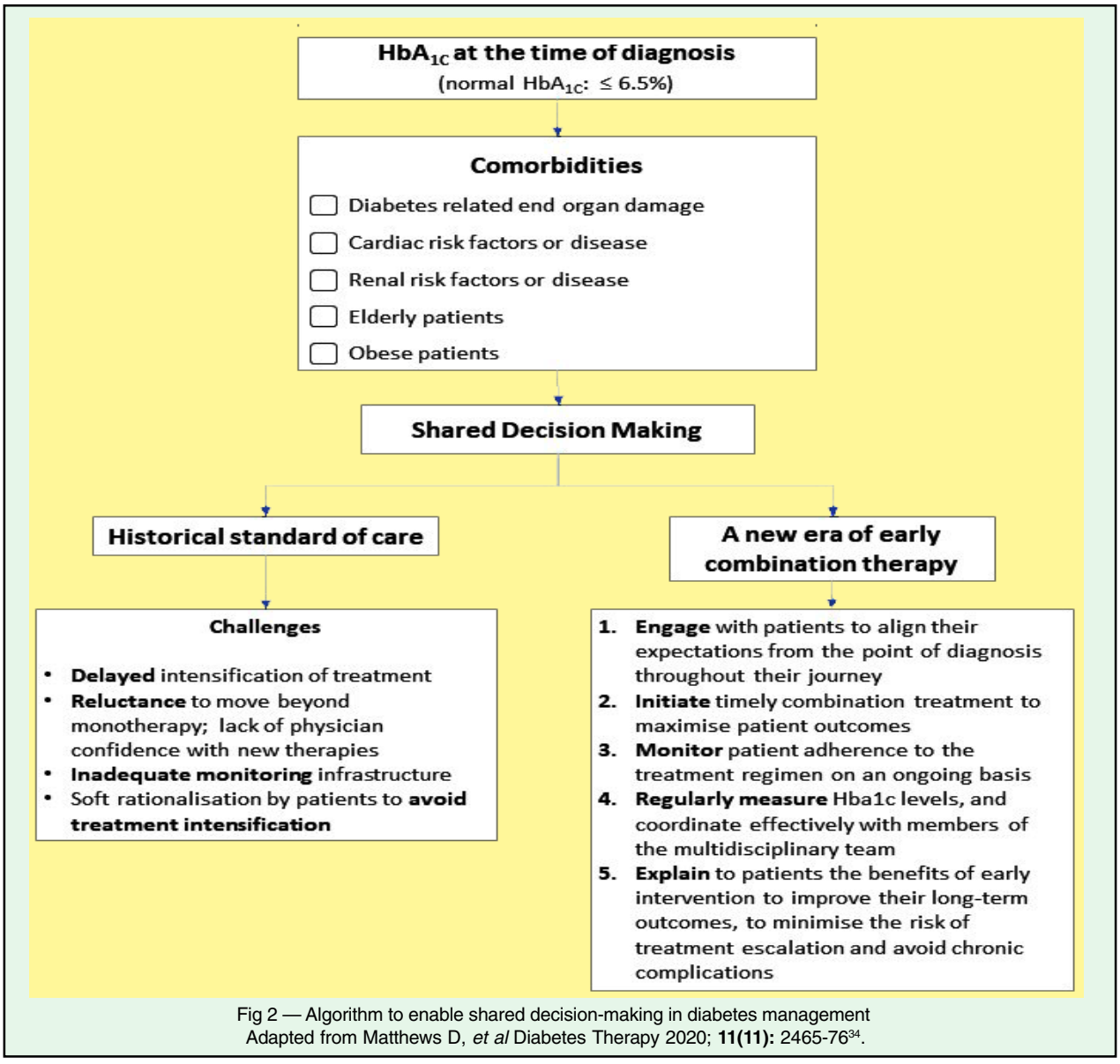

Fig 2 — Algorithm to enable shared decision-making in diabetes management
Adapted from Matthews D, *et al* Diabetes Therapy 2020; **11(11):** 2465-76[34].

Final Expert Opinion

- Combination therapy is required for sustained glycemic control in patients with type 2 diabetes mellitus.
- Early combination therapy could potentially alter the course T2DM, thereby providing longer periods with stable HbA_{1c} levels, delaying the need for therapy intensification, and reducing the risk of chronic complications.
- Initial combination therapy with Metformin Sustained Release (SR) and Vildagliptin Immediate Release (IR) Fixed Drug Combination (FDC) should be considered in:
  - Patients presenting with A1C levels 1.5– 2.0% above target,
  - Patients with any one of the below comorbidities:
    - # Patients with diabetic end-organ damage manifestations
    - # Patients with Cardiac or renal risk factors.
    - # Elderly patient
    - # Obese patients and patients in whom weight gain is undesirable.
- Diabetic patients who can be started or switched to Metformin SR + Vildagliptin IR Fixed Drug Combination (FDC):
  - Practice fasting during Ramadan or Navratra
  - Are at high risk for hypoglycemia
  - Are intolerant to Metformin IR formulations
  - Patients on Metformin and Vildagliptin combination therapy can also be switched to FDC.

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Drug Corner

Consensus Statement : The Need for Tobacco Harm Reduction in India

Shashikant Pawar[1], Subhrojyoti Bhowmick[2], Jijo Joseph John[3], Sunil Khetarpal[4], Jitendra Mohan Hans[5], Anirban Dalui[6], Shubhra Jain[7]

Cigarette smoking is a major public health issue in India and leads to significant morbidity and mortality. Addressing the issue of smoking is a major challenge to public health, as the addiction is hard to break. Counseling smokers regarding smoking cessation is the first step to achieving cessation, but the quit rates remain low. Several pharmacological interventions have been developed over the years. Nicotine replacement therapy is available in a variety of formulations, each with different advantages, drawbacks, acceptability among smokers and quit rates. In addition, a range of novel nicotine and tobacco products, including Heated Tobacco Products (HTPs), have been developed which leverage nicotine to aid in smoking cessation. A group of medical experts convened to review the evidence on the burden of smoking, the concept of Tobacco Harm Reduction (THR), novel nicotine and tobacco products for THR, and the potential of HTPs to aid in smoking cessation. This paper outlines the findings and recommendations regarding THR in the Indian context. The panel opined that tobacco cessation centers and counseling remain the foundation of tobacco cessation in India. At the same time, there appears to be potential for the application of THR products in India. The relevant authorities must review the potential of THR products, and make these available, to provide the best possible cessation strategy for the Indian population that is currently at risk of mortality and severe morbidity.

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Key words **: Cigarette smoking, Nicotine, Tobacco, Tobacco harm reduction, Heated tobacco products, Novel nicotine, Tobacco products.**

The epidemic of smoking looms large over the Indian population, with millions of adult smokers at risk of developing life-threatening diseases. Overcoming the nicotine addiction is the key to preventing morbidity and mortality associated with smoking[1]. Several modalities are available to aid in smoking cessation, including non-pharmacological and pharmacological therapies. These have varied acceptability among smokers, and varied efficacy of cessation and impact on risk of disease[2,3]. Over the years, a number of Nicotine Replacement Therapies (NRTs) have been introduced as smoking cessation aids[4]. In addition, a class of Noncombustible Nicotine and Tobacco Products (NNTPs) has been developed, which present lower health risks than conventional cigarettes[5]. A process of regulatory approval is required before introduction of any smoking cessation interventions, which follows a thorough review of the science of a given intervention. Products such as electronic cigarettes (e-cigarettes) and heated tobacco products (HTPs) are not approved for use in India, thus depriving the at-risk groups from potentially life-saving therapies. The consensus statement presented in this paper describes the opinion of Tobacco Harm Reduction (THR) products of a panel of experts, in the Indian context.

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Methodology :

A group of medical experts convened to review the evidence on the burden of smoking, the concept of Tobacco Harm Reduction (THR), novel nicotine and tobacco products for THR, and the potential of Heated Tobacco Products (HTP) to aid in smoking cessation. The HTPs are currently not approved for use in India. The group of experts reviewed the available evidence and presented their conclusions on the same. The objective was to discuss the current scientific evidence on novel nicotine and tobacco products to develop a consensus on potential of THR to alleviate the health burden faced by smokers.

Panelists :

The group included Dr Subhrojyoti Bhowmick (Clinical Director at Peerless Hospital & B K Roy Research Center), Dr Sunil K Khetarpal (Director, Association of Healthcare Providers), Dr Jijo Joseph John (Professor and Head of Department, Pediatrics,

Dean of Research, Believers Church Medical College), Dr Shubhra Jain (Assistant Professor, Chest and TB Hospital, Jaipur), Dr Jitendra Mohan Hans (Chairman & Director Dr Hans Centre for ENT and Cochlear Implant), and Dr Anirban Dalui (Public Health Specialist, Assistant Finance Secretary, Indian Medical Association, Bengal). The discussion was moderated by Dr Shashikant Pawar (General Manager, Dr L H Hiranandani Hospital).

FINDINGS AND RECOMMENDATIONS

- *Establishing a tobacco cessation center at every medical college including the district medical college is a useful approach to address the issue of counseling and should be made mandatory.*
- *Counseling of youth is a crucial aspect in reducing the dependence on tobacco. Towards this, counseling centers should be established which focus on preventing initiation of smoking among youth. Furthermore, the use of social media could also prove useful.*
- *Patients at high risk must be made aware of the need for smoking cessation and the risks of continuing to smoke. Regular follow-up of these patients is required to ensure continued abstinence from smoking.*
- *Stringent implementation of laws prohibiting smoking in public places should be taken up with the relevant authorities.*
- *Relevant authorities must review the potential of THR products, and make these available, to provide the best possible cessation strategy for the Indian population.*
- *Regulatory aspects regarding sale of tobacco products, such as high cost, should be addressed.*

THE SMOKING EPIDEMIC : INDIAN SCENARIO AND IMPACT OF SMOKING

India has the second highest burden of tobacco consumption in the world, second only to China. Tobacco smoking remains a significant concern, with nearly 100 million adults smoking tobacco, and over one million adult deaths attributed to tobacco consumption each year. The maximum prevalence among men is estimated to be 17.5% while that among women is estimated to be 1.2%[1,6].

Smoking is known to significantly impact health, causing more deaths from vascular, respiratory, and other causes than from cancer. Worldwide, the annual deaths attributed to tobacco smoking are 4-5 million, with over 1 million deaths attributed to tobacco smoking in India[6,7]. It is concerning that a majority of the projected tobacco-related deaths are from middle- and low-income countries such as India, and these countries are expected to carry the majority of the burden of tobacco-related deaths until 2035[7].

Tobacco is a potent carcinogen and is associated with cancers at various sites. Over 90% of lung cancers are due to tobacco smoking, with a risk ratio of 15-30. Similarly, the risk ratio for cancer of the urinary tract is 3, that of the pancreas, nasal cavity and liver is 1.5-2.5, and that of the kidney is 1.5-2.0. Alarmingly, about one-third of deaths from cancer are due to tobacco smoking. The risk of death from lung cancer is highest among current smokers compared with never smokers, and smoking cessation reduces the risk of death from lung cancer in an age-dependent manner[7].

A comprehensive analysis on the burden of tobacco use in India revealed a higher risk of all cause-mortality from smoked tobacco rather than smokeless tobacco (relative risk [RR] 1.67 *versus* 1.16 among men; RR 1.53 *versus* 1.30 among women).When analyzed by cause of death, the trend remained constant for deaths from Respiratory Diseases, Tuberculosis, Cardiovascular Disease (CVD), and cancer. Economic analysis indicated that smoked tobacco accounted for 78% of the total cost attributed to tobacco use, with higher costs reported among men than women. For all diseases attributed to smoking, the share of the cost was higher among men than women[8].

Conclusion :

Even after varied awareness campaigns and traditional nicotine replacement methods, the number of smokers is >100 million. What measures can be taken to improve individual and public health?

- As compared to the burden of tobacco smoking, there are very few tobacco cessation centers and counseling centers in India.The knowledge deficit regarding the harms of smoking, and addiction itself also play a role in the low rates of quitting. *Establishing a tobacco cessation center at every medical college including the district medical college is a useful approach to address the issue of counseling and should be made mandatory.*
- There is a need to address smoking among the younger population, and target prevention of initiation of smoking among the youth. The harms are noted in the long-term, and therefore, preventing the initiation of smoking is important. *Counseling of youth is a crucial aspect in reducing the dependence on tobacco. Towards this, counseling centers should be established which focus on preventing initiation of smoking among youth. Furthermore, the use of social media could also prove useful.*

- Counseling of patients at higher risk, such as those with Chronic Obstructive Pulmonary Disease (COPD) should be mandatory. *Patients at high risk must be made aware of the need for smoking cessation and the risks of continuing to smoke. Regular follow-up of these patients is required to ensure continued abstinence from smoking.*
- The Cigarettes and Other Tobacco Products Act (COTPA) is existent but is not implemented in mass gathering places. *The issue of stringent implementation of laws should be taken up with the relevant authorities.*
- There are several THR products available across the globe. These products are proven to be successful in achieving smoking cessation. *Relevant authorities must review the potential of THR products, and make these available, to provide the best possible cessation strategy for the Indian population.*
- Lastly, *regulatory aspects regarding sale of tobacco products, such as high cost, should be addressed*.
- THR can be an alternative to reduce the harm caused by smoking tobacco. The options available in India are limited at the current time. There is therefore scope for expanding the portfolio of available options to lower the risk of disease among the population of smokers in India.
- *Although the use of e-cigarettes is banned in India, it may be necessary to re-consider this decision. The availability of a THR product on prescription as a smoking cessation aid has the potential of achieving the target of reduction of the risk of disease.*
- *The evidence in favor of HTPs could be presented to regulatory authorities in India, for consideration as use as a smoking cessation therapy.*
- *There is a need to test HTPs in India to understand the efficacy, safety, and viability of use in the Indian population. To successfully carry out a study, the product must be in sustained use for a prolonged period, in order to evaluate the effects on the users and the community.*

TOBACCO HARM REDUCTION

Cigarette smoke is generated when tobacco is burned at high temperatures (600-900°C). This complex mixture consisting of solid particles and liquid droplets has over 6,000 known chemicals. There are several Harmful and Potentially Harmful Constituents (HPHCs) in cigarette smoke and are responsible for the development of chronic smoking-related diseases[9].

Tobacco Harm Reduction (THR) is considered to minimize the harm of exposure to tobacco. National Institute for Health and Care Excellence (NICE) defines Tobacco Harm Reduction (THR) as "reducing the illnesses and deaths caused by smoking tobacco—among people who smoke and those around them"[3]. The WHO Framework Convention on Tobacco Control defines "tobacco control" as a range of supply, demand and harm reduction strategies that aim to improve the health of a population by eliminating or reducing their consumption of tobacco products and exposure to tobacco smoke[10]. The concept of harm reduction is not new, and has been used in medicine and social policy in cases where hazardous behaviors cannot be completely avoided. This concept aims to minimize the harm to individuals and society when certain harmful behaviors cannot be prevented. In the context of tobacco, it is hoped that THR would allow smokers to gain some control of their addiction to nicotine[3,11].

This approach has gained traction in several countries, including USA, UK, Japan, and Sweden (among many other countries), where less toxic nicotine-containing products are available as alternatives to smoking. The purpose is to reduce death and disease caused by cigarette smoking. In fact, the use of snus in Sweden is a prime example of the potential of THR. The availability of snus has reduced the prevalence of smoking among males in Sweden, resulting in one of the lowest rates of smoking-related deaths across Europe[3].

Addiction to nicotine stems from nicotine content rather than tobacco. Regular cigarette smoking creates a pleasurable sensation mediated by the Central Nervous System (CNS), leading to nicotine addiction. When a person abstains from nicotine exposure for a few hours, withdrawal symptoms arise which sustain the nicotine addiction. To overcome this addiction, Nicotine Replacement Therapies (NRTs) have been developed which deliver steady but lower concentrations of nicotine. This allows for blunting of the pleasurable effect of nicotine and reduction of the intensity of withdrawal symptoms. Cigarettes rapidly deliver nicotine to the brain, thus creating an immediate pleasurable sensation. In contrast, NRTs deliver low levels of nicotine with a blunted pleasurable sensation[12].

While there are a number of approved NRTs, a major drawback across all the products is that nicotine is not delivered in the same way, nor at the same rate and dose as cigarettes. Additionally, the sensory cues and rituals associated with cigarette smoking are not replicated by NRTs, thus impacting user acceptance. There are also concerns among users that NRTs may become addicting, and doubts about the effectiveness and safety of these products. As with several medical treatments, premature withdrawal has been reported with NRTs as well, which affects the efficacy of these products[3,4,11].

Discussion :

Do novel nicotine and tobacco products have potential to improve individual and public health and manage the overall harm caused by consumption of conventional cigarettes? What are the potential options for adopting THR in India?

Studies have indicated the introduction of non-combustible tobacco products has reduced the consumption of combustible tobacco products, and thus it can be inferred that these products are acceptable to the users. It is necessary to separately consider nicotine (which causes addiction) and harmful byproducts (which cause diseases). Therefore, THR products should play a role as cessation therapy. While no product would be completely safe, the focus should be on the outcome (reduction of harm, and lower risk of disease). The panelists unanimously agreed that THR products will be useful. Although medical treatment has been available in India, these treatments are expensive and require a long duration. Furthermore, varenicline which is commonly prescribed has adverse effects and is expensive. Therefore, there is a need for less harmful products, as medication is not the solution. *THR can be an alternative to reduce the harm caused by smoking tobacco. The options available in India are limited at the current time. There is therefore scope for expanding the portfolio of available options to lower the risk of disease among the population of smokers in India.*

NOVEL NICOTINE AND TOBACCO PRODUCTS

THR products which are associated with low risk of disease include electronic cigarettes (e-cigarettes) and other vapor products, snus and low-risk non-combustible nicotine or Heated Tobacco Products (HTPs)[11].

- Snus is an example of a successful THR product, as the use of snus has progressively replaced cigarette smoking in Sweden (58% of daily tobacco users use snus), with consequent low mortality rates (reduction in mortality from 26% in 1990-95 to 10% in 2002-07 among men). Snus has the advantage of not producing toxic combustion products and Tobacco-Specific Nitrosamines (TSNAs), as well as having lower risks of cancer, CVD and all-cause mortality compared with cigarette smoking[11].
- E-cigarettes or electronic nicotine delivery systems are a safer alternative to conventional smoking. These products are battery-powered and resemble a cigarette in appearance and in the need for repetitive hand-to-mouth movement, as well as the visual cue of smoke-like vapor. Unlike conventional cigarettes, combustion of tobacco does not occur. Furthermore, e-cigarette vapor has substantially lower levels of potentially toxic compounds compared with conventional cigarettes. Maximum TSNA levels are 500-fold to 1,400-fold lower in e-cigarettes than conventional cigarettes. Formaldehyde, acetaldehyde, and acrolein (potentially toxic carbonyl compounds) have been detected in e-cigarette vapor in 12 brands of e-cigarettes but at levels substantially lower than in cigarette smoke[11].
  - Comprehensive toxicological analysis of e-cigarette vapor indicates that the use of e-cigarettes may lead to lower exposure to harmful constituents, as well as lower cytotoxic and mutagenic effects[13]. In fact, the health risks are similar to those of smokeless tobacco, which has 1% of the mortality risk of smoking. Data indicates that current e-cigarette use does not increase the risk of Myocardial Infarction (MI). Rather, the association between e-cigarette use and MI depends on the history of conventional cigarette use[14]. Modeling studies have estimated that switching from conventional cigarettes to e-cigarettes for 10 years could lead to 6.6 million fewer premature deaths and 86.7 million fewer life-years lost due to cigarette use[15]. With respect to smoking cessation, the use of e-cigarettes is twice as effective as NRT in helping smokers quit[16]. Harnessing the potential of alternative products may be effective in achieving THR[15]. E-cigarettes are not associated with increase in serious health concerns and can be considered a much safer alternative to conventional smoking[11].
- Conventional cigarettes involve the combustion of tobacco, wherein the temperature at the tip is 700-950°C during puffs. The generation of toxic components occurs at 200-600°C. This gives rise to the concept that heating tobacco to lower temperatures could prevent the generation of toxic chemicals. Heated Tobacco Products (HTPs) utilize this concept and apply controlled heating to uniquely processed tobacco. HTPs heat tobacco to a maximum of 350°C[9]. Studies have reported that exposure to HTPs as opposed to conventional cigarettes leads to lower risk of lung cancer and CVD, and lower exposure to HPHCs. Beneficial changes have also been noted in lipid metabolism, endothelial dysfunction and cardiovascular risk factors among individuals who switch from conventional cigarettes to HTPs[17]. Furthermore, after the introduction of HTPs in Japan, there has been a significant reduction in hospitalizations due to COPD and ischemic heart disease (IHD)[18].

Discussion :

Given the potential benefits of THR strategies, what measures can be taken to increase the awareness and understanding of harm reduction principles? Are any specific measures required to regulate the use of THR products among adolescents/youth, so as not to promote cigarette smoking, or use THR products as a stepping stone to cigarette smoking?

All forms of smoking cessation should be available in India as smoking is a lifelong disease that requires multiple treatment approaches. Smoking cessation strategies that are effective in other countries must be considered in India as well, so as not to deprive individuals of an effective solution.It is important to acknowledge the fact that cigarettes are the cause addiction and life-threatening disease, while THR products reduce the risk of disease.

Although the use of e-cigarettes is banned in India, it may be necessary to re-consider this decision. The availability of a THR product on prescription as a smoking cessation aid has the potential of achieving the target of reduction of the risk of disease. As per the regulatory requirements in India, the e-cigarette is a "device" and thus it cannot be bought directly by customers. Appropriate regulatory procedures could be applied to ensure that the products meet the desired quality standards, and the availability and sale of these products occur only based on a prescription. The aim of introduction of THR products is to aid in smoking cessation and reduce the risk of disease in individuals exposed to tobacco. *Simultaneously, awareness campaigns among youth to highlight that tobacco consumption in any form is harmful could be undertaken.*

INDEPENDENT RISK ASSESSMENT OF HTPs

Several countries (USA, UK, Netherlands, Japan, Germany) have assessed the evidence and generally conclude that HTPs may be less harmful than cigarettes. In a ruling by the United States Food and Drug Administration (USFDA), they state "the proposed products, as actually used, reduces a user's exposure to Harmful and Potentially Harmful Constituents (HPHCs) if they switch completely from combusted cigarettes to the HTPs. A measurable and substantial reduction in morbidity or mortality among individual tobacco users is reasonably likely in subsequent studies"[20]. Authorities in the United Kingdom concluded that "The available evidence suggests that heated tobacco products may be considerably less harmful than tobacco cigarettes and more harmful than e-cigarettes"[21]. The National Institute for Public Health and the Environment, Ministry of Health, Welfare and Sport, The Netherlands in an evaluation of e-cigarettes stated that "It may be concluded that the health risks associated with smoking conventional cigarettes are considerably higher than those associated with using e-cigarettes"[22]. There appears to be a general consensus that e-cigarettes and HTPs are less harmful than conventional cigarettes.

Discussion :

How can the evidence of evaluations from Government Agencies of other countries for HTPs be taken forward for developing regulatory strategies for THR in India? Based on the current ban on NNTPs in India, what are the important considerations for developing a policy-making document of THR? What measures can be taken to uplift the ban on NNTPs for THR?

It may be useful to conduct a detailed analysis of the conclusions of the agencies. Based on the findings, *the science of HTPs could be presented to regulatory authorities in India, for consideration as use as a smoking cessation therapy. In view of the lack of data from India, data from studies conducted in other countries could be presented.*

Is there a need for further studies demonstrating the reduced harm of HTPs or is the real problem a lack of awareness of the data? How can gaps in awareness be addressed?

There is information on the potential of HTPs from other countries, but studies from India are lacking, as these products are not available in the country. There is a need to test HTPs in India to understand the efficacy, safety, and viability of use in the Indian population.To successfully carry out a study, the product must be in sustained use for a prolonged period, to evaluate the effects on the users and the community. Furthermore, it is not ethically correct to carry out a randomized controlled trial. Nonetheless, if the manufacturer aims to conduct a trial in India, the relevant authorities must consider the dual outcome of aiding smoking cessation and reducing the risk of disease in individuals using tobacco. To achieve this dual outcome, the availability of effective, safe, and cost-effective products (whether pharmacological products or "devices" such as HTPs) that meet stringent quality standards and are available strictly under prescription for the purpose of smoking cessation, could benefit the community as a whole.

IMPACT OF NNTPs ON CIGARETTE SMOKING: EXPERIENCE FROM OTHER COUNTRIES

Japan is the largest consumer of HTPs, accounting for nearly 85% of the global market. The increasing market share of HTPs in Japan has led to a concomitant decline in annual cigarette sales, and a decline in aggregate consumption of tobacco products.

Nearly 70% of those who use HTPs in Japan have switched completely to HTPs, with dual use noted only in 9% of tobacco users. The introduction of HTPs led to a decline in cigarette smoking. Furthermore, usage among the youth remains low (0.1%). HTPs have a low impact on the use of tobacco by never-smokers (0.5%) and re-initiation by former smokers (<0.1%) in Japan. Similar data has emerged from UK as well[19].

Discussion :

How can a balance be formed between heavily regulated nicotine pharmaceuticals and THR products, and unregulated tobacco products?

Cost is expected to be a major factor impacting the use of such alternative products. While the cost may initially be high, it is expected that a competitive market of HTPs may lead to reduction in costs. The HTPs would be available only on the prescription of a registered medical practitioner for the purpose of smoking cessation in an individual who aims to quit smoking. The products would be classified as "devices", and hence would not be available for purchase without a prescription. It follows that the quality and composition of the product would be strictly regulated, unlike the tobacco products available in the open market.

SUMMARY

The road to smoking cessation is marred in controversy on the potential for misuse of smoking cessation therapies. While the panel acknowledges that the THR products in question carry the potential for misuse, the benefits of introduction of these products in India cannot be denied. In the context of cigarette smoking, the ideal is complete cessation, and the objective of harm reduction can be achieved with the use of multiple approaches. Towards this, several NRTs and other products have been developed over the years, with varying efficacy in achieving sustained cessation. The products must not only be effective, but also acceptable to the users, to ensure appropriate use for the desired duration, to achieve the required outcome. Novel nicotine and tobacco products such as electronic cigarettes have demonstrated considerable efficacy over NRTs and have a lower risk of disease. Several countries have adopted these products for the purpose of smoking cessation. In light of the evidence of reduction in disease and the toxicological studies, it would be useful to consider THR products for use in India. Given the burden of tobacco smoking and the consequent health effects, it is necessary to make available the most effective products as smoking cessation therapies. There is hope that the evidence on THR products can be reviewed objectively by the relevant authorities, so that the individuals currently at increased risk of potentially life-threatening disease could benefit from a policy change that grants them an alternative smoking cessation aid that could improve the health of the individuals using it and the community.

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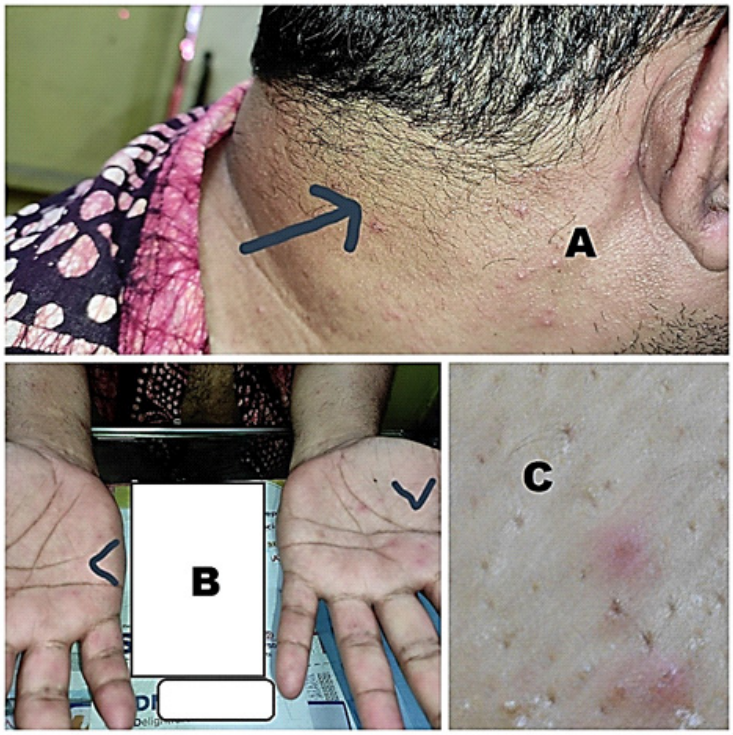
Pictorial CME

A Man with Rash

Rudrajit Paul[1]



A 30-year-old man came to the OPD with a sudden onset rash (Fig 1) on his hands (arrowhead), feet and neck (arrow). The rash was tender. Panel C shows closeup of the rash. He also complained of severe sore throat with mild fever. His son had recently been afflicted with similar symptoms.

(1) What is the most likely diagnosis?

(2) What is the causative agent?

(3) What are the other types of rash in this disease?

(4) What is a close mimicker of the oral lesion?

Answers : -

(1) The typical morphology and distribution of the rash, along with history of contact is suggestive of hand-foot-and-mouth disease, a contagious viral illness. There has been recent resurgence of this infection in Eastern India.

(2) This viral exanthem is most commonly caused by Coxsackie virus A16 and Enterovirus A71.

(3) As panel C shows, the commonest type of rash in this case is a macule or papule surrounded by a zone of erythema. In children, the rash is typically not painful. But in adults, as in our case, the rash may be tender. The other type of rash isvesicular, which may rupture to form superficial ulcers, which heal without scarring. Oral lesions, located on lips, tongue or buccal mucosa, are usually painful, as in our case. Also, although the disease is named "hand-foot-mouth", in adults, the distribution of the rash may be more extensive.

(4) One closely related disease, caused by the same family of enterovirus, is Herpangina. The differentiating point is, in herpangina, the exquisitely tender oral lesions are located in posterior soft palate and pharynx.

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Image in Medicine

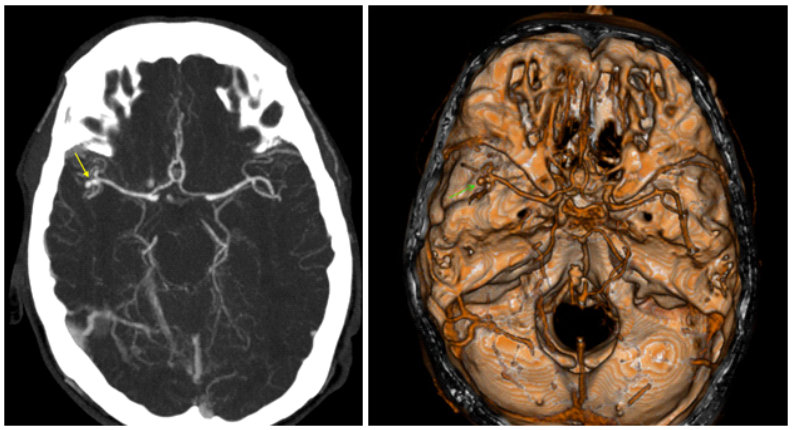
Bhoomi Angirish[1], Bhavin Jankharia[2]

Quiz 1

CT Brain Angiogram images of a 42-year-old Female Patient who presented with Headache.

Questions :

(1) What is the diagnosis?
(2) What are the common locations?



Answers :

(1) Well defined round outpouching is seen from the junction of M1-M2 segment of right middle cerebral artery suggestive of saccular cerebral aneurysm.

(2) The common locations of cerebral aneurysm are:

Anterior circulation : more common

a) Anterior cerebral artery /Anterior Communicating artery

b) Supraclinoid Internal carotid artery and ICA/Posterior Communicating artery junction

c) Middle cerebral artery (M1/M2 junction) bi/trifurcation

Posterior circulation :

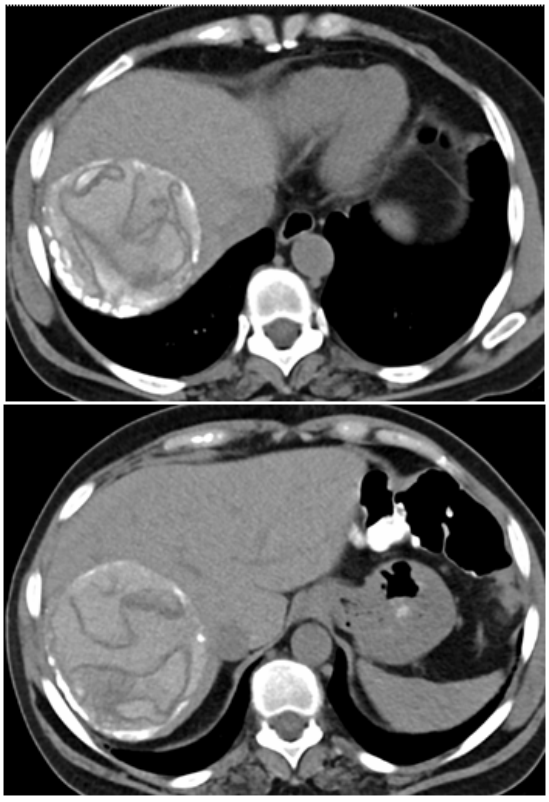
d) Basilar tip e) Superior cerebellar artery f) Posterior inferior cerebellar artery

Quiz 2

CT Scan Images of a 28-year-old Male who presented with Abdominal Pain since 5 months.

Questions :

(1) What is the diagnosis?
(2) Name the signs of ruptured endocyst.



Answers :

(1) Well defined partially calcified cystic lesion with internal hyperdense contents and multiple curvilinear serpentine membranes is seen in right lobe of liver , these imaging findings are suggestive of hepatic hydatid cyst.

(2) A) Serpent (snake) sign: Wavy membranes within the cyst.

B) Spin (whirl) sign: Twisting membranes within the cyst.

C) Congealed water lily or ball of wool sign: Solid conglomeration of membranes settled in the dependent portion of the cyst.

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Student's Corner

Become a Sherlock Holmes in ECG

M Chenniappan[1]

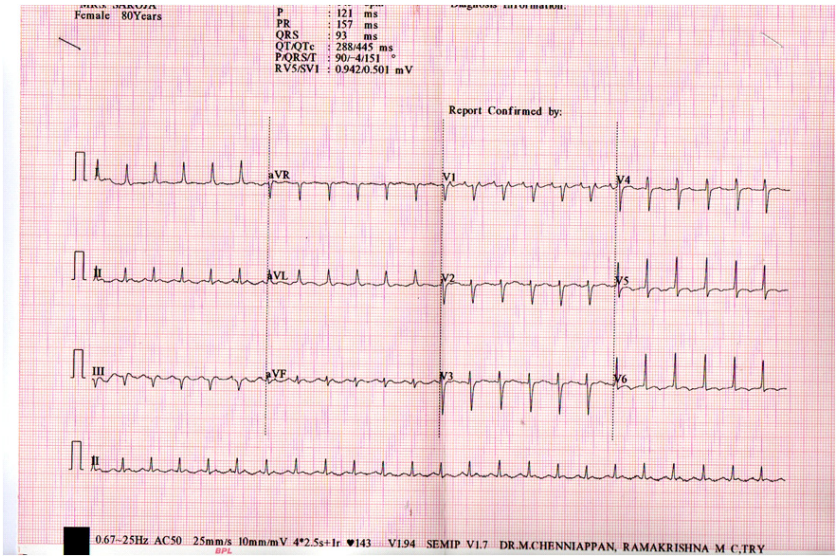
Series 11 :

"Massage to Unmask"

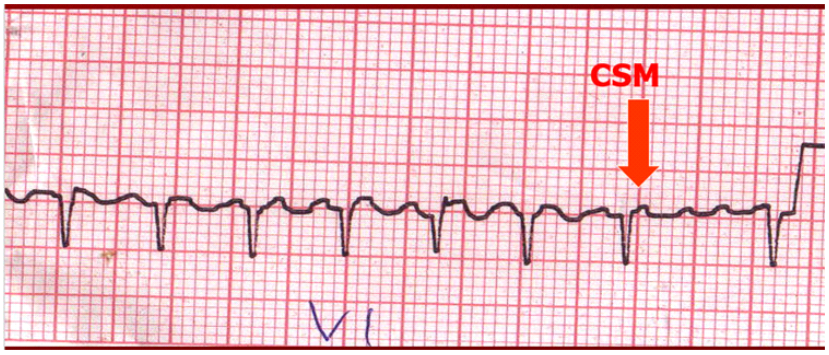
This is the ECG of 80 years old female with intermittent palpitation (ECG-1)

Questions :

(1) Describe the ECG Finding?
(2) Why is this Clue?
(3) What is Practical Implication?



ECG 1



ECG 2 — The last portion of this strip shows rapid blocked P waves confirming atrial tachycardia

Answers :

(1) The ECG Findings :

This ECG shows narrow QRS regular tachycardia. Each QRS is preceded by p wave which mimics sinus tachycardia. There seems to be another P wave at the end of QRS which means that atrial rate is almost 286/mt. So this is atrial tachycardia with 2:1 AV block. But it is difficult to differentiate between sinus tachycardia and atrial tachycardia with 2:1 AV conduction. That's why some other maneuver is necessary to confirm the diagnosis of atrial tachycardia with 2:1 AV block.

(2) The Clue :

Whenever there is confusion about sinus tachycardia vs atrial tachycardia it is preferable to employ a vagal maneuver to delay the AV conduction. The simple bedside vagal maneuver is carotid sinus massage (CSM). If it is sinus tachycardia there will be gradual slowing of sinus tachycardia as long as the massage is applied; once the massage is stopped, the original rate is restored. If it is atrial tachycardia, due to increase in A.V. nodal refractory period, more p waves are blocked resulting in long R-R interval within which we can see rapid, blocked p waves, confirming the diagnosis of atrial tachycardia. Hence the clue "massage to unmask" is given. The ECG of this patient after CSM is given (ECG-2) which shows rapid blocked P waves due to long R-R interval produced by CSM.

(3) Practical Implication :

If this ECG is diagnosed as sinus tachycardia, active intervention may not be necessary other than treating underlying cause. If atrial tachycardia is diagnosed by CSM active intervention like cardio version or pharmacological intervention is needed to covert the rhythm to normal sinus rhythm or controlling ventricular response.

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Letter to the Editor

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

What they didn't teach us in Medical College — An Indian Perspective

Sir, — In the last four decades the world has changed beyond recognition and so has the world of doctors, but the question is ' has the medical education changed too'? With an exploding population and enhanced awareness because of the internet,a doctor today is expected to know many new things and develop many new skills which the past medical students perhaps never required to master. There isa huge set of skills that they still don't teach students in medical school, and they are expected to pick them up by osmosis from unsubstantiated sources. Needless to say, these medical students miss these skills dearly all their lives. The science of medicine is important, but the art of medicine can no longer be ignored. A renewed emphasis is today needed on the professional aspect of medicine, rather than catering only to the knowledge basefor a doctor to be maximally useful to the society. We have tried to enumerate all these skills, which a doctor should have but the busy medical curriculum leaves no time for them.

Biostatistics & Data Science :

Today's doctors are jotting notes on an iPad and navigating various electronic medical record systems. Medical practices and hospitals are generating and dealing with a deluge of data. Smarter and smarter software's are being to record this data. But none of the medical students knows why they are generating this data or equipped enough to use them or understand the data fully. The aim is to connect the collected data to patient outcome to understand the disease and improve treatment. This is the road to 'Evidence based medicine' form the less accurate 'Eminence based medicine'.

From good data, protocols are developed and if the designed are implemented properly, it saves patients' lives and good data generate good protocols[1]. Standardization of the steps in routine patient care that do not utilize physician intellect frees up time to focus on actually practicing medicine. If everyone has a different way to treat a disease, say Hypospadias, for which there are over 300 surgeries, and each surgeon can't all be doing it the best way! By following protocols two things happen - quality of health care goes up and costs go down giving rise predominantly to evidence based medicine.

Information technology 101 :

Doctors are increasingly using technology in their practices, whether it's to record notes or store patient data in an electronic medical record[2]. Some doctors are using the newest telemedicine tools to consult with patients online. Almost all medical journals are today available online and conferences held continents apart can be attended and webinars conducted on handheld electronic devices. So why are medical graduates not being taught to use information technology both for their own education as well as for patient care?

Communication skills :

Doctorsneed to be nice people and doctors need to be nice to people too and for that good communication skills is mandatory[3]. What to say, whom to say, when to say and how to say cannot be left for chance. The most effective doctors understand how to communicate with patients. That doesn't mean rattling off a diagnosis and sending them home. It requires picking up on the subtle indications that a patient has not understood something or is too upset to take in information.

Only 35% of communication is verbal and the remaining 65% involves facial expression, tone of voice, movement, appearance, eye contact, gesture, and posture! A consultation involves listening, writing, presenting, negotiating, influencing, and finally establishing a professional relationship. The crux is who should be teaching the medical students all this, and the reply is obviously a communication expert who need not be a doctor.

Personal Finance :

The medical profession may be a gold mine for some, but majority of the doctors are poor in managing personal finance. Outlandish lifestyle and block-buster success stories, owning palatial mansions, fancy speed boats, helicopters and airplanes are usually anecdotaland not the rule. The reality is that too many of the doctors are in debt, paying too many EMIs and as a result, cannot afford to retire when they should. It's now imperative that doctors learn to manage their money, or they risk drowning in debt. Recent medical school graduates could benefit from some formal education about how to use the latest web and mobile tools to manage their finances. The present generation feels that investment managers and property dealers usually take them for a ride because of their ignorance of the subject. From personal finances, to dealing with loans, to contract negotiation to basic skills involved in setting up a practice, there is no formal education in medical schools.

Teaching skills :

A doctor will remain an educator all his life. Whether he is a resident or a medical educator or a consultant or a family physician he has to impart the knowledge of good health. Teaching is such an invaluable skill for the doctors. Butare oblivious about the difference between adult or child learning and what is worse, we don't even know how to keep on learning ourselves! As a teacher one wears many hats - a communicator, a disciplinarian, a conveyor of information, an evaluator,a classroom manager, a counselor, a member of many teams and groups, a decision-maker, a role-model, and even a surrogate parent. Unfortunately, the doctors are not trained for any one of these!

The four core qualities are essential for teaching are knowledge, the skills to convey that knowledge, the ability to make the teaching material interesting and relevant, and a deep-seated respect for the student.Except the first none of the other three are taught in medical colleges. And all this is an established science today supported by information technology.

Management and Entrepreneurship :

Doctors need to be taught how to run a business, the basics of money, the basics of running a hospital or clinic, the realities of the world of taxes and how to be competitive and yet commercially viable. A very unfortunate reality is that when it comes to financial stability, it takes a long time for the Doctor of Medicine who has been in school for at least 8 years! The business of medicine is not

taught in medical school, and sadly, that is where the money is. Some courses in business management and entrepreneurship specially tailored for medical students need to be a part of their curriculum.It is estimated that India needs about 6,00,000-7,00,000 additional beds over the next five to six years - indicative of an investment opportunity of $25-30 billion[4].

Leadership and Man Management :

Doctors are often placed in leadership roles even in their residency years. Doctors have torun teams of interns, coordinate with other physicians and nurses, conduct multi-disciplinary planning sessions and align families around shared treatment goals. And yet there is almost no training on how to succeed in the working world! Man management involves managing oneself, managing communication, managing relationships and managing teams. It is a complex interplay and very difficult to pick up if not properly taught. Doctors can be benefited from basic management skills - delegating work, providing feedback, motivating others, and collaborating with other teams. They could use training on how to lead a room full of people with different roles, experiences, and emotions, especially in the trauma emergency. A medical graduate needs to know how to interact with juniors, seniors, teachers, nurses, ministerial staff, patients, relatives, administrators, Class IV employees.

Time management :

Time is our most precious asset and yet right from the medical college days , majority of the doctors fail to respect it. It is known that 20 percent of patients consume 80 percent of healthcare resources and our energy. In medical colleges, the medical professionals spend 80 percent of their time on 20 percent of diseases, including a litany of esoteric rare disorders that are academically illuminating but most clinicians will never see in their entire careers. The medical professional does not need to know about rare, complex and difficult to pronounce syndromes and fancy investigations being done in laboratories nowhere near their practice, but they need to know how to manage dementia, manage pain thoughtfully and assess patient safety. The biggest gap in 21st century medical training is a lack of old-school skills, and not high-tech coding. Thankfully we, the past generation were taught clinical signs[5] which have been replaced today by a battery of investigations. Picking uppapilledemais far quicker way of diagnosing raised intracranial tension than a CT scan. In a study from India, more than two-third of the students were found to have poor to average time management skills[6].

Research skills :

If India still remains a developing country despite being the fastest growing economy in the world, then it is because we lack research skills. A medical graduate is expected to understand:

- how to critically read a research article?
- how to cite sources and find good articles?
- how to understand basic statistics?
- how to get a research grant?
- how to get ethical clearance for clinical trials ?
- how to train in GLP – good laboratory practices?
- how does one start a lab and get funding?

The medical graduates,in most Indian colleges, don't even know what a career in research looks like and how does it even start!

Nutrition, Fitness and Disease prevention :

Though the doctor spends a lot of time studying Social & Preventive Medicine but how much of that is brought to clinical use? What proportion of the consultation time is spent on conveying the message of nutrition, fitness and disease prevention? Lifestyle diseases drive some of the biggest costs in healthcare and have some of arguably the biggest impacts on patients' lives but how many of us find ourselves adequate enough to discuss about lifestyle changes, nutrition, and exercises to our patients?[7] Keeping people healthy is far easier and cheaper than treating them when they are sick. In a study from University of Florida, it was highlighting the need for significant improvement in education of physicians about nutrition and physical activity and need for physicians to focus on good personal health behaviors, which may potentially improve with better education[8].

Biotechnology :

The medical community need not know the entire subject, but they at least need to know how the instrument in their hand works and what can be done to prolong its life? Whether it is X- Ray, CT Scan, MRI, Lasers, or Endoscopes, Medicine is surrounded by technology and ever changing ones. How long can one keep on wearing blinkers and relying on company engineers? They think the doctor are too demanding, don't understand machines and the doctor think they don't understand our demands and make machines first and then start searching for their use. This dichotomy can only be solved if the medical professionals become more tech savvy and make way to the boardrooms of these medical technology companies. Interestingly enough Texas A&M University has plans to create such a program in creating "Physician Engineers"[9].

Ethics :

Is it not an irony that the first time a medical student hear about it is when the thesis proposal goes to the Institutional Ethics Committee? Though the introduction to bio-ethics should start in 1st. Semester and go right up to the end of stay in the medical college with booster doses at every stage of MBBS or postgraduate education, it is hardly ever discussed as a subject. The topic can be taught as didactic lectures, group discussions- knowing another student's thought process, case presentations – review different ethical cases and seminars –with different sections of the society – judiciary, teacher, journalist, home maker, hospital owner and so on. The purpose is to make the budding medical doctors passionate about ethical medicine[10].

Health policies and Health Insurance :

This freaks out most doctors. They feel they should have a say in the formulation of health policies of the government, but they know nothing about it. Doctors are not taught how health policies are formulated and how they are brought into action. They are unaware of how they are lobbied for and how to make changes in them. The doctors think black ribbons, candlelight marches and strikes are the only weapon .

Very few of the medical professionals understand how different health insurance schemes work and end up burning their fingers by treating diseases and patients not covered by insurance and not getting remunerated at the end of the day! Doctors are never taught how expensive different medications are, how patients get billed, how can they lower costs for patients in general. Doctors don't even know the different policies, restrictions, and costs it takes to run a clinic or hospital. They are not market ready! Every doctor should be aware of 4 insurances - ***Professional***

Indemnity Insurance,Personal Accident Insurance, *Property Liability Insurance and Public Liability Insurance*[11].

Humanities:

The "humanistic" side of medicine is routinely ignored in the Indian medical institutions as they are 100 % geared towards the "scientific" side of medicine. Bedside manners are neither taught nor tested. Manners are easy to teach to a kid and very difficult to a 20+ year old. The purpose is to change in a manner that is amenable to what patients want in their doctors and change according to the patient's beliefs and religious and social compulsions. When a procedure goes fine, a good bedside manner can be a luxury. When serious complications arise, empathy and communication can be the difference between acceptance and a dangerous false hope[12].

Patient's place a lot of importance on the way a doctor interacts with them. If they can travel miles and wait for hours, they have every right to expect quality time during consultations, uninterrupted by ringing phones and barging in nurses and technicians.

Sustaining empathy for the patients and providing encouragement to them at all times while not keeping them in the dark about the prognosis is absolutely non-negotiable. No problem, however trivial it may sound, can be dismissed without giving due attention. The doctors are overburdened but it's not the patient's fault! Spoken words should be carefully chosen and the medical community should be taught this art. Patients being berated for being overweight or noncompliant or smelly or difficult areabsolutely unacceptable. They may repeat, recall and really take to heart….so they need patience and encouragement!There is again a lot of patience and hand holding involved in this art of communicating a poor prognosis, a complication, news of an impending amputation of limb or worst of all, death. Even telling a new mother that her newborn has to stay an extra day because of jaundice can be difficult. 90% of the time, even this little disappointment results in tears. Are the doctors trained to handle this?If not then they will have to face emotional outbursts.

Taking care of ourselves :

The doctors are expected to give – time, effort and energy and keep on giving…….But they should not give so much of themselves away that patients, whom they once enjoyed treating, become burdens and the doctors become empty shells. The doctors need hobbies and interests and days off and vacations and permission to breathe sometimes. Doctors need family time and crazy friends and people around us who let us just be a mom/dad or a wife/husband or a referee in a football game. They need people who don't keep putting us on an impossible pedestal and who allow us to be humans. In a study from India, the pooled prevalence of burnout was 24% in the emotional exhaustion domain, 27% in the depersonalization domain, and 23% in the personal accomplishment domain. Younger age, female gender, unmarried status, and difficult working conditions were associated with increased risk of burnout[13].

Conclusion :

Good communication, patience and encouragement prepare our patients for our imperfections. While the science of medicine is invaluable and is being both taught and updated with time, the art of medicine is lagging behind as our medical education it too science heavy. Thanks to the internet, the savvy patient often knows what his/her disease is and smart medical apps will soon offer treatment too, but it will not be able to offer empathy, comfort and understanding. Are the doctors of today offering the same? Or are they in a mad rush jotting online forms, getting irritated by huge patient load and suffering early burnouts? With time our medical education must change and our doctors, the product of that education, must be market ready for all eventualities.

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ABBREVIATIONS USED

(C) Correspondence, (CR) Case Report, (DC) Drug Corner, (Ed) Editorial, (IM) Imaging in Medicine, (MH) Medical History, (OA) Original Article, (PCME) Pictorial CME, (RA) Review Article, (SC) Student's Corner, (SA) Special Article, (Spl C) Special Correspondence, (VE) Voice of the Expert

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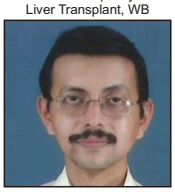
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