



Risk Factors for Extrapulmonary Tuberculosis in Bangladesh: A Country with High Tuberculosis Prevalence

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Authors' contributions

This work was carried out in collaboration among all authors. Author Md. FH wrote and finalized the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Tuberculosis (TB) is a major public health problem in Bangladesh. In this case-control retrospective study, a total of 348 patients, either with pulmonary TB (PTB) or extrapulmonary TB (EPTB), were surveyed from April 2020 to January 2023 from five different districts of Bangladesh to identify risk factors of EPTB. The results revealed that most of the surveyed TB patients were infected with PTB (225 patients) while 123 patients were infected with EPTB. Males were more susceptible to PTB while females were more prone to EPTB. EPTB was more prevalent in younger people than older

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people as compared with PTB. Likewise, married patients were more prone to PTB than EPTB while unmarried patients were equally susceptible to both PTB and EPTB. Brain, lymph node and intestine were major organs which were infected by EPTB, but the prevalence of EPTB of intestine, lymph node and breast were higher for female than for male. BCG vaccination showed more preventive role against EPTB than PTB. EPTB was prevalent in certain blood groups and occupations. Similarly, the people with very dark brown skin and underweight in childhood were more prone to EPTB. The data also revealed that family members with EPTB, regular medication, less exposure to direct sunlight, and mental stress increased the prevalence of EPTB. Contrary, addiction to smoking, average sleeping hours, and use of mosquito coil were dispensable factors affecting the prevalence of EPTB. All these findings emphasize the necessity for addressing specific risk factors, to decrease the burden of EPTB in Bangladesh.

Keywords: Tuberculosis; extrapulmonary; risk factor; Bangladesh.

1. INTRODUCTION

Roughly one-third of the world's population has been infected with *M. tuberculosis*, and new infections occur at a rate of one per second (Houben & Dodd 2016). Moreover, tuberculosis (TB) is a major public health problem in Bangladesh. Considering the estimated number among total population, Bangladesh is a high Tb burden and high drug resistant (DR) TB burden country and it ranks 7th among 22 high Tb burden countries (Kundu et al. 2020). People with TB can infect up to 10-15 other people through close contact over the course of a year (Chinenye 2015). Without proper treatment up to two thirds of people ill with TB will die (Bhatt et al. 2012). Although, a considerable progress has been made to decrease the mortality rate of tuberculosis by DOTS but this success is undermined by very slow rate of decline as well as emergence of multidrug-resistant (MDR) and extremely drug-resistant (XDR) tuberculosis during the past decade. Moreover, Extra-pulmonary tuberculosis (EPTB) which can infect nearly every type of organs such as the lymph nodes, urinary tract, reproductive organs, meninges of the brain, bones and joints, pleural cavity, skin, and peritoneal cavity is becoming more notorious day by day because of lack of effective treatment and low recovery rate (Haque et al. 2015). Thus, the threat of MDR-TB and XDR-TB are accompanied by an increasing trend of extra-pulmonary TB (Miuro et al. 2023). Hence, even after the remarkable attempt to control TB worldwide, it remains a major global health threat because of the emergence of extra-pulmonary TB by drug-resistant mycobacteria. However, not all infections with *M. tuberculosis* cause TB disease and many infections are asymptomatic, called latent TB (Khabibullina et al. 2022). The risk of development to infection and disease is two different aspects and accurate understanding

of these factors is critical for planning TB control policies. The risk of TB infection is principally governed by exogenous factors as well as is determined by an intrinsic blending of the infectiousness of the source case, closeness to contact and social and behavioral risk factors including smoking, aerosol, alcohol, and indoor air pollution etc. (Narasimhan et al. 2013). However, factors that increase the progression of infection to disease are primarily host related, called endogenous such as alteration of immune response due to HIV co-infection (Gautam et al. 2021, Anes et al. 2021). Therefore, several studies have been undertaken addressing some socio-economic, cultural, and healthcare seeking related factors that influence TB (Nidoi et al. 2021, Hussain et al. 2020, Onyango et al. 2020). It has been reported that the social and demographic factors such as, poor housing, low-income, overcrowding, lack of education, smoking habit, drug addiction etc. contribute to the incidence and transmission of TB (Etim et al. 2024, Zarakpege 2023). However, recent data on risk factors of extra-pulmonary TB in Bangladesh are inadequate. Hence, this study was designed to explore the risk factors of extra-pulmonary tuberculosis in Bangladesh.

2. MATERIALS AND METHODS

2.1 Patient Population

A total of 348 patients, either with pulmonary or extrapulmonary TB, were surveyed from April 2020 to January 2023 from five different districts of Bangladesh, i.e. Rajshahi, Chapai Nawabganj, Sirajgonj, Moulvibazar and Chittagong. Rajshahi and Chapai Nawabganj are northwestern districts of Bangladesh while Moulvibazar is a northeastern district of Bangladesh. Sirajgonj is located near the center of Bangladesh while Chittagong is located in southern side of Bangladesh.

2.2 Case and Control Definitions

The patients with pulmonary TB only who were confirmed by the *M. tuberculosis* infection limited to the lung were classified as control patients (n=225). Conversely, the patients whose infection with *M. tuberculosis* was detected in organs or tissues outside the lung, either with or without pulmonary TB, were classified as a case of extrapulmonary TB (n=123).

2.3 Data Collection

A standardized survey tool which was developed for collection of data on demographic variable, lifestyle variables, physical and clinical characteristics of the patients was used for identification of risk factor of tuberculosis in Bangladesh. The addresses of the patients were collected from patient's records at different hospitals and NGOs who worked on TB in the surveyed districts. Then, data were obtained from detailed epidemiological interviews conducted by investigators at the hospitals or homes of patients using the survey tool. Oral informed consent was taken from each participant for data collection. Original clinical records were reviewed as needed.

2.4 Statistical Analysis of Data

Then, data entry was made from the survey tool into the SPSS program. Descriptive statistics were used to present role of different factors on

prevalence of tuberculosis with an intention to identify the risk factors of extrapulmonary tuberculosis in Bangladesh.

3. RESULTS

In this study total 348 people were surveyed from 5 different districts (Rajshahi, Chapai Nawabganj, Sirajgonj, Moulvibazar and Chittagong) of Bangladesh. The results revealed that most of the surveyed TB patients were infected with pulmonary TB (PTB) (225 patients) while 123 patients were infected with extrapulmonary TB (EPTB) (Table 1 and Fig. 1). The highest percentage of EPTB was found in Rajshahi and Moulvibazar districts, while the lowest percentage of EPTB was observed in Chittagong district (Fig. 1).

In this study, the mean age of patients for PTB was around 42 years while mean age for EPTB was around 35 years indicating that EPTB was more prevalent in younger people than older people as compared with PTB (Fig.2). It was also found that there was variation in prevalence of different types of tuberculosis for male and female patients in Bangladesh (Fig. 2). The results revealed that males were more prone to PTB than females. Conversely, females were more susceptible to EPTB than males (Fig. 2). This result has been supported by other studies reporting that female is more prone to EPTB than male (Pervin et al., 2024, Lin et al., 2013, Fang et al., 2022).

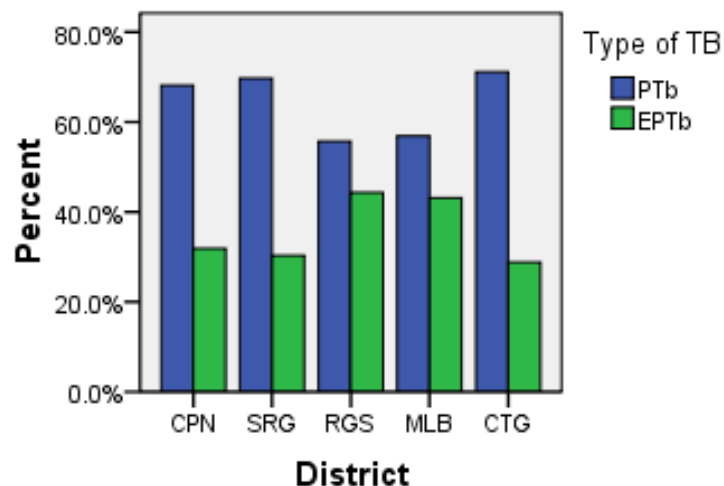


Fig. 1. Prevalence of different type of tuberculosis in different districts of Bangladesh. CPN=Chapai Nawabganj, SRG=Sirajgonj (SRG), RJS=Rajshahi, MLB=Moulvibazar and CTG=Chittagong (CTG)

Table 1. Number of surveyed PTB and EPTB patients from 5 different district of Bangladesh

Type of TB	District					Total
	Chapai Nawabganj (CPN)	Sirajganj (SRG)	Rajshahi (RJS)	Moulvibazar (MLB)	Chittagong (CTG)	
Pulmonary (PTb)	47	69	39	33	37	225
Extra-pulmonary (EPTb)	22	30	31	25	15	123
Total	69	99	70	58	52	Grand Total = 348

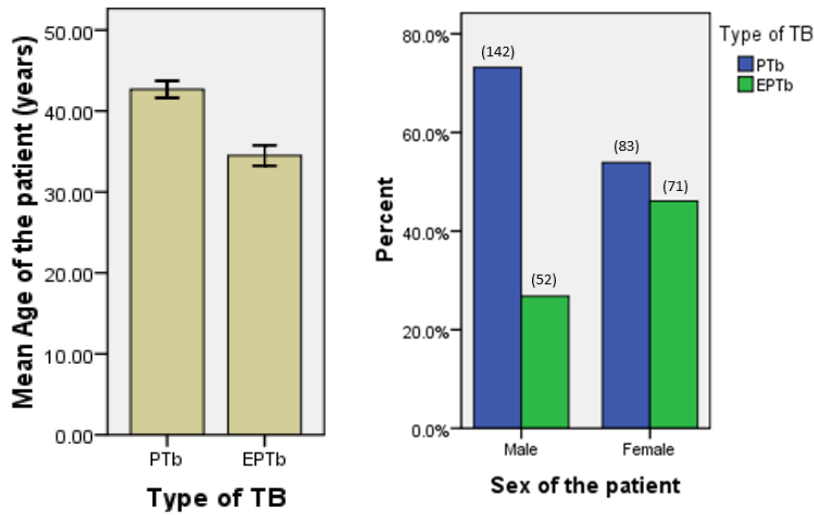


Fig. 2. Role of age and gender of patients on prevalence of tuberculosis (Mean Age ± SE). The number in bracket “()” shown on the top of each bar is the actual number of patients

The results revealed that the lung was the most affected organ to tuberculosis in both male and female (Fig. 3 and 4). However, the brain, lymph node and intestine were major organs which were infected by EPTB (Fig. 3). The prevalence of EPTB of intestine, lymph node and breast were higher for female than for male (Fig. 4).

The results revealed that the prevalences of PTB and EPTB were different for married and unmarried patients (Fig. 5). However, married patients were more prone to PTB than EPTB

while unmarried patients were equally susceptible to both PTB and EPTB (Fig. 5). It was also found that the numbers of siblings of patients were comparatively higher for PTB than EPTB indicating that higher number of siblings was not a risk factor for EPTB (Fig. 5).

Surprisingly, this survey showed that incidence of EPTB was higher than that of PTB in patient with no BCG vaccination (Fig. 6). Thus, the results indicates that the BCG vaccination is more effective for prevention of EPTB than PTB (Fig. 6).

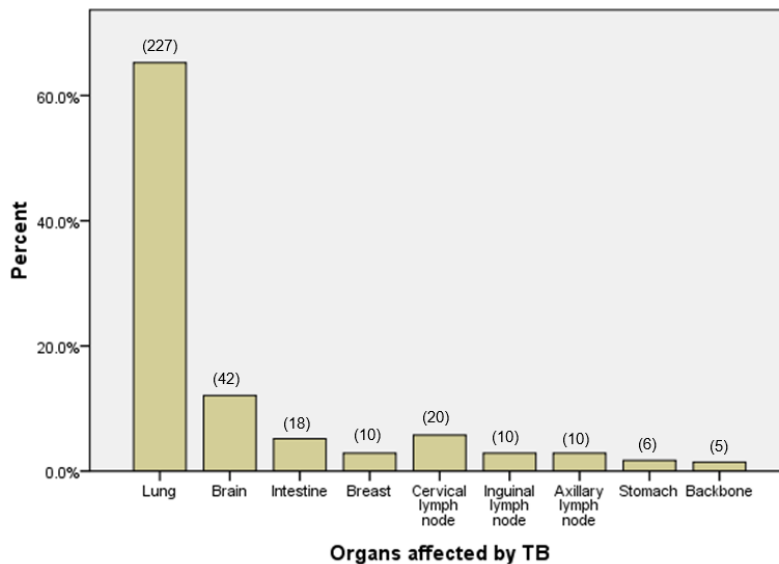


Fig. 3. Percentage of different organs infected by tuberculosis in Bangladesh. The number in bracket “()” shown on the top of each bar is the actual number of patients

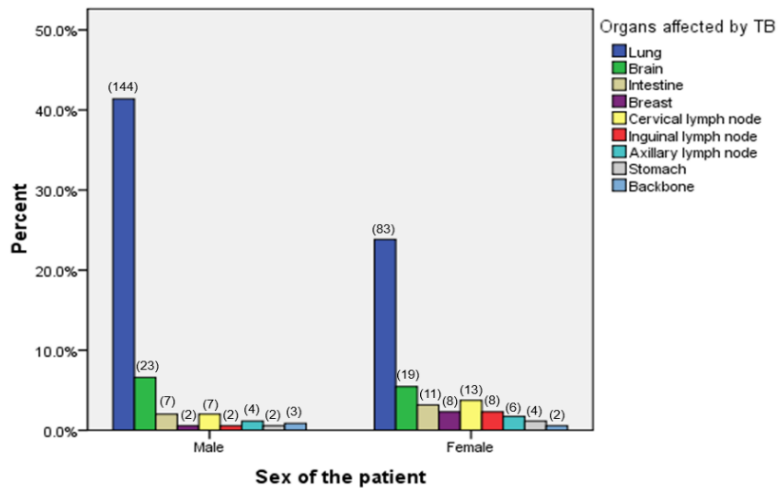


Fig. 4. Role of gender of patients on types of organs infected by tuberculosis. The number in bracket “()” shown on the top of each bar is the actual number of patients

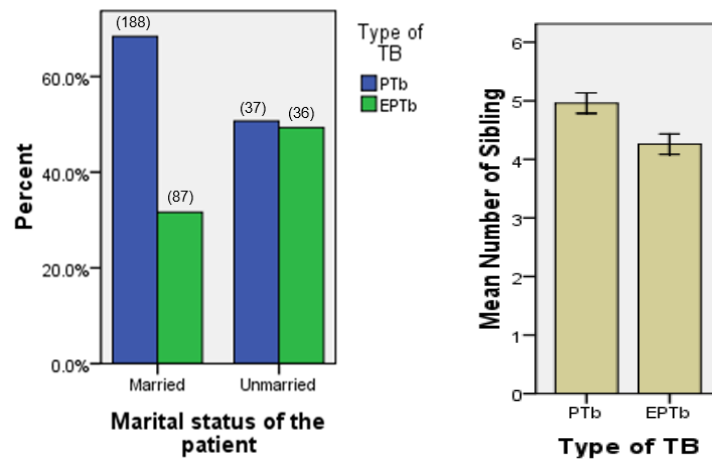


Fig. 5. Role of marital status and number of siblings on prevalence of tuberculosis. The number in bracket “()” shown on the top of each bar is the actual number of patients

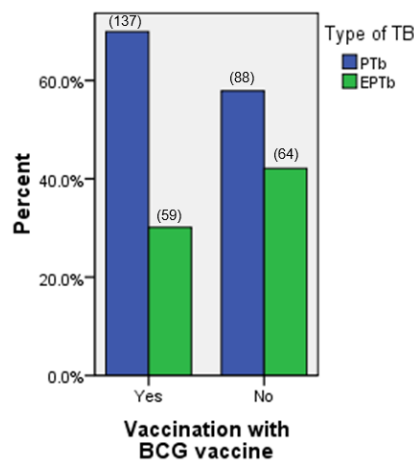


Fig. 6. Role of BCG vaccination on prevalence of tuberculosis. The number in bracket “()” shown on the top of each bar is the actual number of patients

As shown in Fig. 7 the prevalence of different types of tuberculosis varied with the blood group of the patients. For PTB, the highest percentage of patients was observed to carry O-positive blood group followed by B-positive and A-positives blood group (Fig. 7). Conversely, the highest percentage of EPTB patients was found to carry B-positive blood group followed by O-positive and O-negative blood group (Fig. 7). Surprisingly, the prevalence of EPTB was higher in patients carrying O-negative and AB-negative blood groups as compared with that of PTB (Fig. 7).

The results of this survey revealed that the prevalence of different types of tuberculosis varied with the occupation of the patients. The highest percentage of TB patients was student

followed by housewife and farmer (Fig. 8). However, incidence of EPTB was higher in the case of bankers, advocates and government servants as compared with that of PTB (Fig. 8).

The colorimetric scale with five colour i.e. very fair (skin color type 1), fair (skin color type 2), medium brown (skin color type 3), dark brown (skin color type 4), and very dark brown (skin color type 5) was used in this study. The scale was not based on race or ethnicity of the patients. The results showed that prevalence of EPTB was higher in people with very dark brown skin colour as compared with the percentage of EPTB for other skin colour indicating that very dark brown skin may be a risk factor of EPTB (Fig. 9).

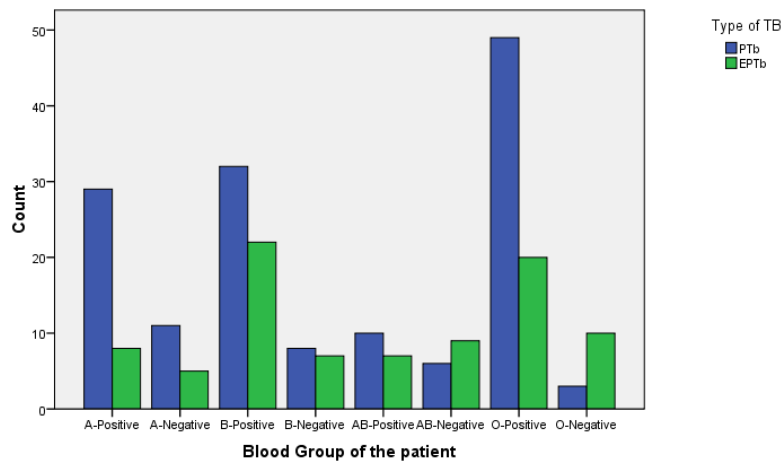


Fig. 7. Role of blood groups of patients on prevalence of tuberculosis

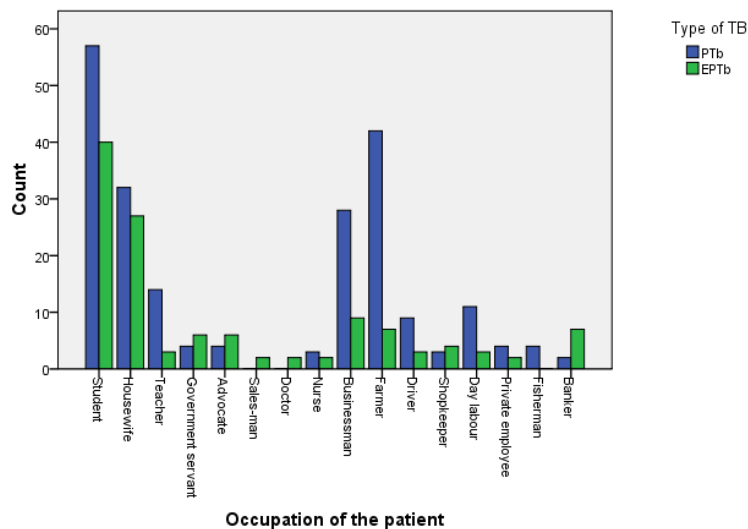


Fig. 8. Role of occupation of patients on prevalence of tuberculosis

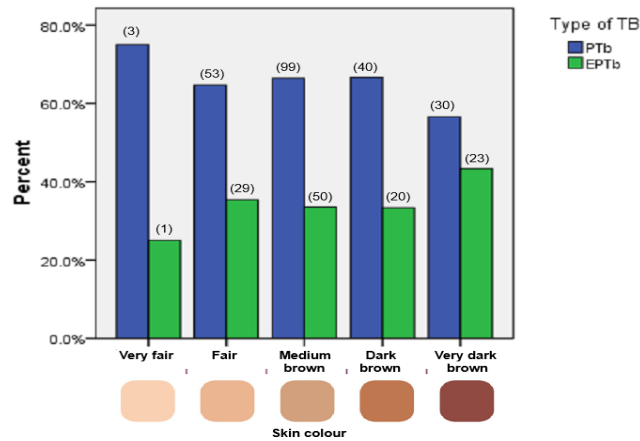


Fig. 9. Role of skin colour of patients on prevalence of different types of tuberculosis. The number in bracket “()” shown on the top of each bar is the actual number of patients

Depending on BMI, body weight was categorized into three types, i.e. Underweight (BMI below 18.5), Normal weight (BMI 18.5-24.9), and Overweight (BMI above 25.0). As shown in Fig. 10 the prevalence of tuberculosis varied with childhood body weight of the patients. The highest percentage of EPTB was recorded in patients who were underweight from childhood. However, prevalence of EPTB in overweight patients was little bit higher than normal weight patients but the pattern of incidence was similar (Fig. 10).

for asthma, hypertension, diabetics etc., and antibiotic use for any other disease before active infection of tuberculosis had a remarkable role in the increase of prevalence of EPTB (Fig. 11).

The results showed that the regular use of long-term control medicines such as medication

As shown in Fig. 12, higher percentages of PTB and EPTB were observed for the patients who had family members with tuberculosis. However, this increase of incident of EPTB was more prominent when family members having EPTB indicating that the infection of EPTB might be related to the availability of those strains of *Mycobacterium tuberculosis* which can cause EPTB (Fig 12).

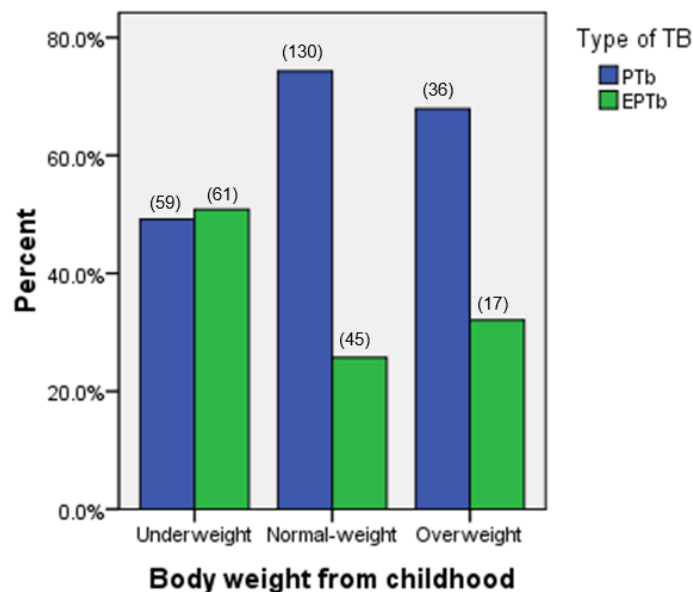


Fig. 10. Role of childhood body weight of patients on prevalence of tuberculosis. The number in bracket “()” shown on the top of each bar is the actual number of patients

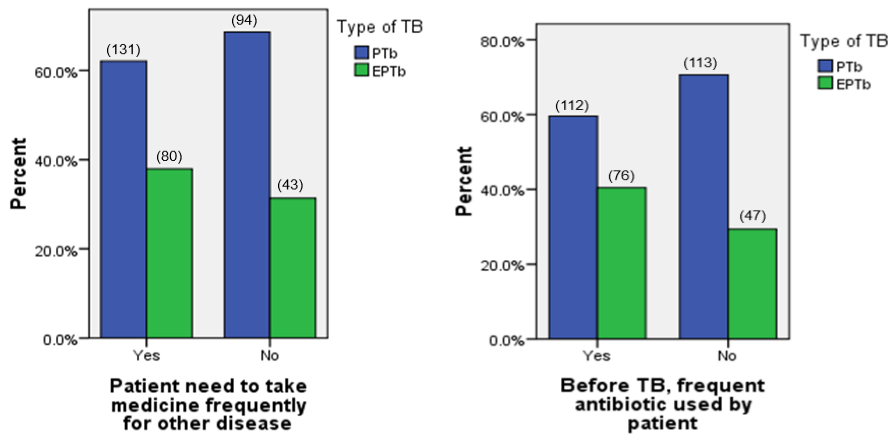


Fig. 11. Role of regular medication and antibiotic use on prevalence of tuberculosis. The number in bracket “()” shown on the top of each bar is the actual number of patients

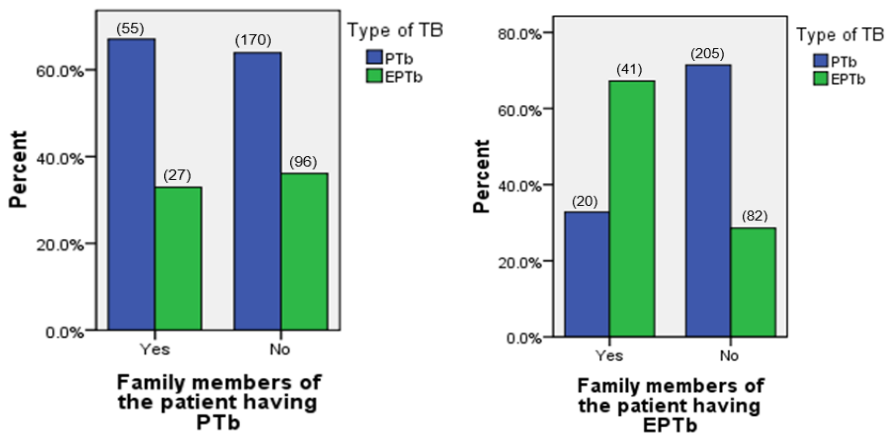


Fig. 12. Role of active TB infection of family members of patients on prevalence of different types of tuberculosis. The number in bracket “()” shown on the top of each bar is the actual number of patients

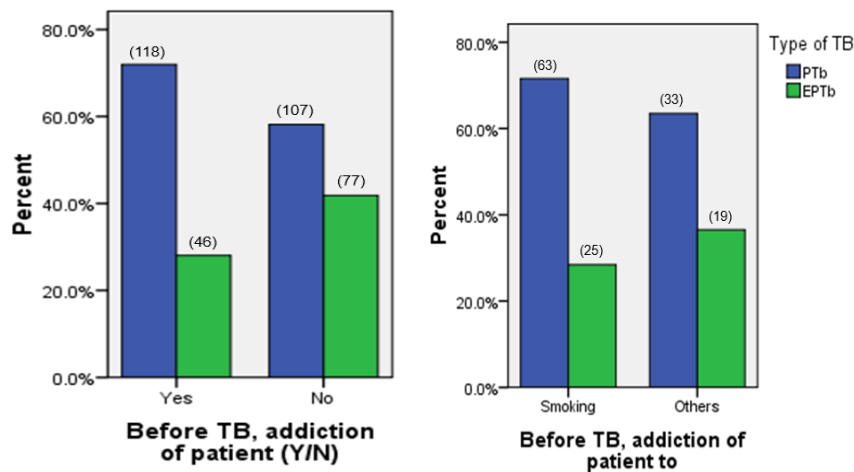


Fig. 13. Role of addiction on prevalence of different types of tuberculosis. The number in bracket “()” shown on the top of each bar is the actual number of patients

The results showed that addiction of patients to smoking had a remarkable role in high prevalence of PTB but not for enhancing the prevalence of EPTB (Fig. 13). Moreover, the results showed that higher number of EPTB patients were addicted to other drugs as compared to smoking indicating the relation of prevalence of EPTB to other drugs rather than smoking (Fig. 13).

As shown in Fig. 14, parentage of EPTB was increased for the patients who were suffering from mental stress before his/her infection of tuberculosis as compared with patient who did not suffer from mental stress. Thus, the results indicate that mental stress is a risk factor of EPTB.

As shown in Fig. 15, before TB infection, the average sleeping hours per day for PTB and

EPTB patients was comparable indicating that the role of sleeping hours on prevalence of EPTB was obscure. But there was prominent difference between PTB and EPTB in case of average exposure of the surveyed patients to direct sunlight before their TB infection (Fig. 15). Before TB infection, the average exposure to sunlight (hours per day) was lower for EPTB than PTB patients indicating that lack of sufficient sunlight exposure to human body is a risk factor for EPTB (Fig. 15).

The results showed that the frequent use of mosquito coil by the people had a remarkable role in enhancement of prevalence of PTB, but no similar effect was observed for EPTB (Fig. 16). Thus, it indicated that the frequent use of mosquito coil might be a risk factor for PTB but not for EPTB.

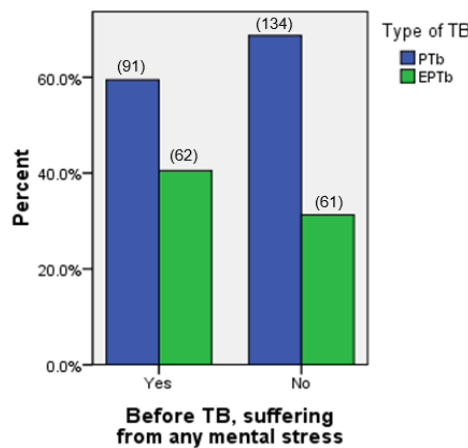


Fig. 14. Role of mental stress on prevalence of tuberculosis. The number in bracket “()” shown on the top of each bar is the actual number of patients

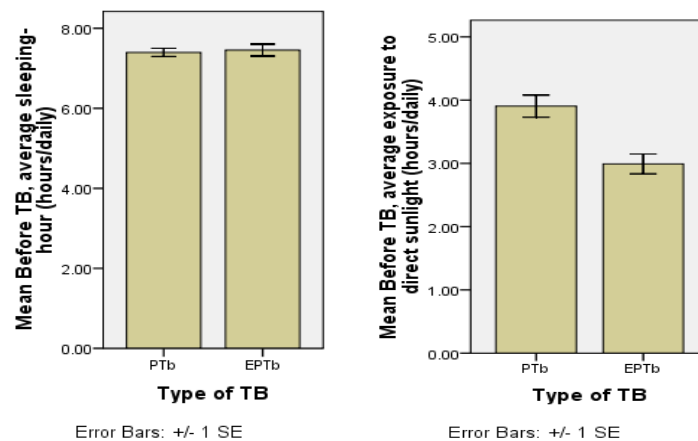


Fig. 15. Role of sleeping hours and direct sunlight exposure hours on prevalence of tuberculosis

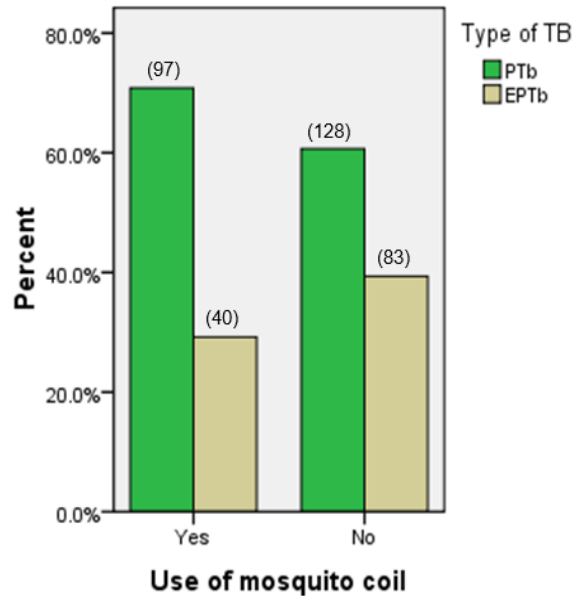


Fig. 16. Role of frequent use of mosquito coil on prevalence of tuberculosis. The number in bracket “()” shown on the top of each bar is the actual number of patients

4. DISCUSSION

In this study it was found that there was variation in prevalence of different types of tuberculosis for male and female patients in Rajshahi city. Female was more susceptible to EPTB than male. It was supported by other studies reporting that females were more prone to EPTB than male (Thakur et al. 2021, Rolo et al. 2023). Another study conducted in Rajshahi city with a view to analyze the socio-demographic and epidemiological factors among registered DR TB cases at two chest disease hospitals of northern part of Bangladesh. Among the study subjects, male was more prevalent to PTB and the age group from 16-45 were mostly vulnerable (Karmaker et al. 2016). In the present study, EPTB was more prevalent in younger people than older people. Similar results were also reported by other studies showing that young patients were more likely to be affected by EPTB than elderly ones (Arega et al. 2020, Rolo et al. 2023). We found that BCG vaccination has no remarkable role on prevention of PTB, but its preventive role was observed against EPTB. It has been reported by others that BCG vaccination protects against EPTB for up to 10 years (Ben et al. 2018). We also found that the prevalence of different types of tuberculosis varied with the blood group of the patients. The highest percentage of PTB patients was observed to carry O-positive blood group followed by B-positive while the highest

percentage of EPTB patients was found to carry B-positive blood group. A study on distribution of ABO and Rh blood groups in patients with tuberculosis in Rohilkhand region of Uttar Pradesh, India showed that the most TB patients were of B-positive group, followed by O-positive (Tiwari et al. 2015). In the present study, the highest percentage of TB patients was student followed by housewife and farmer. However, a study on latent tuberculosis infection in family members in household contact with active tuberculosis patients in Semarang City, Central Java, Indonesia reported that the occupation of laborers/farmers/fishers was the most dominant risk factor associated with latent TB infection (Karbito et al. 2022). We found that prevalence of EPTB was higher in the people with very dark brown skin indicating that very dark brown skin may be a risk factor of EPTB. Likewise, a study on extra-pulmonary manifestations in a large metropolitan area with a low incidence of tuberculosis in USA concluded that African American ethnicity (people with black skin) was an independent risk factor for EPTB (Gonzalez et al. 2003). The present study revealed that the highest percentage of EPTB was recorded in patients who were underweight from childhood. Similar results are reported in other studies indicating that children underweight is risk factors of TB, especially of EPTB (Laghari et al. 2018, Mushtaq et al. 2021, Laghari et al., 2019). We found that the regular medication and antibiotic use for any other disease before active infection

of tuberculosis was a risk factor of EPTB which was supported by another study on outcome of EPTB in India (Anaghashree, 2019). The present study showed that people were more frequently infected with EPTB when family members were EPTB patients. It has been reported by others that high prevalence of EPTB disease was resulted from the close contacts of adults with EPTB (Wingfield et al., 2018). We found that smoking had a remarkable role in the high prevalence of PTB but not for enhancing the prevalence of EPTB. However, few study reported that smoking is a risk factor for both PTB and EPTB (Gambhir et al., 2010).

5. CONCLUSION

This study highlights notable differences in the susceptibility and risk factors for PTB and EPTB. Males were more prone to PTB, while females and younger individuals were more susceptible to EPTB, particularly affecting organs like the brain, lymph nodes, and intestines. Certain demographic and lifestyle factors, such as underweight status in childhood, family history of EPTB, reduced sunlight exposure, and mental stress, were identified as key contributors to EPTB prevalence. In contrast, factors like smoking, sleep patterns, and mosquito coil use were found to have minimal impact. Importantly, BCG vaccination demonstrated a more protective role against EPTB. These findings underscore the need for targeted interventions, including improved vaccination strategies and addressing specific risk factors, to reduce the burden of EPTB in Bangladesh.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of manuscripts.

CONSENT

Written informed consent was taken from each participant

ETHICAL APPROVAL

For our study, we received research authorization from the Department of Zoology, Faculty of Biological Sciences, University of Rajshahi, Bangladesh.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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