ORIGINAL ARTICLE

To study the prevalence of latent tuberculosis infection among medical students.

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Abstract

Background: Risk of developing latent tuberculosis infection increases in medical students with their higher exposure to TB care facilities. **Objective:** To study the prevalence of latent TB infection among students attending professional degrees MBBS, BDS, MD, MS, MDS at King George's Medical University, India. **Methods**: This study was carried out with Tuberculin skin testing among students and active TB cases were excluded. A standard dose of 0.1 mL of purified protein derivative was slowly injected intra dermally into non-dominant forearm. After 48-72 hours, the reaction was estimated by measuring the transverse diameter of the induration. **Results:** Total 561 students had given consent to get enrolled. Prevalence of latent tuberculosis infection was significant with period of clinical exposure (*p-value* < 0.05), average size of induration (*p-value* < 0.001), and history of prior Tuberculin Skin Test (*p-value* < 0.001). However it was not significant with the age (p-value > 0.05), gender (*p-value* > 0.05), and history of contact with active cases of TB (p-value > 0.05). **Conclusion:** The prevalence of latent tuberculosis infection is higher in post graduate students followed by interns and final year students due to more exposure to patients in wards and clinics at King George's Medical University, India.

Keywords

Latent Tuberculosis Infection; Tuberculin Skin Testing; Purified Protein Derivative; Medical Students; Dental Students

Introduction

Latent Tuberculosis Infection (LTBI) is a state of patient vulnerable response to mycobacterium tuberculosis (MTB) antigen stimulation with no substantiation of clinically manifest active TB.(1) Around 5-20 percent LTBI cases, devoid of any signs and symptoms, could convert into active TB case within 2-5 years.(1, 2) In India 40 percent population is estimated to suffer from LTBI.(3, 4) Medical students attending bedside teaching could be exposed to LTBI risk in TB treatment facilities, infectious disease wards, etc. (5,6) In medical students, LTBI screening, early diagnosis, treatment is remarkable intervention to prevent recurrence and active TB progression.(7,8) India is the highest TB burden country in the world although epidemic TB is on the decline.(9,10) The best screening for the high burden countries considered is Tuberculin skin Test (TST) or Monteux test or Interferon Gamma Release Assay (IGRA) to assess LTBI.(6, 10) TST is the widely used and recommended to identify MTB infection even in absence of signs and symptoms, by skin reaction at injection site.(11, 12) TST conversion is presumptive evidence of acquired LTBI and a potential risk for progression to TB disease.(13) Chest radiographs and Sputum examination can be interpreted as beneficial in pulmonary lesions assessment.(14)

Aims & Objectives

This was the first study conducted regarding the prevalence of latent tuberculosis infection in medical students with increasing years of exposure to clinical teachings and hospital duty from first professional under graduation to post graduation at King George's Medical University (KGMU), Lucknow.

Material & Methods

Study Population and design: A cross-sectional descriptive study of Prevalence of LTBI among medical and dental students pursuing MBBS, BDS and MD, MS, and MDS based on Tuberculin Skin Test (TST) and chest radiograph investigation was established in the Department of Respiratory Medicine, King George's Medical University (KGMU), Lucknow, India, between December 2020 and March 2021. Students with active tuberculosis infection were excluded from the study.

Study Procedures: The participants with written consent were enrolled in this study. With the help of stratified sampling students were arranged in order of increasing years of clinical exposure right from first professional year in under graduation to final year in post-graduation.

Socio-demographic and clinical characteristics were assessed including comorbid illness, history of exposure to active cases of TB in community(not more than a year) and history of TST and Bacillus Calmette-Guerin (BCG) vaccination. A standard dose of 0.1 mL of purified protein derivative (PPD) was slowly injected intra dermally into non-dominant forearm. The reaction was read after 48–72 hours. The size of the reaction was determined by measuring the transverse diameter of the induration.

Outcomes: The PPD administered was 0.1 mL on flexor aspect of non-dominant forearm intradermal and reaction was being read after 48-72 hours, by measuring transverse diameter of the induration. Outcome and categorisation of participants was done on the basis of size of induration as follow 0-5 mm, 5-10 mm and ≥10 mm.

Ethical Clearance: The Institutional Ethics Committee (IEC) of King George's Medical University, Lucknow, India has approved all the study methods to conduct this study.(Ref Code: 98th ECM II B IMR-S/PI)

Statistical analysis: Categorical and clinical variables for socio-demographic and clinical characteristics were summarized using mean, standard deviations, and medians with interquartile range (IQR) respectively, and p-values ≤ 0.05 were deemed statistically significant. Prevalent LTBI was calculated as a proportion with a corresponding 95 per cent exact binomial confidence interval for several exposures of interest. Finally, the reliability between years of clinical exposure and PPD measurement was evaluated using cronbach's alpha to check the dependency of clinical year's exposure of medical students with the results of their PPD testing. All the data in this study were analysed using IBM SPSS Statistics (version 24.0.0.0).

Results

Study Population: In 561 participants, 95.7 per cent were MBBS & BDS Undergraduates and 4.3 per cent were postgraduate students. The mean of age was 21.7 years (18-22 years age group).

About 65.2 per cent and 34.8 per cent were male and female students respectively. There were about 2 per cent participants reported history of contact with patients of tuberculosis and 2.5 per cent participants reported prior exposure of TST. All participants were covered with BCG immunization as per National Immunization Schedule at time of birth. (16) Using the Pearson Chi-square test, the p-value ≥0.05, which indicates the age group, was not statistically significant in the mean size of induration by TST. Reliability was tested using cronbach's alpha (α = 0.554) indicative of poor reliability. [Table 1]

The average PPD measurement was 11.5 mm. This was an indication that medical students of KGMU were on the verge of developing LTBI. The highest mean of PPD measurement was 16.5 mm for postgraduate students, and the lowest mean was about 9 mm among first-year students. These mean values indicated that the prevalence of LTBI was two folds in postgraduate students in comparison to first-year students. [Table 1]

In the final year medical undergraduates, who had completed 4 years of clinical rotations in their academic session, the mean was 10.7 mm. Meanwhile, in medical interns, with 5 years of clinical exposure, the mean value was 13.6 mm. This was indicative of the highest prevalence of LTBI in medical interns as compared to final year students. [Table 1]

The mean was 10.2 mm in final year dental undergraduates, with clinical exposure of 3 years, and in dental interns, with clinical exposure of 4 years, the mean value pertained to 10.6 mm. This was indicative of the increasing risk of developing LTBI with progression to clinical rotations in wards and clinics in the dental department. [Table 1]

Postgraduate students with clinical exposure of nine years pertained to the highest mean value of 16.5 mm. The average of postgraduate students with 8 years of clinical exposure was 15.0 mm. The third highest mean value pertained to the postgraduate students with clinical exposure of 7 years which was 14.6 mm. This showed that from under graduation to post graduation, the risk of developing latent tuberculosis infection increased significantly with increasing clinical exposure in medical students. [Table 1]

[Figure 1] presents and compared relation between prevalence of LTBI and years of clinical exposure. Among 17.82 per cent participants, the size of induration was ≥ 5 mm with a mean value of 9.1 mm by TST. The size of induration was between 5-10 mm in 14.4 per cent participants with a mean value of 7.3 mm. The size of induration ≥ 10 mm was seen in 67.7 per cent participants

with a mean value of 34.5 mm [Table 1]. Prevalence of Latent Tuberculosis Infection was 67.7 per cent with the highest fold of risk towards the postgraduate students as compared to undergraduates and Intern. Prevalence of LTBI is statistically significant, p-value < 0.50, with the period of exposure to clinical settings.

Of the three hundred and eighty participants, with the size of induration ≥ 10 mm compared to the level of graduation and courses enrolled in, the highest mean was in postgraduate students of the department of Obstetrics and Gynaecology, KGMU followed by the department of General Surgery and the department of Respiratory Medicine, KGMU with the value of 2 mm, 1.8 mm and 1.7 mm respectively. [Table 2]

About 2 per cent students reported exposure to active cases of tuberculosis either in the community or during rotatory hospital duty in academic sessions. In the department of Obstetrics and Gynaecology, KGMU, one post graduate student had a history of Hilar lymphadenopathy and two residents were active cases of TB a year ago. Four medical undergraduates, with 4 years of clinical exposure, tested positive for COVID 19 and one student was an active case of TB. Six dental undergraduates, with 3 years of clinical exposure, had a history of contact with an active case of TB to their class fellow and one of them had a history of bronchial asthma. Using Pearson Chi-squared Test, the p-value was >0.05, although this variable of contact with an active case of TB was statistically not significant with the size of induration by TST. [Table 3]

About 2.5 per cent participants presented with a history of TST and p-value < 0.001, this variable could be statistically significant with the size of induration by TST. [Table 3]

For 22.1 per cent of students with an average size of induration ≥ 10 mm, the p-value was 0.74. Showing the size of the induration was statistically not significant for the gender of the participants. Reliability was assessed using cronbach's alpha (α = -0.149), which indicated poor reliability. [Table 3]

In 2.49 per cent participants, who were exposed to TST before, came out with an average size of induration ≥ 10 mm. Using the Pearson Chi-squared test, the p-value was < 0.001, this was indicative of the statistical significance of previous PPD testing and an average size of induration ≥ 10 mm. [Table 3]

Discussion

This cross-sectional descriptive study of the prevalence of LTBI among undergraduate and postgraduate medical and dental students at KGMU has several important findings. In our study, 67.7 per cent participants had shown the prevalence of LTBI using TST. This result was higher than those in previous studies by Kinikar et al. in 2019. (5) The TST positivity rate of our study was even higher than previous studies (Verso et.al 2019), (Durando Pet. Al 2015). (20, 21) Overestimation of the incidence of latent tuberculosis infection with TST was probably due to BCG booster dose vaccination at birth. (16) In our study, the prevalence of LTBI in dental students was higher than in a study by Lamberti et.al in 2017. (22) The most probable cause for this higher prevalence in dental students could not be only higher clinical exposure but also the high incidence of TB in India.

Furthermore, notably, a history of contact with active cases of TB infection significantly increased the risk of prevalent LTBI.(23) Being a medical resident and increasing age was associated with a higher risk of incident LTBI, suggesting that greater TB exposure increases the risk even though our analysis found no significant association between any exposure variable and incident LTBI. Even though, post graduate students have a higher risk fold of prevalent LTBI than the general population.(17) Our analysis indicates post graduate students are at a twofold greater risk of prevalence of LTBI as compared to Interns and Undergraduate medical and dental students in KGMU. We ended up with a conclusion, in our study that postgraduate students are at lower risk of developing TB infection as compared to previous studies with 15-fold risk.(17) Such increased risk is expected given that postgraduate students have more direct interaction with patients in wards and clinics. Prior studies have also reported that time spent in the wards and clinics are an independent risk factor for TB. (18, 19)

Similarly, we identified that increasing age was associated with higher LTBI risk. This is because postgraduate students are older than undergraduate students, and as mentioned before, medical residents have higher exposure. Also, the postgraduate students have spent more time in the hospital during their MBBS/BDS training, and internship. Since the exposure period is longer, residents are at a higher risk of incident TBI.

Another significant finding of the study is the low prevalence of LTBI among first-year and second-year undergraduate students as compared to final-year students and Interns reported both from MBBS and BDS courses. The reason could be feeble interaction with the patients. In KGMU, hospital duty is commenced from the second year onwards, and with further succession in the professional year; students have a good exposure towards patients in wards and clinics. Therefore, advancement in the professional year until residency, the trend of prevalence of LTBI keeps on progressing.

Our study has several limitations such as the sample size was 2000 but only 561 were covered. Preference of Written consent over digital consent forms proved cumbersome and time taking. As per the guidelines of the National TB control program, only the suspected cases, that is those who are presenting with symptoms of TB, are supposed to be done with sputum test and radiological examination, none of the participants did undergo the same. (15) It was mentioned in previous studies that two-

step TST to be done over healthcare settings rather we did only single-step TST. (24) A better measure to assess the association of the number of exposures to risk of LTBI would be to obtain real-time data on exposure rather than collect annual data as recommended by the CDC, which is subject to recall bias. Finally, we did not collect information on how much time was spent in the wards and clinics or the number of encounters with active TB patients, thus potentially underestimating the association of exposure with incident LTBI

Conclusion

The prevalence of latent tuberculosis infection is higher in post graduate students followed by interns and final year students. The probable cause of this trend could be years of clinical exposure in post graduates students as compared to under graduation and internship students. Moreover, consideration of TST as screening test for LTBI estimation, the post-graduation students are at verge of developing active TB cases at KGMU.

Recommendation

In TB burden countries like ours, awareness regarding LTBI should be priority. Screening of medical students for LTBI in different medical colleges could prevent progression to active cases. Moreover, early diagnosis and treatment at initial stage will not only prevent the disease rather alleviate financial burden of patient.

Limitation of the study

The limitation of this study was estimated sample size of 2000 could not be done.

Relevance of the study

As per the prevalence of LTBI concerned, screening should be done at particular time interval in order to prevent its progression to active TB infection in medical students in different medical colleges, especially in TB burden countries.

Authors Contribution

PKD: concept, study design, analysis, drafting of the manuscript; SK: concept, study design, analysis; SK: literature review; SKV: Final approval of the manuscript; SK: collection of data; AK: collection of data, drafting of manuscript; EC: revising of manuscript

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Tables

TABLE 1 DEMOGRAPHIC AND EPIDEMIOLOGICAL CHARACTERISTICS OF THE STUDY POPULATION (N=561)

S. No.	Characteristics	Values	
1)	**Mean age (in Years)**	21.72	
2)	**GENDER**	**N (%)**	
	A) MALE	366 (65.2)	
	B) FEMALE	195 (34.8)	
3)	**Duration of Clinical exposure (in Years)**	**N**	**Mean (mm)**
	a) M(1)	111	8.9
	b) M(2)	166	9.3
	c) M(3)	35	9.0
	d) M(4)	101	10.6
	e) M(5)	55	13.6
	f) D(4)	39	10.2
	g) D(5)	29	10.6
	h) P(9)	2	16.5
	i) P(8)	17	15.0
	j) P(7)	5	14.6
4)	**History of Previous PPD Injection**	14 (2.5 %)	
5)	**TST Measurements**	**N (%)**	**Mean(mm)**
	a) 0-5mm	100 (17.8)	9.0
	b) 5-10mm	81 (14.4)	7.4
	c) ≥ 10 mm	380 (67.7)	34.5

N: Total Number of Students; TST: Tuberculin Skin Test; M: MBBS Undergraduate; D: Dental Undergraduate; P: Postgraduate Students; ( ): Duration of clinical exposure in years

TABLE 2 DISTRIBUTION OF AVERAGE SIZE OF INDURATION ≥ 10 MM USING TST STRATIFIED ACCORDING TO THEIR GRADUATION LEVEL (N=380)

S. No.	Graduation Level	N	Mean ±SD
1)	BDS	59	1.00±0.54
2)	MBBS	343	0.93±0.49
3)	MD(OBSTETRICS & GYANECOLOGY)	5	2.00±0.00
4)	MD(PULMONARY MEDICINE)	7	1.56±0.72
5)	MS(GENERAL SURGERY)	4	1.75±0.50
6)	MS(OPHTHALMOLOGY)	6	1.67±0.51

TST: Tuberculin Skin Test; SD: Standard deviation

TABLE 3 ASSOCIATION OF CHARACTERISTICS OF STUDY PARTICIPANTS WITH OUTCOMES OF TST (N=561)

S. No.	Characteristics	Total	Size of induration (%)			*p*-value*
		N (%)	0-5 mm	(5mm-10mm)	(>10 mm)	
1)	**History of contact with active case of TB**	11 (2)	0	81.8	18.1	0.3
2)	**Gender**					
	a) Male	366 (65.2)	16.4	13.6	69.9	0.74**
	b) Female	195 (34.8)	20.5	15.8	63.5	
3)	**Previous PPD Injection**	14 (2.5)	14.2	28.5	57.1	<0.001

*TST: Tuberculin Skin Test; PPD: Purified Protein Derivative; TB: Tuberculosis; N: Number of students. *Test of significance: between total number of participants and average size of induration in each category mentioned in table. ** After considering total number of male and female participants.*

Figures

FIGURE 1 GRAPHICAL REPRESENTATION OF RELATION BETWEEN PREVALENCE OF LTBI (IN %) AND YEARS OF CLINICAL EXPOSURE OF STUDENTS IN MEDICAL COLLEGE AND HOSPITALS.