

Original Article

Prevalence of Tuberculosis among bedside contacts of Smear Positive Tuberculosis Patients at The University Teaching Hospital, Lusaka, Zambia

Patrick Lungu¹, Duncan Chanda¹, Gershon Chongwe², Shabir Lakhi¹

¹Department of Internal Medicine, University Teaching Hospital, Lusaka

²Department of Epidemiology and Biostatistics, University of Zambia, School of Public Health, Lusaka

ABSTRACT

Background: Screening of contacts of tuberculosis (TB) patients is not routinely done in resource-limited countries like Zambia despite the World Health Organization (WHO) recommendations, leading to missed opportunities for prevention, early diagnosis and high mortality.

Objective: Main objective was to establish the prevalence of latent and active tuberculosis in bedside contacts of smear-positive index patients and associated risk factors.

Methods: The study was carried at the University Teaching Hospital, a tertiary level facility. We conducted a cross sectional analytical study. We included 64 TB-unexposed and 69 TB-exposed contacts in this analysis. We recruited bedside contacts of smear-positive TB patients (TB Exposed group) in medical wards and contacts of surgical patients (TB Unexposed group) as a comparison group. A structured questionnaire was used to collect data on demographic, laboratory and clinical parameters among them being, age, gender, residence, relationship index patient's sputum grades BMI and HIV status. Active TB was diagnosed microbiologically and radiologically, while latent tuberculosis infection (LTBI) by tuberculin skin test (TST). Collected data was analysed using STATA 13 to determine the prevalence of TB and LTBI and the associated factors. A p value of < 0.05 was considered statistically significant.

Results: The mean age for TB unexposed and that of TB exposed was of 41.2 [\pm 13.5] years and 40.2 [\pm 14.7] years respectively. The Prevalence of active TB in TB exposed and in TB unexposed was 13.0% and 0% respectively. The prevalence of LTBI among TB exposed and TB unexposed was 83.1% and 38.3% respectively. Active TB in TB exposed bedside contact was associated with duration of hospital stay (AOR 2.45, 95% CI 1.0 – 5.9, p = 0.03) and index patient's sputum grade of 2+ (AOR 4.4, 95% CI 1.07 -18.3, p = 0.04).

Conclusion: Bedside contacts of active TB patients are at an increased risk of contracting both latent and active TB. Further, our findings suggest a significant prevalence of LTBI in the general population of Lusaka. Bedside contact tracing is an effective approach to finding the missing TB patients our setting of a high TB burden country/community. The findings call for an urgent need to institute effective TB control/preventive measures with active case finding as a priority and LTBI screening finding and treatment.

INTRODUCTION

Tuberculosis (TB) remains a significant cause of preventable morbidity and mortality in developing countries. A third of the world's population is infected with Mycobacterium tuberculosis. The high burden of Human Immunodeficiency Virus (HIV)

Keywords: Bedside contacts, TB exposure, background exposure, active TB, LTBI.

has led to an increase in tuberculosis incidence. Undernutrition, chemotherapy, and diabetes are among the other predisposing factors of TB.'

In developing countries, resource constraints hinder screening of close contacts of TB patients. Despite the current control measures, the incidence rate of TB in Zambia remains high with the current incident rate being at 376/100,000 with a low treatment coverage of 59%. The prevalence survey done in Zambia between 2013 and 2015 did highlight the high magnitude of the TB burden in Zambia than earlier than earlier estimated. It is after this survey that Zambia was classified as one of the 30 high TB burden countries. One key highlight of the survey was that participants found with TB during the survey had been to the health facilities two or three times and TB was missed until the survey. This highlights the point that TB control remains a challenge due to, among other factors, diagnostic delays.' About 41% of TB cases in Zambia are undetected, untreated and continue to infect others hence driving the TB epidemic. The lack of implementation of active case finding is the major contributor of the missed cases. Active case finding is an essential part of the initial TB control strategy yet is woefully implemented. Latent TB infection (LTBI) treatment is an important public health intervention especially among people living with HIV yet the uptake of TB preventive therapy (TPT) remains suboptimal. Zambia's TPT uptake stands at 18% among adult living with HIV and 3.8% among children exposed to TB.⁹ The burden of LTBI in Zambia like in many third world countries is unknown as it has not been prioritised due to resource limitations and unawareness of its importance.

Paucities in contact tracing allows disease progression and leads to a poor outcome. A study by Muchemwa *et al.* in Lusaka, Zambia revealed a TB bacteraemia of 34.8% in patients with sepsis, with a mortality of 70% in that subgroup. Mateyo *et al.* in their study showed that TB was the leading cause of respiratory distress in HIV patients.¹⁶ A post-mortem

study in Zambia revealed that 25.6% of TB cases were diagnosed posthumously. From the point of TB exposure to the development of sepsis, respiratory distress and death there exists a window of missed opportunities for prevention, early detection and intervention.

Globally and regional studies have shown that contacts of TB patients are at risk of contracting both LTBI and active TB.'''

The virulence of the *Mycobacterium tuberculosis* strain, type and duration of contact greatly influences the chance of acquiring TB infection. The risk of developing active TB is highest during the initial 48 months of the first contact and decreases subsequently.'

TB is spread from person to person through inhalation of nuclei aerosolised by coughing, sneezing or talking. Aerosol from a person with active pulmonary TB remains suspended for up at least 30 minutes. Thus, Proximity by bedside contact is high risk.

Exposure to TB has various outcomes which may be primary-TB, LTBI or immediate clearance. In HIV negative people with untreated LTBI, the estimated risk of developing active TB is 5-10% over a lifetime. On the other hand, the risk increases in people living with HIV, 5% - 10 % per year in progress to active TB.¹⁸ Risk of TB infection in close contacts is influenced by intensity of exposure, duration of exposure and infectiousness of the index patients. We presumed that the rate of both LTBI and active disease would be high in the bed side contacts of TB patients as there is repeated exposure to the index patient and other known and unknown TB patients in the wards. It is known that high bacterial load (high sputum grade) corresponds with high rates of TB infections among close contacts..

At the University Teaching Hospital (UTH) a national referral hospital in Lusaka, Zambia relatives of TB patients are often at the bedside, defying limitation of visits set by the hospital. In

extreme cases relatives sleep in the TB wards. These wards lack environmental TB control measures such as negative pressure ventilation and ultraviolet germicidal irradiation. Presumed TB patients are only isolated after confirmation of active TB disease. Besides, TB preventive therapy national coverage in Zambia remains suboptimal at less than 18%. The focus has been on the treatment of active TB.

The motivation for this study was the anecdotal evidence of a number of bedside contacts found with TB during the course of admission of the index patient at the University Teaching Hospital. This study aimed to determine the prevalence of LTBI and active TB among bedside contacts and the risk factors of contracting TB in this study population

METHODOLOGY

Study environment

We conducted a cross-sectional study at the University Teaching Hospital. The Study population were bedside contacts of TB patients in the medical wards called "TB-exposed group" and bedside contacts of surgical patients in surgical wards, designated "TB-unexposed group". Simple random sampling was used to select participants for both groups.

Sample size determination

Using a two-sided chi-square test (two sample proportion test) in STATA version 13, the sample size was calculated at 78 participants in TB unexposed group and 78 in TB exposed, with an expected difference of 14% in LTBI in the two groups at 85% power. We took the study done in Yaoundé Cameroon as a reference, where the prevalence of active TB 14% in the close contacts.

Recruitment and eligibility

We recruited relatives aged 18 and above who were bedside contacts of the bacteriologically confirmed TB patients and bedside contacts of surgical

patients. They were then grouped as TB exposed and TB unexposed respectively. We excluded participants with a previous history of TB and those who had a Mantoux test in the last three months or a Bacillus Calmette–Guérin BCG boost during the previous two months.

Study assessment and laboratory evaluations

Following enrolment, we administered a structured questionnaire, recording demographic characteristics, cardinal symptoms and medical history. Physical examination was done to elicit signs of TB, as well as to look for the presence of a BCG scar. We injected 02 tuberculin units (TU) of 0.1ml purified protein derivative into the epidermis on the forearm, and the induration size read 48-72 hours later using Vernier callipers.

A spot sputum sample was collected either spontaneously or through induction and subjected to microscopy, Gene-xpert or liquid culture. The study nurse drew blood for FBC/ESR, HIV test and CD4 count. Anterior-posterior chest x-rays were done and were independently reported by a consultant radiologist as follows: normal, non-tuberculous abnormality, inactive TB or active TB.¹⁴

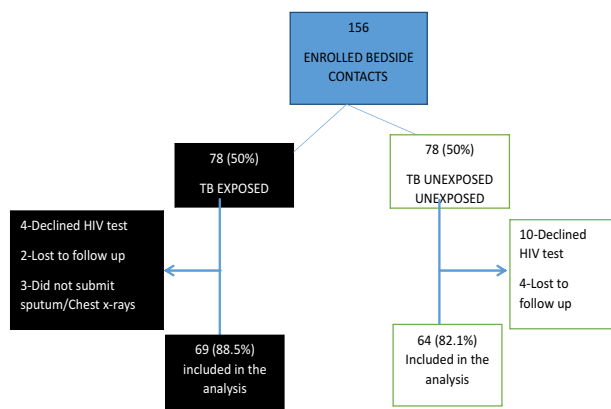
Data Collection and Analysis

The data was collected and double entered into Excel 2010. We analysed the data using STATA version 13. Pearson's Chi-square or Fisher's exact tests were used to determine associations between dichotomous variables where appropriate. Student's T-test was used to analyse continuous variables. Active TB and LTBI were primary outcome variables of interest. Associations of LTBI and active TB with independent variables such as age, duration of contact and type of contact were investigated using stepdown logistic regression models, with a threshold of 0.20. We calculated p-values as two-tailed, taking a p-Value of 0.05 as statistically significant.

Study Process

Between August 2015 and January 2016, we enrolled 70 TB patients and 64 surgical patients from which we enrolled a total of 156 bedside contacts, 78 (50%) were TB exposed (TB contacts), and 78 (50%) were TB unexposed (contacts of surgical patients in different sections of the hospital). 69 of 78 (88.5%) TB exposed and 64 of 78 (82.1%) TB unexposed were included in the analysis. See Figure 1.

Figure 1: Participant enrolment



RESULTS

Baseline characteristics of participants

The demographic characteristics of the study population are as shown in Table 1. The mean age [±SD] was 41.2 [±13.5] years and 40.2[±14.7] in TB-unexposed and TB-exposed respectively. There was a predominance of females, with 50 (78.1%) in TB-unexposed and 49 (70.0%) in TB-exposed. Fourteen (21.9%) of the TB-unexposed and 16 (22.9%) of TB-exposed were spouses to the index patients. There were 38 (59.4%) first degree relatives to the index patient in TB-unexposed and 35 (50%) in TB-exposed. 52 (80%) of the TB-unexposed and 38 (53.5%) of the TB-exposed were always at the bedside and median days (IQR) duration of hospital stay up to the point of enrolment was 6, (1.5-29.3) and 7.5 (1.3-14.5). [Table 1].

Table 1: Baseline characteristics of bedside contacts of tuberculosis patients (TB exposed) and surgical patients (TB unexposed)

Characteristics	TB Unexposed		TB Exposed		p value
	N or (Mean), [Median]	% or (SD),[IQR]	N or (Mean), [Median]	% or (SD),[IQR]	
Gender					
Female	50	78.1%	49	70.0%	0.29
Age mean (SD)	41.2	(±13.55)	40.4	(±14.86)	0.74
Relationship with index					
Spouse	14	21.9%	16	22.9%	
1st degree relative	38	59.4%	35	50.0%	0.46
2nd degree relative	12	18.8%	19	27.1%	
Residence (High density)	51	79.7%	48	68.6%	0.14
Duration of hospital stay median, [IQR]	6	[1.5-29.3]	7.5	[1.3-14.5]	0.02
Type of contact					
Only during visiting hour	12	18.8%	8	11.4%	
Shared the same dwelling	2	3.1%	24	34.3%	<0.01
Always at the bedside	50	78.1%	38	54.3%	
Number of Household members with TB					
None	64	100.0%	4	5.7%	
One	0	0.0%	50	71.4%	< 0.01
Two or more	0	0.0%	16	22.9%	
Past medical history (Uneventful)					
HIV status positive (participant)	17	26.6%	25	35.7%	0.25
Cough (yes)	7	10.9%	18	25.7%	0.03
Chest pain (yes)	1	1.6%	9	12.9%	0.02
Weight loss (yes)	4	6.3%	10	14.3%	0.13
Drenching night sweats (yes)	1	1.6%	5	7.1%	0.21
Fever (yes)	0	0.0%	7	10%	0.01
BCG scar Present	55	85.9%	65	92.9%	0.19
Chest findings Crackles	0	0.0%	5	7.1%	0.25
BMI	25.3	(±4.5)	25.2	(±5.34)	0.96
HB (mean, SD)	13.5	(±1.68)	12.5	(2.6)	<0.01*
ESR (mean, SD)	23.3	(±20.15)	25.2	(±22.41)	0.25
CD4 participant median, [IQR]	524	[266-821]	461.5	[256.3-675]	< 0.01*

Table 1: The most common type of contact was bedside contact, 78.1% of the TB unexposed and 54.3% of the TB exposed were always at the bedside. The mean CD4 in TB exposed was lower than in the TB unexposed. There were 10% of the TB exposed reported history of fever and none among the TB unexposed.

The prevalence of active TB was at 13% in TB-exposed and 0% in TB-unexposed (p = 0.014) while the prevalence of LTBI in the TB-exposed was 83.1% and 38.3% in TB-unexposed (p = <0.001). See figure 2

Figure 2

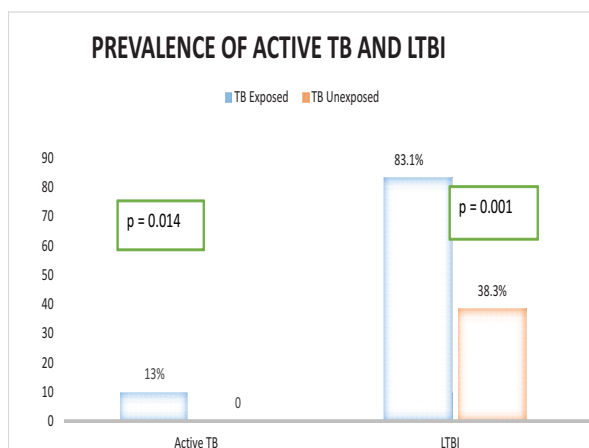


Figure 2: The prevalence of active TB among TB exposed bedside contacts is 13%, none of the contacts in the TB unexposed group had active TB. LTBI prevalence was very in the TB exposed population at 83.1%, The TB unexposed population equally had a significant prevalence of LTBI at 38.3%

Factors associated with latent TB infection (LTBI) in TB exposed and TB unexposed

The odds of LTBI were independently associated with exposure to an index patient's sputum grade of 1+ is 16.1 (2.52 – 103) $p < 0.01$, that of exposure to an index patient with sputum grade of 2+ is 33.3 (2.9 - 383.8) $p < 0.01$ and that of exposure to a patient with sputum grade 3+ is 9.5 (2.04 – 44.0) $p < 0.01$. Other factors were not statistically significant (Table 2).

Factors associated with active TB among the TB exposed bedside contacts

The odds of active TB among bedside contacts of TB were independently associated with the contacts having a productive cough 2.42 (1.06 – 5.55) $p = 0.035^*$ and having had a duration of hospital stay of 8-14 days (being at the bedside for 8-14 days) 2.45 (1.0-5.9) $p = 0.045^*$ The other factors among them HIV, sputum grade, relationship and type of contact were not statistically significant (Table 3).

Table 2: Factors associated with latent TB infection (LTBI) in TB exposed and TB unexposed

Characteristics	LTBI negative N (%)	LTBI positive N (%)	Crude OR	95% CI	p value	Adjusted OR	95% CI	p value
Gender								
Female	43 (79.6%)	56 (70.0%)	1			1		
Male	11 (20.4%)	24 (30%)	1.68	0.74 - 3.79	0.216	1.72	0.54 - 0.42	0.355
Age (years)								
Less or equal 25	8 (14.8%)	11 (13.8%)	1			1		
26 – 35	21 (38.9%)	32 (40.0%)	1.09	0.35 - 3.40	0.880	2.76	0.53	0.231
>36	25 (46.3%)	37 (46.3%)	1.09	0.40 - 3.0	0.867	3.24	0.67	0.143
Relationship with index								
Spouse	14 (25.9%)	16 (20.0%)	1			1		
1st degree relative	28 (51.9%)	45 (56.2%)	1.4	0.6 - 3.32	0.436	0.84	0.42-1.67	0.616
2nd degree relative	12 (22.2%)	19 (23.8%)	1.39	0.50 - 3.84	0.530	0.72	0.28 - 1.85	0.496
Duration of hospital stay (days)								
0 - 7 days	22 (40.7%)	42 (52.5%)	1			1		
8 - 14 days	10 (18.5%)	16 (20%)	1.48	1.05 - 2.09	0.026	0.81	0.20 - 3.28	0.767
More than 14 days	22 (40.7%)	22 (27.5%)	0.52	0.24-1.11	0.094	0.59	0.21-1.61	0.300
Cough etiquette by index patient								
Yes	1					1		
No	38 (70.4%)	43 (53.8%)	2.04	1.0 - 4.24	0.05	0.69	0.20 - 2.35	0.553
Sputum grading (index patient)								
N/a	43 (79.6%)	21 (26.3%)	1			1		
1+	4 (7.4%)	16 (20.0%)	14.3	2.98 - 68.9	<0.01	16.1	2.52 - 103	<0.01
2+	1 (1.9%)	16 (20.0%)	2.10	1.52 - 2.91	<0.01	33.3	2.9 - 383.8	<0.01
3+	2 (11.1%)	27 (33.8%)	9.21	3.3 - 25.7	<0.00	9.5	2.04 - 44.0	<0.01
Episode of TB (index patient)								
1 st	51 (94.4%)	51 (63.8%)	1			1		
2 nd	2 (3.7%)	20 (25.0%)	10	2.22 - 45.0	<0.01	3.28	0.50 - 21.0	0.216
3 rd	1 (1.9%)	9 (11.3%)	9	1.1-73.7	0.040	2.14		0.538
Type of contact								
Only during visiting hour	11 (20.4%)	9 (11.3%)	1			1		
Shared the same dwelling	5 (9.3%)	21 (26.3%)	5.13	1.4 – 19.1	0.015	1.30	0.22 - 7.78	0.774

Table 2: A slight majority (33%) of participants found with LTBI were exposed to TB patients with a sputum grade of 3+. All grades of sputum were associated with LTBI. HIV and BCG vaccination did not influence the status of LTBI. On Univariate analysis sharing the same household and 2nd episode of TB were significantly associated with LTBI.

Table 3: Factors associated with active TB among the TB exposed bedside contacts

Characteristic	Active TB	No active TB	Crude	95% CI	p value	Adjusted OR	95% CI	p value
Gender								
Female	6 (67%)	18 (30%)	1			1		
Male	3 (33%)	42 (70%)	1.16	0.26-5.19	0.842	17	1.3-221	0.310
Type of cough								
Dry cough	1 (11%)	20 (33%)	1			1		
Productive cough	8 (89%)	40 (67%)	2.45	1.11 - 5.37	0.025	2.42	1.06 - 5.55	0.035*
Relationship								
Spouse	4 (44%)	12 (20%)	1			1		
1 st Degree relative	4 (44%)	30 (50%)	0.4	0.14 - 1.18	0.098	0.10	0.09 - 1.22	0.072
2 nd degree relative	1 (12%)	18 (30%)	1.7	0.17-1.68	0.128	3.22	0.49-2.20	0.225
Duration of Hospital stay								
1-7 days	1 (11.1%)	36 (60%)	1			1		
8-14 days	4 (44.4%)	7 (11.7%)	0.5	0.3-0.81	0.006*	2.45	1.0-5.9	0.045*
≥15 days	4 (44.4%)	17 (28.3%)	8.4	0.88-81.0	0.065	57	6.81-407	0.063
Sputum grading of index TB patients								
1+	1 (11.1%)	19 (32%)						
2+	3 (33.3%)	14 (23%)	1.15	1.52 - 2.54	0.336	0.20	0.04-8.5	0.400
3+	5 (55.6%)	27 (45%)	2.78	0.30-26.0	0.371	0.89	0.25-31.0	0.950
Type of contact								
Only during visiting hour	1 (11%)	7 (11.7%)	1			1		
Shared the same dwelling	1 (11%)	23 (38.3)	0.03	0.01-5.0	0.421	3.74	0.01-6.3	0.205
Always at the	7 (88%)	30 (50%)	1.63	0.17-15.5	0.669	0.65	0.02-18.7	0.801

Table 3: *Bedside contact whose patients stayed in the hospital 8-14 days were at a high risk of contracting TB, adjusted odds ratio of 2.45 (95% Confidence Interval 1.0-5.9) and Bedside contacts with a productive cough were 2.42 times likely to have active TB.

*statistically significant, IQR =interquartile range, SD = standard deviation, CI = confidence interval

DISCUSSION

Our study has shown that LTBI and active TB are highly prevalent among bedside contacts of smear-positive TB patients. Further, this study shows that contact tracing at bedside is feasible and a low-hanging fruit in finding the missing people with TB. The results also affirm that there is an alarming level of background LTBI in the population with no documented TB exposure; we attribute this to high

TB burden in Lusaka. "This is an important finding and a source of concern in that the background cases of LTBI forms the reservoir for active TB. The prevalence of active TB in our study is comparable to the findings in other studies in the region."

TB diagnosis in this study was based on clinical grounds i.e. the radiological features were aligned to the history of exposure and clinical presentation. This is similar to the findings of the national prevalence survey done in Zambia, where there were more cases of TB diagnosed clinically. A chest radiograph is a highly sensitive screening tool for TB, especially among immune competent individuals. These findings amplify the efficacy of chest radiography as a screening tool for TB especially in the presence of symptoms. TB diagnosis in the absence of microbiological diagnosis was made by a constellation of clinical features and radiological features.

LTBI prevalence was higher in our population than the findings in the region. We attribute this to the difference in the level of TB exposure in the study populations, in this study the level of TB exposure was higher when compared to studies testing all household contacts.^{11,12,22} The findings of Agarwal *et al.* who noted that the prevalence of tuberculosis among individuals visiting a general healthcare facility is considerably higher than that in the general population support our findings. Additionally, studies done in industrialised countries have shown a higher frequency of tuberculin conversion and significant cases of tuberculosis among nurses caring for TB patients. Further, in support of our findings is an observations study where inoculation of guinea pigs with dust from restrooms frequented by medical students led to the death of the animals to a cause attributable to TB. This actually highlights the high level of risk among close contacts (bedside contacts).

Our study showed that the prevalence of TB was higher in those that were in the inner-ring circle of the index patients. We are ascribing this to closer proximity and repeated exposure during and before

hospital admission and diagnosis of the index patient. This supports the approach of prioritising close contact in tracing under programmatic settings. On the other hand, it is possible that ethnicity and genetic factors could be and other background factors at play as the majority of the contacts found with LTBI and active TB were first-degree relatives to the index patients. To explain this observation, Sheriff *et al.* observed that certain ethnic groups were more susceptible to acquiring LTBI, suggesting a constitutional predilection to LTBI and active TB.^{11,12,22}

Unsurprisingly the majority of participants in this study were females (78.1% in TB unexposed and 70% in TB exposed) and had a higher level of LTBI. We attribute this to the cultural norms in our setting where the women are the active care providers of a sick relative.^{10,12,21} Contrary to the findings of Jitendra *et al.* and Amelia *et al.*, active TB was not associated with gender in our study.^{10,12}

About knowledge attitude and practice, this study showed a considerable deficit in knowledge on TB preventive measures. About 86.6% of contacts had never used N-95 masks and denied knowing about their existence. Our observation is in concordance with other authors.²⁹ Further; we found a lack of cough etiquette by the index patient as a risk factor for contracting LTBI, though contrary to the findings of Gustavo *et al.*

This study established a significant association between LTBI and sputum grading. The result is explicit because patients with high sputum grading have a high infectious dose of bacilli and likely to remain infectious for a longer time.'

Similar to the findings of Khalilzadeh *et al.* in Iran, one of the high TB burden countries. there was no relationship between the duration of contact and LTBI or active TB. However, in line with Jitendra *et al.* and Amelia *et al.*, we found the type of contact to be significantly associated with acquiring LTBI or active TB, possibly due to high levels of exposure in close contacts.¹¹ We recognise that TB patients once

put on effective treatment become less infectious. We cannot rule out that bedside contacts got the infection prior to the admission of the index patients. However, we also documented TB infection in contacts that had only casual contact. This could be attributed to background exposure in the community.

As expected, we found the duration of symptoms and the duration of treatment of the index patients to be significantly associated with both LTBI and active TB. We attribute this to the increased level of exposure, poor health-seeking behaviour by the index patients and delays in establishing TB diagnosis and initiating treatment prolong the infectious window.

We observed a positive association of TST results with increasing age, suggesting cumulative exposure to TB. However, there was no association between active TB and age." HIV was not a factor in the development of either LTBI or active TB. Furthermore, there was no anergy observed to TST; this finding is at odds with other studies that have reported anergy in HIV patients. Janis *et al.* found no case of LTBI among HIV participants, and attributed it to anergy, although they did not establish the cause of anergy. In support of our finding, Gutierrez *et al.* only observed a PPD positivity in HIV patients with mean CD4 count of 220 cells/ μL . Our HIV population in this study had a CD4 count higher than 220 cell/ μL and had no AIDS-defining illness.

BCG vaccination (infant vaccination) did not have any significant effect on the TST results.¹⁰ The reasons for this observation can be derived from findings of Moreno *et al.* who established that PPD response to BCG vaccine varies with the number of years since the BCG vaccination and induration of 14 mm is unlikely to be due to BCG.

All the participants found with active TB were diagnosed based on the presence of constitution symptoms and radiological features that were in keeping with active TB disease. The low

bacteriological yield is attributable to the lowly quality of sputum obtained. We could not ascertain whether participants acquired TB from index patients as DNA finger typing was not part of the study. However, we are confident that the results of this study are a precise reflection of the burden of LTBI and active TB in the study population.

CONCLUSION

Bedside contacts of TB patients are at an increased risk of contracting both latent and active TB. Further, our findings suggest that there is a significant prevalence of LTBI in the general population of Lusaka. Bedside contact tracing is an effective approach to finding the missing TB patients our setting of a high TB burden country/community. The findings call for an urgent need to institute effective TB control/preventive measures with active case finding as a priority and LTBI screening and treatment.

CONFLICT OF INTEREST DECLARATION

The authors declare that they have no conflicts of interest.

ETHICS STATEMENT

The study was approved by the University of Zambia Biomedical research committee. We All participants gave written consent. Participants found with active TB and LTBI were referred to appropriate service areas for further management.

ACKNOWLEDGEMENTS

The authors would like to acknowledge the support given by the management of the University Teaching Hospital and all the staff members of the Department of Internal Medicine that rendered support during the study.

REFERENCES

1. Maher, D. *et al.* The Growing Burden of Tuberculosis. *Arch. Intern. Med.* **163**, 1009 (2003).

2. Sudre, P., Dam, G. & Kochi, A. Tuberculosis? a global overview of the situation today. *Bull World Heal. Organ* **70**, 149–159 (1992).
3. Narasimhan, P., Wood, J., MacIntyre, C. R. & Mathai, D. Risk Factors for Tuberculosis. *Pulm. Med.* **2013**, 1–11 (2013).
4. Thompson, V., Mangura, B. T., Ford, J., Valway, S. E. & Onorato, I. M. Evaluation of Investigations Conducted of Tuberculosis. *JAMA* **287**, 991–995 (2002).
5. Kapata, N. *et al.* The Prevalence of Tuberculosis in Zambia? Results from the First National TB Prevalence. 2013–2014 (2016) doi:10.1371/journal.pone.0146392.
6. Tembwe, R. *et al.* Prevalence of Tuberculosis, HIV and Respiratory Symptoms in Two Zambian Communities: Implications for Tuberculosis Control in the Era of HIV. *PLoS One* **4**, e5602 (2009).
7. Harries, A. & Kumar, A. Challenges and Progress with Diagnosing Pulmonary Tuberculosis in Low- and Middle-Income Countries. *Diagnostics* **8**, 78 (2018).
8. Marks, S. M. *et al.* HHS Public Access. **162**, 2033–2038 (2017).
9. TUBERCULOSIS. 2018 (2018).
10. Chimoga, C. *et al.* Tuberculosis at post-mortem in inpatient adults at a tertiary referral centre in sub-Saharan Africa – A prospective descriptive autopsy study. *Int. J. Mycobacteriology* **4**, 75–76 (2014).
11. Aabye, M. G. *et al.* The Prevalence of Latent Mycobacterium tuberculosis Infection Based on an Interferon- γ Release Assay: A Cross-Sectional Survey among Urban Adults in Mwanza, Tanzania. *PLoS One* **8**, e64008 (2013).
12. Fox, G. J., Barry, S. E., Britton, W. J. & Marks, G. B. Contact investigation for tuberculosis: A systematic review and meta-analysis. *Eur. Respir. J.* **41**, 140–156 (2013).
13. Mwenebabu, M. *et al.* Tuberculosis Transmission Attributable to Close Contacts and HIV Status, Malawi. *Emerg. Infect. Dis.* **12**, 729–735 (2012).

14. Gopinath, K. *et al.* Incidence and Prevalence of Tuberculosis among Household Contacts of Pulmonary Tuberculosis Patients in a Peri-Urban Population of South Delhi, India. *PLoS One* **8**, e69730 (2013).
15. Khan, M. T., Ahmed, Z., Zafar, M., Qayyum, S. & Shafi, K. *Active case finding of sputum positive pulmonary tuberculosis in household contacts of tuberculosis patients in Karachi, Pakistan. The Journal of Association of Chest Physicians* vol. 2 (2014).
16. E. VYNNYCKY & M. FINE, P. E. The natural history of tuberculosis: the implications of age-dependent risks of disease and the role of reinfection. *Epidemiol. Infect.* **119**, 183–201 (1997).
17. (MACET), M. A. C. for the E. of T. Latent Tuberculosis Infection: A Guide for Massachusetts Providers. (2009).
18. Acuña-Villaorduña, C. *et al.* Intensity of exposure to pulmonary tuberculosis determines risk of tuberculosis infection and disease. *Eur. Respir. J.* **51**, (2018).
19. 29. Al. Kuaban C, Koulla-Shiro S, Lekama Assiene T, H. P. Tuberculosis screening of patient contacts in 1993 and 1999 in Yaounde, Cameroon. *Med. Trop.* (1996).
20. Sepkowitz, K. A. Tuberculosis and the Health Care Worker: A Historical Perspective. *Ann. Intern. Med.* **120**, 71–79 (1994).
21. Sia, I. G. & Wieland, M. L. Current concepts in the management of tuberculosis. *Mayo Clin. Proc.* **86**, 348–361 (2011).
22. Aggarwal, A. N. Tuberculosis transmission at healthcare facilities in India. *Lung India* **26**, 33–34 (2009).
23. Sepkowitz, K. A. Tuberculosis and the Health Care Worker? A Historical Perspective. (2017).
24. Zayas, G. *et al.* Effectiveness of cough etiquette maneuvers in disrupting the chain of transmission of infectious respiratory diseases. 1–11 (2013).
25. S., K., H., M., M.R., B., S., Z. & A.A., V. Prevalence of tuberculosis in close contacts smear positive TB patients. *Tanaffos* **5**, 59–63 (2006).
26. Lienhardt, C. *et al.* Factors affecting time delay to treatment in a tuberculosis control programme in a sub-Saharan African country? the experience of The Gambia. **5**, 233–239 (2001).
27. Berkowitz, N. *et al.* The prevalence and determinants of active tuberculosis among diabetes patients in Cape Town, South Africa, a high HIV / TB burden setting. *Diabetes Res. Clin. Pract.* **138**, 16–25 (2018).
28. M. Janis, E. *et al.* Tuberculin skin test reactivity, anergy, and HIV infection in hospitalized patients. *American Journal of Medicine - AMERJMED* vol. 100 (1996).
29. Persons, H. *et al.* Tuberculin and Anergy Testing in HIV-Seropositive and. 185–193 (2016).
30. Investigation, O. The Effect of BCG Vaccination on Tuberculin Reactivity and the Booster Effect Among Hospital Employees. **161**, 1760–1765 (2001)