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Research Article

Individual and community level response for pulmonary tuberculosis patients in India

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ABSTRACT

Background: Host-related and environment-related factors have been shown to play a role in the development of tuberculosis (TB), but few studies were carried out to identify their respective roles in Central India.
Methods: This was a descriptive case control study, which was conducted at tertiary care government hospital. The duration of the study was from January 2011 to September 2013. A total of 822 sputum smear-positive TB patients were included in the study. Cases were newly detected smear positive TB patients. Two controls were recruited for each case, one within the household of the case, and one in the community.
Results: Regarding host-related factors, univariate analysis by conditional logistic regression of 687 matched pairs of cases and household controls showed that TB was associated with male sex, family history of TB, smoking, alcohol, anaemia, HIV infection, and history and treatment of worm infection. In a multivariable model based on 601 matched pairs, male sex, family history of TB, smoking, and HIV infection were independent risk factors of TB. The investigation of environmental factors based on the comparison of 816 cases/community control pairs showed that the risk of TB was associated with single marital status, family history of TB and adult crowding.
Conclusions: TB is a multifactorial disorder, in which environment interacts with host-related factors. This study provided useful information for the assessment of host and environmental factors of TB for the improvement of TB control activities in developing countries.

Keywords: Tuberculosis, Risk factors, Host factors, Environmental factors

INTRODUCTION

The development of tuberculosis (TB) in man is a two-stage process in which a susceptible person exposed to an infectious TB case becomes infected and may later develop the disease, depending upon various factors. In individuals infected with Mycobacterium tuberculosis, any condition modifying the balance established in the body between the host's immune defenses and the tubercle bacilli can have an impact on the risk of developing the disease. Factors that have been shown to influence this balance have been investigated for a long time, and were reported to be both 'intrinsic' and 'extrinsic' to the host.[1] However, in most studies investigating risk factors for TB, host-related and environmental factors were usually investigated separately, using different designs, making it impossible to assess their respective effects.[2,3]

Several approaches can be considered to target tuberculosis control and there is an urgent need to design new interventions against tuberculosis, integrating the epidemiologic and sociologic approaches.[4] Comparison of the prevalence of individual risk factors for TB in various populations using standardized indicators would elicit useful information.

In India, few studies have been carried out to understand the effect of individual factors on the development and progression of the disease. Unfortunately, no study integrating the total sum of these factors has been carried out.

This study intends to help health system policy makers, health officials, faculty in medical institutions, non-governmental organizations and health care providers in India, particularly in Sagar, Madhya Pradesh to understand the predisposing factors that are most alarming in our society and will also help them in concentrating their resources which are most affected by TB.

METHODS

Pulmonary TB was confirmed by two consecutive smears positive for acid-fast bacilli and/or a positive culture. The household (in this study, household was defined as the extended family living together in the same area and eating from the same pot) of each case was visited and information collected on various demographic and socioeconomic variables.

For each case, two types of controls were recruited. First, a healthy control was selected at random within the household of the TB case. This control was age-matched to within 10 years of the case. Then, a healthy community control was selected at random in the neighborhood of the case's household.

Information was collected from cases and controls on a wide range of potential host-related and environment-related risk factors for TB. These included factors already identified in previous studies and factors expected to predispose to TB in the particular situation of developing countries.[2,3] Standardized questionnaires were addressed to the study subjects by field assistants.

Informed consent was taken from all subjects. Approval for this study was also obtained from the review board of our institution. Ethics has been respected throughout the whole study period.

Data were double entered using Epi-Info (version 6, CDC, Atlanta, GA) and transferred to STATA (version 7, Stata Corporation, College Station, TX) for analysis. Analysis was conducted on data using index case and household control pairs to assess the effect of host-related factors and index cases and community control pairs to assess the effect of environmental risk factors. Finally, cases and community controls were compared to assess the combined effect of host-related and environmental factors. Odds ratios (OR) and their 95% confidence intervals (CIs) were estimated using conditional logistic regression, with TB as an outcome. The likelihood ratio test was used to test the association between the explanatory variables and the risk of TB and for linear trend and interaction. Univariate analysis was performed to examine the effect of each variable of interest on the risk of TB. Multivariate models were then constructed, including variables that showed a significant statistical effect in the prediction of TB in univariate analysis ($P < 0.05$).

RESULTS

822 index cases that satisfied the case definition were included in the analysis. Of these, 687 had a household control and 816 had a community control, allowing matched-pair analysis. Results from univariate analysis carried out on the 687 cases/household control pairs are displayed in Table 1.Male are found to be higher risk of developing TB than female. Widowed/divorced and single individuals were at a higher risk of developing TB than married individuals.

A former episode of TB in the case, or among his/her family, strongly increased that risk. The risk of TB was also found to increase with smoking, with a significant dose–response trend according to duration of smoking ($P < 0.001$), as well as with alcohol intake and drug use. The presence of a BCG scar appeared protective against TB. HIV infection, history of worm infection, and recent treatment of worms were found to increase the risk of TB, but there was no effect of history or treatment of asthma. Finally, TB was associated with diabetes and anaemia, with a significant linear trend for decreasing levels of hemoglobin ($P < 0.001$).

Environmental factors were investigated using a wide range of variables collected at the household level (Table 2). The risk of TB increased with the number of households in the compound, and with the number of persons in the household. More particularly, the risk increased with the number of adults in the household (P-value for linear trend < 0.01) although TB was not associated with the number of persons per room in the household.

The risk of TB increased if houses were built with mud-brick compared with cement walls, and if the floor was made of earth/soil rather than cement, but these effects were not statistically significant. The absence of a ceiling in the house was protective against TB. The risk of TB was not associated with the number of windows in the house.

Table 1: Host-related factors for TB: Comparison of TB cases and household controls (univariate analysis).

Variable	Total no. of pairs	Controls *n* (%)	Cases *n* (%)	OR (95% CI)	*P*-value
Sex					
Female	687	362 (53)	215 (31)	1	<0.0001
Male		325 (47)	472 (69)	2.32 (1.85, 2.94)	
Marital status					
Married	671	359 (54)	310 (46)	1	
Single		289 (43)	323 (48)	1.86 (1.30, 2.64)	
Widowed/divorced		23 (3)	38 (6)	2.34 (1.30, 4.22)	0.0003
Former TB					
No/unsure	675	660 (98)	638 (95)	1	0.001
Yes		15 (2)	37 (5)	2.69 (1.42, 5.09)	
Family history of TB					
No/unsure	673	558 (83)	504 (75)	1	<0.0001
Yes		115 (17)	169 (25)	2.38 (1.64, 3.47)	
Smoking					
Never	669	526 (79)	377 (56)	1	<0.001
Past		32 (5)	59 (9)	2.38 (1.50, 3.77)	
Current		111 (17)	233 (35)	3.14 (2.35, 4.21)	
Alcohol					
Never	672	546 (81)	509 (76)	1	<0.001
Current/past		126 (19)	163 (24)	1.84 (1.28, 2.66)	
Drug					
No	663	657 (99)	646 (97)	1	0.02
Yes		6 (1)	17 (3)	2.83 (1.12, 7.19)	
BCG scar					
No/unsure	687	325 (47)	364 (53)	1	0.02
Yes		362 (53)	323 (47)	0.77 (0.61, 0.97)	
HIV status					
Negative	609	562 (92)	537 (88)	1	0.002
Positive		47 (8)	72 (12)	2.34 (1.29, 3.54)	
History of worms					
No	673	503 (75)	468 (70)	1	0.01
Yes		170 (25)	205 (30)	1.43 (1.08, 1.90)	
Treatment for worms					
No	673	532 (79)	507 (75)	1	0.05
Yes		141 (21)	166 (25)	1.37 (1.00, 1.88)	
History of asthma					
No	674	665 (99)	669 (99)	1	0.28
Yes		9 (1)	5 (1)	0.56 (0.19,1.66)	
Treatment of asthma					
No	674	669 (99)	670 (99)	1	0.74
Yes		5 (1)	4 (1)	0.80 (0.21,2.98)	
Diabetes					
No/unsure	674	672 (100)	665 (99)	1	0.03
Yes		2 (0.3)	9 (1)	4.5 (0.97, 20.8)	

Table 2 - Environment risk factors for TB: Comparison of TB cases and community controls (univariate analysis).

Variable	Total no. of pairs	Controls *n* (%)	Cases *n* (%)	OR (95% CI)	*P*-value
Demographic and household related factors					
Number of HHs [a] in the compound					
1	816	231 (28)	209 (28)	1	
2–4		431 (53)	347 (42)	0.95 (0.72, 1.25)	
>4		154 (19)	260 (32)	2.25 (1.61, 3.15)	<0.001
Number of people in HH					
1–5	813	265 (33)	264 (32)	1	
6–10		344 (42)	274 (34)	0.81 (0.64, 1.03)	
>10		204 (25)	275 (34)	1.39 (1.07, 1.82)	<0.01
Number of adults in HH					
1–5	813	203 (25)	176 (21)	1	
6–10		356 (44)	298 (37)	1.40 (1.11, 1.76)	
>10		254 (31)	339 (42)	2.85 (1.88, 4.29)	<0.001
Persons per room (ppr)					
<1	746	35 (5)	31 (4)	1	
1–2		367 (49)	345 (46)	1.07 (0.64, 1.82)	
>2		344 (46)	370 (50)	1.26 (0.73, 2.16)	0.4
Family history of TB					
0	813	772 (95)	676 (83)	1	
1 member		38 (4.6)	100 (12)	2.90 (1.96, 4.29)	
>1 member		3 (0.4)	37 (5)	13.37(4.10, 43.61)	<0.001
Walls					
Cement	567	292 (52)	279 (49)	1	
Mudbrick/other		275 (48)	288 (51)	1.54 (0.92, 2.57)	0.09
Floor					
Cement	1132	517 (91)	505 (89)	1	
Mud, earth		49 (9)	61 (11)	1.32 (0.86, 2.01)	0.2
Ceiling					
Yes	741	327 (44)	352 (47)	1	
No		414 (56)	389 (53)	0.79 (0.63, 1.00)	0.05
Number of windows					
0	816	85 (10)	104 (13)	1	
1		619 (76)	608 (74)	0.73 (0.52, 1.01)	
>2		112 (14)	104 (13)	0.71 (0.47, 1.09)	0.11
Socioeconomic factors					
Marital status					
Married	805	466 (58)	388 (48)	1	
Single		276 (34)	358 (44)	1.92 (1.48, 2.46)	
Widowed/divorced		63 (8)	59 (7)	1.13 (0.75, 1.71)	<0.001

[a]HH=Household

DISCUSSION

The present study is one of the first in Central India to examine risk factors of TB consistently in a large sample. The observed association of TB with male sex is in agreement with what has been reported in most countries.[5,6] Whether the male excess among the study population reflects a selective under-reporting or under-diagnosis of female patients or a true background sex difference is difficult to assess.[7] There are considerable sex differences with regard to stigma and its social consequences, which may result in differential health-

seeking behaviour and access to care between males and females.[8,9] However, the consistent effect of male gender observed, both with household and community controls and throughout the sites, suggests that selective under-diagnosis relating to gender is unlikely. Of note, a genome-wide linkage study searching for regions of the human genome containing TB susceptibility genes suggested a linkage between regions of the chromosome X and TB, with a lod score of 1.77, which could contribute to the excess of TB in males in many population.[10]

Smoking results in histological changes in the lower respiratory tract, including peribronchial inflammation, fibrosis, vascular intimal thickening, and destruction of alveoli.[11] This leads to alterations in the epithelial function, such as reduced ciliary activity, decreased clearance of inhaled substances, and abnormal vascular and epithelial permeability. In this study, cigarette smoking was an independent risk factor for TB, with a clear dose–response effect with duration of smoking. These results are consistent with those reported in a case–control study carried out in Spain.[12] Our findings thus support the hypothesis of an increased vulnerability of smokers to the infection and development of TB, most probably owing to patho-physiological changes in the lungs induced by chronic smoking.[11,12] As smoking is becoming an increasing public health problem in resource-poor countries, especially in the younger age groups, these results reinforce the need to take appropriate public health measures.

Since the start of the pandemic, HIV infection has emerged as the most important risk factor for the development of TB in individuals infected with M. Tuberculosis.[4] According to WHO there is a continuous 10% per year increase in TB projected in countries most severely affected by HIV infection.[13] The major factors contributing to the HIV associated TB epidemic in India are the high risk of reactivation of latent TB infection in HIV infected persons and the high risk of progressive TB disease owing to HIV infection, associated with the high TB transmission rate in the community. Therefore, it is essential to include HIV infection as a risk factor when trying to identify the role of other factors on the risk of developing TB.[14]

We observed a consistent effect of former experience of TB within the household, and this effect increased with the number of persons who had TB in the past. Furthermore, there was some evidence that this effect was higher when the former TB case was in close family link with the index TB case, as compared with unrelated household members. The risk of TB infection increased with social proximity to the case, and that this effect was persistently higher in first-degree than in more distant relatives.[15] This clustering of TB within families, already noticed by epidemiologists decades ago could reflect not only the facility of transmission within the household, but also a genetic contribution to the susceptibility to TB.[16-18] This aspect has been investigated in the present study and results from combined case–control and linkage analysis have so far showed that vitamin D receptor variants might have an impact on susceptibility to TB.[19,20]

Marital status similarly reflects both demographic and SES of individuals. In India, widowed and divorced persons, especially women, rely heavily on family solidarity, and in the absence of this solidarity, may experience severe socioeconomic difficulties. Thus, in this study also, being single and living alone was an independent risk factor for TB.[21]

Subjects with TB were less likely to report a history of asthma than community controls. A putative link between exposure to mycobacteria and a decreased risk of atopic disease was suggested in a study of Japanese children in whom strongly positive tuberculin responses in early life were associated with a reduced risk of asthma in later childhood.[22] In an ecological study carried out in 23 industrialized countries, TB notification rates were inversely associated with lifetime prevalence of wheeze and asthma.[23] These findings are consistent with the hypothesis that natural exposure to M. tuberculosis in childhood may have a role in inhibiting atopy. It has been shown that mycobacteria elicit a Th1 immune response in humans leading to the production of IL-12, IFN*, and TNF which has been shown to cross-inhibit Th2 responses.[24,25] Thus, it is possible that mycobacterial exposure decreases the development of atopy through the inhibition of Th2 immune mechanisms, which is consistent with both the above epidemiological findings and our earlier findings of a high Th1 activity in exposed household controls.[25]

There are several limitations of this study. The validity of information obtained by patient recall cannot be established with certainty. Another limitation is that the study does not prove whether these patients had these risk factors by chance or if TB could predispose to these factors. Thus, further studies linking the relationship of these factors to the occurrence of the disease need to be carried out. This will contribute to developing a holistic approach in the management of TB.

CONCLUSION

This present report highlights social dysfunctions faced by TB patients. Understanding of these issues will help the providers in planning more comprehensive efforts to educate the community on TB and thereby reduce the social sufferings faced by the people with tuberculosis. Currently the entire country is covered by RNTCP and every year more than one million patients are being initiated on treatment. The findings of this study bring out the need to provide adequate psycho-social support to patients enrolled in the programme, which will help in enhancing their compliance.

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