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Latent Tuberculosis Infection among Household Contacts of Pulmonary Tuberculosis Cases in Central State, Sudan: Prevalence and Associated Factors

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Abstract

Introduction: Tuberculosis is a major health problem in developing countries including Sudan. Screening for TB cases through Household contacts (HHCs) investigation is an appropriate strategy to interrupt transmission of TB. **Objectives:** To determine the prevalence tuberculosis infection and risk factors for tuberculosis infection among household contacts in Wadimadani locality, Central State, Sudan, between November 2015 and April 2016. **Methods:** An analytical cross-sectional study conducted. During study period, to confirm TB diagnosis, all suspect contacts were tested through sputum samples, tuberculin skin test or chest X-ray. Structured questionnaire was used to collect socio-demographic and environmental factors. **Results:** One hundred forty six patients of smear-positive pulmonary tuberculosis were included in the study, 657 household contacts were identified and screened. Forty three new TB cases were detected from household contacts, yielding a prevalence of 6.5% (95% confidence interval = 0.05, 0.09) of latent tuberculosis infection (LTBI). Two factors were significantly associated with LTBI among HHCs: duration of contact with a TB patient ≤ 4 months (P = 0.03) and the educational status (P = 0.02). **Conclusion:** Screening of HHCs of index case of TB will contribute in early detection and treatment of new cases, and considered as a forward step towards eliminating TB.

Keywords

Tuberculosis, Latent Tuberculosis Infection, Household Close Contact, Central State, Sudan, Prevalence, Risk Factors

1. Introduction

Tuberculosis (TB) is one of the top ten causes of death worldwide. In 2015, 10.4 million people fell ill with TB and 1.8 million died from the disease (including 0.4 million among people with HIV). Over 95% of TB deaths occur in low- and middle-income countries [1].

Although people with LTBI do not manifest overt symptoms of active TB and are not infectious, but they are at increased risk for developing active disease, about one in ten latent infections eventually progresses to active disease, which, if left untreated, kills more than 50% of its victims [2].

Globally, nine million people annually developed active disease attributed to LTBI, and one third of the world population, approximately 2 billion people are thought to be latently infected with TB [3].

The global goal of tuberculosis control programs is to eliminate the disease by breaking the chain of transmission, which can effectively be achieved by rapid identification and effective treatment of infectious cases [4]. Once these cases are detected, it is imperative to detect infected people in contact with them so that the chain of transmission can be broken.

Therefore, in recent years contact tracing has started gaining importance and is now incorporated into the revised National Tuberculosis Programs (NTPs) of many countries even those of limited source [5].

In Sudan, TB is also considered as a major public health problem as in many other African countries, and according to FMOH data, it is the most frequent reason for hospital admission and hospital deaths constituting 11.6% and 16% respectively [6]. A pervious study on prevalence of LTBI among household contacts of Sudanese patients with pulmonary tuberculosis was done in Eastern district of the Sudan that came out with significant different point prevalence for HHC (461/1000) compared to (367/1000) for community contacts (CCs). This study was done in Eastern part of the Sudan and has not studied the risk factors that associated with LTBI among household contacts [7].

This study aimed at screening household contacts (HHCs] of smear positive pulmonary TB cases, to estimate the prevalence of LTBI among household contacts of TB index cases and identify socio demographic and environmental factors associated with the development of LTBI among household contacts of pulmonary TB cases in Wadmadani, Gezira State; Sudan.

2. Materials and Methods

2.1. Study Design and Setting

This was an analytical cross-sectional study, conducted between, November 2015 and April 2016 in Wadimadani, Sudan, Central (Gezira) state (central region in the Sudan), at the main center of TB control program.

2.2. Study Population

Index case was defined as smear positive pulmonary tuberculosis patient aged >

15 years who had at least one household contact, with no previous history of TB or taking anti tubercular treatment in the previous 6 months. One hundred forty six index cases were enrolled in the study.

Household contacts were defined as all people who shared meals and rooms with the index case and living together for at least the previous 3 months. Symptomatic contacts were defined as those who were showing any symptoms or signs of tuberculosis (cough, expectoration, hemoptysis, weight loss, or fever irrespective of duration at baseline during study period. Six hundred fifty seven HHC of the index cases were recruited during the study period.

Sputum smear for acid fast bacilli test were done for all adults suspected contacts 55.71% (366/657). An early morning sputum samples examination for three consecutive days were obtained, if the results were positive the contact would be identified as latent TB infection (LTBI) case and referred to TB management unit to complete their management, while the negative results were shifted to chest x-ray confirmation. Cavitations were defined as the presence of cavitations on a chest radiograph.

2.3. Tuberculin Skin Test (TST)

TST was performed for all suspected children of the household < 15 years old, 44.29% (291/657), by injecting 0.1 ml of tuberculin purified protein derivative (PPD) into the inner surface of the forearm, then after marking around injected site, that followed by reading the diameter of indurations after 72 hours using ball point technique, and it was considered to be positive if it was 10mm or more indurations [8].

All investigations were conducted in the main tuberculosis center laboratories and radiological departments by expert staff in both Wadmadani Teaching Hospital and Wad-madani Pediatrics Hospital.

All participants who diagnosed after investigations as latent TB were referred for management in DOTS center of the community.

Ethical clearance was obtained from ethical committee of Gezira state—MOH. Also an informed consent was also obtained from all participants.

2.4. Questionnaire

The structured questionnaire [9] (see **Appendix 1**) used in this study was divided into three parts: index case, contact, environmental factors. Index case information included socio demographic data, residence, relationship with contact, tuberculosis symptoms, duration of tuberculosis symptoms, and number of family members. Contact information included gender, age, sleeping in the same room with the index case and duration of contact with tuberculosis patient. Environmental factors included type of house, number of rooms, house size.

2.5. Measurement

Duration of contact was measured as the period of time per month that the contact was exposed to the index case.

House size was measured as the number of rooms in the house. Household size that measured as the number of family members in the household and crowding was measured as the average number of people per room.

2.6. Statistical Analysis

Data were cleaned and entered into spreadsheet and then into STATA version 13, which was used for analysis of data. Univariate analysis was performed using Chi-square test was used to assess the association of all categorical risk factors with smear positive acid fast bacilli test or tuberculin skin positive or presence of cavitations on chest x-ray radiograph. Odds ratio and their 95% confidence intervals were also calculated. Factors that found significantly associated with tuberculosis infection in univariate analysis were considered for inclusion in the multivariate model In multivariate analysis generalized estimating equation (GEE) was used to determine risk factors for tuberculosis infection among household contacts, due to the presence of clusters of contact to the same index case within the household. Adjusted odds ratios and their 955 confidence intervals were estimated. For all statistical test association were considered significant at p-value ≤ 0.05.

2.7. Results

Six hundred fifty seven household contacts were identified through contact tracing of 146 newly diagnosed index cases. Only 43 newly pulmonary T.B cases were detected from house to house tracing of the contacts that revealed a prevalence of 6.5% (43/657) Latent TB (LTB) cases. Sixty five percent (28/43), were identified by Sputum Acid Fast Bacilli, 23.4% (10/43) were identified by chest radiograph, and 11.6% (5/43) were identified by tuberculin skin test. The mean age (±sd) of smear positive pulmonary TB and smear negative was 33.07 ± 14.87 years and 32.35 ± 14.87 years respectively. LTB cases were 4.47% (22/291) among children < 15 years old and it was 10% (14/143) among adults, productive age group between 25 - 35 years old. LTBI of HHCs was 7.0% and 6.10 among males and females respectively (Table 1).

Table 1 summarizes the socioeconomic status of the study population. Prevalence of LTBI cases among illiterates was 8.65% (27/312), compare to 4.65% (16/345) prevalence among educated.

Figure 1 illustrated family members' relationship for TB positive household contacts with index cases. The majority of contacts who got T.B were the sons (32.60%) and sisters (28%) of index respectively.

Table 2 Summarized the predicting factors of with LTB of the HCC. Only two factors, Illiterates and duration of contacts less than 4 months were found significantly associated with LTB of HHC (P value was 0.05, and 0.03, respectively).

Education reduced the risk of LTB among HCC by 54% in crude analysis, and when adjusted by other factors, education reduced the risk of LTB among households by 12% (Table 3).

Table 1. Socioeconomic factors of study population-Wad Madani locality-Gezira 2015/2016, (N = 647).

Socio-demographic factors	Smear positive household contacts (n = 43) (%)	Smear negative households contacts (n = 614) (%)	Total (n = 657) (%)
Gender (number, %)			
Male	22 (7.03)	291 (92.97)	313 (100)
Female	21 (6.10)	323 (93.90)	344 (100)
Age (mean ± SD*)	33.07 ± 14.87	32.35 ± 14.87	
Age categories:			
<15 years	13 (4.48)	278 (95.53)	291 (100)
16 - 24	5 (5.81)	81 (94.19)	86 (100)
25 - 35	14 (9.79)	129 (90.21)	143 (100)
+35	11 (8.03)	126 (91.92)	137 (100)
Income/month (SDG‡)			
<500	9 (4.13)	209 (95.87)	218 (100)
>500	34 (7.76)	405 (92.24)	439 (100)
Education			
Illiterate	27 (8.65)	285 (91.35)	312 (100)
Some education	16 (4.64)	329 (95.36)	345 (100)
Occupation			
Student	5 (2.96)	164 (97.04)	169 (100)
Housewife	15 (8.43)	163 (91.57)	178 (100)
Worker	12 (7.14)	156 (92.86)	168 (100)
Child	11 (7.86)	129 (92.14)	140 (100)

*SD=Standard Deviation. †SDG=Sudanese Genah (Pound).

The cases of LTB among HCC with duration of contacts of less than 4 months were twice more likely to have LTB, compared to those with longer duration (more than 4 months) in crude analysis, Crude OR (95% CI) = 2.02 (1.07, 3.79). The adjusted exposure odds ratio of the duration less than 4 months compared to a long duration of more than 4 months, were 1.94 (95% CI = 0.74, 0.94), as shown in Table 3.

3. Discussion

The prevalence of LTBI disease among household contacts in Madani locality, which was 6.5% had great difference from the results of contact tracing conducted in Eastern state (2017) that revealed prevalence 44% of T.B among household contacts [10] and it was considered to be a lower prevalence compared to those reported in South Africa, where prevalence among gold mines contact was 89% [11]. However prevalence of LTBI in Morocco contact tracing was done through evaluation continued for 12 years of follow up among household contacts of TB in different regions, results show that the overall prevalence of T.B was 2.5%. However Morocco is one of low-middle income countries where the DOTS strategy has been successfully implemented [12]. There are several studies which reported different prevalence of T.B among household contact, this leads to the assumption that many of these current cases were actually

Table 2. Predicting factors associated with household contacts of pulmonary TB cases.

Risk factors	TB positive contacts (%)	Normal contacts (%)	P-value*
Gender (number, %)			
Male	22 (7.03)	291 (92.97)	0.63
Female	21 (6.10)	323 (93.90)	
Age categories:			
<15 years	13 (4.48)	278 (95.53)	0.17
16 - 24	5 (5.81)	81 (94.19)	
25 - 35	14 (9.79)	129 (90.21)	
+35	11 (8.03)	126 (91.92)	
Income/month (SDG‡)			
<500	9 (4.13)	209 (95.87)	0.08
>500	34 (7.76)	405 (92.24)	
Occupation			
Student	5 (2.96)	164 (97.04)	0.10
Housewife	15 (8.43)	163 (91.57)	
Worker	12 (7.14)	156 (92.86)	
Child	11 (7.86)	129 (92.14)	
Education			
Illiterate	27 (8.65)	285 (91.35)	**0.02**
Some education	16 (4.64)	329 (95.36)	
Household size (members)			
1 - 4	13 (9.92)	118 (90.07)	0.27
5 - 8	23 (6.04)	358 (93.96)	
>8	7 (4.83)	138 (95.17)	
House size{rooms}			
1 - 2	42 (6.58)	596 (93.42)	0.97
>2	1 (5.26)	18 (94.74)	
Type of building			
Mud	11 (25.58)	264 (43)	0.07
Bricks	32 (74.42)	350 (57)	
Relation with index case:			
Grandfather/mother	8 (4.37)	175 (95.63)	0.08
Wife/husband	11 (7.48)	136 (92.52)	
Son/sister	24 (7.34)	303 (92.66)	
Duration of contact			
<4 months	25 (5.16)	440 (94.84)	**0.05**
>4 months	18 (5.98)	174 (94.02)	

*Chi-square.

infected by a member of their own family [13].

With respect to the sex distribution of pulmonary T.B cases, although this study revealed that there was no significant gender difference in prevalence of LTBI among HCCs, but majority in other studies, as a study conducted in Malawi, found male, were more likely to be named by subsequent Smear-positive tuberculosis patients [14].

In this study only 4.68% of children age less than 15 years had positive tuberculin reaction; however, almost all of them had been BCG vaccinated at birth, a

Table 3. Crude and adjusted exposure odds ratio (OR) of the latent tuberculosis cases of the household contacts, Wadmadni, 2015, 2016).

Risk factors	TB positive contacts	Normal contacts (%)	Crude OR (95% CI)	Adjusted OR (95% CI)
Education				
Illiterate	27	285	1 (Reference)	1
Some education	16	329	0.46 (0.24, 0.88)	0.88 (0.74, 0.94)
Duration of contact				
<4 months	25	440	1	1
>4 months	18	174	2.02 (1.07, 3.79)	1.94 (1.00, 3.4)

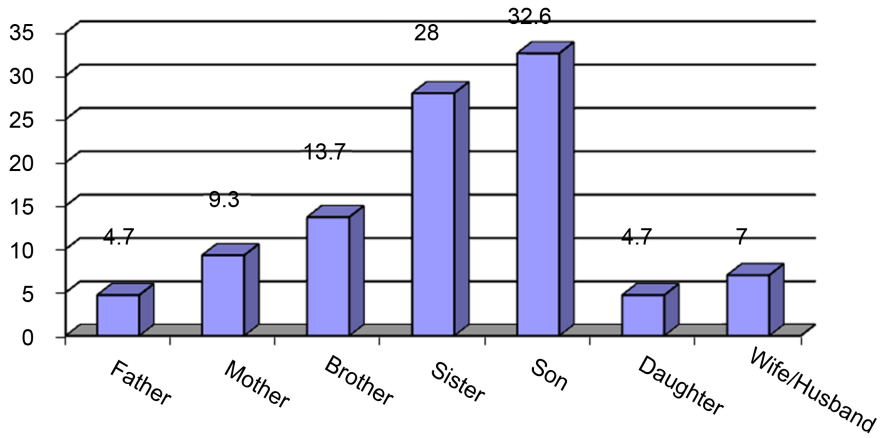

Figure 1. Family members relationship for TB positive household contacts among pulmonary TB cases, Wadmadani locality, Gezira state (P value = 0.7).

similar study in a Hong Kong study which found a percentage of 8% for the same age group, which is considered less to the result of this study [15].

For the factors associated with development of TB disease among infected contacts discovered during study period, results shows that although gender distribution revealed that males acquire more T.B disease 7.3% than females 5.8%, however there was no statistically significant difference (OR 0.71 95% CI 0.38 - 1.32, p = 0.44).

These values are similar to the findings of the study conducted in South Glamorgan (UK), which involved Indian subcontinent group which also found no significant difference between males and females {M:f 10:12} to acquire the disease [16], and another study was carried out in Osaka-Japan showed that there was a significant difference in gender distribution, causing secondary T.B cases {male: 5.6%, female: 1.8%, p < 0.05} [17].

Although association of age on occurrence of LTBI {25 - 35} years old was not significant (P value = 0.17), the study conducted in Osaka [18], confirmed the effects of age in acquiring the disease, as it was statistically significant at age 49 years (P value < 0.01). In contrast of those children who had contact with T.B patient had a very high risk of getting T.B, even though they were vaccinated at birth [19]. Further to that in Alaska, a study of children under 15 years of age

who were household contacts of adults with culture-positive pulmonary tuberculosis found that 25% developed infection and 9.6% progressed to active disease [20], which is differ to the result of this study; found the development of T.B infection among contacts children < 15 years was found in 4.48% of them.

The duration of contact between the pulmonary TB cases and their household contacts, in this study, showed the risk of getting T.B infection within 4 month and less, was 5.16%, however, it was insignificantly associated with development of LTBI (P value = 0.05).

This result was similar to a study carried out in Hong Kong in 2008 and revealed that LTBI among HHCs developed within 3 month period of time spent with contact, especially if there is another environmental factors or increase in the degree of closeness with the index T.B case [21]. Also in the study conducted in north Spain, and took 10 years of study, found that majority of household contacts (73%) developed the disease within 12 months. Transmission of mycobacterium T.B usually follows close and prolonged contact between the infectious patients and a susceptible individual. The factors that influence transmission include the environment where the organisms are dispersed, quantity of bacilli expelled by the index patient and the duration of exposure to the infectious patient. Further to the aspect of communicability of TB which has more effect in early period of contact with infectious pulmonary TB cases [18].

Women as housewives, in term of occupational aspect, have accounted for the highest percentage of 8.43% compared to all occupational contacts, that explained by the prolonged time spent with the pulmonary T.B patient at household level; that increases the likelihood of T.B disease, even the difference is not statistically significance (P-value 0.10). As for relationship between acquiring T.B disease and the number of family members for each contact, results showed that a majority of contacts who got T.B were the sons of index cases (**Figure 1**). But the association was statistically insignificant (P value = 0.07). These findings reflect the role and importance of degree of closeness with the index case for accruing the disease, particularly the son and daughter who have more exposures to their parents so they found more care and all kinds of social emotions. Thus, it also had been confirmed in the previous study in Bangkok which proved that, the risk of tuberculosis infection was still significantly associated with close contacts to mother with tuberculosis and father with tuberculosis [21].

Educational status related to confirmed pulmonary TB among household contacts showed that illiterate contacts constituted more occurrence versus educated contacts (P value = 0.04).

With respect to the monthly income of the families with infected contacts in this study, prevalence of LTABI among HHCs contacts of monthly income of lower than 500 SDG was 4% compared to 8% of those with income higher than 5000 SDG, as expected in terms of limited income among households contacts and thus inability to provide the basic needs for housing, water and food in an appropriate manner, and increased the possibility of acquiring T.B disease, but that the association was insignificant (P value = 0.08) (**Table 2**).

4. Limitation of the Study

The limitations of our study need to be considered in the interpretation and application of our results.

We conducted our study in specific population of Wadmadani city and locality of the Central State; they may not represent all other regions of the state.

The design of our study (cross sectional design) lack temporality of association between the risk factors and the outcome, therefore the interpretation of our results of the association of risk factors and LTBI, should acknowledge this limitation.

However, in spite of above limitations our findings are supported by other studies as discussed above.

5. Conclusions

Prevalence of pulmonary TB among household contacts in this study was 6.5%, which is high if compared to similar studies in different countries.

Results suggest that contact tracing, if conducted well, will be a powerful means of improving case detection rates for pulmonary TB disease. While education reduced the risk of LTB among HCC by 12%, short duration of contact increased the risk of LTB by 1.94 times.

Conflict of Interest

The authors declared that they did not have any conflict of interest.

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Appendix 1

Household Contacts of pulmonary tuberculosis index cases Questioner

Wad Madani Locality—Gazira State {Central of Sudan}

Date ……/……../……

Patient name: ……age……gender: ……..residence: ……..

Index case no……Tel……..Investigator……

Date of onset of TB: ….…Number of Household contacts……....Address……..….

Identifiers, education, socioeconomic factors and symptoms & signs suggesting TB disease

Contact Name	Age	Gender	Relationship with the index patient	Education level/years	Occupation	Duration of contact with the patient	Cough > 2 weeks	Hemoptysis	Weight loss	Night fever	BCG Vaccine	Sputum test			CXR	Tuberculin skin test
												1	2	3		

Environmental information about exposure settings for household contacts of TB index cases

No of family members			Room no		Type of house builds		Monthly income level/SDJ	
1 - 4	5 - 8	8<	2 - 1	2<	MUD	BRICKS	≥500	>500

Result of Sputum Culture:……..

Result of CXR…….Referred/ treatment……..