Tuberculosis in Staff and Students of Patan Hospital, Kathmandu

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ABSTRACT

Background: There is a high risk of occupational exposure to tuberculosis among healthcare workers in endemic countries. Regular screening for tuberculosis among healthcare workers is not carried out in Nepal. Infection control measures are also not routinely implemented. The aim of this study was to determine the prevalence of active tuberculosis among staff/students at Patan Hospital.

Methods: Participants were given a self-administered questionnaire and invited to undergo chest radiography. Cases were scored and reviewed based on predetermined criteria, and presumptive tuberculosis cases were invited to undergo sputum smear and culture. Participants were categorized according to the extent of patient contact and asked about history of tuberculosis medication.

Results: Among 560 participants, 76.8% had direct contact with patients. Fifty-eight (10.4%) gave history of cough >2 weeks. Based on symptom history and chest radiography, 20.0% (n=112) cases were reviewed, and 12.5% (n=14) of those reviewed had sputum tested for acid-fast bacilli. One participant had culture-positive tuberculosis. Fifty participants (8.9%) reported tuberculosis in the past, among which 42.0% (n=21) occurred after employment at Patan Hospital and 42.0% before joining Patan Hospital. Security staff, radiology technicians and ward cleaning staff had the highest proportion of cases with a history of tuberculosis. History of tuberculosis medication had no relation with age, sex, education, body mass index and smoking. The incidence rate of tuberculosis at Patan Hospital was 3.6 per 1000 person-years.

Conclusions: Overall incidence of tuberculosis among healthcare workers is noteworthy. However, this study suggests when symptomatic tuberculosis occurs in healthcare worker at Patan Hospital, it is diagnosed and there is not a large pool of undiagnosed tuberculosis.

Keywords: Health personnel;occupational health; tuberculosis.

INTRODUCTION

A substantially increased risk of tuberculosis(TB) among healthcare workers has been documented in many studies. Asystematic review conducted in 2007 showed a wide variation inthe annual risk of TB disease attributable to nosocomial exposure ranging from 25 to 5,361 per 100,000 (median 228) in low and middle income countries.[1] There is considerable variation in risk by occupation within individual institutions; laboratory staff, radiologists and nursing staff tend to have higher risks while administrative staff have the lowest risks, due to limited exposure[1-3] randomly selected from the 6,003 subjects employed at the facility. Cases and controls were compared with respect to clinical and demographic variables. The cases and controls were of similar age. Logistic regression analysis showed that body mass index (BMI). Systematic screening for TB can facilitate early diagnosis of TB in healthcare staff and hence interrupt the chain of transmission to other staff, patients, and the wider community.[4,5] However, at present, screening for TB among healthcare workers is not carried out in

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hospitals in Nepal.

Guidelines on infection control and prevention of nosocomial TB transmission are well established and implemented in healthcare institutions in high-income countries.[6-8] Although negative isolation of TB cases is desirable, in low resource settings with a high number of TB cases this is not feasible, and simpler, practical measures need to be applied to reduce the risk of nosocomial transmission.[9] TB Infection control measures are not currently implemented in Nepalese healthcare settings.

In the year 2014, the incidence rate of TB in Nepal was 156 per 100,000 populations.[10] There is no data on TB among healthcare workers in Nepal. The aim of this study was to determine the prevalence of active tuberculosis among staff and students working in Patan Hospital, Lalitpur, Kathmandu.

METHODS

The study was conducted at Patan Hospital between November 2014 and June 2015 using a cross-sectional study design. Patan Hospital is a 450-bedded teaching hospital for the Patan Academy of Health Sciences (PAHS) in Kathmandu, the capital of Nepal. There are approximately 1,050 staff. The hospital provides primary care as well as specialty services to over 300,000 people per year coming from the local urban catchment area and from diverse geographic areas within Nepal.

All hospital staff and fourth and fifth (final) year medical students over the age of 18 years were invited to participate in the study. Staff information sessions were held to inform staff about the study. Question and answer sessions followed and staff were also invited to discuss the study individually in confidence with the research staff. If written informed consent was obtained, study participants were given a self-administered questionnaire, which included data on age, gender, employment history and role within the hospital as well as self-reported assessment of symptoms consistent with TB. The questionnaires were returned to the study staff in sealed envelopes via designated departmental collection boxes. The study staff assisted participants who were unable to fill out the questionnaires independently. Study participants were also invited to undergo chest radiography unless contraindicated (e.g. pregnancy). Two radiologists independently reported the chest X-rays (CXR) and any discrepancies resolved by consensus. The study staff systematically scored each participant using the questionnaires and chest radiography (Table 1). The participants meeting criteria consistent with TB specified in table 1 were subsequently invited for clinical evaluation and asked to provide 3 sputum samples for acid – fast bacilli (AFB) examination smear with Ziehl-Neelsen stain. A single sample from each of these participants was tested by GeneXpert MTB/RIF (Cepheid, USA) testing and Bactec MGIT (Becton Dickinson, USA) liquid culture.

Table 1. Criteria for review and sputum testing of study participants.
Stage 1: Study Participants contacted for a clinical evaluation
– Any participant with any abnormality on CXR. .
– Participants with cough $\geq$ 2 weeks.
– Participants with >2 other symptoms consistent with TB
Stage 2: Study Participants invited to provide sputum for smear examination
– Participants with cough $\geq$ 2 weeks.
– CXR suggestive of active tuberculosis.
– Any other significant symptom present without other cause (eg. Weight loss >10% without dieting) deemed necessary by the study clinician.
– Close Contacts of known TB cases under antituberculous treatment if deemed necessary by the study clinician based on symptoms and CXR findings.

The study participants were categorized as Direct Contact with Patients and No Direct Contact with Patients according to the occupational role. Those with Direct Contact with Patients were further categorized as those with Frequent direct contact with Patients and those with Limited direct contact with Patients (Table 2)[3] randomly selected from the 6,003 subjects employed at the facility. Cases and controls were compared with respect to clinical and demographic variables. The cases and controls were of similar age. Logistic regression analysis showed that body mass index (BMI).

Table 2. Categorization of health care works according to the extent of patient contact.	
Extent of Contact	**Health care workers included**
Frequent direct contact with patients	Doctors, Nurses, Medical Students

Limited direct contact with patients	OPD/ Ward/ ER Attendants, Radiology Technicians, Physiotherapists, Pharmacists, and Ward Cleaning Staff.
No direct contact with patients	Administrators, Academicians, Cashiers, Kitchen staff, Security staff, Housekeeping staff including Laundry workers& Maintenance staff, and Laboratory personnel.

Participants who responded 'Yes' to the question 'Have you ever taken medicine for TB?' were categorized as havinga history of TB, while those who responded 'No' were categorized as having No history of TB.

Zhiel-Neelsen staining for AFB was performed at Patan Hospital using the standard WHO protocol. GeneXpert testing was performed at the Oxford University Clinical Research Unit-Nepal laboratory at Patan Hospital using the manufacturer's protocol. Automated commercial liquid culture using Bactec MGIT culture (Becton Dickinson, USA) was performed at the German-Nepal-TB Project (GENETUP) NationalTB reference laboratory in Kathmandu, following the standard protocol.

Chi-Squared (x^2) tests, Fisher's exact test and independent sample t-tests were used, where appropriate, to examine the differences in characteristics of study participants with and without a history of TB and study participants who had TB before and after joining Patan Hospital/ PAHS. Univariate logistic regression was used to examine the association between extent of contact of the health care workers with patients and TB. Incidence rate was calculated as a ratio of the total number of cases with a history of TB and the total person-time of duration employed in the hospital in years. Person –time was calculated as a sum of total time contributed by each participant. It represents the population at risk during the period of time starting from time of employment to when they developed TB i.e. the change from non-disease to disease or to the date when the study was conducted for those who did not develop TB in the course of employment. All statistical analyses were performed using STATA version 13.0. *P*-values less than 0.05 were considered statistically significant.

RESULTS

Five hundred and sixty hospital staff (366 female and 194 male) were enrolled into the study (53.3% of the hospital staff), reflecting male: female ratios among hospital staff. Among them, 76.8% (n=400/560) had direct contact with patients (Frequent direct contact = 53.6% (n=300/560); Limited direct contact = 23.2% (n=130/560)), while 23.2% (n=130/560) had no direct

contact with the patients. CXR was performed in 508 (90.7%) participants.Fifty-eight (10.4%) gave history of having cough lasting longer than 2 weeks (Table 3). Based on the symptoms and CXR findings, 20.0% (n = 112/560) of participants were clinically evaluated, and 12.5% (n=14/112) of those evaluated had sputum tested for AFB by smear, GeneXpert and Bactec MGIT culture. One study participant tested positive by the GeneXpert in 2 hours (rifampicin susceptible) and was started on standard antituberculous therapy (ATT). The MGIT culture for this participant was also positive after 12 days of incubation.

Table 3. Results of self-reported assessment of symptoms consistent with TB.

History / Symptoms	Response N(%)		
	Yes	No	Don't know
Do you have a cough that has lasted 2 weeks or longer?	58 (10.4)	491 (88.0)	9 (1.6)
Have you lost your appetite?	14 (2.5)	538 (97.5)	0 (0.0)
Have you lost weight without dieting?	4 (0.7)	548 (98.0)	7 (1.3)
Have you had fever, chills, or night sweats?	5 (0.9)	547 (98.0)	6 (1.1)
Have you coughed up blood?	12 (2.1)	541 (96.8)	6 (1.1)
Have you been feeling very tired?	62 (11.1)	486 (87.1)	10 (1.8)
Have you ever had a positive tuberculin skin test (TST) result?	18 (3.2)	515 (92.6)	23 (4.2)
Have you ever had an abnormal chest x-ray?	52 (9.3)	472 (84.6)	34 (6.1)
Have you recently had the mucous you coughed up tested for TB?	46 (8.2)	505 (90.4)	8 (1.4)
Have you ever been told you had TB?	37 (6.7)	512 (91.9)	8 (1.4)
Have you ever taken medicine for TB?	50 (9.0)	501 (89.8)	7 (1.2)
Have you ever lived with or had close contact with someone who had TB?	233 (41.8)	297 (53.3)	27 (4.9)

Nine percent (n=50/560) of the study participants reported a history of medication for TB, among which 42.0% (n=21/50) took antituberculous therapy after joining Patan Hospital, 42.0% (n=21/50) before joining Patan Hospital and 16.0% (n=8/50) did not respond to the question. The mean duration of employment at Patan among those who had TB prior to and after joining

Patan Hospital was 12.6 (IQR 12.2)and 14.0(IQR 11) years respectively (P=0.566). There were no significant differences in the characteristics of participants who had TB before and after joining the hospital.The incidence rate of TB in staff at Patan Hospital was estimated as 3.6 per 1,000 person years (95% CI 2.4 – 5.5 per 1,000 person years).

Table 4 compares the characteristics of those who had a history of TB with those who did not have TB in the past based on self-reported history of taking antituberculous chemotherapy. There were no significant demographic differences between the two groups. The mean age for those with a history of TB and those with no history of TB was 37.4 years and 34.6 years respectively. Those with a history of TB had been employed for a median duration of 13.0 years (range 0.4-35) while those with no history of TB had been employed for a median of 6.7 years (range 0.1- 49.5, P=0.025).Educational levels were similar between the two groups (P=0.752). The history of contact with TB patients was similar in both groups (39.5 % and 39.5% respectively for those with and without history of TB respectively, P=0.995). A greater proportion of those with a history of TB reported TB in a family member (34.9% vs. 20.1%, respectively, P=0.024).

Table 4. Characteristics of hospital staff & medical students based on history of taking ATT (N=551).

Characteristics	No TB 501 (90.9)	TB 50 (9.1)	P – value
Sex (N=551)			
Female	326 (65.1)	36 (72.0)	0.325
Male	175 (34.9)	14 (28.0)	
Age (N=529)			
Mean (SD)	34.68 (10.2)	37.39 (8.5)	0.075
Education (N=540)			
Bachelors and above	242 (49.1)	21 (44.7)	
Intermediate**	128 (26.0)	12 (25.5)	0.752
Grade 10 and below	123 (24.9)	14 (29.8)	
BMI (N=531)			
Mean (kg/m^2) (SD)	24.8 (3.6)	24.3 (3.7)	0.3916
Underweight	12 (2.5)	1 (2.0)	
Normal Weight	251 (52.6)	28 (57.1)	
Overweight	171 (35.9)	15 (30.6)	0.897
Obese	43 (9.0)	5 (10.2)	

Duration of Employment at Patan (years) (N = 546)			
Median (Range)	6.7(0.1 – 49.5)	13.0 (0.4 – 35)	0.024
Smoking (N=550)			
No	455 (90.8)	45 (91.8)	0.813
Yes	46 (9.2)	4 (8.2)	
BCG in childhood (N = 431)			
No	395(9.1)	4 (10.8)	
Yes	351 (90.9)	33 (89.2)	0.764
TB contact in the past 3 months (N = 509)			
No	282 (60.5)	26 (60.5)	
Yes	184 (39.5)	17 (39.5)	0.995
History of TB in a family member(N = 481)			
No	350 (79.9)	28 (65.1)	
Yes	88 (20.1)	15 (34.9)	0.024

*9 participants answered 'don't know' or did not respond to the question. ** Intermediate = education above grade 10 but below bachelors level.*

Table 5 shows the job categories at risk of TB. The nurses represent the largest group of staff and the largest group with history of TB medication (n=25/50, 50%). Within each job category, Security staff (n=2/6, 25.0%), Radiology Technician (n=2/9, 22.2%) and Ward Cleaning Staff (n=8/51, 15.7%) have the highest number of cases with a history of TB within each group.

Overall, those with direct contact with patients had a significantly higher risk of having previously had TB (OR= 2.8 [95% CI 1.1 – 7.3], P=0.031) compared to those who have no direct contact with patients (Table 6). When further stratified by the degree of contact, increased risk was observed for those with limited direct contact (OR=3.7 [95% CI 1.3-10.3], P=0.013) but was not significant for those with frequent direct contact (OR=2.5 [0.9-6.6], P=0.067).

Table 5. Job categories at risk of TB.

Job Category	Total number of Participants (n=550)*	Percentage of total participants	Participants with TB history(n=50)	Percentage of those with TB history	Percentage of occupational category with TB history
Nurse	199	36.2	25	50.0	12.6
Doctor	44	8.0	2	4.0	4.5
Medical Student	54	9.8	1	2.0	1.9
OPD/Ward/ ER Attendants	47	8.5	4	8.0	8.5
Radiology Technicians	9	1.6	2	4.0	22.2
Pharmacist	9	1.6	1	2.0	11.1
Physiotherapists	4	0.7	0	0.0	0.0
Ward Cleaning Staff	51	9.3	8	16.0	15.7
Housekeeping	56	10.2	1	2.0	1.8
Academicians	2	0.4	0	0.0	0.0
Administrators	22	4.0	0	0.0	0.0
Laboratory Personnel	26	4.7	2	4.0	7.7
Kitchen Staff	14	2.5	2	4.0	14.3
Cashier	5	0.9	0	0.0	0.0
Security Staff	6	1.5	2	4.0	25.0
Total	550	100	50	100	

*10 participants did not fill out their job description.

Table 6. Patient contact is a significant risk factor for a history of TB at Patan Hospital.

	No TB n (%)	TB n (%)	Odds Ratio (95% CI)	P-value
No Direct Contact with Patients	120 (96.0)	5 (4.0)	Reference	-
Direct Contact with Patients	381 (89.4)	45 (10.6)	2.8 (1.1 – 7.30)	0.031
No Direct Contact with Patients	120 (96.0)	5 (4.0)	Reference	-
Limited Direct Contact with Patients	111 (86.7)	17 (13.3)	3.7 (1.3 – 10.3)	0.013
Frequent Direct Contact with Patients	270 (90.6)	28 (9.4)	2.5 (0.9 – 6.6)	0.067

DISCUSSION

In our study, only one case was diagnosed with active TB. This would equate to a rate of 179 per 100,000, [95% CI 32– 945]). This is an imprecise estimate due to there being only a single case, but is broadly consistent with the rate of TB in the Nepalese population. The participant was sputum smear negative, but the GeneXpert MTB/RIF assay detected *Mycobacterium tuberculosis* susceptible to rifampicin.This finding of a single case was contrary to our hypothesis that the incidence of undiagnosed TB among the healthcare workers is high. However, five healthcare workers were receiving treatment for TB during the study period. Self-reported medical history showed a high number of cases (9.07%) with a history of TB. This was equivalent to an incidence rate of 3.6 per 1,000 person years (95%

CI 2.4 – 5.5 per 1000 person years, or, with 1,000 staff at Patan 3.6 health care workers developing active TB each year, which is substantially higher than the national TB incidence. However, this also suggests that while incidence is high and infection control measures need to be strengthened, the awareness of TB is high among staff. We did not detect a large number of undiagnosed cases of active TB in staff suggesting those who are symptomatic seek a diagnosis. However, only half of the eligible staff participated in the survey (53.3%) and it remains possible that staff with TB did not participate due to fear of stigma or fear of receiving a TB diagnosis. Surveillance of active TB among the health care workers should be in place to identify active cases.

Overall, the nurses represented the largest occupational category with a history of TB (50%), followed by the

ward cleaning staff and the OPD/Ward/ERattendants. Within each job category, the security staff, radiology technicians and the ward cleaning staff has the highest proportion of history of TB. This aligns with the existing literature which identifies nurses, hospital attendants and radiology staff as the high risk groups[1]. In a systematic review, reported incidence rate ratios as high as 27.9 among nurses, 53.0 among radiology technicians and 52.2 among patient attendants.[1] Other staffs are also in constant contact with patients and their caretakers, which could explain the high number of TB cases in these particular groups. The relation between TB infection and the development of the disease is complex, and an unknown proportion of cases would have acquired TB outside the hospital, with socio-economic factors also playing a role in risk of TB disease. The high number of healthcare workers with a history of TB highlights the need for proper infection control to curb the disease transmission to patients and coworkers in the hospital setting. The WHO guidelines recommend infection control at three levels: administrative control, environmental control and personal respiratory protection[9]. Administrative control is the most important level of control that plays a central role in reducing the risk of exposure to health care workers and patients.This includes enforcing proper outpatient TB management, inpatient management and isolation policies, implementation and evaluation of infection control interventions. There is inevitably a compromise between ideal infection control standards and feasible solutions that can be implemented within the extreme resource limitations of the Nepalese health care system.

Many studies have tested for latent tuberculosis among health care workers. Prevalence of latent tuberculosis ranges from 33% to 79% among health care workers in low and middle income countries[1]. In our study, we have not assessed for latent tuberculosis. Most studies have used tuberculin skin tests (TST) to detect latent disease. TST is affected by BCG vaccination, which is an important cause of false-positive results and makes itdifficult to interpret in our population. Moreover, TST results are also affected by random errors.Interferon-γ release assays (IGRA) have been developed as an alternative to TST and are widely used to detect latent disease in high income countries, especially in migrant populations, where the incidence of TB is low[11]. However recent studies have shown the test result is influenced by many variables including sample time, storage, transport and operator experience. High intra-subject variability (reversions and conversions over a series of tests) occurs in IGRA results that complicate the interpretation of the results[12]. Furthermore, the aim of the study was not to identify latent TB prevalence and there is no set policy

for the treatment of latent TB disease in the hospital or in Nepal; therefore the test was not performed.

The survey questions required the participants to self-report medical history and were therefore subject to recall bias. For example, we asked participants to recall the specific year when they had TB.

CONCLUSIONS

Overall, the study results suggest that although TB is relatively common among healthcare workers at Patan hospital; it is recognized and diagnosed when cases occur among healthcare workers. Infection control policies should be comprehensively reviewed and strengthened to protect health care workers, patients and visitors from nosocomial TB transmission, using a stepwise incremental approach to apply sustainable measures.

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