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Factors Associated with Relapsed Tuberculosis in Males and Females: A Comparative Study

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ABSTRACT

Background: *Tuberculosis (TB) is the leading cause of death from an infectious disease in women worldwide especially in developing countries. There is limited number of literature available on factors associated with the relapse of TB and very few studies on gender differences in this regard. This study aimed to compare the factors associated with the relapse of TB in males and females.*

Materials and Methods: *A cross-sectional study was conducted in the medical department of Civil Hospital in Hyderabad from August 2008 to November 2008. A total of 100 consecutive patients of any age or gender, diagnosed with relapse of TB who had positive sputum smear after completion of a standard course of anti-tuberculosis therapy (ATT) were included in this study. Those with newly diagnosed tuberculosis and cases of treatment failure or treatment defaulters were excluded from the study. Demographic variables, factors associated with the previous TB infection and underlying medical conditions were among the variables compared in both sexes.*

Results: *The mean age of patients was 36.84±17.40 years in males and 36.21±16.41 years in females. There were 38 females and 62 males. Among the factors associated with the relapse of TB, there were statistically significant differences between males and females in regard to addiction (p=0.01), employment (p<0.001), weight gain (p=0.01) and mean hemoglobin value (p=0.05).*

Conclusion: *Further studies with larger sample sizes are required for evaluation and comparison of factors associated with the reactivation of TB in males and females. This would provide solutions for TB control agencies in the future.* ***(Tanaffos 2009; 8(3): 22-27)***

Key words: *Tuberculosis, Relapse, Gender Identity*

INTRODUCTION

Tuberculosis (TB) is the most common infectious disease that represents a major public health threat to the global population. Up to 8 million new cases and 2-3 million deaths are attributed to this infection annually. It is twice as much common in men than in women in developing countries (1). TB is the leading cause of death from an infectious disease in women worldwide (2). The World Health Organization has therefore encouraged gender-specific comparisons in

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TB incidence to determine whether women with TB are less likely to be diagnosed, reported, or treated compared to men.

Several studies have been conducted internationally and also in Pakistan addressing factors associated with resistant and multi-drug resistant tuberculosis and TB control (3,4). However, only a few studies have shown gender-based differences in patients with pulmonary TB (5,6). A study conducted in Mexico showed the male to female ratio in incidence rate for overall, reactivated, and recently transmitted disease to be 1.58 (95% CI 1.34 to 1.86), 1.64 (95% CI 1.36 to 1.98), and 1.41 (95% CI 1.01 to 1.96), respectively (7).

The literature is scarce on gender differences in relapsed TB patients. Also little information is available on high prevalence of relapsed, disseminated and Multi Drug Resistant (MDR) TB cases in developing countries like Pakistan, India, Bangladesh and etc. This study aimed to explore and compare the factors associated with the relapse of TB in males and females. This study would provide a basis for future researches in this regard.

MATERIALS AND METHODS

A cross-sectional study was conducted in the medical department of Civil Hospital in Hyderabad from August 2008 to November 2008 after taking an informed consent from the participants. Since it was not an experimental study, further anonymous data collection did not warrant any formal ethical approval. A case of relapsed TB was defined on the basis of clinical and radiologic manifestations confirmed on positive smear after completion of standard course of Anti TB therapy (ATT) and was labelled cured previously. A total of 100 patients were selected consecutively of any age and either gender who presented to the tertiary care outpatient department (OPD). Patients with newly diagnosed tuberculosis and cases of treatment failure or treatment defaulters were excluded from the study.

The selected patients were interviewed by two medical doctors using a structured questionnaire. The interviewer bias was controlled by proper training of the interviewers and use of a structured questionnaire. The recall bias was controlled by multiple questions and validating the answers mentioned in that questionnaire.

Gender differences in factors associated with relapsed TB were evaluated in this study including the demographic variables, factors associated with the previous TB infection and associated medical illnesses. Demographic variables included age, gender, overcrowded families, level of education, occupation, monthly income, nutritional status, addiction, history of close contact with a TB patient, severity of disease and previous treatment. Factors associated with the previous TB infection included extent of radiological and residual lesions, presence of initial cavitation and weight gain. Associated medical conditions included presence or absence of other diseases/conditions i.e. anemia, diabetes, asthma or etc.

Age distribution was noted in years. All subjects were residing in an area adjacent to the District Hospital. There was no common definition of overcrowding in the literature; however, for the purpose of this study, it was defined as two or more people of opposite sex sleeping in the same room (except they are married or under ten years old). Educational status was divided into literate and illiterate, based on the person's ability to read a newspaper.

The occupational status was divided into employed and unemployed (housewife, student, etc). For analysis of the socioeconomic status, subjects were divided into three groups according to their total monthly income i.e. < 5000 Rupees /month (low income), 5000-10000 Rupees /month, (middle income) and > 10000 Rupees /month (high income).

Family income included salaried employment (full-time or part-time job), self-employment, investments, real estate income and etc. Habits and addictions like smoking, and alcohol consumption were specifically sought. Subjects were also asked about the consumption of meat, eggs, and milk. History of close contact was defined as a person living or coming into contact with an individual with infectious TB. Body mass index (BMI, defined as the weight in kilograms divided by the square of the height in meters) of each subject was recorded as the measure of nutritional status. Patients were grouped into underweight (<19), normal (19-24) and overweight (≥25) based on their BMI.

Previous chest x-rays were reviewed to measure the extent of the radiological lesions (one or more than one lobe involvement), presence of initial cavitation, and extent of the residual lesion. In regard to the previous course of treatment, delay in negative conversion of sputum cultures (measured within two months after the initiation of anti-tuberculous drug therapy), weight gain (patients were asked whether there was a change in their weight compared to their previous weight record if available or feeling the looseness of clothes), time of relapse (calculated in month from the end of the course of previous ATT till the re-diagnosis of active disease) were all noted.

Anemia was noted and defined as a reduction in hemoglobin concentration below the normal range for age, sex, physiological condition and altitude from the sea level of a person. This study has taken the cutoff value of Hb 12 gm/dL (gram/deciliter) for women and 13 gm/dL for men. Diagnosis of asthma and COPD was based on clinical criteria. Fasting and random blood sugars were noted in unknown diabetics for screening purposes. Other illnesses associated with relapse like anemia, asthma, COPD and etc were evaluated by blood tests, x-rays etc.

Statistical analysis

All data were entered and analyzed using SPSS version 12 software. Mean ± standard deviation was calculated for quantitative variables like age, BMI, time of relapse and concentration of hemoglobin. Frequency and percentage were calculated for qualitative variables like gender, place of residence, smoking, nutritional status, factors associated with the previous infection and associated illnesses. As this study was pertained to a single group of patients, and application of statistical tests was not possible, subjects were divided into two groups based on gender and these groups were compared in terms of presence or absence of a risk factor for statistically significant associations. Chi-square and student's t-test were used to compare quantitative and qualitative variables. P value < 0.05 was considered significant.

RESULTS

The mean age of patients was 36.84±17.40 years among males and 36.21±16.41 years among females. There were 38 females and 62 males. The mean hemoglobin value was 11.49±1.47mg/dl in males and10.64±1.35mg/dl in females. The majority (36%) of patients were in the age range of 21 to 30 years. All (100%) patients were residents of inner city area with overcrowded families. About 62% of patients were literate; 62% were employed, 72% had monthly income <5000 rupees per month and 44% were addicts. Sixty percent had adequate nutrient consumption, 64% had history of close contact with a TB patient.

About 70% of patients were anemic, 10% had diabetes mellitus, 45% were asthmatics and 8% had COPD. Eighty four percent had one lobe involvement, 14% had initial cavitation, 18% had an extensive residual lesion, 4% had delay in conversion of sputum cultures for AFB and 52% gained weight.

In this study, statistically significant differences (p value < 0.05) were noted between men and women

in terms of occupation, addiction, no weight gain and etc. (Table 1). Similar comparisons regarding associated medical illnesses were noted (Table 2). This study also showed factors associated with the previous TB infection i.e. the extent of radiological lesion and presence of initial cavitation (Table 3).

Addiction (p=0.01), employment (p<0.001), weight gain (p=0.01) and mean hemoglobin value (p=0.05) were among the factors associated with the relapse of TB which showed statistically significant difference between males and females. Differences in other demographic variables, factors associated with the previous TB infection and associated medical illnesses are shown in Tables 1-3.

Table 1. Demographic characteristics of the sample.

Demographic characteristics		Male	Female	P-value
Age		36.84±17.40	36.21±16.41	0.9
Crowding	Yes	62 (100.0%)	38 (100.0%)	-
	No	--	--	
Educational status	Literate	26 (41.9%)	12 (31.6%)	0.66
	Illiterate	36 (58.1%)	26 (68.4%)	
Occupation	Employment	56 (90.3%)	6 (15.8%)	P<0.001
	Unemployment	6 (9.7%)	32 (84.2%)	
Monthly income (Rs)	<5000	44 (71.0%)	28 (73.7%)	0.90
	5000-10000	16 (25.8%)	10 (26.3%)	1
	>10000	2 (3.2%)	-	1
Addiction status	Addict	36 (58.1%)	8 (21.1%)	0.01
	Non-addict	26 (41.9%)	30 (78.9%)	
Consumption of nutrients	Adequate	36 (58.1%)	24 (63.2%)	0.95
	Inadequate	26 (41.9%)	14 (36.8%)	
History of close contact	Yes	38 (61.3%)	26 (68.4%)	0.83
	No	24 (38.7%)	12 (31.6%)	
BMI (kg/m²)	<19	16 (25.8%)	10 (26.3%)	1
	19-24	40 (64.5%)	22 (57.9%)	0.64
	≥25	6 (9.7%)	6 (15.8%)	0.66
Mean BMI		21.94±2.86	21.87±2.97	0.9

Table 2. Associated Medical Illnesses of the sample.

		Male	Female	P-value
Mean Hb (g/dL)		11.49±1.47	10.64±1.35	0.05
Anemia	Yes	38 (61.3%)	18 (47.4%)	0.50
	No	24 (38.7%)	20 (52.6%)	
Diabetes Mellitus	Yes	2 (3.2%)	8 (21.1%)	0.06
	No	60 (96.8%)	30 (78.9%)	
Asthma	Yes	8 (6.5%)	0 (0%)	-
	No	58 (93.5%)	38 (100%)	
COPD	Yes	8 (12.9%)	0 (0%)	-
	No	54 (87.1%)	38 (100%)	

Table 3. Factors associated with the previous TB infection.

Factors associated with the previous TB infection		Male	Female	P-value
Extent of radiological lesion (> One lobe involvement)	Yes	14 (22.6%)	2 (5.3%)	0.13
	No	48 (77.4%)	36 (94.7%)	
Presence of initial cavitation(s)	Yes	6 (9.7%)	6 (15.8%)	0.66
	No	56 (90.3%)	32 (84.2%)	
Extent of residual lesion	Yes	14 (22.6%)	2 (5.3%)	0.13
	No	48 (77.4%)	36 (94.7%)	
Delay in conversion of sputum culture	Yes	2 (3.2%)	2 (5.3%)	1
	No	60 (96.8%)	36 (94.7%)	
No weight gain	Yes	20 (32.3%)	26 (68.4%)	0.01
	No	42 (67.7%)	12 (31.6%)	
Time of relapse	--	11.94±6.15	11.42±7.24	0.79

DISCUSSION

The results showed that involvement of more than one lobe and extensive residual lesion were more common in males whereas factors like presence of initial cavitation, delay in conversion of sputum culture, diabetes mellitus and weight gain were more common in females. Addiction, employment, weight gain and mean Hb value were significantly different between males and females.

A study by Gustafson et al. has shown that living in overcrowded families is a risk factor for relapse of

tuberculosis and addition of each adult to the household increases the risk of tuberculosis by 5% (8). In our study, all 100 patients were living in overcrowded families. Studies have also shown that addiction is an important cause of relapse (9,10). Our study also found that 58.1% of males and 21.1% of females were addicts.

Risk of TB infection among household contacts is associated with the intensity of exposure and extent of activities that they share (11). In our study, 64% of patients had positive history of contact with a TB patient who was either a family member or a close friend.

Caminero et al. in their study noted that recurrence of tuberculosis occurs in less than a year (12). But van Rie et al. in their study noted that the median interval between the cure and the subsequent diagnosis of tuberculosis was 25.5 months (13). In our study, rate of relapse during the first year after cure was 62 % which is comparable with other studies. The majority of these patients were illiterate, poor, anemic and underweight and were living in crowded families, similar to our study cases.

Jimenez-Corona et al. reported similar results in their study on 623 pulmonary TB patients. Recurrence was more common in males who had some formal education and had higher socioeconomic level compared to women. Men were also more likely to have been living in a shelter, been imprisoned, or using alcohol or drugs (7). Our study also noted that relapse of TB was more common in more educated, socioeconomically stable men who had adequate food consumption.

Khan A et al. also claimed that a weight gain of 5% or less was significantly associated with more than twice risk of relapse (14).

In a study conducted in Mexico on 623 patients with pulmonary TB including those with reactivated TB it was reported that the male to female ratio in incidence of overall, reactivated, and recently transmitted disease was 1.58 (95% CI 1.34 to 1.86), 1.64 (95% CI 1.36 to 1.98), and 1.41 (95% CI 1.01 to 1.96), respectively (7). Similarly, our study also showed that relapse of TB was more common in males.

Another study showed that smoking (OR 2.53, 95% CI 1.23-5.21) and living in an area where the family health program was not implemented (OR 3.61, 95% CI 1.46-8.93) were the factors independently associated with the relapse of tuberculosis. These results were similar to ours as well (15).

The main limitation of this study was the small sample size. In order to evaluate and compare the selected factors between males and females we must have a larger sample size and this might be the reason for most of our insignificant results. However, it was a unique study of its kind and the purpose was only to highlight the possible differences between males and females in terms of factors associated with the relapse of TB. The other limitation was the lack of data and previous studies on this topic.

CONCLUSION

In our study, greater than one lobe involvement, and extensive residual lesion were insignificantly more common in males; whereas, factors like presence of initial cavitation and delay in conversion of sputum culture were insignificantly more common in females. Only the weight gain was significantly more common in females. Among factors associated with the relapse of TB, addiction, employment, weight gain and mean Hb value were significantly different between males and females. We recommend further studies with larger sample sizes to be conducted for further evaluation and reaching a firm conclusion. Such studies would definitely provide key solutions for TB control agencies in the future.

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