



The Risk Factors for Pulmonary Tuberculosis Incidence in Ghana: A Small Matched Case-control Study

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Authors' contributions

This work was carried out in collaboration among all authors. Author MB conceptualized the study. Authors TA, DAA, SB and BJ revised the original design. Authors MB and ESC analyzed the data. All authors participated in interpreting the results, drafting the manuscript and revising it critically for important intellectual content. All authors read and approved the final manuscript.

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ABSTRACT

Aims: Knowing the risk factors for tuberculosis (TB) opens up avenues for identifying target groups for intensified case finding. We aimed to identify the risk factors for pulmonary TB (PTB) incidence in a rural district in northern Ghana.

Study Design: A matched case-control study.

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Place and Duration of Study: The Kassena Nankana West District of the Upper East Region of Ghana, between February 2019 and March 2019.

Methodology: This study was conducted in 4 public health facilities. Cases were newly confirmed PTB patients aged 15 years or over, controls were age and sex matched outpatients. A pre-tested questionnaire collected information on a range of possible risk factors from participants. Conditional logistic regression identified independent risk factors for PTB incidence in a multivariable model at 95% confidence level.

Results: The analysis included 174 cases and controls. Multivariable analysis showed that the risk of PTB was increased with low household monthly income (AOR=3.45; 95% CI: 1.08-10.97; $P=.03$), smoking (AOR=2.69; 95% CI: 1.13-6.43; $P=.02$) as well as household exposure to a known TB case (AOR=2.57; 95% CI: 1.08-6.10; $P=.03$).

Conclusion: Low household monthly income, smoking, and household exposure to a known TB case were independent risk factors for PTB incidence. These factors can be used to actively screen for PTB in the population.

Keywords: Infectious diseases; morbidity; risk factors; tuberculosis; case-control; Ghana.

1. INTRODUCTION

Tuberculosis (TB) has remained an issue of public health concern globally with a devastating effect on health and wellbeing. Current TB control strategies focus on early diagnosis and treatment of people with active TB disease. Although the availability of chemotherapy, together with socioeconomic development around the 20th century, helped to reduce TB morbidity and mortality rates in developed countries, high incidence rates of TB are still reported from, especially low and middle-income countries in Africa [1].

Ghana has achieved the 85% global target for TB treatment success rate. However, case detection rate has remained low and below the international target for about three decades, specifically, in the northern part of the country [2]. It is reasonable to assume that the low case detection could imply a low prevalence of the disease in the population or failure of the surveillance system to identify undiagnosed TB patients. However, there is epidemiological evidence that suggests that passive TB patient finding is inadequate for the early diagnosis of TB disease in rural populations that bear the highest burden of the TB epidemic [3,4]. Moreover, an assessment of the impact of the internationally recommended Directly Observed Treatment Short-course (DOTS) strategy on case finding and treatment success concluded that the package improved overall treatment success, but had no notable effect on early case identification [5].

Despite the evidence, TB case finding in Ghana and elsewhere still follows the DOTS guidelines and depended primarily on detecting TB among

patients presenting to health facilities with signs and symptoms of the disease. Consequently, poor access to health services and poor health-seeking behaviour of patients could negatively affect the early diagnosis of TB in individuals, thereby contributing to disease transmission in the population. Indeed, undiagnosed pulmonary smear-positive TB patients are the primary source of secondary infections in most communities [6,7]. Nonetheless, our search for literature on the risk factors for pulmonary TB (PTB) in Ghana revealed that these factors have not been explored adequately. Elsewhere in Africa, the risk factors for PTB incidence have been documented, including marital status, sex, smoking, family history of TB, adult crowding, and human immunodeficiency virus (HIV) infection [8,9].

To end TB as a global epidemic, understanding the risk factors for PTB is a means under the purview of the national TB control programme (NTP) that could improve the early identification of undiagnosed TB patients for treatment and subsequently decrease disease transmission in the population. This study sought to identify the risk factors that were associated with PTB incidence (the most infectious form of TB) in a predominantly rural district in the Upper East Region of Ghana.

2. MATERIALS AND METHODS

2.1 Study Setting

The study was conducted in the Kassena Nankana West (KNW) district located in the Upper East Region of Ghana. The district was carved from the Kassena Nankana Municipal in 2007 per the Legislative Instrument (LI) 1855 and

lies approximately between latitude 10.97° North and longitude 01.10° West, with Paga as its administrative capital. The district shares boundaries with Burkina Faso to the north, Builsa North District to the south, Kassena-Nankana Municipal to the east, and Sissala East Municipal in the Upper West Region to the west (www.ghanadistricts.com).

It is a predominantly rural district with a population of 84,585 in 2018, projected from the 2010 Population and Housing Census (PHC) [10]. This population is served by 35 public health facilities including a district hospital, 5 health centres and 29 Community-based Health Planning and Services (CHPS)¹ centres and zones. Six of these facilities can undertake sputum smear microscopy to confirm PTB disease. The district lies in the Sahel savannah zone, characterized by two seasons; the dry and wet seasons. Agricultural pursuit is the mainstay of the local economy, employing more than 70% of the active population. During the agricultural-off season (late November to early March), a substantial number of people, especially the youth migrate to the southern zone in search for jobs to sustain the livelihood of family members back home [11].

The district was selected for the study because the TB case notification rate has consistently been lower than the international target of 70%. TB case detection rate in the district has decreased since 2013 and on average below the international target of at least 70% between 2012 and 2018 (Fig. 1). More importantly, rural populations bear the burden of undiagnosed TB disease because they lack adequate knowledge about the disease and face challenges in accessing health care services for diagnosis and treatment of infections [12].

2.2 Study Design and Selection of Participants

First, the TB registers available in the TB facilities were reviewed to ascertain the number of documented cases of PTB in the district. Data were found from 2007 to 2018 for some facilities and not others. Over that period, 285 cases were registered of which 276 were PTB cases. Also, it

¹ CHPS is a national programme of community-based care provided by resident nurses referred to as community health officers. CHPS, introduced in 1999, reduces geographical barriers to healthcare access and provides basic level preventive and curative services for minor ailments at the community and household levels

was identified that through the creation of the district, new TB facilities were also created. Consequently, many records on TB cases for the years preceding 2007 were not available. After carefully studying the information available on the patients, the time available for the data collection, and constrains with funding and logistics, the study was limited to four of the health centers (there were no eligible cases in one of the 5 health centers) and the period was limited to between 2015 and 2018.

All newly confirmed PTB patients aged ≥ 15 years registered during 2015-2018 in the four purposively selected health centres in the district were eligible to participate in the study (n=108). PTB was confirmed according to the WHO and NTP guidelines. The confounding effect of age and gender on TB has long been recognized [13–16]. Therefore, cases were matched 1:1 on age (± 5 years) and gender with the controls. Cases and controls were recruited from the same catchment area. The controls were patients with no previous history of TB attending the same health centres from where cases were registered for conditions that were not respiratory-related. The physicians at the health centres helped in ruling out TB symptoms in controls. The controls were recruited within 3 days after a case was interviewed. Data collection was carried out between 5th February and 6th March 2019.

2.3 Data Collection

Information on a wide range of host-related factors was collected from TB patients and controls using a piloted pre-coded questionnaire in a face-to-face interview [17–19]. A TB knowledge index was created from six questions which assessed respondent's knowledge on 1) signs and symptoms of the disease; 2) mode of transmission; 3) whether the disease is curable; 4) whether the patient knows TB treatment is free; 5) the standard duration of TB treatment and; 6) whether treatment could be discontinued earlier with improvement in health status. The TB knowledge was evaluated by a score based on the responses given to the six questions, with one point given for each correct response. Thus a maximum score of 6 points was given when a respondent answered correctly to all the six questions. An arbitrary criterion of 'good knowledge' was set if a respondent obtained at least 4 out of the maximum 6 points. A household monthly income group (low, average and high) was constructed from a tertile of monthly household income.

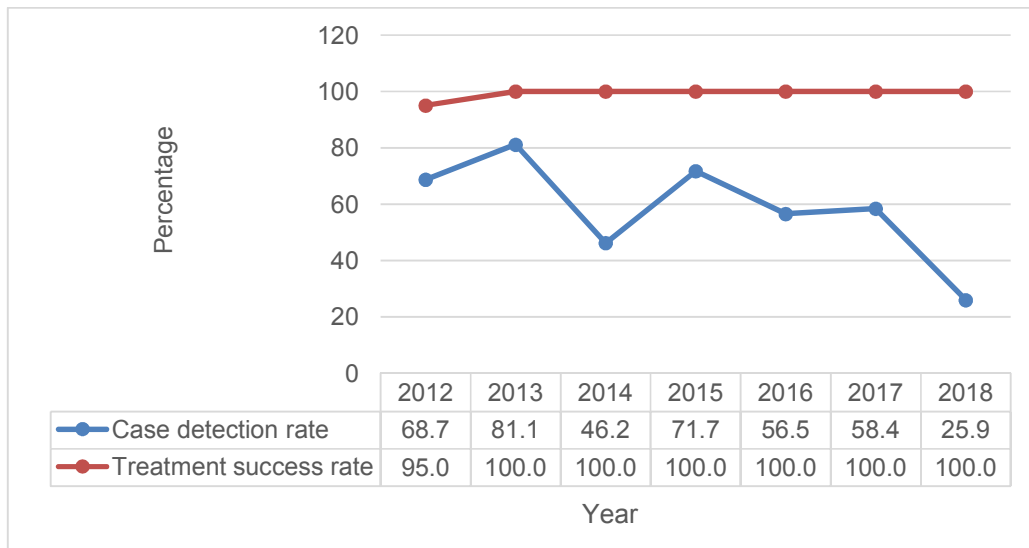


Fig. 1. Trends of tuberculosis case detection and treatment success rates in the Kassena Nankana West district, 2012-2018. Source: District's annual reports (unpublished data)

The questionnaires were administered to cases and control in health facilities or their homes by trained data collectors with at least a diploma in educational level and with previous experience in data collection. The interviews were conducted in the appropriate local language. The interviewers were blinded to the respondents and so could not tell whether the respondent was a TB patient or a non-TB patient. The presence of a Bacillus Calmette-Guerin (BCG) scar on the right arm was used as a confirmation of BCG vaccination history. Administered questionnaires were checked daily for completeness and consistency. Owing to the lack of funding and other logistical constraints, we could not assess the HIV infection status and nutritional status of the study participants. These factors have been associated with the risk of TB [20].

2.4 Data Analysis

The information collected was entered in EpiData Entry Client (v.4.4.3.1, EpiData Association, Denmark) and exported to STATA /IC version 15.0 for Windows (StataCorp LLC, College Station, USA) for cleaning and analysis. The Chi-square (χ^2) test was used to examine differences in proportions while differences in continuous outcomes were assessed using the t-test.

Conditional logistic regression models were used to estimate the odds ratio (OR) and their corresponding 95% confidence intervals (CIs), with TB disease as the outcome. The likelihood

ratio test was performed on associations between explanatory variables and the outcome. Univariate analysis was performed to examine the association between explanatory variables and the risk of TB. A multivariable model was then built including variables that were significantly associated with TB risk in the univariate analysis. A $P < .05$ was considered statistically significant for a factor to be classified as a risk factor. All tests were two-tailed.

3. RESULTS

3.1 Age and Sex Distribution of Participants

Of the 108 eligible PTB patients to participate in this study, 87 patients were interviewed giving a response rate of 80.6%. The remaining 21 patients could not participate because, at the time of the data collection, 15 had travelled out of the district, 3 had died, and 3 could not be located using the documented address. An equal number of controls were also interviewed giving a total of 174 PTB patients and controls participating in the study. The mean age (in years) of the cases and controls was 50.1 (± 14.0 years) and 50.6 (± 14.3 years) respectively. Statistically, there were no significant differences in the age and sex distribution between the cases and controls, an indication that the cases were properly matched with the controls. Nonetheless, 70.1% of the cases were males (Table 1).

Table 1. Age and sex distribution of cases and controls (N=174)

Indicator	N	Controls	Cases	P-value
Age, years	174			.89 ^a
Mean (standard deviation)		50.1(14.0)	50.6(14.3)	
Median (range)		47(21-85)	48(18-83)	
Sex, n (%)				1.00
Male	122(70.1)	61(50.0)	61(50.0)	
Female	52(29.9)	26(50.0)	26(50.0)	

^aWilcoxon rank-sum test; N: total sample size

3.2 Univariate Analysis of the Risk Factors Associated with Pulmonary Tuberculosis in Ghana

A univariate conditional logistic regression analysis was conducted to identify the factors that were associated with PTB incidence. The results showed that the risk of PTB was increased with low household monthly income (OR=4.78; 95% CI: 1.81, 12.62), smoking (OR=5.50; 95% CI: 2.59, 11.68), alcohol consumption (OR=4.83; 95% CI: 2.01, 11.64) as well as household exposure to a known TB patient (OR=2.90; 95% CI: 1.41, 5.95). On the other hand, the risk of PTB incidence was lowered with poor knowledge about TB disease (OR=0.29; 95% CI: 0.12, 0.71) (Table 2).

3.3 Independent Risk Factors of Pulmonary Tuberculosis in Ghana

The multivariable analysis identified socioeconomic and behavioural factors that were independently associated with the risk of TB. The results showed that household monthly income, smoking status, and household exposure to a known TB patient were important risk factors for the development of PTB. The risk of PTB was increased with low household monthly income (AOR=3.45; 95% CI: 1.08, 10.97; $P=.03$), smoking (AOR=2.69; 95% CI: 1.13, 6.43; $P=.02$), and exposure to a known TB patient (AOR=2.57; 95% CI: 1.08, 6.10; $P=.03$) (Table 3).

4. DISCUSSION

The small matched case-control study identified that household income, smoking, alcohol consumption, household exposure to a known TB patient, and knowledge about TB disease were statistically significantly associated with the risk of developing PTB. However, household income, smoking, and household exposure to a known TB patient were independent risk factors

for PTB in Ghana. The findings identified a high-risk group for active TB case detection and treatment.

The analysis found an association between low household monthly income and increased risk of TB, which was supported by findings from earlier studies [21,22]. TB is a disease of the impoverished and socioeconomic status can affect the development stages of TB: exposure, progression to disease, delayed diagnosis and treatment, and poor treatment compliance and success [23]. It can be explained that low household income is a catalyst to enable TB transmission via poor living environments such as overcrowding and poor ventilation, increasing the risk from latent TB infection to active TB through undernutrition, and barriers to early diagnosis and treatment due to low levels of awareness on the disease and poor access to health services [24].

The study found an association between smoking and the risk of TB, which was contrary to previous studies [14,25] but in consonance with findings from a study in three West African countries [8] and elsewhere in Asia [26]. Smoking has far-flung effects on lung function in the human host. Nicotine in tobacco impairs the phagocytic function of macrophages in the alveolar and consequently suppressing specific immune response [27]. This ultimately renders the individual more susceptible to TB infection and progression to active TB from latent infection [28]. Smoking also promotes disease transmission by motivating infectious patients to cough, thereby excreting the *Mycobacterium* bacilli into the environment [29]. Smoking was not only linked to TB morbidity but has been associated with adverse treatment outcomes, including mortality [30]. The complex interaction between smoking and TB epidemiology underscores the need for smoking cessation interventions to be implemented to combat the TB epidemic in low and middle-income countries.

Table 2. Univariate analysis of the risk factors associated with pulmonary tuberculosis in Ghana

Category/variable	N	Controls n (%)	Cases n (%)	OR (95% CI)	P-value
Demographic factors					
Marital status					
Single (Never married)	20	7(35.0)	13(65.0)	2.50(0.78, 7.97)	.12
Married	109	58(53.2)	51(46.8)	Referent	
Previously married	45	22(48.9)	23(51.1)	1.08(0.51, 2.29)	.84
Place of residence					
Urban(Town)	28	19(67.9)	9(32.1)	Referent	
Rural (outskirts)	146	68(46.6)	78(53.4)	2.25(0.99, 5.17)	.05
Travel time to Heath facility					
less than 30 minutes	62	35(56.5)	27(43.5)	Referent	
30 minutes to1 hour	88	42(47.7)	46(52.3)	1.47(0.72, 2.97)	.29
More than 1 hour	24	10(47.1)	14(58.3)	2.03(0.69, 5.98)	.20
Socio-economic factors					
Educational attainment					
No formal education	61	21(34.4)	40(65.6)	1.80(0.67, 4.88)	.24
Basic education	90	55(61.1)	35(38.9)	0.65(0.26,1.61)	.34
Secondary or higher	23	11(47.8)	12(52.2)	Referent	
Employment status					
Unemployed	37	21(56.8)	16(43.2)	0.58(0.23,1.48)	.25
Employed	137	66(48.2)	71(51.8)	Referent	
Household monthly income group					
Low	63	21(33.3)	42(66.7)	4.78(1.81,12.62)	.002
Average	67	38(56.7)	29(43.3)	1.33(0.61, 2.93)	.47
High	44	28(63.6)	16(36.4)	Referent	
Biological and behavioral factors					
BCG vaccination					
Yes	115	61(53.0)	54(47.0)	Referent	
No	59	26(44.1)	33(55.9)	1.64(0.77, 3.46)	.19
Smoking status					
Never smoked	94	65(69.1)	29(30.9)	Referent	
Smoked/current smoker	80	22(27.5)	58(72.5)	5.50(2.59, 11.68)	<.001
Alcohol consumption					
Never	53	38(71.7)	15(28.3)	Referent	
Previous consumer/current consumer	121	49(40.5)	72(59.5)	4.83(2.01,11.64)	<.001
History of diabetes					
Yes	28	17(60.7)	11(39.3)	0.45(0.16, 1.31)	.14
No	146	70(47.9)	76(52.1)	Referent	
Household exposure to a known TB patient					
Yes	53	17(32.1)	36(67.9)	2.90(1.41, 5.95)	.004
No	121	70(57.9)	51(42.1)	Referent	
History of imprisonment					
Yes	9	4(44.4)	5(55.6)	1.33(0.30, 5.96)	.70
No	165	83(50.3)	82(49.7)	Referent	
Knowledge about TB disease					
Poor	47	31(66.0)	16(34.0)	0.29(0.12, 0.71)	<.001
Good	127	56(44.1)	71(55.9)	Referent	

Table 3. Independent risk factors of pulmonary tuberculosis in Ghana

Category/Variable	AOR (95% CI)	P-value
Household monthly income group		
Low	3.45(1.08, 10.97)	.03
Average	1.35(0.52, 3.48)	.53
High	Referent	
Smoking status		
Never smoked	Referent	
Smoked/current smoker	2.69(1.13, 6.43)	.02
Alcohol consumption		
Never	Referent	
Previous consumer/current consumer	2.41(0.81, 7.16)	.11
Household exposure to a known TB patient		
Yes	2.57(1.08, 6.10)	.03
No	Referent	
Knowledge about TB disease		
Poor	0.53(0.18, 1.58)	.25
Good	Referent	

AOR: Adjusted odds ratio (adjusted through multivariable analysis); CI: Confidence interval; TB: tuberculosis

Proximate risk factors of TB measure direct exposure to infectious droplets. The risk of infection following exposure to *Mycobacterium tuberculosis* (MTB) depended on the degree of infectiousness, and proximity to the source case [20]. Having a history of household exposure to a known TB patient was associated with an increased risk of TB in this study. This observation may reflect a within-household transmission, and or genetic susceptibility of household members to the disease [31]. The positive association between household exposure to a known TB case with TB incidence in this study, nonetheless, was consistent with findings from other studies [9,14,19]. Indeed, 8-19% of TB transmissions take place at the household level [32,33]. This implies that the majority of infections occurred outside of the household. Therefore, from a public health perspective, TB contact tracing should not be limited to only household contacts but should include community contacts in order not to miss infectious individuals at the community level.

We noted no statistically significant association between having a history of diabetes and PTB risk in the univariate analysis. This finding was contrary to published reports which have associated diabetes with TB incidence [21,34]. Here, 60.7% of controls reported having a history of diabetes compared with 39.3% of cases (OR=0.45; 95% CI: 0.16-1.31, $P=.14$). In this study information on the history of diabetes was collected through participants' self-report. Thus,

this finding may reflect a limitation associated with our question on diabetes. This is because mild types of this condition may not have been diagnosed in cases. Moreover, TB patients in the study area are not routinely tested for diabetes. It is, therefore, likely that the true prevalence of diabetes among the TB cases in this study might have been underestimated.

There are some limitations with our study which should be noted. First, the exposures were identified retrospectively. In consequence, it is difficult to determine if the association was a true temporality. That is to say, it is hard to establish if the exposure preceded the outcome or whether the outcome might have preceded the exposure. Secondly, we ascertained exposure from participants' self-report of exposure to risk factors using an interviewer structured questionnaire. Therefore, the validity of the information provided by the respondents depended, in part, on the subject matter. Cases and controls may have different recollections of exposures and sometimes the cases are more likely to recall their exposure to potential risk factors better than the controls. We tried to minimize recall bias by blinding the data collectors to whether the respondent was a case or control during the interviews. This we believe prevented the interviewers from unintentionally prompting the respondents, especially the cases to remember past events relating to the exposures. Thirdly, the selection of controls from the health centers followed a non-random methodology, thus

rendering the sample of controls less representative of the general population in terms of health. We minimized selection bias by selecting the controls from the same catchment area as the cases, as well as matching the cases with the controls. Lastly, we were not able to measure and then control for, through statistical analysis, all factors that may have affected the development of PTB. For example, HIV infection and undernutrition are well-known risk factors of TB. Information on these factors could only be ascertained by conducting a primary evaluation of the respondents. This required procuring the necessary HIV testing kits and measuring tools for assessing body mass index (BMI). However, this was not possible due to the lack of funds for the project and other logistical constraints.

5. CONCLUSION

Low household monthly income, smoking and household exposure to a known TB case are independently associated with increased risk of PTB incidence in rural northern Ghana. Our findings provide information that is vital for identifying target groups in rural populations for intensified case finding and preventive treatment. More broadly, the currently implemented DOTS strategy to TB control in Ghana needs to be complemented with interventions that would reduce susceptibility and progression from latent TB infection to active disease. These interventions should address socioeconomic inequalities and smoking cessation in the communities to offer broad population-level benefits.

CONSENT

Informed consent was obtained from participants before the interview. The purpose of the study including the risks, benefits and their right to participate or refuse were explained to participants. The confidentiality of participants was guaranteed. Their anonymity was ensured by excluding personal identifiers during data entry and analysis.

ETHICAL APPROVAL

This study was approved by the ethics committee of Harbin Medical University.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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