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Launching UJMS: Where do we go From Here?

PIYUSH GUPTA

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Starting a scholarly journal is no mean feat for an academic institution. With the launch of this inaugural issue of “UCMS Journal of Medical Sciences (UJMS)”, University College of Medical Sciences (UCMS) reinforces its position as an elite medical institution with an in-house journal. The journal is another cog in the wheel of continued learning which is the spirit of UCMS. In addition to providing a nurturing environment for research, we plan to increase scholarly publishing by providing a platform to enable our researchers to showcase their academic potential. This would allow them to take their research work to its logical end-point in addition to giving them better career opportunities and secure funding for further research. UJMS aims to further our commitment to pragmatic and integrative learning across the curriculum. The open access format adopted by the digital version of UJMS is in alignment with the principle of providing a free platform for dissemination of research.

The scope of UJMS has been kept broad to cover all medical specialties while allowing dissemination of academic content for increasingly targeted or specialized readerships. *Health Humanities* section has been added in the journal to give a new dimension which draws on creative and fine arts to add altruistic touch to healthcare and well-being. UCMS has always been a robust MBBS campus, hence, a *Student's Voice* section is our endeavour to empower the students to co-lead the institution by

collaborating with faculty and peers. Additionally, it helps students to hone their leadership capabilities and shape their educational experiences.

We must remember that “Rome wasn’t built in a day” and likewise sustaining a journal is a major commitment and requires passion, dedication, motivation and hard work on part of all stake holders. Regular submission from faculty and students is the most crucial element for running a journal. The seniors need to hold hands of their juniors and guide them in not only initiating research but also to take it to its logical end-point of publication. A vibrant editorial board provides both energy and oversight for the content. A robust peer review process adds credibility to the journal. Additionally, institutional support in the form of funding, logistic support in the form of manuscript submission and plagiarism check software, supportive staff, and office space are needed. Indeed, an army marches on its belly!

Many logical questions and apprehensions follow any major project. All authors justifiably wish their work to be suitably cited and indexed. This process has its own path, and I have personally felt that biomedical researchers should have material suitable for all levels of presentation, starting from the basic rounds, the local newsletter, and culminating in high-value internationally indexed work. Hope we get there soon as a close team!

Comparison of Metabolic Profile of Lean and Obese Patients with Type 2 Diabetes Mellitus

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ABSTRACT

Background: Obesity induced insulin resistance has long been used to explain the development of type 2 diabetes mellitus (T2DM). However, it cannot be used to explain the development of T2DM in lean individuals. Given the lifelong morbidity associated with T2DM and its sequelae, it is necessary to properly understand the disease process. Therefore, this study was designed to compare the physical and biochemical parameters in lean and obese patients of T2DM.

Materials and Methods: We included newly diagnosed patients of T2DM and categorized them as lean (BMI < 18.5 kg/m²) and obese (BMI > 25 kg/m²) individuals; 30 patients in each of the two groups. Routine biochemical parameters such as fasting blood glucose (FBG), 2-hour post-prandial blood glucose (PPBG) and lipid profile were estimated using autoanalyzer. Glycated hemoglobin (HbA_{1c}) levels were estimated in whole blood using BIO-RAD D-10 autoanalyzer. Serum insulin was measured by ELISA.

Results: Glycemic parameters (FBG, PPBG, and HbA_{1c}) were higher in the lean group compared to the obese group. Dyslipidemia was present in both groups but was worse in the obese group. Fasting serum insulin levels were higher in the obese group compared to the lean group. Atherogenic index of plasma was high in both groups.

Conclusion: Hyperglycemia was greater in lean compared to obese T2DM patients predisposing them to a greater risk of hyperglycemia induced cellular damage. Dyslipidemia was present in both the groups but was worse in the obese patients.

Keywords: Fat, Glycemic parameters, Lipid profile, Obesity, Thinness.

INTRODUCTION

Diabetes mellitus (DM) is defined as a group of metabolic diseases characterized by hyperglycemia, resulting from defects in insulin secretion and/or insulin action.¹ The incidence of DM continues to rise with the International Diabetes Federation (IDF) projecting a steep rise in the caseload of Type 2 Diabetes Mellitus (T2DM) by the year 2045.² The rise in cases of T2DM has been linked to the obesity pandemic in the developed world.^{3,4}

Although majority of T2DM patients are obese (body mass index, BMI > 25 kg/m²), 10-20% of patients of T2DM are non-obese or lean (BMI < 18.5 kg/m²). The proportion of lean patients with T2DM is higher in developing countries compared to developed countries.⁵ However, the exact etiopathogenesis of the disease in lean individuals is yet to be elucidated as the model of obesity induced insulin resistance does not hold true in these patients.

Most of the studies done till date solely focus on obese patients of T2DM. The very few studies done in

lean T2DM patients have certain limitations namely difference in the methodology and analysis (for example, use of different BMI cut-offs for leanness, treatment status of the patients) which makes their comparison with studies done in the obese group difficult.^{6,7}

A high prevalence of cardiovascular-related morbidity and mortality in T2DM and associated dyslipidemia, warrants early diagnosis and management in order to prevent these complications. Keeping this in mind the current study was designed to compare the physical and biochemical profile of newly diagnosed lean and obese patients with T2DM at diagnosis prior to initiation of pharmacotherapy.

MATERIALS AND METHODS

This descriptive study was designed and conducted in the Department of Biochemistry and Endocrinology of University College of Medical Sciences and Guru Teg Bahadur Hospital, Delhi. Prior approval of the Institutional Ethics Committee for Human Research (IEC-HR/2019/41/25) was obtained.

Newly diagnosed, age and sex matched patients of T2DM belonging to the age group of 20-65 years, who were not on any pharmacotherapy for T2DM, were recruited from the out-patient clinic of endocrinology department after obtaining a written informed consent. The diagnosis of T2DM was made as per WHO criteria.⁸ The patients were divided into two groups – lean (BMI <18.5kg/m²) and obese (BMI >25kg/m²) based on Body Mass Index (BMI) as per WHO Asia-Pacific Guidelines.⁹ Other causes of lean diabetes such as diabetes arising out of pancreatic insufficiency (secondary diabetes), and type 1 diabetes were excluded based on history, clinical examination and laboratory findings. Lean patients of T2DM were recruited first, followed by obese patients. Given the fixed duration of the study (18 months and the low frequency of lean patients (newly diagnosed) of T2DM, 30 patients were enrolled in each group. Patients with renal and hepatic disorders, severe co-morbid illnesses, thyroid disorders, chronic alcoholics, and pregnant and lactating women were excluded from the study.

A detailed history was taken from the patients recruited in the study, which was followed by a clinical examination and anthropometric measurements as per standard guidelines.¹⁰ Fasting blood glucose (FBG), 2-hour post-prandial plasma blood (PPBG), and lipid profile were estimated using RANDOX RX Imola autoanalyzer, (RANDOX, UK) as per the instructions of the manufacturer. HbA_{1c} levels were estimated in whole blood using BIO-RAD D-10 autoanalyzer (BIO-RAD, USA) as per the instructions of the manufacturer. Fasting serum insulin level was estimated by sandwich ELISA (DRG International, USA) following the protocol provided by the manufacturer [sensitivity: 1.76 µIU/mL; precision: intra-assay 2.8%, inter-assay 5.99%]. Atherogenic Index of Plasma (AIP) was calculated using the formula $AIP = \text{Log} [\text{Triglyceride}/\text{High Density Lipoprotein-Cholesterol}]$.¹¹

Statistical Analysis: Statistical analysis was carried out using SPSS version 26.0 (IBM Corporation, USA) software. Biochemical parameters such as fasting serum insulin, fasting plasma blood, 2-hour plasma blood, HbA_{1c} and lipid profile were compared between the groups by the unpaired student t-test or Mann-Whitney U test. P value less than 0.05 was considered significant.

RESULTS

Out of the 30 patients in each group, 8 (26.7%) were female and 22 (73.3%) were male in both groups. **Table I** shows the demographic characteristics of the study participants.

Out of the 30 patients in the lean group, there was

TABLE I. Physical Parameters in Lean and Obese Patients of Type 2 Diabetes Mellitus

Variable	Lean (n=30)	Obese (n=30)
Age (years)*	52.1 (±10.7)	51.5 (±10.4)
Male sex#	22 (73.3%)	22 (73.3%)
BMI (kg/m ²)*	17.9 (±0.9)	27.2 (±2.7)
Percentage body fat (%)*	22.1 (±5.9)	36.0 (±5.8)

*Expressed as mean (± SD); # Expressed as n (%).

positive family history of diabetes in a total of 7 (23.3%) patients. Out of these 7 patients, 2 had the presence of T2DM in both parents while 3 had only maternal history of T2DM and 2 had only paternal history of T2DM. In the obese group, out of 30 patients recruited, 12 (40%) reported a positive family history for T2DM. Out of these 12 patients, 3 had both parents suffering from T2DM, 5 had only maternal history and 4 had only paternal history of T2DM

Routine biochemical parameters were comparable between both groups. Glycemic parameters and lipid profile values are depicted in **Table II**. As seen in **Table II**, dysglycemia was worse in the lean group and dyslipidemia was worse in the obese group at diagnosis.

DISCUSSION

Diabetes is characterized by hyperglycemia and tends to be accompanied by dyslipidemia.¹² In this study we compared the glycemic parameters and lipid profile in newly diagnosed lean and obese patients of T2DM.

Glycemic status at diagnosis was worse in the lean group compared to the obese group. A significant difference was seen in the mean fasting blood glucose levels between the two groups. Post-prandial blood glucose level was also higher in lean patients of T2DM as compared to obese patients but the difference was not statistically significant. Glycated hemoglobin (HbA_{1c}) levels also followed the same trend as blood fasting glucose levels with a highly significant difference between the two groups. Conflicting reports exist on the glycemic parameters in lean and obese patients of T2DM mainly due to the non-uniformity in BMI cut-offs used which makes comparison of these studies difficult. Coleman, *et al* reported a worse glycemic status in lean patients (BMI <25 kg/m²) of T2DM compared to obese patients (BMI >30 kg/m²).¹³ Asegaonkar, *et al* reported a higher FBG level in obese patients (BMI >25 kg/m²) of T2DM compared to lean patients (BMI <25 kg/m²).¹⁴ Bautista, *et al* reported higher values of glycemic parameters in obese patients (BMI >25 kg/m²) of T2DM compared to lean patients (BMI <18.5 kg/m²).¹⁵

TABLE II. Glycemic Parameters and Lipid Profile in Lean and Obese Patients of Type 2 Diabetes Mellitus

Parameter [mean (\pm SD)]	Lean (n=30)	Obese (n=30)	P value
Glycemic parameters			
Fasting blood glucose (mg/dL)	254.2 (\pm 63.1)	207.3 (\pm 73.8)	0.01
2-hour post prandial blood glucose (mg/dL)	361.2 (\pm 76.6)	329.2 (\pm 88.0)	0.13
HbA _{1c} (%)	11.5 (\pm 2.6)	9.4 (\pm 2.1)	0.001
Lipid Profile			
Serum total cholesterol (mg/dL)	207.0 (\pm 35.2)	214.1 (\pm 35.4)	0.43
Serum triglyceride (mg/dL)	152.6 (\pm 66.4)	156.2 (\pm 53.7)	0.81
Serum low density lipoprotein (LDL) cholesterol (mg/dL)	124.3 (\pm 31.0)	137.5 (\pm 36.9)	0.13
Serum high density lipoprotein (HDL) cholesterol (mg/dL)	34.2 (\pm 11.1)	30.8 (\pm 7.5)	0.16
Miscellaneous Parameters			
Fasting serum insulin (μ IU/mL)	16.1 (\pm 8.4)	27.1 (\pm 4.9)	0.001
LDL-C/HDL-C	4.0 (\pm 1.6)	4.8 (\pm 2.1)	0.09
Atherogenic index of plasma	0.61	0.77	0.006

Our findings suggest that lean individuals are exposed to higher levels of blood glucose compared to their obese counterparts. A possible explanation for higher blood glucose levels could be earlier β -cell failure in lean patients which is supported by our finding of lower fasting insulin levels in lean patients compared to obese patients,¹³ or defects in insulin signalling pathways.¹⁶

Dyslipidemia although present in both groups was worse in the obese group. Although both groups had comparable high density lipoprotein (HDL) cholesterol and serum total cholesterol levels, serum triglycerides and low density lipoprotein (LDL) cholesterol levels were comparatively higher in obese patients which can be explained by the increased rate of lipolysis in their abundant fat reserves.¹⁷ As with glycemic parameters conflicting data on lipid profile exists in lean and obese patients of T2DM. Bautista, *et al* reported no significant difference in lipid profile.¹⁵ Barma, *et al* reported no significantly deranged lipid parameters while comparing lean (BMI <19 kg/m²) vs obese patients (BMI >25 kg/m²) of T2DM.¹⁸ Some studies have reported normal serum lipid profile in lean patients of T2DM.^{19,20} Our lipid profile findings are in line with the findings of Asegaonkar, *et al* the only difference being in the BMI cut-offs used.¹⁴ In contrast to our study, Sinharoy, *et al* reported higher levels of serum triglyceride levels in lean patients (BMI <18.5 kg/m²) of T2DM compared to obese patients (BMI >25 kg/m²).²¹

Although dyslipidemia was worse in obese group, the lipid profile is also deranged in the lean group with a high LDL to HDL ratio predisposing them to the atherosclerosis and its sequelae. AIP is commonly used a predictor of

cardiovascular risk with values higher than 0.24 be labelled as high risk.¹¹ In this study both lean patients and obese patients had an AIP value of more than 0.24 at diagnosis. Therefore, these patients can be considered to be at high risk of developing coronary sequelae, obese patients having a higher risk compared to their lean counterparts.

One of major limitations of this study is the small sample size. A study with a larger sample size and long-term follow up will enable a better understanding of the disease process especially in lean individuals.

CONCLUSIONS

Based on the available literature and our findings we can conclude that hyperglycemia tends to be more severe in lean patients compared to their obese counterparts. Lean T2DM patients are consequently exposed to the ill effects of deranged lipid metabolism *i.e.*, atherosclerosis and its sequelae as evidenced by a high LDL/HDL ratio and high AIP. Therefore, there is a need to control blood sugar levels more aggressively in lean T2DM patients to delay the chronic complications associated with the disease. Studies need to be planned to decipher the exact etiopathogenesis of hyperglycemia in lean individuals so that appropriate treatment protocols can be established.

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CONTRIBUTORS: EAA, MM: Conceptualization and study design, funding acquisition, data curation, formal analysis and interpretation of data, project administration, drafting the manuscript; SVM: Conceptualization and study design, supervision, analysis and interpretation of data, project administration, review of draft and critical inputs; RK: Study

design, supervision, validation, analysis and interpretation of data, project administration, review of draft and critical inputs; DP: Visualization, supervision, validation, investigation and data analysis, project administration, review of draft and critical inputs. All authors approved the final manuscript and will be accountable for all aspects of the work.

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A Cross-Sectional Study Evaluating Disparities in Knowledge and Awareness Regarding Diabetes Amongst Patients, Family and General Population in Rural India

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ABSTRACT

Background: The data regarding the knowledge and awareness regarding diabetes among patients, their family members, and the general population is sparse in India, especially from the rural population. We conducted this study to ascertain the knowledge and awareness regarding diabetes in the rural population and to find the disparities that exist in knowledge between the diabetic patients, their family members and the general population.

Material and Methods: A community-based cross-sectional study was conducted over 2 years amongst respondents selected by convenience sampling. Data was collected using pretested structured face-to-face interviews after taking informed written consent. The respondents were categorized as people with diabetes, their family members and the general population.

Results: A total of 4244 persons were interviewed. Only 51.8% of the respondents had knowledge of diabetes, with glaring disparities between the three groups. Amongst the general population, only 27.4% had knowledge of diabetes. Similarly, the awareness of prevention, complications and risk factors of diabetes was much lower in the general population compared to diabetics and their families, and this group had a significantly lower composite knowledge score of diabetes.

Conclusion: Nearly half of the rural community in the study was found to have inadequate knowledge of diabetes. Even amongst the diabetics and their families, the knowledge and awareness were poor. A greater emphasis on the dissemination of community education regarding symptoms, prevention and risk factors for diabetes is necessary.

Keywords: Asian, Diabetes, Non-diabetes, Population, Risk.

INTRODUCTION

One-fifth of all the adults with diabetes in the world reside in the South-East Asia Region, with India having the second-highest prevalence of diabetes among adult population.¹ Currently, data from population studies indicates that 9.1% of the adult population; which is around 463 million people have diabetes, of which 88 million reside in India. This burden is expected to expand to 115 million by 2030, accounting for 12.1% of the adult population. Currently, around 31 million people are estimated to be having impaired glucose tolerance, and this may increase to around 50 million by the year 2050.¹

Around 1.1 million people die from diabetes-related illnesses in India every year.¹ Unfortunately, more than half (56.1%) of all people with diabetes in India remain undiagnosed, and even among the known diabetes

patients, less than one-third have their diabetes under good control.^{2,3} Evidence suggests that poor access to health care, poverty, coupled with low education, are associated with a higher rate of diabetes-related complications.^{4,5} Education remains one of the key measures for ensuring better treatment and control of diabetes. There is also evidence to show that increasing knowledge regarding diabetes and its complications can lead to an increase in compliance with therapy, thereby reducing the complications of diabetes.^{6,7}

Nearly 70% of the Indian population still resides in rural areas and growing urbanization and changing lifestyle habits (e.g. higher calorie intake, increasing consumption of processed foods, sedentary lifestyles) contribute to the increasing prevalence of type 2 diabetes at a societal level. While the global prevalence of diabetes in urban areas is

higher, this gap is closing with the rural prevalence being on the rise.¹ There is evidence to suggest that diabetes mellitus and its related complications show a threefold rise in rural areas.⁸ While there have been studies on the subject of diabetes awareness in India, there is a paucity of studies from the rural belt. Moreover, most of these studies were hospital-based rather than at population level. Hence, the data available is not representative of the country as a whole. There is a need to assess the knowledge and awareness among people living in rural areas to steer the future development of awareness programs and techniques for effective health education and patient counselling. Identification of lacunae in the knowledge amongst diabetic individuals will help us in providing a better insight towards further management and education. Hence, this study was aimed to ascertain the knowledge and awareness in the rural population and to find the disparities that exist in knowledge between the diabetic patients, their family members and the general population.

MATERIAL AND METHODS

The present study was a single centre study done at Uttar Pradesh University of Medical Sciences (UPUMS), Saifai, Etawah, Uttar Pradesh. It was conducted to ascertain the prevalence of diabetes in nearby rural areas of Western Uttar Pradesh, India, between 1 January 2018 and 31 December 2019.⁹ This study was a part of our ongoing project on the evaluation of prevalence of diabetes and its complications in rural India. The study was approved by the Institutional Ethics Committee (192/UPUMS/DEAN/2016-17). After excluding non-responders, a total of 4244 participants were recruited for the study via the health camp approach i.e. non-probability or convenience sampling. Village heads and local panchayats were consulted to ensure maximum participation. After obtaining a written informed consent, data was collected using a pre-tested structured questionnaire used previously in the ICMR-INDIAB study (after obtaining due permissions).¹⁰ Specific questions were asked to assess the participant's knowledge regarding the risks of diabetes, causative factors, complications and prevention of complications. Knowledge of causative factors and complications of diabetes was assessed using open-ended questions. The questionnaire was translated into hindi and administered by an interviewer trained for the same. The questionnaire used and calculation of KAP composite score is shown in *Appendix 1*.

Individuals diagnosed by a physician and receiving anti-diabetes medications (self-reported) and/or those who had 2-h post-prandial glucose value ≥ 200 mg/dL and/or fasting blood glucose ≥ 126 mg/dL were classified as having diabetes.

Statistical analysis: Statistical analysis was carried out using SPSS version 24 (SPSS Inc., Chicago, IL, USA). Data were presented as numbers (%) and mean (\pm SD). Quantitative variables that followed normal distribution were compared using ANOVA. *P* value <0.05 was considered significant.

RESULTS

A total of 4244 participants were included in the study, of which 2328 (54.85%) were male and 1916 (45.15%) were females. Amongst them, 341 (8.03%) were diabetics, 598 (14.1%) were their family members (non-diabetic) and the remaining 3305 were part of the general population. The mean age of diabetics (51.6 years) was higher than the other two groups. *Table I* summarizes the data regarding the demographic profile and awareness regarding diabetes amongst the study participants.

Overall, a total of 1713 (51.8%) participants reported that they knew about the illness called diabetes. However, on including only the general population, just 907 (27.4%) reported that they knew about diabetes. Even amongst the family members of diabetics, 133 (22.2%) did not know about diabetes. Amongst those who had heard about diabetes in the general population, 59.8% thought that more people were being affected by diabetes, 55% answered that diabetes can affect other organs and 48.6% reported that diabetes could be prevented. Corresponding numbers for the diabetic groups were 95.8%, 71.2% and 52.5%; while amongst the family members the numbers were 85%, 61.9% and 60.2%, respectively. Interestingly, more participants' family members thought that diabetes could be prevented as compared to the other two groups.

The knowledge of the risk factors for diabetes in the participants has been shown in *Table II*. The major risk factor for diabetes was stated as consuming more sweets by 71.7%, whereas overweight or obesity was listed by 49.8%, family history of diabetes by 38.1%, high blood pressure by 29.3%, lack of physical activity by 21.8% and mental stress by 15.2% of the general population. The knowledge regarding risk factors for diabetes was better among the known diabetic subjects (consuming more sweets 84.2%; obesity 60.2%; family history of diabetes 54.6%; high blood pressure 56.2%; lack of physical activity 51.6%; and mental stress 41.2%). Amongst the family group, lack of physical activity and family history was significantly higher than the diabetes group (67.3% and 65.2% respectively, $P=0.001$ for both)

Among the preventive factors, diet modification was reported by 65.2% of the diabetics and exercise by 58.1%. There was no significant difference between the distribution of participants reporting exercise as a preventive measure amongst the three groups. See *Table II*.

TABLE I. Demographic Features and Awareness Regarding Diabetes of the Study Participants

	Diabetics (n=341)	Family members (n=598)	General population (n=3305)	P value
Age distribution (years)				
18-30	8.2%	17.4%	25.7%	>0.05
30-39	9.4%	19.2%	22.2%	>0.05
40-49	22.6%	21.1%	19.6%	>0.05
50-59	29.3%	19.2%	18.1%	>0.05
60-69	21.7%	17.6%	10.8%	>0.05
>70	8.8%	5.5%	3.4%	>0.05
Mean age (years)	51.6	43.8	38.9	0.001
Sex				
Male	50.7%	48.2%	56.5%	>0.05
Female	49.3%	51.8%	43.5%	>0.05
Awareness				
Have you heard of a condition called diabetes?	341 (100%)	465 (77.8%)	907 (27.4%)	0.01
If yes, do you think in general more and more people are getting affected with diabetes nowadays?	327 (95.8%)	395 (85%)	542 (59.8%)	0.001
Do you think diabetes can affect other organs?	243 (71.2%)	288 (61.9%)	498 (55%)	0.02
Can diabetes be prevented?	179 (52.5%)	280 (60.2%)	441 (48.6%)	0.01

Knowledge of the organs affected by diabetes is shown in **Table III**. On comparing the composite knowledge score of diabetes amongst the three groups, the mean composite score (\pm SD) of the general population was 17.9 (\pm 4.0), of the family members was 45.2 (\pm 30.5), while the diabetic population had a significantly higher score of 68.2 (\pm 45.2) ($P=0.001$). The least score of "0" was obtained by 72.6% of the general population and 22.2% of the family members. The maximum score of "100" was obtained by 2.7% of the general population and 10.2% of the diabetic population and 8% of the family members.

DISCUSSION

In the current study, we assessed the knowledge and awareness amongst 4244 participants with the help of a pre-validated questionnaire. Previously a few studies assessing the knowledge of diabetes have been reported from India, but most of these studies are hospital-based. There is a paucity of data from rural India. The major finding in the study is the lack of knowledge and awareness regarding diabetes among the rural population with just over half (51.6%) knowing about diabetes. What

TABLE II. Risk Factors And Preventive Factors of Diabetes As Stated By The Participants

Risk factors	Diabetics (n=341)	Family (n=465)	General population (n=907)	P value
Consuming sweets	84.2%	78.8%	71.7%	0.011
Family history	54.6%	67.3%	38.1%	0.004
Obesity	60.2%	54.9%	49.8%	0.014
Hypertension	56.2%	38.5%	29.3%	0.003
Lack of physical activity	51.6%	65.2%	21.8%	0.03
Mental stress	41.2%	39.6%	15.2%	0.001
Preventive factors				
Balanced diet	65.2%	69.4%	52.6%	0.01
Exercise	58.1%	60.2%	58.9%	0.32

TABLE III. Knowledge of Organs Affected by Diabetes Among The Study Participants

	<i>Diabetics (n=243)</i>	<i>Family (n=288)</i>	<i>General popu- lation (n=498)</i>
Eyes	61.5	53.4	32.6
Kidneys	68.9	46.8	45.3
Nerves	55.3	41.2	22.3
Hands	45.8	19.3	12.5
Lungs	2.5	1.0	1
Stomach	6.8	2.6	3.6
Feet	48.9	36.5	18.6
Brain	7.9	6.5	11.2
Heart	23.5	12.6	17.8
Any other relevant answer	2.1	1.2	3.8

Values expressed as %.

is more worrisome is that 72.6% of the general population is unaware of diabetes itself. This is worrying in the context of the fact that India has a mostly rural population, and an estimated 56.1% of the diabetics in India remain undiagnosed. Even amongst the family members of diabetics, 22.2% did not know about diabetes. ICMR-INDIAB study reported a 36.8% awareness of diabetes in the rural areas with figures ranging from 55% in rural Tamil Nadu to 16.5% in rural Jharkhand.¹⁰ This is in contrast to findings reported by Islam, *et al* who reported a much higher proportion of 93% in rural areas of Bangladesh.¹¹ Mohan, *et al* reported a higher awareness of diabetes, albeit from an urban area in India.² A lower score in our study could be a reflection of the lower literacy rate in rural areas.

A finding of great public health importance in the study was that even amongst those who knew about diabetes, 59.8% of the general population reported that there was an increasing prevalence of diabetes and less than half amongst these (48.6%) reported that diabetes was preventable; a still lower proportion were aware of the major risk factors of diabetes. Even amongst those who thought diabetes was preventable, only 58.9% were aware of the effects of exercise and 52.6% were aware of the role of diet in prevention of diabetes. The people will transform their behaviour and attitude regarding diabetes only if they think themselves to be at high risk. Even amongst diabetics, only 52.6% reported that diabetes is a preventable disease despite evidence for the same having been reported by many studies such as the Finnish Diabetes Prevention Study¹² and the Diabetes Prevention Programme.¹³ This points towards a need to ensure robust participation of the population under the already undergoing National Program for Control of Diabetes,

Cardiovascular Disease and Stroke, and this can help improve diabetes awareness levels at the rural level.

In the diabetic population, the knowledge regarding prevention, risk factors and complications of diabetes was higher than both the other groups, but it still paints a dismal picture. Amongst the risk factors, obesity was considered by most (60.2%), while diet as a preventive measure was reported by only 65.2%. Amongst the diabetic complications, renal involvement was reported maximum at 68.9%. This reflects a poor attitude towards patient counselling and education regarding various aspects of diabetes. It should be well understood that diabetic care involves intensive education and counselling along with medical management. This forms a strong basis for recommending the presence of a diabetes educator at each centre that caters to diabetics.

On considering the composite score, the disparities between the diabetic group and the general population come to the fore with a vexatious difference of 68.2 vs 17.9. This reveals an unsettling knowledge gap regarding diabetes in the general population. Such data gives an indication of the various levels at which public health policies need to be planned and aimed at for preventing diabetes at the rural level.

The strengths of our study are its large sample size and representation of data from a usually poorly represented population. There are a few limitations of our study. Ours was a questionnaire-based study wherein the respondents may try to guess answers and verbal ability also becomes a deciding factor. While a health camp-based approach may be convenient, it does not ensure accurate representation of the population.

To summarize, this study provides a glimpse of the current status of knowledge and awareness of diabetes from rural India. There is an increasing need to conduct diabetic awareness activities in the rural population which can be done via public talks, use of mass media and use of local resources such as leaders, religious assemblies and door-to-door campaigns to increase awareness regarding diabetes.

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CONTRIBUTORS: HSh and NR: Conception and drafting of the study and collection of data; VR, MK and PI: Literature search and drafted the manuscript. HSo: Analyzed the data and interpreted the results. All authors approved the final version of the manuscript and are accountable for the manuscript.

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Appendix 1. Questionnaire and Calculation of KAP Composite Score (Reproduced with permission from ICMR-INDIAB with permission)¹⁰

The Interview Schedule consisted of 7 questions which were closed or semi-closed as follows: 1 Have you heard of a condition called diabetes? Yes/ No 2 If yes, do you think in general more and more people are getting affected with diabetes now a days? Yes/No 3 Do you think diabetes can affect other organs? Yes/No 4 If yes, which organs? Eyes/Heart/Lungs/Stomach/Kidneys/Feet/Brain/Hands/Nerves/Others (Specify)/Don't know 5 What are the risk factors for diabetes? Overweight/High blood pressure/Family history of Diabetes/Consuming more sweets/Lack of physical activity/Mental stress/Others (Specify)/Don't know 6 Can diabetes be prevented? Yes/No/ 7 If yes, how can it be prevented? Diet/Exercise/Others (Specify)

A composite score for knowledge of diabetes was used for this study. The scoring was done as follows: (a) For closed questions, correct answers were graded as one and incorrect answers (inclusive of "don't know") as zero. (b) For causative factors for diabetes, the highest score of '4' was awarded to subjects who ticked obesity, high blood pressure, lack of physical activity or family history of diabetes, '3' was given to those who ticked "consuming sweets," '2' to those who ticked "mental stress" and '1' for any other answer which made sense or was close to the above answers, while all other answers were scored '0'. (c) Thus the least possible score was '0' if all answers were incorrect, and the maximum score was '8' if all answers were correct. (d) A composite score in percentage was then derived by dividing each individual's score by the maximum score possible. E.g., if an individual's score was '6', then the composite score would be $6/8 \times 100 = 75\%$. Questions 4 and 7 were not included in the score.

Isoniazid Preventive Therapy in Persons Living with HIV attending an Anti-retroviral Clinic in North India

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ABSTRACT

Background: The risk of developing tuberculosis (TB) is several times greater in people living with HIV (PLHIV) than those without it. The TB/HIV syndemic continues to be a global public health challenge. Isoniazid Preventive Therapy (IPT) was found to be effective in reducing incidence of TB by almost 50%, under programme conditions in India. However, data on efficacy, safety, and completion rates of IPT among PLHIV in India are limited. Thus, this study aimed at documenting outcomes of IPT in terms of completion rate, adverse events and incidence of active tuberculosis.

Materials and Methods: An outpatient antiretroviral therapy (ART) centre-based cohort of 101 PLHIV aged ≥ 18 years in whom IPT (300 mg isoniazid + 50 mg pyridoxine) had been initiated in the last 28 days, after ruling out active TB were recruited and followed up. Participants lost to follow-up or expired (due to causes not related to IPT) were excluded from the adverse events and TB occurrence analysis.

Results: About 92.1% participants completed IPT and 24.7% developed minor adverse events during IPT. None of the patients who received IPT developed active TB infection at the end of follow-up.

Conclusion: Co-administration of IPT with ART does not compromise safety or compliance.

Keywords: Antiretroviral, Isoniazid Preventive Therapy, Tuberculosis.

INTRODUCTION

Tuberculosis (TB) is the most common opportunistic infection amongst people living with human immunodeficiency virus (PLHIV) and accounts for 25% of deaths amongst them in India. The risk of developing TB is 21-34 times greater in PLHIV compared to those without HIV infection.¹ The TB/HIV syndemic is a global public health challenge which needs to be addressed on a war footing.

The widespread institution of antiretroviral therapy (ART) has been instrumental in lowering the risk of TB through immune reconstitution, but the risk remains high despite achievement of good CD4 cell recovery, thereby underlining the need to implement other preventive interventions such as Isoniazid Preventive Therapy (IPT). The World Health Organization (WHO) and Joint United Nations Programme on HIV/AIDS (UNAIDS) issued a statement in 1998 recognizing the effectiveness of IPT among PLHIV and recommended its use as part of an essential care package for these patients.² A systematic review found that IPT reduced the overall risk of TB by

33% and by 64% when targeted to PLHIV who had a positive tuberculin skin test.³

Despite strong recommendations globally, the uptake of IPT has been limited due to difficulties in excluding active TB, added pill burden for patients, side effects, poor adherence to IPT, and concerns about development of drug resistance. In a review done by the WHO Guidelines Group, adherence for IPT ranged from 34-98%.⁴ A prospective multicentric study with phased implementation was conducted to assess the uptake and effectiveness of IPT in reducing TB incidence in a cohort of PLHIV enrolled into HIV care between 2013 and 2016 at seven ART centres in four states of India. IPT was found to be effective in reducing TB incidence by almost 50%, under programme conditions in India.⁵ However, there is dearth of data regarding feasibility, efficacy, safety, and completion rates of IPT among PLHIV in India. There are specific concerns about adverse events of isoniazid in those with concurrent ART. Our study had a value addition as it addressed several aspects regarding IPT in the Indian population.

MATERIALS AND METHODS

A hospital-based prospective cohort study was conducted in an ART centre of a tertiary care teaching hospital of Delhi, India. The study population constituted all PLHIV aged ≥ 18 years, initiated on IPT (< 28 days from recruitment to the study) from the ART centre. Participants lost to follow-up or expired (due to causes not related to IPT) were excluded from the adverse events and TB occurrence analysis. Information regarding socio-demographic profile (age, gender, religion, educational status), baseline characteristics (CD4 count, ART regimen, viral hepatitis co-infection, biochemical profile including serum alanine aminotransferase level) was collected. All participants were followed up at 2, 6 and 9 months after initiation of IPT.

The outcomes of interest in this study were the IPT completion rate, incidence of adverse events and occurrence of active TB infection during 9-month follow-up. Patients who were lost to follow-up or expired (due to causes not related to IPT) were excluded from the adverse events and TB occurrence analysis. Patients who were transferred to other hospitals were excluded from all outcome analysis.

Adherence was assessed using the pill count method at 2, 6 and 9 months (where applicable) of follow up. Adherence assessment for the remaining months of IPT not evaluated by participant interaction were supplemented by monthly adherence records of the ART Clinic. The reasons for interruptions in IPT intake were noted from records and it was ensured that the participant underwent counselling to improve adherence for ensuing months. Assessment for adverse events was guided by appearance of symptoms and signs in the participant. The participant was enquired regarding the appearance of the various commonly reported adverse effects of isoniazid. Occurrence of TB was considered if the participant was removed from IPT and initiated on antitubercular therapy at any point of time within 9 months of start of IPT.

Statistical analysis: The data collected as a part of this study were entered in a computer based spreadsheet and analysed using SPSS version 20.0. The continuous variables were reported as mean (\pm standard deviation,

SD). The categorical variables were reported as number (percentage).

RESULTS

A total of 101 PLHIV aged ≥ 18 years in whom IPT (300 mg isoniazid + 50 mg pyridoxine) had been initiated from the ART centre in the last 28 days, after ruling out active TB were enrolled for study. The mean (\pm SD) age of the study population was 39.9 (\pm 10.9) years. There were 58.4% ($n=60$) male participants and 40.6% ($n=41$) female participants. The most commonly reported mode of HIV transmission was heterosexual ($n=87$; 86.1%). The majority of the participants (92.1%) in the study group belonged to WHO clinical stage I. The mean (\pm SD) CD4 count at the time of recruitment was 461 (\pm 240) cells/ μ L.

Out of 101 participants in the study, 68 (67.3%) participants received cotrimoxazole prophylaxis therapy (CPT) in the past and 56 (55.4%) participants were on CPT at the time of recruitment. Past history of tuberculosis was present in 22 (21.8%) participants with 2 participants giving a prior history of tuberculosis on two occasions.

Out of 101 participants, 85 (84.2%) completed 6 months of IPT without any interruption. However, 8 (7.9%) participants completed IPT with some interruption while 8 (7.9%) subjects did not complete IPT. Thus, the cumulative IPT completion rate of the study population was 92.1%. The reasons for interrupted IPT uptake in 16 study participants are shown in **Table I**.

Around 24.7% patients developed minor adverse events during IPT (**Table II**). The most common adverse events recorded were weakness or fatigue (44.0%) followed by nausea and vomiting (32.0%). Some of the participants experienced more than one adverse event. On clinical examination during follow up at 2nd, 6th and 9th months, none of the participants reported symptoms of hepatotoxicity and none had jaundice. One participant complained of paraesthesia but showed no signs of peripheral neuropathy and managed to continue IPT. None of the patients who were exposed to IPT (including those who stopped IPT prematurely) developed active TB infection at the end of follow-up.

TABLE I. Reasons For Interruption in Isoniazid Preventive Therapy (IPT) amongst Study Participants (N=16)

Reasons for interruption	IPT completed with some interruption (n=8)	IPT not completed (n=8)
Lack of conviction due to not having tuberculosis	8	8
Pill burden	0	3
Concerned about adverse reactions	1	2
Good CD4 count	1	2

Table II. Adverse Event Profile Amongst Study Participants While Receiving Isoniazid Preventive Therapy

<i>Adverse event</i>	<i>No of participants</i>
Weakness or fatigue	11
Nausea and vomiting	8
Skin rash	7
Allergic reaction with swelling of lips and face	2
Gastric discomfort	2
Paraesthesia	1
Fever	1

DISCUSSION

The present study was a hospital-based prospective cohort study that assessed the outcome of IPT in 101 PLHIV taking treatment and care from ART centre of tertiary care teaching hospital in Delhi. The overall completion rate of IPT in our study was high (92%) and comparable to previous studies.⁶⁻⁸ Despite the increase in pill burden, IPT was well tolerated with concurrent ART. A previous study reported IPT completion rate as 77.1% which was even higher in subjects on ART (78.3%).⁹ Another study by Takarinda, *et al* reported 80.6% IPT completion rate.¹⁰ Such a high completion rate in our study could probably be due to the fact that all participants were on ART at the time of study and majority were in WHO clinical stage I with higher mean CD4 counts. This result is also a reflection of services provided at the centre through an effective national program like appropriate preparation with synchronized IPT and ART supplies; trained nursing staff and counsellors educating participants regarding IPT at every follow up visit, financial benefits to patients on ART etc. In our study the major reason for interruption of IPT was a lack of conviction to consume IPT in the absence of tuberculosis. Two participants did not complete IPT due to adverse events like nausea, vomiting and weakness in one and swelling of lips and face in the other. In the study by Takarinda, *et al* non-completion of IPT was attributed to loss to follow up in majority of participants; adverse effects of IPT and non-availability of IPT were reported as reasons in 7.2% and 4.5% of the participants for non-completion of ART.¹⁰ Another study quoted that severe adverse drug reaction like skin rash and transaminitis were reasons behind stopping IPT in 6.5% (n=3) participants; other reasons were loss to follow up and stopping IPT on their own by participants.⁸

Although the benefit of IPT among PLHIV is well established, there have been concerns about adverse events of isoniazid, particularly when co-administered with ART. In our study all participants were clinically stable

during the follow up period over 9 months. None of the study participants reported any major adverse event while minor adverse events were reported by 25 (24.7%) subjects. The most common adverse event noted was weakness or fatigue. Other studies from different parts reported hepatotoxicity as a common adverse effects.^{7,8,10} The relatively low incidence of adverse events recorded in our study may be because of lower incidence of hepatitis B or C coinfection, higher mean CD4 counts, absence of advanced (stage III/IV) illnesses. It is also possible that some less severe adverse events may be understated as they were recorded on the basis of recall or from records maintained by staff at the centre.

It was seen that concomitant IPT with ART had significant protective effect on occurrence of TB compared to ART alone.⁹ Zero incidence of TB in our study could not be attributed to IPT alone as our study was not a comparative study against IPT naïve participants. Other studies reported different incidence of TB in patients on IPT ranging from 2.2% to 3.1%.^{7,8} It is also plausible that since majority of our study participants were in WHO clinical stage I, had good CD4 counts and the mean duration of consumption of ART had been for more than 4 years, which could have resulted in zero incidence of tuberculosis in our study.

Our study found that IPT is a feasible and relatively safe strategy in PLHIV. Coadministration of IPT and ART gives additive prophylaxis against reactivation of TB and has not been shown to compromise safety or compliance in our study. However, this was a single centre study with a small sample size and thus there are limitations in statistical power to detect small subgroup effects and generalizability. Due to a limited number of follow up visits, the majority of data was collected by recall leaving scope for inaccurate estimates. Multicentre studies with longer follow up of participants across all stages of HIV are needed to determine the outcomes of IPT in PLHIV. Future studies also need to address the risk of developing drug-resistant TB after exposure to IPT.

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Basic Tenets of Obtaining A Biomedical Research Grant

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“A grant is a mechanism by which an agency awards money to fund a research study or other activity, such as an educational program, service program, demonstration, or research project.”¹

Obtaining a grant for a research project provides the principal investigator (PI) an opportunity to work in an area of science which enables him/her to contribute meaningfully to the body of science. It is also a great contribution for the parent institute as it provides funding to develop a new service or research environment.

In order to secure funding for research, the PI develops a research proposal which is a description of the research question or hypothesis and also provides a description of the background of research, aims and objectives and the detailed methodology planned. A tentative budget for the research project and the timeline for conducting the research work including the process of implementation are the key elements of the research protocol. It is imperative that the project should have qualities that would appeal to the scientific review board members and justify its approval for funding.

The grant proposal must be written as per the guidelines of the funding agency. The usual format includes an introduction to the topic with an emphasis on the background and justification for the research envisaged, which is followed by the aim and objectives of the proposal, detailed methodology including the outcome variables, references, a tentative budget proposal and the proposed timeline for the research project.

Identifying the appropriate extramural funding agency which will provide funds for the research is a very crucial step. The PI must carefully read the scope and guidelines for research proposal before submitting a research proposal to obtain funding from a particular funding agency. The thrust areas of the funding agency should

match with the proposed research. The timeline for submission of research proposal to the funding agency must be noted carefully. The PI should prepare the concept in advance with plenty of literature search and inputs from seniors or peers. It is also essential to obtain the approvals from the institutional scientific committee and ethics committee to enable timely submission.

NEED FOR EXTRAMURAL FUNDING

The idea of asking for funds from an external agency is to enable the PI to conduct research which is different from the routine work that is being carried out at his/her institution. Often, most institutes have a basic laboratory infrastructure but lack the specific equipment or reagents needed. The instruments and equipment so purchased in a research project, remain in the custody of the researcher till the project is completed and thereafter it should become an asset of the department. Additionally, conducting scientific research systematically and meticulously involves additional manpower which can be hired for the tenure of the research project with the monetary support from the funding agency.

FUNDING AGENCIES

There are two major sources for funding of research, i.e., public funding (governmental agencies or research councils) or private agencies (corporations through research and development departments). For health research or life sciences, some of the important government funding agencies are: Department of Biotechnology (DBT), Department of Science and Technology (DST), Indian Council of Medical Research (ICMR), University Grants Commission (UGC), and Council of Scientific and Industrial Research (CSIR), all of which provide both major and minor projects in different biomedical research areas.

GOVERNMENTAL FUNDING AGENCY

Indian Council of Medical Research (ICMR)

The ICMR provides funding support for health research projects. The research projects can be submitted under the following categories:

Short duration low-cost proposals (minor projects): The ICMR provides grants to support short-term *extramural research projects* that cover the biomedical needs. Scientists/professionals employed at a medical college, research institute, or university, research and development laboratories, government and semi-government organizations, and NGOs can apply for extramural research grants with documentary evidence of their employment and a requisite Department of Scientific and Industrial Research (DSIR) certificate required to allow the researcher to avail exemption from customs duty while purchasing any equipment, reagents, consumables, etc for the research project. These projects have a financial cap of Rs 10 lacs with a duration not exceeding 1 year.

Adhoc projects: ICMR provides financial support in the form of ad-hoc projects to researchers employed in teaching and research institutes or non-governmental organizations along with evidence to support their employment and DSIR certificate. These projects have a financial cap of Rs 1.5 crores for a duration of upto 3 years (may be extended upto 5 years).

Task Force: These are centrally planned and implemented on a multi-centric basis with time-bound defined targets with a focus on research areas of national priority. The collaborating scientists with expertise are encouraged to undertake activities. The financial cap is Rs 5 crore per collaborating centre for the total duration.

Cohort study: Prospective, observational, demographic information is collected over prolonged duration with an aim to assess the cause of disease and analyze the association between risk factors and disease. These studies are without any experimental work. The financial cap is Rs 2 crore per year.

National Registry: An organized system that uses observational studies to collect data regarding topics of national priority like clinical trials intervention with patient involvement.

Centre for Advanced Research (CAR): It is like creating an advanced centre of technology in medical sciences e.g., Biosafety level 3 laboratory, advanced centres for fungal identification and research.

Capacity building/support for sustained quality research: Evidence-driven process of strengthening the

abilities of an organisation to perform core functions and continue to improve and develop on time.

Table I provides details of research programs supported by ICMR.^{2,3}

Department of Biotechnology (DBT)

It is one of the major sources of funding for research in various fields of science and technology, including agriculture, plant biotechnology, bioinformatics, medical biotechnology and basic science research. Funding is provided for infrastructure facilities, societal developments, biotechnology product and process development, international cooperation, bioresources, and human resource development. DBT provides funding under individual fellowship programs for young faculty, post-doctoral students, post-graduates and students pursuing Masters in Sciences (M.Sc). The eligible candidates can apply during their career break and gain research experience by submitting their proposal at any university or institute (under a faculty/supervisor) for conducting their research work. Even permanent faculty may apply for such fellowships to pursue higher education overseas or at other higher educational institutes in India providing specialized research support. Under these schemes DBT provides prestigious and popular fellowships like the TATA innovation, Har Gobind Khorana, S Ramachandran Award and Janaki Ammal Women Bio-Scientist Award. **Table II** provides a list of programs funded by DBT.^{2,4}

Department of Science and Technology (DST) and Science Engineering Research Board (SERB)

Science Engineering Research Board (SERB) is an offshoot of DST which offers various schemes to scientists for pursuing a career advancement course or planning to work in institutes with high throughput technology.

Atmanirbhar Bharat: Indian women scientists and researchers can apply for SERB-Power Research Grants at any higher education institute. The applicant must be a regular academic or research scholar in a recognised institution or lab in India. Indian Institute of Technology (IIT), Indian Institute of Science Education and Research (IISER), Indian Institute of Science (IISc), National Institute of Technology (NIT), Central Universities, and National Labs of Central Government Institutions are Level I Category, while State Universities/Colleges and Private Academic Institutions are Level II Category. Level I applicants can receive Rs. 60 lac for 3 years, while level II applicants can receive Rs. 30 lac for 3 years.

Intensification of Research in High Priority Areas (IRHPA): Projects funded by the IRHPA should take on difficult problems that contribute to the growth of

TABLE I. List of Programs Funded by the ICMR

<i>Program</i>	<i>Specific areas of research supported</i>	<i>Nature of support</i>	<i>Duration of support</i>	<i>Amount sanctioned</i>
Junior Research Fellowship	All areas of life sciences	Contingency	3 years +HRA	Fellowship: Rs. 31,000/- Research grant: Rs. 20,000 per annum
Senior Research Fellowship	All areas of life sciences	Contingency	3 years	Fellowship: Rs. 35,000/- +HRA Research grant: Rs. 20,000 per annum
Research Associateship	All areas of life sciences	Contingency	3 years	Fellowship: Rs. 47,000/- +HRA (with Rs.2000 yearly increment)
Short-Term Low-Cost Proposals	Thrust areas in health research	Contingency	Upto 1 year	Rs. 20,000 per annum (Up to Rs. 10 lac)
Extramural Adhoc	Thrust areas in health research	Staff, contingency, travel, equipment, and overhead charges	3 years	Up to Rs. 1.5 crores
ICMR Emeritus Scientist	Biomedical sciences	One project assistant	Initially for 2 years. Extendable up to 3 years	Honorarium: Rs. 60,000 per month
		Contingency		Contingent grant Rs. 1 lac per annum
Task Force Projects	National priority areas of research; usually multicentric projects		3 Years	Up to Rs. 5 crores for the total duration per center
Support for post-doctoral fellows		HRA, NPA, contingencies, travel	2 years (extendable up to 3 years)	Fellowship of Rs. 65,000 per month plus HRA, NPA, contingency grant of Rs. 3.0 lac per annum, 25% of which can be used for travel.

HRA-House rent allowance, NPA-Non-practicing allowance.

scientific understanding. The IRHPA's projects focus on new areas of study that are not getting enough funding or attention elsewhere. IRHPA fund provided for infrastructure development which provides funding for 5 years for establishing high throughput technology facilities at institutes.

Core Research Grant (CRG) offered by SERB is open to all permanent faculty of universities across the country who wish to initiate research as a part of their promotion and progress in career.

Empowerment and Equity Opportunities for Excellence in Science (EMEQ) scheme of the SERB offers research support and funding preferably to researchers belonging to the Scheduled Caste and Scheduled Tribe.

Scientific Useful Profound Research Advancement (SUPRA) scheme deals with new breakthroughs (out of box ideas) with high-quality proposals consisting of new hypotheses or innovations in technology.

Fellowships: Amongst the other scholarly short-term funding opportunities, the prestigious J.C Bose Fellowship for senior faculty or emeritus scientists and the SERB Women Excellence Award are individual fellowships offered to scientists or researchers of high repute, providing them a chance to pursue their research even at a later age. Innovation in Science Pursuit for Inspired Research (INSPIRE) Fellowship, Satyam-Yoga, Swarna Jayanti Fellowship Scheme, Women Scientist Scheme (WOS) for break in career for female researchers are other schemes which are displayed on DST/SERB website.

Table III provides a description of programs funded by SERB.^{2,5}

Department of Health and Research (DHR)

Department of health research is the parent institute of ICMR which undertakes projects like establishment of a network of laboratories for managing epidemics and

TABLE II. List of Programs Funded by Department of Biotechnology (DBT)

Program	Specific areas of research supported	Nature of support	Duration of support	Amount sanctioned
DBT Research Associateship Program	Frontier areas of biotechnology and life sciences; coordinated by Indian Institute of Sciences, Bengaluru	Contingency	2 years	Stipend: Rs. 47,000 – Rs. 54,000 HRA per month Research grant: Rs. 50,000 per year
TATA Innovation Fellowship	Biological sciences and biotechnology	Consumables, equipment, international and domestic travel, manpower and other contingent expenditure	3 years (extendable up to 2 years)	Rs. 25,000 pm Contingency grant: Rs. 6 lac per annum
Har Gobind Khorana - Innovative Young Biotechnologist Award	Frontier areas in biotechnology/ biotechnology related fields	Equipment, software, consumables, contingency and travel grant	3 years	Rs. 75,000 per month+ HRA for candidates not in regular employment Rs. 1 lac per year for regularly employed candidates
S Ramachandran– National Bioscience Award for Career Development	Basic and applied research in biological sciences including medical sciences	Contingency	3 years	Contingency grant: Up to 10 lac, cash prize: Rs. 2 lac Research grant: Rs. 5 lac per year Citation and trophy
Janaki Ammal Women Bioscientist Award (Senior and Young category)	Biology and biotechnology	Contingency	5 years (young category)	Senior category: One-time cash prize: Rs. 5 lac along with citation and gold medal Young category: One-time cash prize of Rs 1 lac along with citation and gold medal Research grant of Rs. 5 lac per annum

HRA House rent allowance.

natural calamities like Virology Research and Diagnostic Laboratory (VRDL), establishment of Multidisciplinary Research Units (MRU) in medical colleges, human resource development scheme of DHR, etc which provide major funding for infrastructure development, creation of instrumentation facility for the institute to pursue research as well as increase the availability of trained personnel for health research. **Table IV** highlights the programs supported by DHR.^{2,6}

International Fellowship

Indian Science and Research Fellowship (ISRF) from DST offers fellowships to faculty/students from Bangladesh, Bhutan, Maldives, Myanmar, Nepal, Sri Lanka, Thailand and Afghanistan to work in India and gain expertise, and exchange knowledge and ideas for future research.

University Grants Commission (UGC)

The UGC provides funding for research pertaining to varied sciences which could be integral to health research including humanities, social sciences, pure sciences, engineering, technology, pharmacy, medical, and agricultural sciences. It offers funding for minor research projects of amounts upto Rs 5 lac for sciences and Rs. 3 lac for social sciences, arts, law, literature, etc. Additionally, monetary support is offered for organising conferences and seminars. Upto Rs. 1.5 lac is provided for organizing international conferences and upto Rs. 1 lac is given for organizing national conferences. Under the Faculty Development Programme it provides the following: award of teacher fellowship for pursuing M.Phil/ Ph.D degree, participation of teachers in academic conferences in India

TABLE III. List of Programs Funded by Science Engineering Research Board (SERB)

<i>Program</i>	<i>Specific areas of research supported</i>	<i>Nature of support</i>	<i>Duration of support</i>	<i>Amount sanctioned</i>
Intensification of Research in High Priority Areas (IRHPA)	Varies depending of emerging problems	Equipment, man-power, consumables, travel and contingency, overheads	5 years	Variable depending on the project
Start-up Research Grant	Frontier areas of science and engineering	Equipment, man-power, consumables, travel and contingency apart from overheads	2 years	Up to Rs. 30 lac
Core Research Grant (CRG)	Frontier areas of science and engineering	Equipment, man-power, consumables, travel and contingency apart from overheads	3 years	Up to Rs. 35 lac
Scientific Useful Pro-found Research Advance-ment (SUPRA) scheme	High quality proposals consisting of new hypothesis or challenge existing ones	Equipment, man-power, consumables, travel and contingency apart from overheads	3 years (extendable up to 2 years)	Variable depending on the project Projects more than 1 crore budget will undergo international review
Empowerment and Equity Opportunities for Excellence in Science (EMEQ) scheme	Research in frontier areas of science and engineering.	Equipment, man-power, consumables, travel and contingency apart from overheads	3 years	Up to Rs. 50 lac
National Post-Doctoral Fellowships	Research in frontier areas of science and engineering	Minor equipment, consumables, contingencies and domestic travel	2 years	Fellowship: Rs. 55,000/- per month HRA Research Grant: Rs. 2 lac per annum Overhead: Rs. 1 lac per annum
JC Bose Fellowship	All areas of science		5 years Maximum age limit up to 68 years	Fellowship: Rs. 25,000/- per month Research grant: Rs. 15 lac per annum Overhead: Rs. 1 lac per annum
SERB Women Excellence Award	All areas of science		3 years	Research Grant: Rs. 5 lac per annum Overhead: Rs. 1 lac per annum
Indo US Fellowship Program	All areas of science and engineering	Air ticket and contingency grant To carry out a well-defined research project at any institution of repute of their choice in the USA	3-12 months	Fellowship: 3000 US dollars per month

(PTAC) and short term visit of young faculty members to reputed institutes, travel grants (100%) once in three years (for college teachers/college librarians/vice chancellors/commission members and UGC officers) to present research papers at international conferences held abroad.

*Indian Council of Social Science Research (ICSSR)*⁷

It provides opportunities in major and minor projects in the

following subheadings:

1. Fund for collaborative research with foreign countries such as Thailand, Japan, China, European Union, UK, etc.
2. Research Programs
3. Senior and post-doctoral fellowship, doctoral fellowship

TABLE IV. List of Programs Funded by Department of Health and Research (DHR)

<i>Program</i>	<i>Specific areas of research supported</i>	<i>Nature of support</i>	<i>Duration of support</i>	<i>Amount sanctioned</i>
Fellowship program for young scientist	Biomedical and health research	Contingency	3 years	Stipend: Rs. 60,000 – Rs. 70,000 HRA depending on the qualification of the researcher Research grant: Up to Rs. 10 lac per year
Fellowship program for women scientist				Research grant: Up to Rs. 10 lac per year
Start-up grant for fellows undergoing short-term/long-term fellowship	Public health issues and activities, national priority areas	Contingency	3 years	Rs. 30 lac per project

HRA House rent allowance.

4. Organizing national and international conferences, seminars etc.
5. Capacity building program
The research projects are categorized as:
 1. Major Project: Duration from 12 to 24 months with a budget of Rs.5-15 lac
 2. Minor Project: Duration from 6 to 12 months with a budget up to Rs.5 lac

Council of Scientific and Industrial Research (CSIR)

The CSIR encourages research in medical sciences through the following projects and schemes:

1. Funding for promoting research in the field of science and technology including agriculture, engineering and medicine and multidisciplinary collaboration.
2. Interactive programs with university faculty
3. Emeritus Scientist Scheme

4. Research Fellowship/Associateship like Shyama Prasad Mukherjee Fellowship, Senior Research Associateship, Shanti Swarup Bhatnagar Award, CSIR Young Scientist award.
5. Fund for organising national and international seminars, conferences, workshops, symposia, etc.
6. Travel Grant to research scholars
7. Faculty Training Programme and adoption of schools and colleges by CSIR laboratories
8. Fulbright Nehru Fellowship provides support for research, teaching and professional development in the United States.

Table V provides description of programs funded by CSIR.^{2,8}

OTHER GOVERNMENTAL AGENCIES

Some other governmental agencies also offer support as

Table V. List of Programs Funded by Council of Scientific and Industrial Research (CSIR)

<i>Program</i>	<i>Specific areas of research supported</i>	<i>Nature of support</i>	<i>Duration of support</i>	<i>Amount sanctioned</i>
CSIR Sponsored Research Scheme	Medicine (basic and clinical sciences), priority to multi-disciplinary projects	Junior Research Fellowships (JRF), Junior Research Fellowships (SRF) and Research Associate (RA), contingency and equipment	3 years (rarely extendable up to 2 years)	Maximum 20 lac (for the other CSIR research scheme, the maximum is 10 lac)
Emeritus Scientist		Contingency, JRF, SRF and RA	3 years (extendable to 2 years upto 65 years of age)	Scientist allowance of Rs. 20,000 pm during the tenure and variable contingency grant

funding agencies. These include: Indira Gandhi National Open University (IGNOU); Higher Education Department, Tamil Nadu; Ministry of Human Resource Development (MHRD), New Delhi; Inter-University Accelerator Centre (IUAC), New Delhi; Forest Research Institute, Dehradun; Department of Education, New Delhi; Science and Engineering Research Council, New Delhi; Ministry of Health and Family Welfare; Indian National Science Academy; National Council for Economic Research and Training; Ministry of Forest and Environment; and Ministry of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy (AYUSH).

Table VI highlights the programs funded by AYUSH.^{1,8}

Defence Research Development Organisation (DRDO)

It provides support to research sponsored to academic institutions under the extramural project proposal with a Memorandum of Collaboration (MoC) between DRDO laboratories and establishments and academia. Their thrust areas are primarily aeronautics research and development with futuristic, scientific-technological areas having potential applications for aeronautical systems.

FUNDING FOR INCUBATOR CENTER

Incubators Nurturing Entrepreneurship for Scaling Technologies

Certain funding agencies encourage engineering or research institutes to apply for opening incubation centre or a national facility (or platform) which can accommodate smaller budgeted or funded projects or support any start-up companies which require equipment and expertise of an established institute to launch their work. The Atal-Innovation Mission (AIM), SERB SURE (State University Research Centre of Excellence) or Community Resilience Resource Centre (CRRC) under DST are such incubation schemes. Under DST, the Science for Equity Empowerment & Development (SEED) division provides opportunities for establishment of CRRCs. Their mandate was to strengthen community preparedness, response and approach to health challenges, especially during COVID. Science Technology Innovation (STI) capacity building for communities for improved resilience against pandemic and post-pandemic recovery for livelihood was a relatively

new concept with an attempt to improve resilience and livelihood in the community.

DBT Sahaj

This scheme is aimed at infrastructure development and creating a facility or platform with cutting-edge technology. The scheme also provides access to resources that could not be provided by any single research laboratory or scientific department but required for data acquisition and analysis therefore a national facility infrastructure is created.

Biotechnology Industry Research Assistance Council (BIRAC)

It invites proposals for the development, validation and pre-commercialization of a product/technology as opportunities for translation medicine.

Bio-NEST scheme

The Bio-NEST scheme of the DBT provides incubation space to start-ups and entrepreneurs. It aims to connect the industry and academia and enables interactions for efficient exchange of knowledge as well as facilitates technical and business mentorship. It also provides enabling services and required mentorship for intellectual property and technology management, legal and contract, resource mobilization and networking platform. It establishes an efficient governance model.

FOREIGN FUNDING AGENCIES

Foreign Funding agencies also provide opportunities to Indian researchers to apply in such schemes, though competitive but extremely valuable and prestigious to seek for their funds. These are enlisted in **Box 1**.

CALL FOR PROPOSAL VERSUS ADHOC OR CORE RESEARCH GRANT

The call for proposals are usually announced frequently around the year but at times it becomes challenging as the time window is limited, thereby researchers get less time to do a thorough literature search for the proposal. However, if you have identified your area of work or expertise then prepare for such calls beforehand. The intent of “Call for proposal” is to gather a basic idea of the work that the researcher plans to propose, hence the word limit is

Table VI. List of Programs Funded by AYUSH

<i>Name of the program</i>	<i>Specific areas of research supported</i>	<i>Nature of support</i>	<i>Duration of support</i>	<i>Amount/Grant</i>
Extramural Research Scheme	Priority areas in alignment with National Health Programmes	Staff, equipment and contingency	1-3 years	Maximum Rs. 30 lac

Box 1. List of Foreign Funding Agencies

- Universe Foundation, Japan
- International Water Management Institute, Colombo
- FORD Foundation
- United Nations International Children's Emergency Fund (UNICEF)
- United Nations Educational, Scientific and Cultural Organization (UNESCO)
- National Institutes of Health (NIH)
- Brazil, Russia, India, China, and South Africa (BRICS)
- German Academic Exchange Service (DAAD)
- International Foundation for Science, Sweden
- The World Academy of Sciences (TWAS), Italy
- The Third World Network of Scientific Organisations (TWNISO), Italy
- Animal Production & Health Division, Vienna, Austria
- British Council, New Delhi
- International Federation for Women in Agriculture, New Delhi

around 2000 words with emphasis on the justifications that the PI provides specifying clear aims and objectives and well-defined outcomes. The calls are then reviewed by the expert committees of the respective funding agencies and those proposals that are shortlisted as innovative, appropriate and worth funding are invited for submission of the extended proposal with details of methodology and budget.

PRIVATE FUNDING AGENCIES

In addition to government funding agencies, there are private funding options, such as associations, foundations, and societies and sponsors with well-established funding schemes and a wide spectrum of interests, goals and purposes. Companies having a turnover of over Rs 100 crores are required to offer Corporate Social Responsibility (CSR) hence, providing opportunities to give funding. For instance, Bill and Melinda Gates Foundation calls for proposal in areas of challenge in science for which one can visit the Grand Challenges website, Pathogen Genomic Surveillance and Immunology in Asia challenge. Another agency like the Sun Pharma Science Foundation Research Awards and Sun Pharma Science Foundation Scholar Awards offer funds and awards for upcoming brilliant and young Indian researchers under the age of 30 years, for their research projects (Bio-Medical Sciences and Pharmaceutical Sciences) and offer support for excellence in original research work in Medical and Pharmaceutical Sciences by Indian Scientists working in India and Non-Resident Indian Scientists. The DBT-Welcome Trust India Alliance provides early career fellowships to clinicians and Public Health researchers in India. Another agency, Simons offers Global Brain Post-doctoral Fellowships to PhD students. **Table VII** provides the names of a few companies and organizations offering collaborations.

CONCLUSION

There are ample sources of funds and plenty of opportunities for researchers to pursue their work and avail

TABLE VII. List of Programs Funded by Private Funding Agencies

<i>Funding Agency</i>	<i>Link to Website</i>
Amgen Technology Private Limited	https://www.amgen.com/
Biocon	https://www.biocon.com/
Bill & Melinda Gates Foundation	https://www.gatesfoundation.org/
Boehringer Ingelheim India Private Limited	https://www.boehringer-ingelheim.in/
Bristol Myers Squibb India Private Limited	https://www.bms.com/in
ELCIA	http://www.elcia.in/
Eli Lilly and Company (I) Private Limited	https://www.lilly.com/
Fresenius Kabi India Private Limited	https://www.fresenius-kabi.com/in/
KlinEra Corporation Private Limited	https://www.klinera.com/
George Institute for Global Health	https://www.georgeinstitute.org.in/
Glenmark Pharmaceuticals Private Limited	https://www.glenmarkpharma.com/
GSK/PPD Pharmaceutical Private Limited	https://www.ppd.com/
Hamilton Health Sciences	https://www.hamiltonhealthsciences.ca/
Himalaya Drug Company	https://himalayawellness.in/

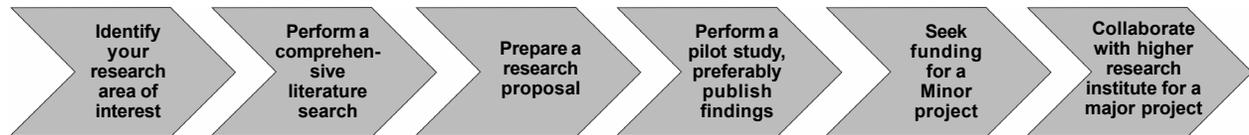


FIG. 1 Roadmap for a researcher aspiring for research grant.

the schemes, but the road to achieve them is tough. Hence, the saying that “It’s not knowledge but the act of learning, not possession but the act of getting, which grants the greatest empowerment” holds true. The greatest challenge in grant writing is to focus on the research hypothesis, finding neglected areas of science, and establishing new paradigms to bridge gaps in the present knowledge and future development. The road map for an aspiring grant writer is summarized in **Fig. 1**. The field is extremely competitive, challenging, time consuming and one must develop the correct grant writing skills. Accepting or rejecting a research proposal for funding support is based upon the thrust areas, delivery of the proposal, development of the hypothesis, and methodology description.

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Rabies Literacy Amongst Medical Undergraduate Students in a Public Teaching Hospital in East Delhi

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ABSTRACT

Background: With the launch of Competency Based Medical Education (CBME) Curriculum in 2019, we need to find out the extent to which medical undergraduates are being trained regarding the management of rabies. The aim of this study was to assess rabies literacy in medical undergraduate students admitted under the CBME curriculum in a public teaching hospital in East Delhi.

Methods: A cross-sectional study was conducted among the medical students of the pre-final year (admission year 2019) and second-year (admission year 2020) pursuing Bachelor of Medicine and Bachelor of Surgery (MBBS) course. The students were approached in their respective teaching sessions in an online survey using a pre-validated questionnaire wherein their responses were scored on a scale of 0 to 10.

Results: A total of 147 responses were analysed. The mean (\pm SD) total rabies literacy score obtained by students was 4.62 (\pm 1.45) out of a maximum possible score of 10. Proportion of students who responded correctly to questions related to basic knowledge of rabies was higher as compared to questions assessing clinical knowledge.

Conclusion: Rabies literacy amongst medical undergraduates was poor. Students performed poorly on clinical decision-making questions and updated guidelines for rabies management. We need to focus on making the future doctors competent in animal bite management for rabies prevention by applying the CBME framework.

Keywords: Competency-based, Literacy, Medical education, Rabies.

INTRODUCTION

Rabies is a viral zoonosis and a 100% fatal disease.¹ It is estimated to cause 59,000 human deaths annually with about 95% cases being reported from Africa and Asia. Rabies is endemic in India and accounts for around one-third of global burden of rabies related deaths.² The Government of India has launched 'National Action Plan for Dog Mediated Rabies Elimination by 2030' which is based on "One Health Approach".³

Rabies is preventable if the animal bite patient receives post-exposure prophylaxis (PEP) as per the recommended guidelines. But certain studies show that the general practitioners and even the medical students have poor knowledge and skills related to management of animal bite cases with respect to rabies prevention.⁴⁻⁷ With the launch of the Competency Based Medical Education (CBME) Curriculum for medical undergraduates in 2019 in India by the National Medical Commission (NMC),⁸ we need to find out the extent to which the medical students are learning about the management of certain health issues such as rabies which is endemic in our country. We conducted this

study to assess the rabies literacy among the medical undergraduates being trained under the CBME curriculum launched by the NMC.

PATIENTS AND METHODS

A cross-sectional study was conducted over a period of three months (August 2022 to October 2022) among the undergraduate students pursuing Bachelor of Medicine and Bachelor of Surgery (MBBS) at the University College of Medical Sciences, Delhi. We enrolled students of two cohorts, i.e., 2019 and 2020 admission years, viz, pre-final year (third-year) and second-year MBBS batches respectively. These were the first two batches to receive MBBS training under the new CBME curriculum.

The topic of rabies is taught in the departments of microbiology and community medicine. Around two lectures in a didactic mode are conducted for a large group of students in both the departments. In addition to this, in the department of community medicine, a single visit to the rabies clinic is conducted. All the students of these two admission cohorts attending their teaching sessions in the

department of community medicine were approached at the end of their teaching sessions where this feedback survey was undertaken and informed consent was obtained to use the data for study purpose.

An online google form consisting of an interviewer-developed pre-tested and pre-validated questionnaire was shared in the WhatsApp groups of the two MBBS admission cohorts at the end of the large group teaching session. These sessions were not on rabies and the students were not aware they would be tested at the end of the class. The questionnaire was developed using “National Guidelines for Rabies Prophylaxis, 2019” and “Current Guidelines on Prevention of Rabies, Consortium Against Rabies”.^{1,9} The domains regarding the basic and clinical knowledge, management of an animal bite, PEP, special situations like PEP in immunocompromised patients and advancement in rabies vaccination were included to make the assessment comprehensive. Two questions consisted of pictures of multiple transdermal bites on the leg and face respectively and the students were asked to categorise the wound as per the NCDC guidelines.⁹ Each correct response was given a score of 1. However, in one question there were two correct responses and each sub-response was given a score of 0.5 in order to retain the overall score of 1. No negative marking was done for incorrect responses. The total score ranged from 0 to 10. A score of less than 4; 4 to 6 and more than 6 were considered as poor; average and good performance, respectively. Incomplete responses were excluded from the analysis.

Statistical analysis: The collected data was entered in Microsoft Excel and analyzed using Student’s t-test and Mann-Whitney U test with the SPSS 20.0 statistical software. Continuous variables such as total rabies literacy score, were checked for normal distribution by Kolmogorov-Smirnov test and Shapiro-Wilk test. If normally distributed, continuous variables were presented as mean (\pm standard deviation, SD); and if non-normally distributed, then presented as median (interquartile range, IQR).

RESULTS

Out of a total of 169 medical students in each of the pre-final and second-year MBBS batches, we were able to approach 102 (60.4%) and 62 (36.7%) students in their respective teaching sessions. Of these, 16 students (9.8%) did not give consent and one student submitted an incomplete form. Therefore, a total of 147 responses were analysed.

The median (IQR) age of the students was 21 years (20,22) and three-fourth of them (75.5%, 111/147) were

males. More (60.5%, 89/147) students belonged to the pre-final year MBBS batch. Most (93.2%, 137/147) of the students reported having attended atleast one teaching session on the topic of Rabies. Among these, majority (60.6%) reported attending rabies related session in both microbiology and community medicine departments; whereas 28.5% attended it only in the microbiology department and 10.9% attended it only in the community medicine department. The overall mean (\pm SD) total rabies literacy score obtained by the medical students was 4.62 (\pm 1.45) out of a maximum possible score of 10. The mean (\pm SD) scores obtained by students of the second-year and pre-final year MBBS batches are 4.27 (\pm 1.51) and 4.85 (\pm 1.37) respectively ($P=0.02$). The median (IQR) scores obtained by students who had attended a teaching session on the topic of Rabies was found to be 4.5 (3.5,5.5) and it was 4.0 (3.0,4.5) among those who had not attended any rabies related teaching session ($P=0.07$). There was no significant difference between the mean scores obtained by students who had attended a rabies related teaching session only in the department of microbiology [4.36 (1.53)], only in community medicine [4.43 (1.59)] and those in both the departments [4.89 (1.36)] ($P=0.13$). **Table I** shows the item-wise distribution of correct responses to rabies literacy questionnaire administered to the medical students of the two MBBS admission cohorts.

DISCUSSION

The average performance of medical students regarding rabies literacy was found to be poor. The proportion of students who responded correctly to questions related to basic knowledge of rabies (e.g., primary system affected in rabies, immediate wound management of a dog bite, etc.) were higher as compared to those who responded correctly to clinical knowledge related questions of rabies (e.g., PEP in an immunocompromised person, preparation of anaphylaxis kit for PEP, updated Thai Red Cross schedule and dose of rabies monoclonal antibodies). We also found that very few students were familiar with the correct dose of rabies monoclonal antibodies (rabies mAbs). This may be because rabies mAbs being a recent development and therefore the incorporation of the same in the teaching-learning resource materials will take some time. The pre-final year students scored higher than the second-year students in rabies literacy score but despite that the rabies literacy score levels were poor (<50% score) than the expectations in both the cohorts of students. Also, the rabies literacy scores obtained by students who had ever attended a rabies related teaching session was not significantly different from those who had never attended any such session.

We found that most of the students were aware

TABLE I: Item-wise Distribution of Correct Responses to Rabies Literacy Questionnaire Among Second Year and Pre-final Year Medical Undergraduate Students (n=147)

<i>Question</i>	<i>Correct response [n (%)]</i>		
	<i>2019 Batch (n=89)</i>	<i>2020 Batch (n=58)</i>	<i>Total (n=147)</i>
<i>Questions related to Basic Knowledge of Rabies</i>			
Rabies is most commonly seen in the age group of	36 (40.4)	27 (46.5)	63 (42.9)
a.) 1-5 years			
b.) 11-19 years			
c.) Below 15 years			
d.) 15-45 years			
The primary system affected in rabies is	79 (88.8)	42 (72.4)	121 (82.3)
a.) Nervous system			
b.) Cardiovascular system			
c.) Musculo-skeletal system			
d.) All of the above			
Immediate wound management of a dog bite includes*	73 (82.0)	50 (86.2)	123 (83.7)
a.) Washing the wound with water and soap for 15 minutes			
b.) Washing the wound with water for 15 minutes			
c.) Application of Povidone-Iodine tincture			
d.) Suturing of the wound			
Rabies is rarely transmitted by which animal	14 (15.7)	07 (1.2)	21 (14.3)
a.) Mongoose			
b.) Bat			
c.) Cattle (Cows/ buffaloes/ camels)			
d.) Rodents and squirrels			
<i>Questions related to Clinical Knowledge of Rabies</i>			
A female was diagnosed with breast cancer one year back for which she was undergoing chemotherapy. A cat scratched her on the face while she was on the way to the hospital. Patient had received pre-exposure prophylaxis against rabies six months back. The next management line would include:	26 (29.2)	32 (55.2)	58 (39.5)
a.) Washing the wound, administration of ERIG and anti-rabies vaccination			
b.) Washing the wound, administration of HRIG and anti-rabies vaccination			
c.) Washing the wound and anti-rabies vaccination			
d.) Washing the wound would suffice			
Categorise the type of wound, Fig.1	48 (53.9)	15 (25.9)	63 (42.9)
a.) Category 1			
b.) Category 2			
c.) Category 3			
Anaphylaxis kit should be kept prepared while inoculation of	38 (42.7)	28 (48.3)	66 (44.9)
a.) ERIG			
b.) HRIG			
c.) Rabies monoclonal antibodies			

table contd...

table from pre-page

Question	Correct response [n (%)]		
	2019 Batch (n=89)	2020 Batch (n=58)	Total (n=147)
d.) All of the above			
Categorise the type of wound, Fig. 2	82 (92.1)	40 (69.0)	122 (83)
a.) Category 1			
b.) Category 2			
c.) Category 3			
Updated Thai Red Cross schedule is	48 (53.9)	18 (31.0)	66 (44.9)
a.) 0.1 mL ID injection in deltoid region at 0,3,7 and 28 days at 2 sites			
b.) 0.1 mL ID injection in gluteal region at 0,3,7 and 28 days at 2 sites			
c.) 0.5 mL IM injection in deltoid muscle at 0,3,7, 14 and 28 days at 1 site			
d.) 0.1 mL ID injection in deltoid region at 0,3,7 and 28 days at 1 site			
Dose of rabies monoclonal antibodies is	14 (15.7)	06 (10.3)	20 (13.6)
a.) 20 IU/kg body weight			
b.) 40 IU/kg body weight			
c.) 3.33 IU/kg body weight			
d.) 0.1 IU/kg body weight			



Fig. 1



Fig. 2

Values expressed as n (%). *Multiple responses allowed. If a student selected even a single correct response, we included her/him in the proportion of students giving the correct response. ERIG Equine rabies immunoglobulin, HRIG Human rabies immunoglobulin, ID intradermal, IM intramuscular.

regarding the primary system affected by rabies and had knowledge regarding the immediate wound management after a dog bite which was assessed by a case scenario-based question. Similar findings were reported by studies conducted previously in which majority of medical

students were aware about immediate washing of the wound with soap and water and application of antiseptic.^{4,5} However, Bhalla, *et al* reported a lower proportion of general practitioners who were aware regarding the immediate wound management.⁶ Similarly,

merely 29% medical students had correct knowledge regarding administration of Rabies Immunoglobulin (RIG) in another study from India.⁴ Various studies have reported that most of the medical students and doctors did not have correct knowledge regarding anti-rabies vaccine schedule.⁴⁻⁷

Some of the limitations of the study include the fact that ours is a single centre study, and therefore the findings of the study cannot be generalised. COVID-19 pandemic disrupted the training of both the MBBS admission cohorts included in the study, and the findings may have been influenced by the modifications in the teaching-learning methods during the pandemic. We did not assess skills by direct observation as our data collection was using an online questionnaire. However, we tried to assess their clinical skills by giving case scenario-based questions which included patient history and images of dog bite wounds to categorise the wound for rabies management. The response from the second-year MBBS batch was lower than expected and we did not attempt to contact the students a second time as it would have led to a contamination of feedback response.

The second-year and the pre-final year medical undergraduate students were found to have a poor level of rabies literacy. The students performed poorly on the clinical decision-making questions and the updated guidelines for rabies management. Rabies being an important public health problem in India, there must be a focused effort on making the future doctors competent in animal bite management and its prevention, by applying the competency-based framework. It seems that there is a need to revisit the specific learning objectives, its teaching-learning methodology and assessment so as to ensure the expected outcomes. NMC now recommends Early Clinical Exposure (ECE) for medical education which facilitates in providing a clinical context and relevance to basic sciences learning. ECE can be used in the teaching learning methodology of rabies as well.¹⁰ Although a visit to the rabies clinic is conducted for the medical students, more attention needs to be given to case discussions and methods of approaching an animal bite case, rather than just demonstrating the technique of anti-rabies vaccination and rabies immunoglobulin at the rabies clinic. Case-based learning and modular training on management of an animal bite and PEP against rabies can be introduced in CBME.

CONTRIBUTORS: AA: Designing the work, acquisition and analysis of data, drafting the work; KAM: Conceptualisation and design

of the work, analysis and interpretation of results, drafting the work, revising for critical inputs; SKB: Interpretation of results, drafting the work, revising for critical inputs. All authors approved the final version and are accountable.

COMPETING INTEREST: None; FUNDING: Nil.

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Successful Management of Oro-Dental Needs in A Child with Down Syndrome Using Holistic Approach

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ABSTRACT

Down syndrome is a chromosomal abnormality associated with mild to moderate intellectual disability. Patients with DS present peculiar orofacial characteristics, which may entail a multitude of oral health issues. Treating such patients can pose a challenge to dental practitioners in terms of behaviour management and safety as the affected individuals experience cognitive delay. This case report intends to present successful management of oro-dental issues including root canal treatment, restoration, oral prophylaxis, and preventive measures in a 10-year-old child with down syndrome.

Key words: Down syndrome, Dental, Oral health

INTRODUCTION

Down syndrome is a chromosomal disorder characterized by delayed psychomotor development and dysmorphic features. First described in a child by Jean-Etienne-Dominique Esquirol, a French psychiatrist, in 1838, down syndrome derives its name from Langdon Down who enumerated some of the characteristic features of this syndrome accurately in his article in 1866.¹ A triplication of material on chromosome 21, caused by an error in cell division results in the presence of an additional third chromosome 21 in down syndrome, hence it is also termed trisomy 21 / trisomy G.² Being one of the most frequent chromosomal disorders in children, it has a prevalence of 1 in 800-1000 live births.³ Three genotypes of down syndrome have been identified, viz, trisomy 21 (94%), translocation (5%), and mosaicism (1%).⁴

The typical phenotype in down syndrome comprises short stature and craniofacial features like brachycephaly, a flat occiput, frontal bossing, flattened nasal bridge, mid-face deficiency, up slanting palpebral fissures and epicanthal folds, short ears, small mouth, deviated nasal septum, and Brushfield's spots in the iris. In addition, there can be hypotonia with increased joint flexibility, an open mouth, hearing disability, protruded tongue, developmental delay in speech and language, and a Simian (single palmar) crease.^{2,4} A risk of concomitant congenital defects and non-inherited mental retardation is seen.^{5,6}

The myriad orofacial manifestations include a small maxilla, mandibular protrusion, fissured and protruding tongue, thick lips, malocclusion (class III), periodontal disease, delayed tooth eruption, hypodontia and hypotonicity of perioral muscles which leads to drooling and difficulty in swallowing and sucking, although, a lower prevalence of caries in down syndrome patients has been found by most investigators in both dentitions.² The poor oral health increases morbidity and adds to the health burden of care-givers of children with down syndrome.⁷ Thus, the populations with developmental disabilities like down syndrome should receive focussed, individualized and comprehensive management of oro-dental issues.⁸ The present case report aims to present the chairside management of a child affected with down syndrome and the challenges faced during treatment.

CASE REPORT

A 10-year-old boy, a known case of down syndrome, presented in the department of pedodontics and preventive dentistry with pain in the upper left back tooth region for the preceding 15 days. The child was suffering from intellectual disability and had been attending a school for children with special needs. He was able to read and write and had a friendly attitude towards people. The child was made comfortable in the hospital environment during his first visit so that a dental check-up could be carried out. The child's extra-oral features had typical Down's facies with upward

slanting palpebral fissures, midface deficiency, and flattened nasal bridge. Intra-oral examination revealed a fissured tongue, poor oral hygiene with plaque deposits on the lingual surface of lower anterior teeth (**Fig. 1a**) and caries in the upper right and left first permanent molar, i.e., tooth 16 and tooth 26 respectively (**Fig. 1b**). Radiographic examination of tooth 16 revealed caries extending from enamel into dentin without pulpal involvement whereas examination of tooth 26 revealed decay extending from enamel, dentin into pulp with widening of periodontal ligamental space and discontinuity of lamina dura. Restoration of tooth 16 and root canal therapy (RCT) of tooth 26 was planned. As preventive therapy, supragingival hand scaling and topical fluoride therapy by the placement of GC MI Varnish™ (5% sodium fluoride with recaldent) was done on the patient's second dental visit to accustom the child and for step-wise escalation of dental procedures. The child was made comfortable through behavioural reinforcement using verbal and non-verbal communication, tell-show-do, euphemisms, modelling, and distraction techniques to enable him to cope with the procedural interventions. In the next follow up visit, chair-side management of the child was tried for which excavation of dental caries was done very slowly for tooth 16, followed by restoration of the tooth with GIC and composite restoration. The child showed reluctance yet cooperative behaviour towards getting chairside procedure. In the subsequent visit, stepwise progression of RCT for tooth 26 was planned following which access opening was performed using round bur (size 2) for gaining access to pulp chamber following which working length was also determined (**Fig. 2a** and **Fig. 2b**). All three canals were prepared in the next visit to keep the visits short and acceptable to the patient to achieve cooperative behaviour with hand K-files (2% taper Mani K-files) and preparation was completed up to size 35 of K-file. After completion of biomechanical preparation (BMP), calcium hydroxide dressing was given as intracanal medicament for two weeks. The patient was asymptomatic in the subsequent visit hence obturation was completed with gutta-percha of the same taper (2%) using lateral condensation technique (**Fig. 2c**). The patient was followed up telephonically after one week for any associated discomfort and the procedure turned out to be uneventful. After completion of root canal therapy, the tooth was restored with composite restoration (3M ESPE™ posterior composite). However, the parent was reluctant for placement of stainless-steel crown due to compromised aesthetics and refused to undergo crown placement for his child. The chairside management in the child was challenging as he had to be counselled each time he underwent any procedure. Behaviour management with the help of modelling, tell-show do and distraction really helped in the completion of chairside procedure for the child without any requirement of general anesthesia.

DISCUSSION

The unique oro-facial traits in children with down syndrome may put them at risk for oral health issues.⁸ It is crucial to comprehend these oral health issues faced by children of down syndrome at the earliest to prevent their Quality of Life (QoL) from being affected adversely.^{4,7} Deps, *et al.* in their meta-analysis found that individuals with down syndrome have significantly lower dental caries, which can be attributed to the presence of spacing between teeth, delay in eruption, and certain salivary characteristics.⁹

Performing pulp therapy in down syndrome may depend on the patient's intellectual quotient (IQ), physical, dental, and soft tissue assessment.⁶ A single visit RCT is given preference in patients requiring endodontic therapy. With the use of advanced dental technologies, the ease of performing RCT has also been simplified for practical management of such cases.¹⁰ The present case was managed chairside with behavioural reinforcement using verbal and nonverbal communication, tell-show-do, euphemisms, modelling, and distraction techniques for achieving cooperative behaviour.² But since the child had to be slowly reinforced for dental treatment, thereby multiple short visits for RCT were preferred over a single visit. The child was practically introduced step by step to the air rotor, endodontic files to simplify ease of access opening, and BMP. The child was particularly fearful on seeing the heated instrument for searing of gutta-percha during obturation. He had to be counselled several times and made at ease while performing obturation.¹⁰

Institution of all possible preventive measures is essential in patients of down syndrome to prevent oral health issues at the earliest and to control the consequent long-term implications. With most parents paying more attention to other health issues, oral health tends to get neglected in children with down syndrome. There should be a prevention strategy individualized for every patient consisting of parental participation and education, a regular visit to dental office starting at 12 to 18 months, assistance in adopting good dietary practices, oral prophylaxis and motivation for oral hygiene, topical fluoride application, pit and fissure sealant, and early intervention.^{10,11} In this case, we have used topical fluoride therapy by the placement of GC MI varnish (5% sodium fluoride with recaldent) as a preventive measure for dental caries and composite resin as a restorative material to restore class II cavity in the right upper first permanent molar. Composite resins can be used successfully for class I and II restorations in permanent molars suggested by strong evidence from meta-analyses.¹¹

CONTRIBUTORS: NK, RT: Conceptualized the work, performed

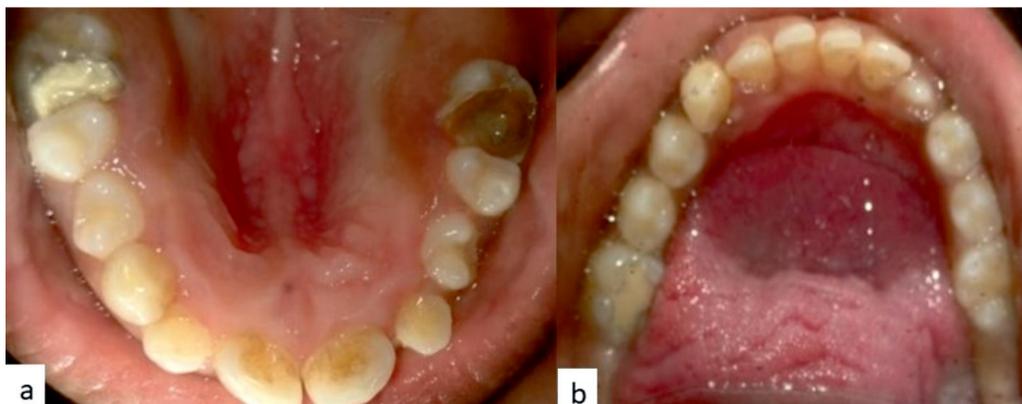


FIG. 1a. Intraoral picture of the maxilla; **1b.** Intraoral picture of the mandible.

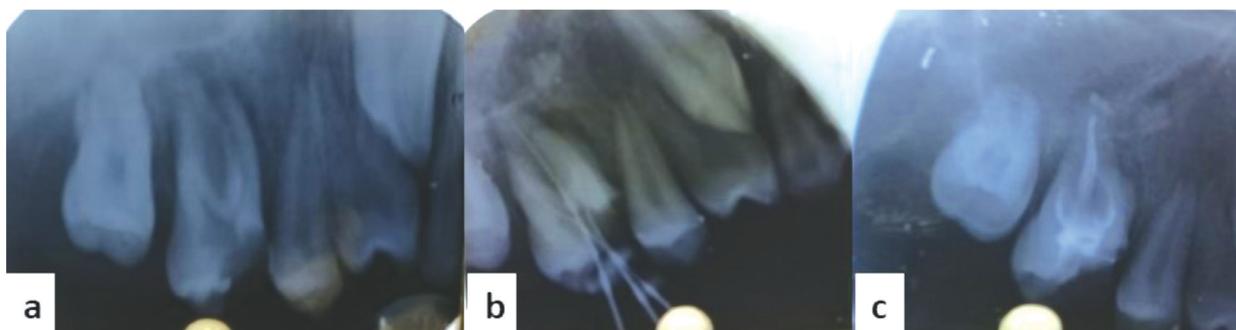


FIG. 2a. Preoperative intraoral periapical radiograph of left maxillary first molar; **2b.** Canal length determination in intraoral periapical radiograph of left maxillary first molar; **2c.** Intraoral periapical radiograph showing obturation of left maxillary first molar.

literature search, acquired data and drafted the manuscript. AK, DK, NG: Patient management, analysis of data, critically revised the manuscript.

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Common condition: Uncommon presentation

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QUESTION

A 2-year-old girl was brought to the pediatric out-patient clinic with complaints of recurrent diarrhea, poor growth and rash over the abdomen for the past few months. Examination revealed generalized lymphadenopathy, mild hepatosplenomegaly and brownish, itchy lesions over the lower abdomen extending upto the genital area (**Fig. 1**). The child had been receiving treatment in the form of oral medications and topical agents from a local practitioner, following which the skin subsided temporarily but flared on stopping the medications. An underlying immunodeficiency was suspected and the child was detected to be reactive for human immunodeficiency virus on ELISA test. Superficial skin scrapings revealed septate hyphae on direct microscopic examination of 10% potassium hydroxide (KOH) mount. What is the likely skin condition?

For answer see Page 47.



Fig 1: Extensive hyperpigmented, scaly plaque involving the lower abdomen and external genitalia, along with the medial aspect of thigh in a young child. Multiple areas of “ring within a ring” appearance (left outer aspect of thigh) and “double-edged scale” (right lower abdomen) can be seen, apart from the typical peripheral scale. Few pustules are also identifiable within the plaque.

Stepping Back to Move Forward: Retrograde Intubation in Carcinoma Epiglottis

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ABSTRACT

A 63 year-old male with an epiglottic carcinoma was posted for surgical excision. Although preanesthetic assessment suggested that intubation using videolaryngoscopy was possible, during intubation lifting the epiglottis to see the vocal cords was not possible as the carcinoma had spread locally. Retrograde intubation was performed as a rescue procedure and surgery was conducted successfully.

Keywords: Cancer, Difficult airway, Epiglottis, Laryngeal Mass.

INTRODUCTION

Laryngeal masses undergoing surgery can present unique anesthetic challenges. Difficult airway can be expected on the basis of preoperative evaluation but in some circumstances unanticipated difficult airway can be encountered.¹ It is therefore necessary to be prepared for such circumstances even though initial evaluation may not suggest major difficulties. Although videolaryngoscopy is the preferred modality to manage such cases, some circumstances may render videolaryngoscopy ineffective. Retrograde intubation is a rescue technique which can be employed when other modalities have failed.² We report a case in which unexpected difficulties were tackled using retrograde intubation.

CASE DESCRIPTION

A sixty-three-year-old male presented with difficulty in swallowing of one-month-duration. The patient had a history of hypertension of five-year duration and diabetes mellitus of nine-year duration which were controlled with oral medications, viz, amlodipine, telmisartan, metformin and glimepiride. Initial clinical and endoscopic assessment revealed a mass on the epiglottis, the biopsy of which was reported as squamous cell carcinoma. Radiological imaging showed a heterogeneous contrast enhancing mass lesion involving the body and fold of epiglottis measuring 1.6 cm×2.2 cm×2.1 cm with few bilateral cervical lymph nodes. Airway assessment showed adequate

mouth opening (>3 finger breadths; Modified Mallampatti Grade 1), and normal neck movements and thyromental distance. Flexible fiberoptic laryngoscopy was done which showed unremarkable nasopharynx, base of tongue, bilateral valleculae and lateral pharyngeal wall (*Fig. 1*). The epiglottis showed a proliferative lesion involving the tip and the left side on both the lingual and laryngeal surfaces. The left sided aryepiglottic fold was also involved while the right aryepiglottic fold was free (*Fig. 2*).



FIG.1 Preoperative flexible fiberoptic laryngoscopy image showing normal glottic opening.



FIG. 2 Preoperative flexible fiberoptic laryngoscopy image showing epiglottic mass.

The patient was posted for trans-oral robotic excision with bilateral modified neck dissection after a week. Based on the initial airway assessment, a plan for nasal intubation with micro-laryngeal tube (size 6.0 mm internal diameter) using videolaryngoscopy was made. After explaining the plan of anesthesia and obtaining a written informed consent, patient was wheeled into the operation theatre. Patient was premedicated with 0.2 mg glycopyrrolate and 1 mg midazolam by intravenous (IV) route; induction was carried out using 100 µg fentanyl and 100 mg propofol given by IV route, followed by 40 mg rocuronium given by IV route for muscle relaxation. Videolaryngoscopy revealed Cormack-Lehane grade III view. We were unable to lift the epiglottis for visualizing the vocal cords and the mass had already started to bleed by then. Flexible fiberoptic bronchoscopy was attempted but the scope could not be negotiated beyond the epiglottic mass due to poor visualization caused by the bleeding (*Fig. 3*). After the failure of intubation by both videolaryngoscopy and flexible bronchoscopy, retrograde intubation was attempted; during this period the patient's oxygenation was maintained using bag and mask ventilation. The cricothyroid membrane was identified by direct palpation and was punctured using 16G hypodermic needle. The placement of needle was confirmed by free air aspiration and an 18G epidural catheter was advanced cephalad through the needle. However, instead of coming out through the nostril, the catheter came out from the mouth. For facilitating nasal intubation, a Ryle's tube (14 Fr) was inserted from the left nostril and pulled out through the mouth. The epidural catheter was then tied to the Ryle's tube and the Ryle's tube was pulled back thus bringing the epidural catheter out from the left nostril. A bougie was railroaded over the epidural catheter followed by a microlaryngeal tube (size 6.0 mm). The endotracheal tube

position was confirmed by auscultation of breath sounds and capnography. Subsequently, an arterial line was inserted and transduced for beat-to-beat monitoring. The anesthesia was maintained with sevoflurane (in a mixture of oxygen with air) with IV infusion of rocuronium in a dose of 0.4 mg/kg/hr. The surgery was conducted uneventfully, and the patient was extubated after an overnight stay in the intensive care unit.

DISCUSSION

Retrograde endotracheal intubation is one of the oldest techniques for the management of difficult airways. Typically, it involves puncturing of the cricothyroid membrane with a needle following which a guidewire is passed upwards through the airway. Then an endotracheal tube is passed over this guidewire.¹ This technique is used in settings of airway obstruction, sub or supraglottic stenosis, non-visualization of vocal cords or failure to intubate by other methods. As this procedure can be life-saving when encountering an unanticipated difficult airway, the knowledge and training on this procedure is essential.² Some complications can occur as a result of this procedure; the guidewire may damage the airway, get coiled or broken or enter the mediastinum.³

The anesthetic management of laryngeal carcinoma is challenging. The initial evaluation should answer whether it is possible to perform ventilation with face mask; is there any anticipated difficulty in laryngoscopy and intubation; and if it will be possible to create a surgical airway if needed. In rapidly progressing tumors, the airway status can change between the initial evaluation and the day of surgery. Hence, the above-mentioned precautions are essential.⁴ Videolaryngoscopy is preferable to direct laryngoscopy in cases with laryngeal carcinoma with an anticipated difficult airway. Awake fiberoptic intubation is

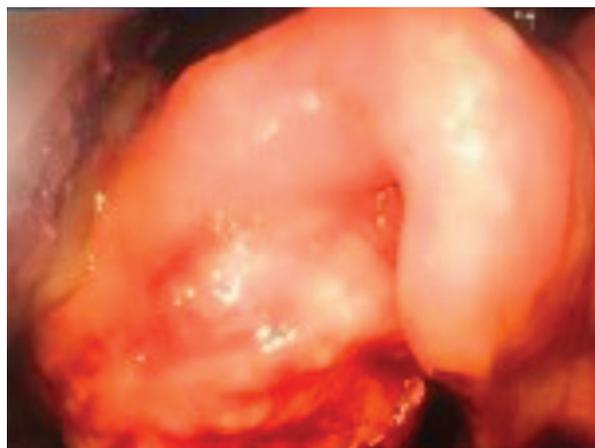


FIG. 3 Videolaryngoscopic view during surgery showing further spread of epiglottic mass with bleeding.

perhaps the safest technique in difficult airway but is not suitable when laryngeal obstruction is present.⁵

In our case, the initial evaluation suggested that intubation using videolaryngoscopy would be possible. However, the carcinoma epiglottis had spread since the last direct laryngoscopy. Further local bleeding obscured vision. The difficulty in lifting the epiglottis rendered other methods futile; in this circumstance retrograde intubation was a savior. In spite of all precautions, the management of airway in laryngeal carcinoma can be tricky and old techniques such as retrograde intubation still have their place in management of such cases.

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COMPETING INTEREST: None; FUNDING: Nil

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Takayasu Arteritis in an Adolescent Girl With Celiac Disease

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ABSTRACT

Takayasu arteritis and celiac disease are immune-mediated diseases. An association between the two conditions has been observed in a few cases. Herein, we present a 12-year-old girl who was diagnosed with celiac disease and one year later detected to also have Takayasu arteritis. Special attention should be given to this possible association as both conditions may have similar abdominal symptoms. Early diagnosis is pertinent as it has therapeutic implications.

Keywords: Autoimmune, Abdominal pain, Vasculitis

INTRODUCTION

Takayasu arteritis (TA) is a chronic granulomatous disease of unknown origin involving the aorta and its major branches. The disease manifestations reflect the extent of involvement of the vessels during the active and chronic phase of the disease. Takayasu arteritis can be associated with other autoimmune diseases.¹ Celiac disease (CD), an autoimmune disorder, occurs due to intake of gluten in genetically predisposed individuals, and primarily affects the small intestine. There are very few reported cases of association of TA with CD, especially in children.

CASE DESCRIPTION

A 12-year-old girl presented with complaints of fever, on and off, for the preceding 3-4 months, headache, bodyache and blurring of vision of one week duration, and multiple episodes of generalized seizures on the day of presentation. In the initial part of her febrile illness, she was hospitalized elsewhere and was detected to have anemia and hepatosplenomegaly; she was managed as enteric fever and discharged. Her past history and records revealed that she was diagnosed as CD one year ago when she had symptoms of chronic diarrhea, abdominal distension, growth failure and anemia. Serum tissue transglutaminase (tTG) IgA antibody levels were elevated (>20 U/ml) and the upper gastrointestinal (GI) endoscopy and biopsy findings were consistent with CD. She was prescribed gluten-free diet (GFD) and hematinics with which her gastrointestinal symptoms resolved. She reported compliance with GFD but the improvement in her

hemoglobin and growth parameters was unsatisfactory. She did not have any family history suggestive of tuberculosis or other chronic illness.

On examination during the present hospitalization, she had pallor, mild hypertension (BP 118/81 mm Hg, >95th percentile as per age and height) and hepatosplenomegaly (liver 3 cm, spleen 5 cm palpable below costal margin). She had short stature (height-for-age < -3 standard deviation, SD) with pre-pubertal secondary sexual characteristics. All peri-pheral pulses were well felt. Neurological examination revealed increased tone with brisk deep tendon reflexes and bilateral extensor plantar response; there was no neck rigidity or focal neurological deficit. Laboratory findings were: hemoglobin 8.1 g/dL, total leucocyte count 10,000/mm³, platelet count 90×10⁹/l, normocytic normochromic red blood cells on peripheral smear, unremarkable liver and kidney function tests and blood sugar. Chest radiograph showed a prominent aortic knuckle causing mediastinal widening (**Fig. 1**), and lumbar puncture was traumatic. She was managed with intravenous antibiotics, phenytoin and mannitol, pending further work-up with differential diagnoses of disseminated tuberculosis with CNS involvement and lymphoreticular malignancy. Her Mantoux test was 12 mm after 48 hours. MRI of brain showed non-specific multifocal hyperintensities. Child was started on empirical antitubercular treatment (ATT). On day 4 of hospitalization, she developed features of congestive heart failure, and was noticed to have high blood pressure (136/87 mm Hg) with prominent supra-sternal and right supraclavicular arterial pulsations with ill-



FIG. 1 Chest radiograph in a 12-year-old girl showing prominent aortic knuckle causing mediastinal widening.

defined ovoid mass with bruit auscultated over supra-sternal area and the mass. Injection furosemide followed by oral metoprolol were added to control hypertension and congestive heart failure. Ultrasonography with doppler of the mass showed dilated ascending aorta and brachiocephalic artery, circumferential mural thickening and irregularity, luminal stenosis with proximal dilatation of subclavian artery, and homogeneous moderately echogenic circumferential mural thickening in left common carotid artery (CCA). A diagnosis of aortoarteritis was suspected. Echocardiography confirmed dilatation of aorta and revealed global hypokinesia with left ventricular ejection fraction of 55% and mild pericardial effusion. Computed tomographic angiography showed dilated and tortuous aorta with areas of stenosis, irregularity of wall and small calcific foci along wall (**Fig. 2a**); dilated and tortuous brachiocephalic artery with narrowing of proximal portions of right subclavian artery and common carotid artery (**Fig. 2b**); luminal stenosis of left pulmonary artery; narrowed superior mesenteric artery (SMA) with wall thickening; attenuated left renal artery (**Fig. 2c**); and mild narrowing at origin of celiac trunk. Child was diagnosed as Takayasu arteritis type V P+ (acute and chronic changes) according to Pediatric Rheumatology European Society and European League Against Rheumatism (EULAR) proposed consensus criteria.² She was further worked up for secondary associations of TA and end organ involvement. ESR was elevated (45 mm/hr), CRP was 4.8 mg/dL, serum anti-neutrophil antibody was

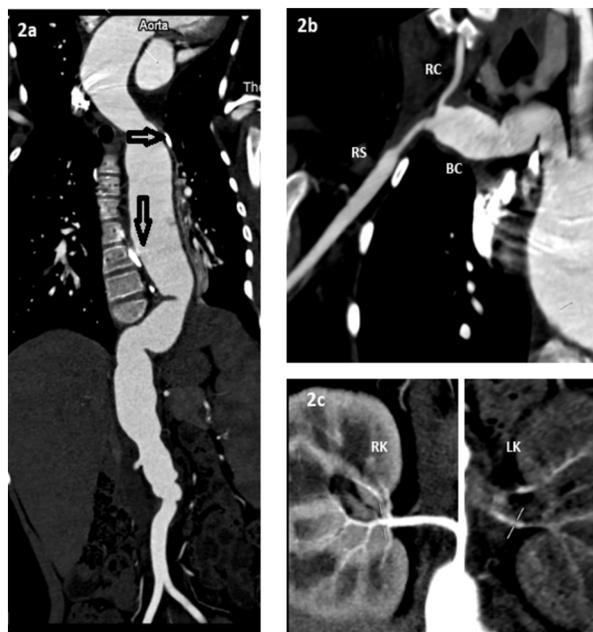


FIG. 2 Computed tomographic angiography (curved multiplanar reconstructions) demonstrating (a) dilated, tortuous aorta with areas of stenosis, irregularity of wall and calcific foci (arrows) along wall; (b) dilated and tortuous brachiocephalic artery (BC) with narrowed proximal segments in right subclavian (RS) and right common carotid (RC) arteries, and (c) attenuated left renal artery.

negative, and serum angiotensin-converting enzyme level was within normal range. Fundus examination showed no retinopathy.

Oral prednisolone (2 mg/kg/day) and aspirin were added on day 6 of admission in view of findings suggestive of TA. ATT was continued in view of positive Mantoux test and well known association of TA with tuberculosis. After 72 hours of treatment the child showed clinical improvement with resolution of tachycardia, tachypnea and regression of hepatomegaly. She was discharged on ATT, oral antihypertensive drugs and tapering doses of oral steroids. On follow-up in the outpatient clinic, she continued to have raised blood pressure for which she was advised to consult an interventional cardiologist. She was advised to undergo renal angioplasty with stent placement for persistent renovascular hypertension but she could not get it done due to various personal and logistic issues. She had an erratic follow-up in the outpatient clinic over the next few months and was subsequently lost to follow-up.

DISCUSSION

The patient described above had a severe form of TA in association with underlying CD for which she was already on GFD. Patients with CD are known to have higher

chances of other autoimmune diseases such as Type I diabetes mellitus, multiple sclerosis (MS), dermatitis herpetiformis, and autoimmune thyroiditis. TA is also known to be associated with autoimmune diseases such as systemic lupus erythematosus, juvenile idiopathic arthritis, sarcoidosis and inflammatory bowel disease.

The association of CD and TA has been reported only rarely. Some shared cytokines may play a role in co-occurrence of these diseases. Almost all the reports of this association are in young to middle aged women.³⁻⁵ On extensive literature search, we could find only one previous report of this association in pediatric or adolescent age group wherein a 12-year-old girl who presented with pallor, short stature and diarrhea and was found to be having poorly palpable pulses on clinical examination.⁶ This patient also had a history of fever of unknown origin and headache for many years before both these diseases were diagnosed. In our case, though the diagnosis of CD preceded the diagnosis of TA, it is difficult to conclude which of the two developed earlier. Our patient had severe short stature as well as extensive involvement of vasculature suggesting that both the diseases had been ongoing for a long duration. In most of the previous reports of this association, the diagnosis of TA preceded the diagnosis of CD. The absence of findings of pulselessness probably contributed to the delayed diagnosis of TA in our case. Presence of tortuous and dilated arteries in this child contributed later to the pulsations in the neck and even a pulsatile mass; thus, the disease presentation was 'pulsatile' rather than a 'pulseless' disease.

The involvement of mesenteric arteries in TA can also cause abdominal symptoms akin to those seen in CD. The tTG positivity, compatible biopsy changes and response to GFD confirmed the presence of CD in our case. However, continuing pallor, fatiguability and appearance of prolonged fever suggested another additional diagnosis which later turned out to be extensive TA.

We conclude that in patients with CD, autoimmune disorders like TA may be suspected if there is unexplained fever or/and inadequate response to GFD despite compliance. Likewise, in patients with TA, symptoms of diarrhea and abdominal distension may suggest CD and warrant further investigations. As each of these diseases involve a different management strategy, timely recognition of association is required improve the outcome.

CONTRIBUTORS: All authors were involved in the diagnosis and clinical management of the child. EA drafted the manuscript which was revised by DS with critical inputs from NG. All authors approved the final version of the manuscript.

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A Dash of Common Salt for Umbilical Granuloma

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CASE 1

A four-week-old male baby was brought by his mother to the outpatient department with complaints of a small reddish pea-sized swelling at the umbilicus noticed after the umbilical cord had fallen off at two weeks of age (**Fig. 1a**). The mother also noticed a scanty, clear and odorless discharge at the site. The surrounding skin was, however, healthy. A possible diagnosis of umbilical granuloma was made. Due to non-availability of silver nitrate stick, a pinch of common salt was sprinkled over the umbilical swelling and covered with a damp gauze for 15 minutes, followed by thorough cleaning of the site. After the first application of salt, the swelling shrunk and became black. The salt pack was repeated the next day, and following it the swelling shriveled and fell off. By the fourth day, the umbilicus was free of any discharge and appeared healthy (**Fig. 1b**).

CASE 2

A two-month-old baby girl was brought by her mother with complaints of a pinkish swelling at the umbilicus noticed since the age of 3 weeks after separation of the umbilical cord. There was associated oozing of some clear and odorless discharge from the swelling (**Fig. 1c**). Considering a possibility of umbilical granuloma, application of silver nitrate was advised to cauterize the lesion. However, due to non-availability of the same, a pack of common salt was applied for 15 minutes. The salt pack was repeated the next day following which the granuloma became black and decreased in size. On the third day, the umbilicus was healthy and clear of any oozing (**Fig. 1d**).

In both the cases, there was complete resolution of granuloma with salt treatment in 2-3 days with no adverse effects and no recurrence was seen at 3 months follow up.

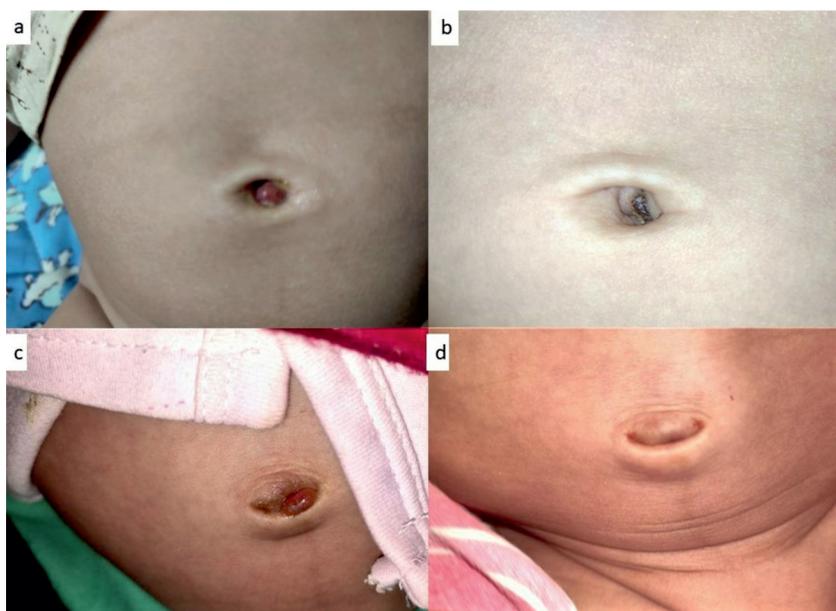


FIG. 1a. A reddish pea-sized umbilical granuloma seen after the cord fell off in case 1, **1b.** Healthy umbilicus following application of salt pack in case 1, **1c.** Umbilical granuloma seen in case 2, **1d.** Healthy umbilicus seen following local application of common salt in case 2.

KEY LEARNING POINT

- Application of common salt pack is an easily available, cheap, rapid, safe and effective treatment option for umbilical granuloma.

DISCUSSION

Umbilical granuloma is the most common umbilical mass observed in the infants and neonates.¹ It is likely due to the overgrowth of umbilical tissue or excessive inflammation of the umbilical cord following improper cutting of the cord after birth.^{2,3} It may present as a protuberant red swelling or with serous or bloody discharge from the umbilicus.

Since umbilical granulomas do not resolve spontaneously, it is imperative to treat them to prevent complications like persistent discharge, omphalitis or bleeding. Conventionally, umbilical granulomas are treated with chemical cauterization using topical silver nitrate or copper sulfate to cauterize the granuloma.^{4,5} Alternative non-invasive treatments include topical steroids like clobetasol propionate or ethanol swabs.^{6,7} Surgical electro-cauterization, cryocauterization and surgical excision are other invasive modalities for managing umbilical granulomas, although used uncommonly. The use of topical silver nitrate and copper sulfate is not cheap, entails the risk of chemical burns and these may not be readily available. Although topical application of steroids can be done easily, it requires daily application for a prolonged period of 4-6 weeks and their use is fraught with complications like local infection. Use of ethanol swabs for treating umbilical granulomas have not had very successful outcomes.

A simple home remedy like application of “common salt” on the lesion can be a cheap and effective alternative solution. The efficacy of salt is explained by its dehydrating action by virtue of its hyperosmolarity. However, prior evaluation of the lesion by a qualified doctor to rule out mimickers of umbilical granuloma like umbilical polyp, umbilical adenoma or urachal anomalies should be done.⁸ The successful treatment of umbilical granuloma with common salt was reported first in 1971,⁹ and subsequently by several authors who reported complete resolution of umbilical granuloma with common salt application with no adverse effects or recurrence on subsequent follow-up.¹⁰⁻¹³

CONTRIBUTORS: MS and PD were involved in patient management, reviewing the literature and writing the manuscript. Both approved the final manuscript and are accountable for all aspects.

COMPETING INTEREST: None; FUNDING: Nil

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Neoadjuvant Immunotherapy: Is this the new Hope in Mismatch-Repair Deficient Locally Advanced Rectal Cancer?

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ABSTRACT

Neoadjuvant chemotherapy and radiation followed by surgical resection of the rectum is a standard treatment for locally advanced rectal cancer. Approximately 5-10% of rectal adenocarcinomas are mismatch-repair deficient (dMMR). These tumours respond poorly to standard chemotherapy regimens, including neoadjuvant chemotherapy in locally advanced rectal cancer. Programmed cell death inhibitors including Dostarlimab and Toripalimab alone or in combination with Celecoxib, offer promising results in the treatment of dMMR locally advanced rectal cancer.

Keywords: Dostarlimab, Immunotherapy, PD-blockade, Toripalimab.

Cancer of the rectum is the third-most incident cancer globally with nearly 44,850 (26,650 men and 18,200 women) new cases of rectal cancer predicted in 2022.¹ Adenocarcinoma accounts for 90% of rectal cancer histologic types; the rest include neuroendocrine, signet ring, squamous cell, adenosquamous, small cell and undifferentiated carcinomas. Neoadjuvant chemotherapy and radiation followed by surgical resection of the rectum is the standard treatment for locally advanced rectal cancer.

Approximately 5-10% of rectal adenocarcinomas harbour deficient mismatch repair (MMR) DNA. MMR deficiency is one of the best-understood forms of genetic instability and is characterized by the loss of function of the MMR pathway. Failure to repair replication-associated errors due to a defective MMR system allows the persistence of mismatch mutations all over the genome which may lead to cancer. MMR deficiency is most common in colorectal cancer as also in gastrointestinal and endometrial cancer, but it may also be found in cancers of the breast, prostate, bladder, and thyroid. MMR deficiency may also be found in an inherited disorder called Lynch syndrome (previously known as hereditary non-polyposis colorectal cancer syndrome). These tumours respond poorly to standard chemotherapy regimens including neoadjuvant chemotherapy in locally advanced rectal cancer.² Knowing if a tumour is MMR

deficient (dMMR) may help plan treatment or predict how well the tumour will respond to treatment.³

In August 2021, US Food and Drug Administration (FDA) approved Dostarlimab (Jemperli®, Glaxo SmithKline), a programmed cell death receptor-1 (PD-1) blocking antibody, for the treatment of adult patients with mismatch-repair deficient (dMMR) recurrent or advanced solid tumours (as determined by an FDA approved test) and which show no response to prior treatment and are left with no satisfactory alternative treatment modalities. The approval of Dostarlimab follows an FDA priority review of the Biologics License Application and is based on the collective results from the dMMR endometrial cancer cohort A1 and the dMMR solid-tumour (non-endometrial cancer) cohort F of the ongoing GARNET trial. The GARNET trial was a multicentre, non-randomised, multiple parallel-cohort, open-label study which began in March 2016 and continued till August 2019. Cohort F included patients with dMMR recurrent or advanced non-endometrial cancers, with the highest prevalence in colorectal, small intestine and stomach cancers. Patients received 500mg Dostarlimab by intravenous route every 3 weeks for 4 cycles, and then 1000 mg every 6 weeks. This treatment was associated with clinically meaningful anti-tumour activity with an acceptable safety profile. Based on the benefits seen in the context of metastatic disease in the GARNET trial, the study team hypothesised that single-

agent PD1 blockade might be beneficial in dMMR locally advanced rectal cancer.⁴ This triggered an interest in PD-1 blockade to be used as a single agent of dMMR tumours. In dMMR rectal tumours, immune checkpoint blockade alone is highly effective as a first-line treatment, as well as in the treatment-refractory disease, with objective response rates of 33-55%, clinically significant duration of response, and prolonged overall survival.

Neoadjuvant immunotherapy has also been investigated in solid tumours, including those that are known to be sensitive to checkpoint blockade in metastatic diseases like non-small cell lung cancer, urothelial carcinoma and melanomas.^{5,6} In a study done on non-small cell lung cancer (NSCLC) patients, it was observed that two doses of PD-1 blockade resulted in a 10% response rate. In another study involving melanoma patients, a 52% response rate was seen with immunotherapy alone.⁷

Another study shows that a single dose of Ipilimumab and two doses of Nivolumab before surgery in dMMR colon cancer resulted in a 50% response.⁸ Toripalimab alone or in combination with celecoxib resulted in an imaging-based response in 55% of patients.⁹ It has also emerged that a longer course of immunotherapy showed better response compared to shorter exposure to checkpoint blockade as a response to immunotherapy takes months rather than weeks to evolve. A recent study by Cercek, *et al* done on 12 patients of dMMR rectal cancer showed that treatment with Dostarlimab, given every 3 weeks for 9 cycles over 6 months, revealed 100% response.¹⁰ This could be a breakthrough in the treatment of rectal cancers as these patients have been seen to have more than 1-year of sustained clinical response without any need for further surgery or chemotherapy. This would save the patients from the associated side effects of bowel, bladder, sexual dysfunction and the hassles of a diverting colostomy. Thus, neoadjuvant immunotherapy has undoubtedly emerged as a potential primary intervention in dMMR locally advanced rectal tumours.

Still, the question of why the localized dMMR rectal tumours respond so well with PD-1 blockade as compared to metastatic colorectal cancer remains to be answered. The probable explanation could be the gut microbiome's influence in the evolution of antitumour response potentiated by immune checkpoint blockade.¹¹ Certain bacterial species like *Fusobacterium nucleatum* were seen to be associated with an immune-responsive environment in mismatch-repair tumours. *Ruminococcus spp.* and *Akkermansia spp.* of gut are associated with notable pathological responses in NSCLC.¹² Thus we can hypothesize that in addition to the burden of mutation defect associated with mismatch-repair deficiency, the gut-

microbiome also has a role to play in eliciting a good clinical response in such tumours.

On the whole, neoadjuvant immunotherapy involving PD-1 blockade along with the influence of the gut microbiome could drastically improve the patient response and survival in locally advanced rectal cancer patients with mismatch repair deficiency. PD-1 blockade with Dostarlimab for 6 months is a promising candidate for complete remission in locally advanced rectal cancer saving the patients from the adverse effects of chemoradiation and surgery. However, this study needs to be followed up for a longer period in a larger cohort to come to a definite conclusion asserting its 100% response. Taken together, neoadjuvant immunotherapy with agents such as Dostarlimab could turn out to be a beacon of hope for such patients in providing the best response with minimal side effects.

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IMAGE QUIZ ANSWER

The child is suffering from a modified superficial dermatophytosis known as ‘Tinea pseudoimbricata’ or ‘Tinea indecisiva’. It forms a subset of ‘Tinea incognito’, or altered tinea, where the typical features of central clearing, peripheral scaling and inflammatory border are absent or reduced. It is characterized by multiple concentric rings with variable scaling. The lesions are similar to Tinea imbricata, which is caused by *Trichophyton concentricum*. On the other hand, Tinea pseudoimbricata has been shown to be caused by multiple dermatophyte species including *Trichophyton tonsurans*, *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Microsporum audouinii* and *Microsporum gypseum*.

Tinea pseudoimbricata is a presentation seen in immunocompromised individuals and in patients with history of topical steroid abuse.¹⁻³ It presents with sequentially appearing concentric scaly rings, giving rise to the characteristic “ring-within-a-ring appearance”.⁴ A high index of clinical suspicion and direct microscopic examination of skin scrapings with KOH and fungal culture on Sabouraud’s dextrose agar (SDA) are vital for the diagnosis.

The condition necessitates systemic antifungal therapy for a prolonged period of at least 6-8 weeks. The drugs recommended are terbinafine and itraconazole. Suboptimal response is expected with fluconazole or griseofulvin. The prognosis is good with adequate and prolonged treatment coupled with management of causes of immunosuppression. This is commonly in the form of topical or systemic steroid abuse, which needs to be stopped. The same was denied in our case. Other causes like HIV infection, like in our case, need to be managed adequately. At the same time, it is important to treat the family members and educate them regarding the infectious nature of the condition, the role of fomites like clothing and bedding, separate washing of infected clothes, avoidance of sharing of towels, clothes, bed linen, and soaps, and the need for good skin hygiene practices.

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Understanding the Facets of Service Bond for Medical Graduates and Post-Graduates in India

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Health equity and availability of health services are major concerns for our country. The shortage of trained doctors in India is particularly perturbing considering that India is the world's second most populous country. According to the World Health Organization (WHO), the average number of medical doctors per 10,000 population is 16.37 globally in 2012-2020.¹ The corresponding figure for India was only 7.4 doctors per 10,000 population.¹

To combat this vexing issue, the solution that most state governments have devised is a service bond for medical students when they join a graduate or post-graduate course. According to the service bond policy in India, medical graduates and post-graduates are obliged to serve for a specific period in state-run hospitals or peripheral health centres after completion of their undergraduate and/or post-graduate degree. Failure to do so warrants a penalty varying from a substantial amount of bond money (specified beforehand by the administration), and in some rare instances, even cancellation of the degree.²

Such policies have long been a part of the world-wide landscape, with the earliest such programmes dating back to the early 20th century.³ These were introduced to encourage students, who received government financial aid for their medical education, to work for the public sector as a way of "giving back to society." Such service bonds come in a variety of forms, from rural recruitment in Thailand, to service in exchange for scholarships in Nepal and Indonesia.

Although, there was no provision for a service bond under the National Medical Commission (NMC) Act 2019 or the Indian Medical Council Act 1956, several states included service bonds as an obligatory requirement for admission to medical courses. These were adopted by state governments to fill up the vacant posts in community

health centres and primary health centres as well as for the implementation of the government's vaccine and woman-and-child medical programmes, especially in peripheral, rural and tribal areas.

Since the state government provides subsidised education in state-run medical colleges, it gets to decide the bond amount. The bond amount has ranged from rupees 5 lakh in Rajasthan and Tamil Nadu, upto rupees 1 crore in Uttarakhand for admission to Bachelor of Medicine and Bachelor of Surgery (MBBS) course. The amount extends to a few crores for post-graduate and super-specialty medical training (**Table I** and **Table II**). The duration of compulsory service also varies from state-to-state ranging from 1 year to 5 years. However, this system of service bonds is ridden with numerous complications in the current scenario of our country's healthcare infra-structure, as well as uncertain and unclear terms of implementation. Very often these postings are not allotted to graduates within a stipulated time and they are left with no option but to find other jobs or join higher studies. However, since the government withholds issuing degrees to medical graduates until the completion of the mandatory service, this often also renders such doctors unable to work elsewhere. In a recent example from Rajasthan, doctors were forced to sit idle for five months without salaries after the completion of their junior residency due to the delayed implementation of bond service.⁴ To prevent the occurrence of such situations, it might be more beneficial for bonds to specify a duration of time after which doctors are no longer required to do mandatory service. It has also been seen that sometimes policies are changed after the students have started the counselling process for admission or when they have already joined the courses. Many states have very strict bond requirements which leave students with no time for individual study. In some states there are different rules for

TABLE I: State-wise rural service bonds in India after completing Bachelor of Medicine and Bachelor of Surgery (MBBS)

State	Service bond	
	Duration of service	Penalty (Rupees)
Andhra Pradesh	-	-
Andaman and Nicobar	1 year	10 lakhs
Assam	5 years	30 lakhs
Bihar	-	-
Chandigarh	-	-
Chhattisgarh	2 years	25 lakhs
Delhi	-	-
Goa	1 year	10 lakhs
Gujarat	1 year	20 lakhs
Haryana	5 years	30 lakhs
Himachal Pradesh	-	-
Jharkhand	3 years	30 lakhs
Karnataka	1 year	10 lakhs
Madhya Pradesh	1 year	10 lakhs
Maharashtra	1 year	10 lakhs
Manipur	-	-
Meghalaya	-	-
Mizoram	-	-
Odisha	2 years	25 lakhs
Pondicherry	-	-
Punjab	-	-
Rajasthan	2 years	5 lakhs
Tamil Nadu	5 years	5 lakhs
Telangana	-	-
Tripura	5 years	20 lakhs
Uttar Pradesh	2 years	10 lakhs
Uttarakhand	5 years	1 crore
West Bengal	-	-

All-India quota (AIQ) seats and state-quota seats, with students joining through AIQ being exempt from service bond. Haryana has introduced a bank loan policy for the bond with unclear specifications regarding interest rates; a 5-year-long service-bond period and no job guarantee. This led to the eruption of widespread protests by medical students all over the country.⁵ In August 2019, the Supreme Court observed that the service bond conditions in some states were too unaccommodating and needed changes. It advised the centre and the Medical Council to develop a uniform national policy regarding the compulsory bond service.⁶

TABLE II: State-wise rural service bonds in India after completing Doctor of Medicine (MD) or Master of Surgery (MS) Course

State	Duration of service	Penalty (Rupees)
Andhra Pradesh	1 year	20 lakhs
Assam	10 years	20 lakhs
Bihar	3 years	25 lakhs
Chhattisgarh	2 years	50 lakhs
Goa	1 year	50 lakhs
Himachal Pradesh	2 years	40 lakhs
Jharkhand	3 years	30 lakhs
Karnataka	3 years	50 lakhs
Kerala	1 year	50 lakhs
Madhya Pradesh	1 year	10 lakhs
Maharashtra	1 year	50 lakhs
Manipur	1 year	20 lakhs
Odisha	2 years	40 lakhs
Pondicherry	3 years	10 lakhs
Punjab	1 year	10 lakhs
Rajasthan	2 years	25 lakhs
Tamil Nadu	2 years	40 lakhs
Telangana	1 year	20 lakhs
Tripura	3 years	50 lakhs for clinical courses; 35 lakhs for pre and para clinical
Uttar Pradesh	2 years	40 lakhs
Uttarakhand	2 years	2.5 crores
West Bengal	3 years	30 lakhs

Students also claim that there are no service bonds applicable to students studying in subsidised educational institutions other than the state-run medical colleges. The state-to-state disparity in service bond has a significant impact on medical students' college choices during the counselling process. This has resulted in students opting for medical courses in those states or institutions which have no service bond. Currently, students studying in medical colleges under the ambit of Institutes of National Importance (INI) including All India Institute of Medical Sciences (AIIMS), medical colleges in few states like Delhi, and unaided private medical colleges have no service bond obligations. Therefore, students preferentially opt for these institutes to bypass the obligatory service bond.

In 2010, the WHO published several recommendations to improve healthcare services in remote and rural areas. They discussed the importance of education and exposure of students to rural healthcare, setting up of medical

colleges outside of big cities, providing personal and professional support, along with financial incentives and scholarships.⁷

NMC's recent guidelines on implementation of the District Residency Programme makes it mandatory for all students pursuing post-graduate medical courses in India to serve at a district hospital for 3 months, on a rotational basis, during the 3rd, 4th or 5th semester of their post-graduation. As this programme is a part of medical training itself, it is a prime example of a policy that enables resident doctors to provide non-bonded service while also improving healthcare facilities at the district level.⁸

A study conducted in Odisha concluded that facilities such as housing, better pay, and improved healthcare resources could give better results with respect to rural service.⁹ The state government of Uttarakhand fired 43 doctors who chose to not join their state service duties on account of inadequate infrastructure at hospitals and poor overall facilities for doctors as well as patients.¹⁰ It was observed that in states like Gujarat, majority of the students chose to pay the penalty amount *in-lieu* of completing the mandatory service and proceed for higher education.¹¹ It is apparent that service bonds can only partially help with the workforce shortage and are by no means the only solution. The infrastructure and management of the peripheral and rural health centres has to be prioritized. A greater impetus to healthcare needs to be the focus to motivate health professionals to serve in remote areas and thereby improve availability of healthcare in rural areas.¹²

Apart from the service bond policy, other implementable measures to increase the availability of manpower in peripheral and rural health care centres can be the provision of in-service quota in post-graduate admissions for candidates who serve in the peripheral areas, ensuring adequate medical infrastructure and support staff in peripheral health centres and hospitals, providing financial incentives apart from the salary for serving in rural and tribal areas, improving infrastructure for living, and creating additional facilities so that doctors can settle with their families in these areas. Any sort of bond should never hinder a medical student's higher education; but it should be flexible enough to make room for it. There needs to be a provision to complete the service bond after completing higher education within a reasonable time frame.

The strategy in some states, which involves banks and has an unacceptably long service time, appears to be more focused on protecting the state and recouping its costs than it is on encouraging public service. Two more considerations further demonstrate this: first, the number

of applicants has recently outpaced the number of openings announced; and second, the most current Rural Health Statistics (RHS), 2020-21, indicate a shortage of positions for rural primary health centre doctors.¹³

The state is required to invest in medical education for the benefit of the general public. Doctors also continue to give back to society even while working in the private sector or abroad, regardless of mandatory public service clauses. Over the last ten years, the number of government and private medical seats, as well as ambitious private-public collaborations in medical education, has increased significantly in the country. Now the programme has also prioritised the vernacularisation of medical education to provide access to the underprivileged members of our community.¹⁴ Service bond rules will create a significant entry hurdle in medical education and produce unfavourable outcomes by discouraging students from pursuing medicine. However, whether the mandated rural service needs to be completely eliminated is debatable. There is a compelling moral and social obligation on the part of the students for returning their financial aid. In locations where there is a recognised shortage of doctors even a tiny contribution from candidates towards bonded service can have a big impact. Evidence-based, well-balanced interventions that are mindful of both society's needs and students' aspirations are urgently needed. The distinction between rural recruitment and rural doctor retention holds the key to the solution. Even if the latter is the ideal outcome, it will be expensive to solve the rural doctor retention issue over a sustained period of time as the rural-urban divide is essentially a developmental issue. It would be simpler to deal with, requiring fewer changes to the current regulations, to make periodic, short-term recruitments attractive. Strict regulatory tools should not tempt governments just because they have lower direct costs. Similarly, potentially beneficial options like rural service requirements should not be completely rejected. Finding a beneficial middle path that benefits the society as a whole without alienating its doctors is the best course of action.

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 **Acharya I, Rohatgi J, Sahu PK. Surgical success of 'W' shaped incision versus Tear trough incision in external dacryocystorhinostomy. *Orbit.* 2022;41(5):572-580.**

In a prospective study, 61 eyes of chronic dacryocystitis underwent external dacryocystorhinostomy randomized into group T (30 eyes) and group W (31 eyes). Intraoperative skin flap button-holing and reversible darkening of their apices were specific complications of group W. In the early postoperative period, lid edema and epiphora were significantly more in group T. Overall, the surgical success in terms of cosmetic, anatomical and functional outcomes in both groups were comparable.

 **Agrawal A, Jha T, Gogoi P, et al. Effect of convalescent plasma therapy on mortality in moderate-to-severely ill COVID-19 patients. *Transfus Apher Sci.* 2022;61(6):103455.**

This study analyzed the records of all COVID-19 patients who received plasma therapy over a period of 6 months in a dedicated COVID-19 hospital in Delhi. Of the 141 patients who received plasma therapy, 62% were discharged after treatment. Age > 60 years, severe COVID-19 infection and pre-existing renal disease were significantly associated with a fatal outcome. The admission-transfusion interval < 5 days was significantly correlated with greater mortality. Patient blood group, plasma antibody levels or donor hemoglobin levels were not associated with death.

 **Aggarwal S, Rajnish RK, Kumar P, Srivastava A, Rathor K, Haq RU. Comparison of outcomes of retrograde intramedullary nailing versus locking plate fixation in distal femur fractures: A systematic review and meta-analysis of 936 patients in 16 studies. *J Orthop.* 2022;36:36-48.**

Six randomized control trials, 2 prospective and 8 retrospective studies with 936 patients with 8 bilateral cases [467: retrograde intramedullary nails (RIMN) and 477: locking plates (LP)] were included. The analysis concluded that there was no statistically significant difference in terms of mean fracture union time, overall complications, implant-related complications, re-operation rates, and duration of surgeries, in both techniques in distal femur fractures. However, a better knee range of motion was seen in the LP method albeit with a greater non-union and infection rate compared to that with RIMN technique.

 **Agrawal T, Dewan P, Gomber S, Agarwal R, Sharma S, Kotru M. Optimum dose of oral folic acid supplementation in transfusion-dependent thalassemia: a randomized controlled trial. *J Trop Pediatr.* 2022;68(6):fmac087.**

A randomized study compared the effect of different doses of oral FA supplementation on the proportion of children with folate and plasma homocysteine (Hcys) excess in transfusion-dependent thalassemia (TDT). After an initial wash-off period of 8 weeks, the median serum folate levels were significantly lower and five children developed folate deficiency. 90 children were randomized to receive different FA doses (5 mg/day Vs 2.5 mg/day Vs 5 mg/week) over 9

months follow up. After 9 months, the median serum folate and Hcys levels and proportion of children with serum and RBC folate excess were comparable in the three groups. Hyperhomocysteinemia was seen in eight children. Routine FA supplementation is recommended in TDT, albeit 5 mg weekly FA may be adequate.

 **Ahmad S, Arora R, Aggarwal AN, Ul-Haq R, Khan K, Tandon A. Comparison between reliability of Schatzker's classification and CT based four quadrant classification for tibial plateau fractures. *J Clin Orthop Trauma.* 2022;32:101986.**

CT based four quadrant classification has been proposed to identify fractures of tibial plateau and aid their surgical treatment. Plain radiographs and CT scans of 35 patients of closed tibial plateau fractures were assessed by 5 orthopedic surgeons and classified by Schatzker's and four-quadrant classification. A similar observation was recorded after 2 months. Four-quadrant classification seemed more reliable in determining tibial fractures having a better agreement on interobserver and intraobserver variation.

 **Bhavya, Rajaram S, Gupta B, et al. PAX1 methylation status in cervical scrapes as novel diagnostic biomarker in CIN 2/3 and invasive squamous cell carcinoma. *J Obstet Gynaecol India.* 2022;72(6):522-528.**

A total of 200 screen positive women (VIA, VILI and Pap test) underwent colposcopy wherein cervical scrapes were taken and stored for DNA analysis and PAX 1 methylation status. Cervical biopsy was performed in women with Swede score ≥ 5 ($n = 98$). Cervical scrapes and biopsy were also obtained from 14 women with obvious cervical growth. PAX 1 methylation percentage was calculated from the DNA extracted from the cervical scrapes. The mean PAX1 methylation percentage in benign lesions, CIN 2/3 and invasive cancer was 9.58% ($\pm 2.37\%$), 18.21% ($\pm 2.67\%$) and 24.34% ($\pm 4.09\%$), respectively, with P-value < 0.001. PAX1 methylation can serve as a marker of high-grade and invasive cervical cancer.

 **Chandra J, Dewan P, Kumar P, et al. Diagnosis, treatment and prevention of nutritional anemia in children: Recommendations of the joint committee of Pediatric Hematology-Oncology Chapter and Pediatric and Adolescent Nutrition Society of the Indian Academy of Pediatrics. *Indian Pediatr.* 2022;59(10):782-801.**

These are the first evidence-based guidelines for the management of nutritional anemia in children. The authors recommend the use of WHO recommended cut-offs of hemoglobin to define anemia in children and adolescents. These guidelines provide an algorithmic approach for the management of iron deficiency anemia and anemia due to vitamin B12 or folic acid deficiency. Screening of infants for anemia at 9 months' age during the routine immunization visit is recommended along with continued iron folic acid supplementation as per the Anemia Mukta Bharat Program.

 **Gangwani N, Singh S, Khaliq F. Trigger films to teach core competencies of ethics and professionalism to first-year medical and nursing students. *Adv Physiol Educ.* 2022;46(3):491–497.**

The study evaluated the role of trigger films, 3-10 minute-long movie clips, as a tool to impart training in professionalism and ethics to under-graduate medical and nursing students. A 2-hour module incorporating an introductory powerpoint presentation and four trigger films based on the four ethical principles of beneficence, non-maleficence, autonomy, and justice, was developed and piloted in the foundation course for the new cohort of students. The students perceived trigger films as an effective and innovative teaching-learning tool.

 **Goel A, Raizada A, Agrawal A, et al. Correlates of in-hospital COVID-19 deaths: A competing risks survival time analysis of retrospective mortality data. *Disaster Med Public Health Prep.* 2022;16(5):1889–1896.**

Data of 1147 COVID-19 patients with a mean age of 50 (± 16.5) years treated at a dedicated COVID hospital in North India, with moderate and severe illness over an 8-week-duration were reviewed. 885 (77.2%) patients were confirmed positive for COVID-19 on reverse transcriptase polymerase chain reaction (RT-PCR). Of 1147 patients, 312 (27.2%) died in hospital and of these 219 had tested positive for COVID-19 on RTPCR. Amongst the COVID-19 positive cases, one-third had died within the first 72 hours of hospitalization; most of them had associated comorbidities. The median time from the onset of symptoms to death was 11 days. After adjusting for sex and COVID-19 test status, advancing age was found to be significantly associated with death.

 **Grover C, Kharghoria G Nail Lichen Planus Severity Index (NALSI): A Novel Severity Score for Nail Lichen Planus. *Indian Dermatol Online J.* 2022;13(5):680–681.**

The authors proposed a score for nail lichen planus to aid evaluation of disease severity and monitor the response to treatment. Each nail is scored based on changes seen in nail matrix, nail bed, and nail fold and presence of irreversible nail changes like dorsal pterygium, atrophy, onychia, or disappearing nail bed.

 **Gupta VP, Beri N, Rohatgi J. Comparative evaluation of outcomes of novel approach of subconjunctival Mitomycin C (MMC) injection at the end of trabeculectomy versus intraTenon injection of MMC prior to the initial conjunctival incision - A pilot study. *Indian J Ophthalmol.* 2022;70(12):4194–4200.**

This pilot study included 40 eyes of 40 patients with uncontrolled glaucoma. Patients below 18 years and failed trabeculectomy were excluded. Patients were randomized to receive subconjunctival mitomycin C injection in the superonasal quadrant at the end of standard trabeculectomy (group A, n=20) or intraTenon mitomycin C injection before the initial conjunctival incision (group B, n=20). Complete success (intraocular pressure < 21 mm Hg without antiglaucoma drugs) was observed in 95% and 75% participants in groups A and B, respectively, 19 months after surgery. Avascular microcystic blebs (70% of group A and 45% of group B) were more common than avascular white blebs (15% in group A and 35% in

group B). Both groups did not report any intra-operative complications, post-operative wound leak, hypotony, choroidal detachment, or endophthalmitis. Subconjunctival mitomycin C during trabeculectomy is a useful modality with greater success rate compared to the intra Tenon mitomycin C.

 **Jain A, Aggarwal R, Gupta N, et al. Reduced fetal urine production rate-An early marker of fetal inflammatory response syndrome in preterm premature rupture of membranes: Prospective cohort study. *Int J Gynaecol Obstet.* 2022;159(2):444–450.**

This prospective cohort study of 70 pregnant women with preterm premature rupture of membranes at 28-34 weeks of pregnancy aimed to find the association between fetal urine production rate (FUPR) and fetal inflammatory response syndrome (FIRS). FUPR was calculated by weekly fetal bladder volume measurements on ultrasound until delivery. After delivery, cord blood interleukin-6 levels, placental tissue histopathology and neonatal outcomes were recorded. Mean FUPR was significantly reduced in neonates with evidence of FIRS. Reduced FUPR can be used as an early predictor of adverse neonatal outcomes.

 **Jindal R, Grover C, Sarkar R, Gupta LK. IADVL Academy position statement on emerging dermatoses in India: Monkeypox. *Indian Dermatol Online J.* 2022;13(5):559–569.**

Through the document, the Indian Association of Dermatologists, Venereologists, and Leprologists aims to sensitize dermatologists to enable prompt recognition and containment of monkeypox which was declared to be a “Public Health Emergency of International Concern” by the World Health Organization in mid-2022.

 **Kaushik JS, Ramachandran P, Kukreja S, Gupta P, Singh T. Delivering electives the clerkship way: consolidating the student doctor method of training. *Indian Pediatr.* 2022;59(9):710–715.**

The authors propose a model to deliver the electives during medical graduate training in India using the clerkship method. This model allows medical students to interact with real patients as a part of a treating team under the guidance of an experienced faculty and allows them to integrate their basic science knowledge with clinical reasoning. Elective posting during under-graduate medical training is a feasible and practical teaching-learning tool.

 **Khairwa A, Kotru M, Dewan P, Narang S. Morphological markers of chromosomal instability in bone marrow aspiration and trephine biopsy of acute leukemia and myelodysplastic syndrome. *Environ Mol Mutagen.* 2022;63(8–9):418–422.**

Seven morphological markers of chromosomal instability (CI) viz., chromatin bridges, multipolar mitosis (MPM), nuclear budding, micronuclei (MN), nuclear heterogeneity (NH), laggards, and chromatin strings in bone marrow aspirate and biopsy, were studied in 37 patients diagnosed with acute leukemia or myelodysplastic syndrome (MDS). All CI markers except laggards were significantly increased in B-acute lymphoblastic leukemia (B-ALL), acute myeloid leukemia (AML) and MDS. The MN, MPM, laggard and NH markers were significantly increased in

patients who met a fatal outcome. Morphological markers of CI are valuable diagnostic and prognostic aids in hematological malignancies.

 **Madan S, Yadav R, Rohatgi J, et al. Demographic and clinical profile of patients presenting with COVID-19-associated rhino-orbito-cerebral mucormycosis at a tertiary care center. *Ann Natl Acad Med Sci.* 2022;58(4):210–219.**

This descriptive study determined the demographic and clinical profile including the risk factors in 117 patients admitted with COVID-19-associated rhino-orbito-cerebral mucormycosis. Diabetes mellitus was noted in 86.2% patients, oxygen supplementation for COVID-19 was received for about 11 days by 34.3% patients. 60% patients were treated with corticosteroids and intravenous amphotericin B was administered to all. External sinonasal debridement was performed in 78.9%, retrobulbar amphotericin B injection administered in 47.9%, and orbital exenteration was performed in 14.5%.

 **Madhu SV, Mishra BK, Mannar V, Aslam M, Banerjee B, Agrawal V. TCF7L2 gene associated postprandial triglyceride dysmetabolism—a novel mechanism for diabetes risk among Asian Indians. *Front Endocrinol (Lausanne).* 2022;13:973718.**

The increase in the risk of type 2 diabetes mellitus (T2DM) in individuals with transcription factor 7 like 2 (TCF7L2) gene is explained by its effect on insulin secretion. Post-prandial lipid responses to a standardized fat challenge test were performed in 620 Asian Indian participants aged 20–60 years (310 with normal glucose tolerance, 155 with prediabetes, 155 with T2DM) and compared between the risk and wild genotypes of the rs7903146 TCF7L2 gene. In 30 participants, adipocyte TCF7L2 gene expression was also performed. Significant upregulation of TCF7L2 gene expression in visceral adipose tissue that correlates with post-prandial hypertriglyceridemia and glycemia was seen in Asian Indians with glucose intolerance which contributes to their increased diabetes risk.

 **Madhu SV, Aslam M, Mishra BK, Gupta A, Jhamb R. Association of 25 (OH) vitamin D and leptin in individuals with insulin resistance. *Indian J Endocrinol Metab.* 2022;26(5):435–438.**

The study assessed association between hypovitaminosis D and hyperleptinemia. 92 individuals; 46 each with insulin resistance (homeostasis model assessment of insulin resistance [HOMA-IR] ≥ 2.0) and without insulin resistance (HOMA-IR < 2.0), were evaluated for serum 25(OH) vitamin D, leptin, anthropometry, and biochemical parameters. Higher circulating leptin levels and lower 25(OH) vitamin D levels were observed in individuals with insulin resistance.

 **Shah HK, Banerjee BD, Thakur GK, Guleria K. Organochlorine pesticides induce epithelial as well as inflammatory mediators following exposure to human ovarian surface epithelial cells: an in vitro study. *J Biochem Mol Toxicol.* 2022;36(11):e23191.**

The study investigated the impact of dichlorodiphenyldichloroethylene (DDE), endosulfan, and heptachlor exposure on

epithelial cadherin (E-cadherin) and proinflammatory mediators in human ovary surface epithelial (HOSE) cells. Exposure to DDE, endosulfan, and heptachlor resulted in epithelial differentiation accompanied by upregulation of E-cadherin expression and overexpression of proinflammatory cytokines (TNF α , IL-1 β , and IL-6) in HOSE cells creates a chronic inflammatory microenvironment that may promote the neoplastic transformation.

 **Sihag P, Tandon A, Pal R, Bhatt S, Sinha A, Sumbul M. Sonography in male infertility: a useful yet underutilized diagnostic tool. *J Ultrasound.* 2022;25(3):675–685.**

Comprehensive sonographic examination including scrotal sonography, testicular doppler and transrectal ultrasound was used to differentiate between obstructive (OG) and non-obstructive (NOG) causes of azoospermia in 30 infertile men with azoospermia and 30 healthy males with normospermia. Ectasia of rete testis/epididymal tubules, altered epididymal echogenicity, dilated terminal vas deferens were significantly more common in OG while inhomogeneous testicular echo-texture and reduced testicular vascularity were more common in NOG. Testicular volume and epididymal head size were significantly higher in OG while resistive index of intra-testicular vessels was higher in NOG. The authors suggest comprehensive sonographic evaluation in the routine diagnostic evaluation of men with azoospermia.

 **Singal A, Bisherwal K, Agrawal S, Bhat S, Diwakar P. Clinico-epidemiological profile and management outcome of subungual digital glomus tumor—Indian experience. *Dermatol Ther.* 2022;35(10):e15745.**

The study analyzed the demographic, clinical, onychoscopic, radiological features and management outcome of 16 subungual glomus tumors in 15 patients. Glomus tumors had a female preponderance (11/15) with thumb being the commonest site. Intractable pain was observed in all patients; nail discoloration was seen in 68.8% (11/16) lesions and nail plate deformity in 37.5% (6/16) lesions. Pink glow and linear vascular structures were seen on onychoscopy. Doppler sonography and/or magnetic resonance imaging confirmed the diagnosis of glomus tumor in all the lesions. Trans-ungual surgical excision was done in all without recurrence.

 **Thuluva S, Paradkar V, Gunneri S, et al. Safety, tolerability and immunogenicity of Biological E's CORBEVAX™ vaccine in children and adolescents: A prospective, randomised, double-blind, placebo controlled, phase-2/3 study. *Vaccine.* 2022;40(49):7130–7140.**

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References: 1. For indication and more information on the product, please refer FEIBA India PI version Oct 2020. 2. Astermark J, et al. Blood. 2007; 109:546-551. 3. VARADI, K, et al. J Thromb Haemost. 2003; 1:2374-2380. 4. Bonnet PO, et al. Haemophilia. 2009;15:1083-1089. 5. Negrier C, et al. Surgical interventions with FEIBA (SURF): international registry of surgery in haemophilia patients with inhibitory antibodies. Haemophilia. 2013;19(3):e143-e150.

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