

# Gender differences in pulmonary tuberculosis in Abbassia Chest Hospital

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**Background** There is growing evidence that tuberculosis (TB) case notifications in men have in many circumstances surpassed those in women. The increase in reported cases among men was often interpreted as the result of barriers to TB diagnosis faced by women in seeking care.

**Aim** To assess Gender differences in patients with pulmonary TB in Abbassia Chest Hospital.

**Patients and methods** This study was carried out between 1 January 2017 and 30 April 2017. Patients were divided into two groups based on Gender difference: males and females. All patients were subjected to history taking, clinical examination, radiological and laboratory investigations, and sputum examination (direct smear and Gene Xpert and sputum culture for relapse TB, treatment failure, default, and suspected smear-negative patients). Pleural aspiration was done for cytological, biochemical, and adenosine deaminase level. Therapy was initiated, and patients were followed up for 6 months.

**Results** The study has been carried out on 126 cases of TB, comprising 98 males and 28 females. The highest prevalence of TB infection among men with respect to different occupations was seen to be manual workers (62%), and among women to be housewives (71.4%). The new cases were 73.5% for males and 89.3% for females. The default was 14.3% for males and 3.6% for females. The frequency of

relapse was 10.2% in males and 7.1% in females, whereas cases of treatment failure were found only in males. Male patients were much more compatible with anti-TB treatment. Drug complications were more common in women. In terms of treatment outcome, the rate of cure was higher in males and defaulters in females were more common.

**Conclusion** In our study, the male-to-female ratio of identified patients with TB is higher than the previously reported global figures. Female patients were more likely to be younger, housewives, had longer symptoms duration before diagnosis, were less compatible with anti-TB therapy, and had more drug complications.

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## Introduction

Tuberculosis (TB) is the ninth leading cause of death worldwide and the leading cause from a single infectious agent. An estimated 10.4 million people (90% adults; 65% male; 10% people living with HIV) fell ill with TB in 2016 [1]. TB remains a public health problem in Egypt. Although the prevalence and incidence of TB has steadily declined over the past two decades, TB still must be considered as a health problem affecting large sectors of society, particularly the poor and the vulnerable [2].

TB epidemiology is markedly affected by age and sex throughout life, as men and women have different combinations of risk factors for TB and follow a variety of ways of seeking diagnosis and treatment [3]. There is increasing evidence that TB case notifications in men have in many circumstances surpassed those in women [1]. These hypotheses have been questioned by other studies that found undernotification and hence undertreatment of female TB cases by passive case finding when compared with active case finding. In some cultural contexts, women are financially dependent on men and cultural Gender roles result in a lack of autonomy. This has been found to reduce women's

access to health care, interaction with health care services, and adherence to TB treatment [4]. Stigma and discrimination in some settings can mean that women ill with TB are ostracized by their families and communities. Cultural and financial barriers can act as major obstacles for women seeking care resulting in delayed presentation and more severe illness. TB mainly affects women when they are economically and reproductively active, and the effect of the disease is also strongly felt by their children and families [5].

The aim of the work was to assess gender differences in patients with pulmonary TB among patients at Abbassia Chest Hospital.

## Patients and methods

This was a prospective observational study of 126 inpatient cases admitted to the Abbassia Chest Hospital in Cairo, Egypt. Cases with pulmonary TB

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were admitted from 1 January to 30 April 2017. Each case was then followed up as an outpatient by its closest chest hospital for 6 months. Patients have been classified into two groups based on gender difference: group A included males and group B included females.

#### Exclusion criteria

The following were the exclusion criteria:

- (1) Patients younger than 14 years old.
- (2) Extrapulmonary TB, except tuberculous pleural effusion.

Before enrollment in the research, every patient gave written informed consent. Patients were entitled to refuse to participate in the study without affecting their care, treatment, or follow-up. Participants' privacy and safety were ensured. The Scientific Research Ethics Committee revised and approved the consent.

The following data have been collected from the following two groups:

- (1) Detailed history.
- (2) Complete clinical examination: general and local chest examination.
- (3) Radiological examination: posteroanterior, lateral plain chest radiography, and computed chest tomography if necessary.
- (4) Laboratory investigation:
  - (a) Complete blood picture.
  - (b) Erythrocyte sedimentation rate.
  - (c) Fasting and 2-h postprandial blood sugar.
  - (d) Liver and renal functions.
  - (e) HIV test (rapid test).
- (5) Diagnosis of pulmonary TB: Sputum inspection: (a) Direct Ziehl–Neelsen smear examination. Each suspected pulmonary TB case presented three sputum samples (at least two samples) for microscopy in accordance with the TB guidelines, Egypt, 2017 [2]). (b) Gene Xpert and TB sputum culture for relapse, treatment failure, defaults, and smear-negative patients still suspected of being pulmonary TB according to their clinical and radiological data.
- (6) Diagnosis of tuberculous effusion: chest x-ray was done for confirmation of effusion then pleural aspiration was done: fluid is usually a straw-color exudate with protein content more than 30 g/l. White blood cell count is high ( $1000 \times 2500$  per  $\text{mm}^3$ ) with lymphocytic prevalence. Adenosine deaminase is increased by more than 30 IU.

- (7) Treatment was given according to the Tuberculosis Control Guidelines, Egypt, 2017 [2].
- (8) Follow-up: Sputum smear after treatment initiation phase (two months) and after treatment maintenance phase (four months). Sputum culture was done for patients who remained positive.
  - (a) Complications of anti-tuberculous drugs.
  - (b) Compliance of drugs.
  - (c) Outcome of treatment:
    - (1) Cure: smear-negative patient in the last month of treatment and at least on one occasion previously.
    - (2) Treatment failure: a patient who is still or returned smear-positive after 5 months or later during treatment. Also a patient who was initially smear-negative before treatment and turned smear-positive after the initial phase of treatment is completed.
    - (3) Died: a patient who died owing to any reason during the course of treatment.
    - (4) Defaulter (lost to follow-up): treatment interruption for 2 months or more.
    - (5) Still on treatment: A patient who was still receiving anti-tuberculous drugs at end of six months of follow up.

#### Statistical analysis

Data have been collected, revised, coded, and entered in version 23 of the Social Sciences Statistical Package (IBM SPSS, Armonk, New York, USA). The quantitative data were presented as mean, SD, and ranges when their distribution found inter-quartile range (IQR) parametric and median when their distribution was not parametric.

Qualitative variables were shown as numbers and proportions. The qualitative data comparison between two groups was carried out using the  $\chi^2$  test. The exact fishing test was used instead of the  $\chi^2$  test, when the expected number in each cell was less than 5.

The comparison of quantitative and parametric data between two independent groups was carried out using independent  $t$  tests. Mann–Whitney tests were used to compare quantitative data and nonparametric distribution between two independent groups.

The confidence interval was set at 95% and the accepted margin of error was set at 5%. Significant was set as follows:  $P$  value more than 0.05 as

**Table 1 Comparison of the sociodemographic data between females and males**

	Males (N=98)	Females (N=28)	Test value	P value	Significance
Age					
Mean±SD	38.90±13.54	30.50±12.38	-2.947	0.004	HS
Range	19-75	18-66			
Residence [n (%)]					
Egyptian	77 (78.6)	23 (82.1)	0.170	0.680	NS
Immigrant	21 (21.4)	5 (17.9)			
Occupation [n (%)]					
Unemployed	15 (15.3)	0 (0.0)	85.501	0.000	HS
Student	8 (8.2)	1 (3.6)			
Housewife	0 (0.0)	20 (71.4)			
Manual worker	61 (62.2)	4 (14.3)			
Office worker	11 (11.2)	3 (10.7)			
Prisoner	3 (3.1)	0 (0.0)			
Education [n (%)]					
Noneducated	24 (24.5)	9 (32.1)	0.740	0.691	NS
School educated	52 (53.1)	14 (50.0)			
Higher education	22 (22.4)	5 (17.9)			
Marital status [n (%)]					
Single	44 (44.9)	10 (35.7)	1.117	0.572	NS
Married	53 (54.1)	18 (64.3)			
Widow	1 (1.0)	0 (0.0)			
Special habits [n (%)]					
No	14 (14.3)	25 (89.3)	57.348	0.000	HS
Ex-smoker	3 (3.1)	0 (0.0)			
Smoker	52 (53.1)	2 (7.1)			
IV addict	1 (1.0)	0 (0.0)			
Smoker and addict	28 (28.6)	1 (3.6)			

HS, highly significant; IV addict, intravenous addict; NS, nonsignificant; S, Significant.

**Table 2 Descriptive data regarding type of the patient and duration of symptoms**

	Males (N=98) [n (%)]	Females (N=28) [n (%)]	Test value	P value	Significance
Type of patient					
New	72 (73.5)	25 (89.3)	3.593 <sup>a</sup>	0.308	NS
Defaulter	14 (14.3)	1 (3.6)			
Relapse	10 (10.2)	2 (7.1)			
Treatment failure	2 (2.0)	0 (0.0)			
Duration of symptoms (months)					
Median (IQR)	2.00 (1-3)	4.00 (2-5)	-3.513 <sup>b</sup>	0.000	HS
Range	1.00-12.00	1.00-11.00			

HS, highly significant; IQR, interquartile range; NS, nonsignificant. <sup>a</sup> $\chi^2$  test. <sup>b</sup>Mann-Whitney test.

nonsignificant; *P* value less than 0.05 as significant, and *P* value less than 0.01 as highly significant.

## Results

Male patients with pulmonary TB were considerably older than females (38.90±13.54 and 30.50±12.38 years, respectively). Manual work is more common in male cases, whereas most female cases were housewives. Smoking and addiction were much more common in male cases: male smokers (53.1%) and female smokers (7.1%). There was also a considerable combination of smoking and addiction (Table 1).

In female cases (median=4 months), the duration of symptoms before diagnosis of TB was significantly longer than in male cases (median=2 months). Most cases in both men (73.5%) and women (89.3%) were new cases (Table 2).

Cough is the most common symptom without a predilection of gender, followed by weight loss and dyspnea (Table 3). Hepatitis C virus and HIV were more prevalent in males (8.2 and 4.1%, respectively) taking in consideration that some cases had combined chronic diseases (Table 4).

Except for pleural effusion, which was significantly more common in female cases (15.3% in males vs. 32.1% in females), radiological findings did not differ between males and females. There have been no significant differences in laboratory studies, sputum work, or treatment between men and women (Table 5).

Male cases were much more compliant to treatment (93.9% of males vs. 71.4% of females). Drug complications were much more common in female cases (95.9% of males did not have complications whereas 75% of females did not). Cutaneous and gastric complications of anti-tuberculous treatment in females were significantly higher (cutaneous complications occurred in 2.0% of males vs. 10.7% of females). Defaulter (lost to follow-up) cases were significantly more common in females (4.1% in males vs. 28.6% in females), whereas the cure rate was higher in males (70.4% in males vs. 60.7% in females) (Table 6).

## Discussion

TB is a major global health problem with more than nine million new TB cases worldwide each year, and approximately two million people die of TB each year.

**Table 3 Presenting symptoms in males and females with pulmonary tuberculosis**

Presenting symptoms	Males [n (%)]	Females [n (%)]	Test value <sup>a</sup>	P value	Significance
Chest pain	2 (2.0)	0 (0.0)	0.581	0.446	NS
Cough	88 (89.8)	27 (96.4)	1.202	0.273	NS
Weight loss	49 (50.0)	12 (42.9)	0.445	0.505	NS
Dyspnea	25 (25.5)	12 (42.9)	3.159	0.075	NS
Fever	15 (15.3)	2 (7.1)	1.243	0.265	NS
Hemoptysis	16 (16.3)	2 (7.1)	1.500	0.221	NS
Loss of appetite	13 (13.3)	2 (7.1)	0.778	0.378	NS

NS, nonsignificant. <sup>a</sup> $\chi^2$  test.

**Table 4 Comparison between concomitant disease between females and males**

	Males (N=98) [n (%)]	Females (N=28) [n (%)]	Test value <sup>a</sup>	P value	Significance
Chronic diseases and concomitant conditions					
No	71 (72.4)	20 (71.4)	10.471	0.033	S
DM	16 (16.3)	6 (21.4)			
HCV	8 (8.2)	0 (0.0)			
CLD	3 (3.1)	0 (0.0)			
Pregnancy	0 (0.0)	2 (7.1)			
HIV					
Positive	4 (4.1)	0 (0.0)	1.180	0.277	NS

CLD, chronic liver diseases; DM, diabetes mellitus; HCV, hepatitis C virus; NS, nonsignificant; S, significant. <sup>a</sup> $\chi^2$  test.

Approximately 33% of the world's population has latent *Mycobacterium tuberculosis* infection, mostly in developing countries [1].

In Egypt, the incidence rate in 2014 was 15/100 000. In addition, this situation is exacerbated by the HIV pandemic, with 13 million people currently co-infected with TB and HIV worldwide. Control of the spread of TB is becoming very difficult owing to the increasing number of multidrug resistant, widely drug-resistant, and extremely resistant strains of TB [6].

Nowadays, increasing evidence has shown that TB case reports among men exceed those among women in most settings. In 2014, the male : female ratio of smear-positive TB cases was 1.7 worldwide and ranged from 1.0 in the Eastern Mediterranean to 2.1 in the Western Pacific region [1]. There is, however, a scarcity in the published literature to determine whether there are gender differences in case reports and whether there are sexual differences in the characteristics of patients with TB. The current study was therefore conducted to evaluate the differences between genders in patients with pulmonary TB at the Abbassia Chest Hospital.

The present study included 126 patients with TB disease, most of whom were male (77.8%). This male-to-female ratio of 2.3 : 1 was higher than the WHO's recent global reports [1]. However, in line with our findings, from January 2015 to May 2016, Mashaly *et al.* [6] conducted a cross-sectional study on 300 patients in the outpatient clinic of Mansoura Chest Hospital for suspected TB, and more than two-thirds of the patients diagnosed with TB were male patients.

There are still unknown reasons for this excess of reported male cases; many postulate that female patients with TB are subjected to greater stigma and barriers to access to health care. It is often suggested that male bias in TB is an artifact of systematic underreporting and underdiagnosis of TB in women [7].

**Table 5 Comparison of the workup and treatment regimen between females and males**

	Males [n (%)]	Females [n (%)]	Test value <sup>a</sup>	P value	Significance
<b>Radiology</b>					
Normal	2 (2.0)	3 (10.7)	4.299	0.038	S
Unilateral pulmonary infiltrates	31 (31.6)	11 (39.3)	0.574	0.449	NS
Bilateral pulmonary infiltrates	57 (58.2)	12 (42.9)	2.059	0.151	NS
Pleural effusion	15 (15.3)	9 (32.1)	4.004	0.045	S
<b>Sputum smear</b>					
Positive	89 (90.8)	25 (89.3)	0.059	0.808	NS
<b>Sputum culture</b>					
Not done	55 (56.1)	14 (50.0)	0.330	0.566	NS
Positive	43 (43.9)	14 (50.0)			
<b>Gene expert</b>					
Not done	64 (65.3)	22 (78.6)	1.769	0.184	NS
Positive and RF sensitive	34 (34.7)	6 (21.4)			
<b>CBC</b>					
Normal	43 (43.9)	13 (46.4)	1.424	0.699	NS
Anemia	51 (52.0)	15 (53.6)			
Leukocytosis	1 (1.0)	1 (3.6)			
Polycythemia	2 (2.0)	0 (0.0)			
<b>Treatment</b>					
Hepatotoxic regimen	4 (4.1)	0 (0.0)	5.041	0.080	NS
Cat 1	67 (68.4)	25 (89.3)			
Cat 2	27 (27.6)	3 (10.7)			

Cat 1, category 1; Cat 2, category 2; CBC, complete blood count; NS, nonsignificant; S, Significant. <sup>a</sup> $\chi^2$  test.

**Table 6 Comparison of the follow-up period between females and males**

	Males [n (%)]	Females [n (%)]	Test value <sup>a</sup>	P value	Significance
<b>Compliance to anti-tuberculous drugs</b>					
Noncompliant	6 (6.1)	8 (28.6)	11.112	0.001	HS
Compliant	92 (93.9)	20 (71.4)			
<b>Complications of drugs</b>					
No	94 (95.9)	21 (75.0)	15.405	0.004	HS
Cutaneous complications	2 (2.0)	3 (10.7)			
Gastric	1 (1.0)	3 (10.7)			
Hepatitis	0 (0.0)	1 (3.6)			
Neuropathy	1 (1.0)	0 (0.0)			
<b>Outcome</b>					
Defaulter	4 (4.1)	8 (28.6)	16.463	0.001	HS
Still on treatment	21 (21.4)	2 (7.1)			
Cure	69 (70.4)	17 (60.7)			
Died	4 (4.1)	1 (3.6)			

HS, highly significant. <sup>a</sup> $\chi^2$  test.

Contrary to this notion, however, a meta-analysis of 29 surveys carried out in 14 countries worldwide found a consistent overt male bias in both notification rates and prevalence rates, strongly suggesting that access to health care is not a confusing factor. Moreover, male prejudice was present in countries where there were no obvious differences in health behavior between the two sexes; unfortunately, Egypt was not included in the EMRO countries [8].

We can attribute the difference between males and females to the variation between cultures and social habits between the countries of the east and the west.

Many reports now show that gender differences observed in case notifications are often reflected by gender differences in prevalent TB cases. These studies show that unfair access to health care facilities and reporting biases are not the main reason for observed differences in case reports and that genuine gender differences exist in TB biology and epidemiology [9].

There is an obvious diversity in mortality, morbidity, and disease varieties of TB between different age groups. The mean age of the patients included in the current study was 37±14 years. Likewise, Zhang *et al.* [10] conducted a case-control study, including

5684 patients with TB bacteriologically confirmed (diagnosed in Denmark and Greenland between 1992 and 2007), and the results showed that most patients with primary TB were between 25 and 44 years of age.

In addition, Sobh *et al.* [11] conducted a cross-sectional study using TB registry medical records at the Aswan Chest Hospital to examine the pattern of TB. The authors reported that more than 60% of the patients were older than 30 years.

Female patients were more likely to be younger than male patients in our correlation analysis ( $P=0.004$ ). Similar to our findings, Feng *et al.* [12] conducted a prospective observational study on 1059 patients with newly diagnosed, culture-positive TB from six Taiwanese hospitals to assess the effect of sex in reporting rates, clinical forms, and outcomes of treatment. The results showed that female patients were significantly younger than male patients and reported a similar ratio between male and female.

Codlin *et al.* [13] also carried out a retrospective review to study sex differences in Pakistan's TB notification. The authors reported a much lower proportion of women in older age groups.

It has been reported previously that some places of work may reflect a higher risk of TB owing to local environmental conditions and that some occupations pose a high risk for the development of TB, including manual workers and miners [14]. In the present study, 61% of male patients were manual workers and 71.4% of female patients were housewives.

In a number of cohort studies, smoking was well documented as a strong risk factor for TB. The higher rate of smoking in men can contribute to the higher proportion of men in TB epidemiology [15–17]. This was similar to the results of the current study in which the majority of male patients were either smokers (52%) or addicts (1%) or both (28%), whereas 89% of female patients had no medically important special habits. Male patients with TB were more likely to get used to smoking. In line with our findings, Feng *et al.* [12] found that male patients with TB had a much higher proportion of smokers than female patients.

There was no significant difference in the frequency of observed symptoms between males and females in clinical presentations, but notably the most common symptom was cough in both. Dale *et al.* [18] conducted

a retrospective cohort study to investigate sex differences between patients with TB in Victoria, Australia. In accordance with our findings, the authors reported no significant differences between males and females in the occurrence of TB symptoms.

In the current study, 77% of patients were new cases; with no significant gender differences but slightly more in female patients (72%) in males and (89%) in females. Eissa *et al.* [19] also conducted a retrospective clinical cohort study in the governorate of Cairo. All TB cases data from the Cairo Governorate's TB registration units (2006–2012) showed that the most common type of patients was new cases (80.3%). Other studies have shown that new cases are the most common type of patient [20,21].

Although there was no statistical difference in the frequency of TB symptoms in this study, women had significantly longer symptom duration than men (about double the median duration). This difference can be attributed to the lower awareness and knowledge of TB between women in our society.

Kamel *et al.* [22] conducted a cross-sectional study to evaluate sex differences in the health care utilization and outcome of pulmonary TB among 334 patients in Alexandria through a structured interview questionnaire to gather the following data: demographic and socioeconomic background; patient satisfaction with the quality of care provided; and patient knowledge, attitudes, and beliefs. Women had considerably lower levels of TB knowledge, beliefs, and attitudes than men [22].

In addition, Hamid Salim *et al.* [23] conducted a prevalence survey to evaluate whether the observed sex difference is epidemiologically true or owing to barriers to accessibility for women with TB. The results showed a much lower awareness of the symptoms among women with TB.

Thorson *et al.* [24] also evaluated the awareness of men and women with smear-positive pulmonary TB using a structural interview. The authors reported a lack of awareness of TB among women. The lack of proper knowledge of constitutional and respiratory symptoms can cause medical assistance to be delayed. Less advanced radiographic findings can also lead to missed pulmonary TB for doctors [24].

Various medical conditions are considered to be risk factors for TB and for poor results in TB treatment. In addition, patients with TB and other communicable

diseases are more likely to develop comorbidity with noncommunicable diseases [25]. For example, the effect of diabetes on the development and severity of TB has recently been established as a result of obesity, changing dietary patterns and physical activity and aging populations [26].

Almost 18% of patients had diabetes in the current study. A cross-sectional study has been carried out in India to evaluate the prevalence of diabetes in patients with TB currently undergoing treatment, similar to our findings. The prevalence of diabetes in patients with TB was found to be 20.7%, with a significantly higher incidence in male patients [27].

In the present study, male patients with TB were more likely than female patients to have a history of chronic diseases such as diabetes and chronic liver disease. Four patients were diagnosed as HIV and all of them were males. These significant differences in the prevalence of comorbidities and immunosuppressive conditions may be one of the factors that contribute to higher TB incidences among males than females.

Contrary to our findings, Feng *et al.* [12] reported no significant difference in diabetes between males and females. The exact reasons for these differences between our findings and the aforementioned study are unclear. However, many methodological differences, such as sample size, study design, and population characteristics can be attributed.

In terms of compliance with treatment, more than 80% of patients reported correct compliance with anti-TB regimens in the current study. In particular, males adhered much more to the scheduled regimes than female patients.

The results of Balasubramanian *et al.* [28] who examined gender differences in TB among adults regarding infection and disease prevalence and compliance with directly observed treatment were not consistent with the previous findings. Their results showed that the treatment was more likely for female patients than for males. Feng *et al.* [12], however, reported no considerable difference in compliance with treatment between men and women. This can once again be attributed to methodological differences. In terms of treatment results, at the end of the follow-up, 68% of patients were cured. Furthermore, female patients were significantly less likely to achieve cure than male patients (60.7 vs. 70.4%), whereas the mortality rate for males was higher.

The current literature, however, showed inconsistent information on the effect of sex on treatment results. Male patients showed a smear conversion rate of 2 months shorter and a culture conversion rate of 2 months shorter. In addition, men were accompanied by a higher 6-month mortality rate and a higher overall mortality on treatment [12].

Faustini *et al.* [29] also reported increased mortality, increased treatment failure, and more treatment default among male patients with TB in Italy. In addition, Balasubramanian *et al.* [28] reported that male sex was considered a risk factor for treatment failure and that males are twice at risk as females. Moreover, Dale *et al.* [18] reported a statistically significant higher mortality rates among male patients with TB than female patients.

In contrast, Begum *et al.* [30] assessed sex differences in the outcome of TB diagnosis and treatment in Bangladesh, with 5632 patients registered in outpatient clinics. There was no statistically significant difference in treatment success (86% female and 84% male patients). Likewise, Hamid Salim *et al.* [23] reported no significant sexual differences in the outcome of treatment: the overall cure rate was 60.5%, and the treatment failure rate was 4.8%.

In the current study, default (lost to follow-up) cases were much more common in women, which is a logical consequence of significantly lower compliance with treatment in women. These differences in treatment results between our results and the other studies point to an obvious problem faced by patients with TB in our community, which requires greater attention and further evaluation.

## Conclusion

The male-to-female ratio of identified patients with TB in this study is higher than the global figures previously reported. Although this ratio can be explained in part by the barriers women face in seeking health care for and diagnosis of TB, the results of the present study show that many biological and demographic characteristics can lead to this high ratio. Occupation can be seen as one of the factors that contributed to the gender difference between the Egyptian population in TB presentation.

Male patients with TB were more likely to be older, manual workers, smokers, and addicts, had diabetes, and had more severe radiological findings, whereas female patients with tuberculosis were more likely to

be younger, housewives, had longer symptoms duration before diagnosis, were incompatible with anti-TB treatment, had more complications with drugs, and had a higher rate of default (lost to follow up). However, further large-scale research is still required to confirm our findings and to evaluate the weight of various factors on the effect of the gender.

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#### Conflicts of interest

There are no conflicts of interest.

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