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## ORIGINAL ARTICLE

## Pulmonary Tuberculosis And Some Underlying Conditions In Golestan Province Of Iran, During 2001-2005

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### ABSTRACT

**Context:** Pulmonary tuberculosis has been a major health problem in Golestan province of Iran.

**Aims:** This descriptive cross-sectional study was performed to evaluate the frequency of coexisting medical conditions and their effects on some epidemiologic factors in patients with pulmonary tuberculosis.

**Setting and Design:** This was a descriptive cross-sectional study.

**Methods and Material:** Demographic information, time of admission in the hospital and coexisting medical conditions (diabetes, chronic renal failure/hemodialysis, corticosteroids consumption and malignancies) were extracted from the patient's file.

**Statistical analysis used:** Chi-square test was used to assess the relationship between variables.

**Results:** Two hundred forty three patients with pulmonary tuberculosis during 5 years were studied. Out of all, 162 cases (66.7%) did not have any co-morbidities. Diabetes mellitus was found to be the most prevalent condition (23.05%) followed by chronic renal failure, corticosteroid consumption and malignancy ranking second, third and fourth in the list (5.8%, 2.5% and 2 respectively). The mean age of the patients was 50.15±19 years old. In the group without co morbidities, male/female ratio was 1.41/1, but co morbidity with diabetes was significantly more prevalent in females ( $p < 0.05$ ).

**Conclusions:** We suggest screening of tuberculosis in patients with chronic renal failure and diabetes mellitus in our area. Also for patients with pulmonary tuberculosis, diabetes screening should be considered essential.

**Key Words:** Pulmonary tuberculosis, Diabetes mellitus, Chronic renal failure, Corticosteroid consumption, Malignancy.

**Key Message:** Pulmonary tuberculosis should be considered in the management of chronic diseases in our area.

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### Introduction

Tuberculosis is one of the most important contagious diseases in the world and approximately 2 million people (1/3 of world population) are infected with mycobacterium tuberculosis [1]. The annual mortality rate of

tuberculosis across the globe is 3 million [2]. Frequent occurrence of co-existing morbidities in patients with tuberculosis is one of the important problems, as the odds ratio for the incidence of active tuberculosis followed by chronic renal failure (Hemodialysis), diabetes and immunosuppressive treatment, is estimated to be around 10-25, 2-4, 10 respectively. An anonymous study in 2003 showed that rate of TB specially in immunodeficient patients and high risk groups such as diabetes mellitus was higher than normal population [3], [4],[5],[6],[7], and also chronic renal failure in the other finding was increased to 6-52.5 more than normal population [8].

Several studies indicated towards a higher prevalence of TB in chronic corticosteroid

consumption and malignancy patients [9],[10],[11],[12].

In Iran, the incidence of reported pulmonary tuberculosis with positive smear of sputum was 7.8 in one hundred thousand people in 2003(WHO had estimated 13 persons in one hundred populations) [13]. Golestan is the second province for the incidence of tuberculosis in Iran [13]. Keeping in mind the high prevalence of tuberculosis in our country and especially in Golestan province, we performed a study to evaluate the frequency distribution of general co morbidities including diabetes, chronic renal failure, corticosteroid consumption and malignancy in patients with pulmonary TB, so that we could be aware of high risk patients, and provide a proper base for future cohort studies based on evaluating the incidence of pulmonary tuberculosis in these groups.

### Materials and Methods

In this descriptive, cross sectional study, 500 files of TB patients were studied. We evaluated the frequency distribution of diabetes, chronic renal failure, corticosteroid consumption, malignancies, age and sex of documented pulmonary TB cases (based on definition of international tuberculosis association) during 2001-2005 in 5th Azar hospital of Gorgan, Iran. Pulmonary TB was defined on the basis of WHO prescription; positive smear pulmonary TB included patients with 2 positive sputum smears or 1 positive sputum smear in addition with radiological changes or positive sputum culture for AFB. Negative smear pulmonary TB cases included patients who did not fulfill the above mentioned criteria but were included due to specialist diagnosis and pulmonary radiographs and also those patients who didn't have proper response to spectrum antibiotics but had proper response to antituberculosis medication, diagnosis of TB was established for them. Patients who had died without exact diagnosis or referred to other centers were excluded. Finally 243 patients were recruited. Demographic information including sex, age, co-existing morbidities (diabetes, chronic renal failure/hemodialysis, corticosteroid consumption and malignancies) and type of tuberculosis and death rate were extracted from patient's file. Patients were categorized in 6 age groups, including 13-20, 21-30, 31-40, 41-50, 51-60 and >60. Fasting blood sugar of higher than 126 mg/dl was considered as diabetes and chronic renal failure/hemodialysis considered for all hemodialized patients and also for patients who

were suffering from renal failure during the 3 last month and more. Corticosteroid consumption was defined for the patients who took steroids with a dosage of more than 40 mg/day for any period of time; and malignancies were confirmed using histopathology results. All data were entered in the computer and analyzed with spss-11.5 software; then one and two dimensional tables of frequency distribution were created and explained.

Considering age and sex of patients, the patients were divided into two groups (one group with patients who had co-morbidities and the other who didn't have any co-existing morbidities) and then they were compared with each other. Chi square and Fisher exact tests were used to explain the results.

### Results

243 pulmonary TB patients were studied during 5 years (2001-2005). Their mean ( $\pm$ SD) age was 50.15 ( $\pm$ 19) years old [Table/Fig 1]. Patients included 130 men (53.5%) and 113 women (46.5%). In our study 162 patients didn't have any co-existing morbidities and 81 patients (33.3%) had at least one co-existing morbidity [Table/Fig 2]. Diabetes was the most common co-existing morbidity in the study (23.05%), followed by chronic renal failure, corticosteroid consumption and malignancy (5.8%, 2.5% and 2%, respectively). In patients with tuberculosis and malignancy, cervix cancer (one case), non-Hodgkin's lymphoma (one case), bronchogenic carcinoma (one case), hepatocellular carcinoma (one case) and brain carcinoma glioblastoma (one case), were reported. Six patients consumed corticosteroids, including two cases of asthma, one case of rheumatoid arthritis, two cases of systemic lupus erythematosus (SLE) and one undiagnosed case. [Table/Fig 1] shows the frequency distribution of TB patients based on co-morbidities.[Table/Fig 3] shows the patients who didn't have any co-existing morbidities, males were found to have higher incidence than females with a ratio of 58.6/41.4. Among patients with co-existing morbidities except malignancy cases, females were found to have a higher incidence than males in diabetes, chronic renal failure and corticosteroid consumption with a range of 57.1, 57.1, and 66.7 respectively. Considering age factor patients higher than 60 years old were found to have a higher incidence of co-existing morbidities(29.6%), similar to patients with co-morbidities such as diabetes and malignancy (41.1% and 40% respectively). Among the

patients with corticosteroid consumption a higher age frequency distribution was observed in patients that ranged 41-50 and higher than 60 years old (33.3%), and chronic renal failure was mostly seen in patients who were 41-50 years old (35.7%). In the patients with TB and DM, female factor play an important role as a risk factor ( $p < 0.05$ ) but in the other groups there weren't any significant statistical difference between male and female.

(Table/Fig 1) Age distribution in TB patients based on co-morbidities

Age group	Without co-morbidity	Diabetes mellitus	Chronic renal failure	Corticosteroid consumption	Malignancy	Total
13-20	19(11.7%)	1(0.8%)	0	0	0	20(8.2%)
21-30	30(18.5%)	1(0.8%)	1(7.1%)	1(16.7%)	0	33(13.6%)
31-40	16(9.9%)	2(3.6%)	1(7.1%)	0	1(2.0%)	20(8.2%)
41-50	23(14.2%)	12(21.4%)	5(35.7%)	2(33.3%)	1(2.0%)	39(16.04%)
51-60	26(16%)	17(30.4%)	3(21.4%)	1(16.7%)	1(2.0%)	48(19.8%)
>60	48(29.6%)	23(41.1%)	4(28.6%)	2(33.3%)	2(4.0%)	75(30.9%)
Total mean age	162(47.3)	56(58.4)	14(52.3)	6(54.8)	5(54.8)	243(50.15)

(Table/Fig 2) Frequency distribution of co-morbidities among pulmonary tuberculosis (TB) patients

Co-morbidity	frequency	Percent
Without co-morbidity	162	66.7
Diabetes	56	23.05
Chronic renal failure	14	5.8
Corticosteroid consumption	6	2.5
Malignancy	5	2
Total	235	100%

(Table/Fig 3) Sex distribution in TB patients with co-morbidities

co-morbidity	Men (percent)	Women (percent)	Total	P-value
Without co-morbidity	95(58.6%)	67(41.4%)	162(100%)	0.023*
Diabetes	24(42.9%)	32(57.1%)	56(100%)	0.07*
Chronic renal failure	6(42.9%)	8(57.1%)	14(100%)	0.41*
Corticosteroid consumption	2(33.3%)	4(66.7%)	6(100%)	0.42**
Malignancy	3(60%)	2(40%)	5(100%)	1**
Total	130(53.5%)	113(46.5%)		

\* chi-square test  
\*\* fisher exact test

## Discussion

In a descriptive retrospective cross sectional study, recorded files of 243 pulmonary TB patients who were admitted in 5<sup>th</sup> Azar hospital during 2001-2005 were studied. Then the frequency distribution of disease and co-existing morbidities which were followed by tuberculosis was estimated. Overall, males formed 53.5% of the patients; predominance of male among the patients without co-morbidities was seen (58.6%) but in patients with co-morbidities (except malignancy cases), females were predominant in number.

Abbasi et al reported that males formed 53% of all TB patients [14] which is similar to the results of this study. The statistical data for sex ratio of all

pulmonary TB patients in the country shows that 51% of all pulmonary TB patients were women and this difference between our study and national figures may be due to the majority of male population in Golestan province or males having more exposure than females. Immigration might be a contributing factor; but this hypothesis requires further evaluations. Evaluating other factors such as alcohol/ opium consumption, and HIV infection in Golestan population and comparing these factors in male and female population may also be of significant help, but in our study, except for malignancy co-existing morbidities (diabetes, etc) were found to be more frequent in females. National figures report a prevalence of diabetes for men as 2.41% and for women as 3.67% [15]. In this study for patients with pulmonary TB and diabetes, females had a higher prevalence than males ( $f/m = 4/3$ ) that was significant statistically ( $p < 0.05$ ). Therefore, due to higher prevalence of diabetes amongst females of this country, contemporary appearance of pulmonary TB with diabetes is to be expected more; but it seems necessary to evaluate other factors as well for incidence of tuberculosis in diabetic females. Nisapattorn and his coworkers in 2006 reported that females had a higher prevalence of coexisting TB and DM than males[4].

In Gulbay et al's study which was done in a hospital of Ankara during 5 years (1999-2004) period, there wasn't any clear difference in sex ratio of TB patients with and without diabetes [16]. Perz-Guzman and his group compared 202 pulmonary TB patients with co-existing diabetes with 226 patients of pulmonary tuberculosis who didn't have diabetes; and their results showed that diabetes was more prevalent among females aged 50 years or old [17] and this study showed approximately similar results. In pulmonary TB patients with chronic renal failure females were found to have a higher prevalence with 57.1% and amongst pulmonary TB patients who had consumed corticosteroids female population had double the prevalence as compared to males. Incidence of most collagen vascular diseases in females, which accompanies corticosteroid consumption, supposedly plays an important role in making females more prone to have pulmonary TB than males. Sazaki and his coworkers in 2000 [18] performed a study on pulmonary TB patients who had received corticosteroids as a treatment for collagen vascular disease; in their study females had a higher prevalence similar to that of our study ( $f/m = 1.5/1$ ). Female gender might be a

significant factor for increasing the incidence of pulmonary TB in individuals with corticosteroid consumption, chronic renal failure and diabetes, but this hypothesis requires further evaluations. In 13 year article's of Coantril and his group in dialytic patients (1986-1999) 24 cases of pulmonary TB reported equal sex ratio[19]. On the other hand another study reported pulmonary TB in 26 dialytic patients that included 6 women and 20 men [20] which is not in confirmation with the results of this study. In review of these studies we couldn't find any relation between sex and chronic renal failure. Males were more prevalent pulmonary TB patients with malignancy by a fraction of F/M =2/3. In Karnak and his coworker's study in 1993-1995 which was about pulmonary TB patients who had malignancy, males were prevalent with a fraction of 4/6.9=f/m; this result is also similar to our results [21]. The mean age of patients without co-morbidities was lower than mean age of all patients (47.3 against 50.15), against the patients with co-morbidities (for example in diabetes 58.4 against 50.15) which is due to higher occurrence of co-morbidities in elderly age. Higher age frequency distribution of TB patients in groups without co-morbidity, patients with diabetes and malignancy was over 60 years old (29.6%, 41.6% and 40% respectively), but in TB patients with chronic renal failure and corticosteroid consumption the higher age frequency distribution was 41-50 years old (35.7% and 33.3%, respectively). This study showed that although co-morbidities like diabetes and malignancy have an increased incidence in higher mean age TB patients than TB patients without co-morbidity, factors like chronic renal failure and corticosteroid consumption are more prevalent in a lower mean age group.

In Gulbay and coworker's study [16] simultaneous prevalence of pulmonary TB with diabetes for patients with mean age 50 years or older (21.3%) was more than for other age groups. In Perz-Guzman and his group's study [17] diabetes had higher incidence of tuberculosis in patients with age more than 50 years. Accompaniment of diabetes with tuberculosis in our study was 23.8% which was higher in Gulbay's study(17.7%) [16] and in Yamagishi's study(13.2%) [22]; this might be because of higher prevalence of pulmonary TB in Golestan province than the total national prevalence. In 2003 the incidence of pulmonary TB with positive smear was 7.8 for 1,00,000 patients in Iran and was reported 22 of 100000 patients in Golestan province [13]. Amongst the four common co-morbidities accompanying

tuberculosis, chronic renal failure was the second most common with a prevalence of 6%. In 1999, Leung and his coworkers in Hong Kong reported the prevalence of pulmonary TB in long term consumers of corticosteroid to be 1.2% [23], while this amount in Cobashy study in 1999 on 162 patients was reported as almost 3.1% [9]. Our findings about corticosteroid consumption and it's relation with pulmonary TB was situated between these two ranges (2.5%). Another common co-morbidity in our patients was malignancy with a prevalence of 2%. In Kamboj study in 2006 the rate of TB among solid organ and blood cancers were reported 102 and 457/100000 cases respectively, although this rate in normal New York population was 24-39/100000 [12].

Leung and coworker's study in 1999 found 4.2% of TB patients with co-existing malignancy (23). This incidence was 10% in Jihad's study in Saudi Arabia [24].

Restrepo BI et al in their study found preliminary evidence of an altered immune response to *M. tuberculosis* in type 2 diabetes, especially type 2 diabetes involving chronic hyperglycemia.

### Conclusion

The results of this study are similar to studies performed in other Asian countries such as Saudi Arabia, Korea and Japan regarding the prevalence of co-existing morbidities with pulmonary TB.

Considering the higher prevalence of TB in this region, regular screening of TB patients for DM and Renal Failure should be considered. Also screening for possible co-existing pulmonary TB in high risk groups (DM, malignancy, chronic renal failure, corticosteroid treatment) by means of chest radiography and sputum smear should be considered.

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