

Clinical and Radiographic Manifestations and Treatment Outcome of Pulmonary Tuberculosis in the Elderly in Khuzestan, Southwest Iran

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Background: Presentation of pulmonary tuberculosis (PTB) in the elderly is expected to be different from that in younger patients because of the debilitating factors and comorbidities. This issue should be considered in the national tuberculosis programs of countries. The purpose of this study was to evaluate the differences in the clinical and radiographic manifestations and treatment outcomes of PTB between the elderly and young patients.

Materials and Methods: This study was conducted as part of a mega project on tuberculosis by the Infectious and Tropical Diseases Research Centre affiliated to Ahvaz Jundishapur University of Medical Sciences. We retrospectively analyzed the medical records of 2,080 relatively young (18–64 years old at the time of diagnosis) and 346 elderly (≥ 65 years) PTB patients, who had been recently diagnosed and treated in the TB unit of Khuzestan Health Center from 2005 to 2010.

Results: Dyspnea and hemoptysis were the most common symptoms and the frequency of positive sputum smear –AFB was lower in the elderly PTB patients. On chest X-ray, elderly patients were less likely to have cavitation in comparison with younger patients. The frequency of favourable treatment outcome in the elderly was significantly lower than that in younger patients (64% vs. 77%, $P = 0.003$).

Conclusion: Dyspnea, weight loss and hemoptysis were more common in the elderly PTB patients. Chest X-ray showed less frequent typical findings of active PTB such as cavitation; and microscopic examination showed fewer sputum smear AFB positive cases in the elderly. The treatment outcome was less favorable in the elderly compared to younger TB patients.

Key words: Tuberculosis, Elderly, Clinical presentations, Radiographic feature; Treatment outcome

INTRODUCTION

Some changes have occurred in the burden of diseases, and non-communicable diseases are now more common than the infectious diseases; however, PTB and human immunodeficiency virus (HIV) infection still remain to be major health problems across the world (1). Although the incidence of TB has decreased in many parts of the world, an increasing percentage of TB occurs among the aged

population (2). Improved living conditions, health promotion, new methods of diagnosis and management of incurable diseases, control of population growth, reduced mortality, low birth rates, and increased life expectancy have resulted in the aging of populations in many parts of the world (3).

It is estimated that about one-third of the world's population are infected with *M. tuberculosis*.

Although HIV infection is a major risk factor for infection with TB, the elderly population is an important reservoir of *M. tuberculosis* infection in the world. Due to changes in physiological, psychological, social and economic states and occurrence of degenerative illnesses in older people, both disease course and TB treatment response are different in the elderly compared to the young population (4,5).

Tuberculosis in the elderly is an important public health issue that should be considered by health officials. In Iran, like other countries, aging of the population has resulted in higher frequency of TB in this age group. A high index of suspicion of TB in an elderly patient, having signs and symptoms of the disease, allows for early detection and appropriate treatment and thus decreases the rate of TB related mortality (6).

Previous studies have reported delays in detection and treatment of PTB in the elderly due to atypical clinical presentation or ignorance of the existence of disease. In some cases, the diagnosis is made after death. Due to negligence or delay in TB treatment, the morbidity and mortality rates of TB are much higher in older people than younger patients (2,4,5).

The aged population of Khuzestan Province also accounts for a high percentage of TB patients (7,8). To the best of our knowledge, studies about tuberculosis in the elderly in this region are very limited; therefore, there is little data on this subject. This study aimed to investigate the clinical manifestations, radiographic characteristics and treatment outcome of TB in the elderly. The current study results may help health officials better manage TB control programs in the region.

MATERIALS AND METHODS

As part of a mega project on tuberculosis, TB patients were studied based on the existing data in Khuzestan Health Center (KHC). TB patients registered during a 6-year period (from 2005 to 2010) in Khuzestan (a southwestern province of Iran with a population of about 4.5 million people living in 23 cities) were reviewed. The

data extracted from the patients' medical files included demographic characteristics, clinical presentation, radiographic features, sputum examination results and the control measures such as: response to treatment and mortality. Elderly patients were defined as patients aged 65 years or older. Patients aged 18–64 years were defined as young patients. Patients were categorized into two groups. The control group included all the young patients with pulmonary TB and the case group included all the elderly PTB patients. The inclusion criteria were all registered patients with documented PTB, diagnosed based on National Tuberculosis Program (NTP) (9). Cases with positive sputum culture for *M. tuberculosis* and those with at least 2 positive sputum smears for acid fast bacilli (SSP-AFB) were defined as definite cases of PTB or smear positive PTB (PTB+). Cases with signs and symptoms suggestive of TB plus 3 sputum smears negative for AFB (SSN-AFB) after two weeks of antibiotic therapy (not effective on *M. tuberculosis*) plus positive chest-X-ray (suggestive of TB) were defined as smear negative PTB (PTB-). If the patient's sputum converted from AFB-positive to AFB-negative after 2-5 months from the start of treatment (with standard anti TB drug regimen according to NTP), the case was defined as cured. A patient, who completed 6 months of treatment and clinically responded to treatment but with unknown bacteriological status was defined as a case of completed treatment. A case was defined as treatment failure if the patient's sputum remained positive 5 months or more after the start of treatment, or changed from negative to positive again. SSN-AFB cases at the beginning of treatment, whose sputum examination became positive after two months of treatment were also considered as treatment failure. Patients with cured or completed treatment were considered as successfully treated and those with failure, defaulted or death were considered as unsuccessful treatment outcome. SPSS version 16 was used for statistical and subsequent multivariate analyses. Chi square and Fisher's exact tests were used to compare the qualitative variables. The differences were considered significant if the P-values were less than 0.05.

RESULTS

Of a total of 2,426 adult PTB cases, 346 (14.3%) were elderly. The mean age of the elderly PTB cases was 77.8 ± 12.2 years, among them 155 (44.8%) were males and 191 (55.2%) were females. The female sex predominated in both groups, comprising approximately 55% of cases. There was no statistically significant difference between the two groups with respect to female predominance. Of the total studied patients, only 155 elderly PTB cases and 814 young PTB cases had complete data including clinical and radiographic characteristics for the purpose of comparison. The patients' clinical symptoms are shown in Table 1. Dyspnea, hemoptysis, and weight loss were more common among the elderly. There were no statistically significant differences between the case and control groups in terms of coughing, expectoration, and fever except for the night sweat. The initial findings in CXR are shown in Table 2. Among the elderly patients, lower lung lesions such as nodular infiltration, fibrotic changes or consolidation were more common. However, the difference for upper lobe nodular infiltration or miliary pattern was not significant between the two groups. Elderly patients had higher frequency of upper lobe consolidation and lower lobe nodular infiltration but fewer cavity findings. In addition, the proportion of patients with normal pattern CXR was not significantly different between the two groups.

The results of treatment in all studied patients are summarized in Tables 3. In the elderly patients, there was no significant difference between mortality and sputum positivity for AFB ($P=0.23$). In this group, there was also no significant difference between successful response to treatment and sputum positivity for AFB ($P=0.14$). Successful treatment after 1 year from the initiation of standard anti-TB treatment between the two groups according to sputum positivity for AFB is summarized in Table 4. Mortality rate for the elderly patients was 26.5%, whereas it was 4.1% for young patients ($P < 0.0001$). Only

54.9% of the elderly patients had successful outcomes (cure or treatment completion) in comparison with 88.1% of young patients ($P < 0.0001$).

Table 1. Clinical presentation of studied patients at the time of pulmonary tuberculosis diagnosis

Clinical presentation	65 years or more N=155	18-64 years N=814	P-value
Cough	141(90.9)	742(91.1)	0.87
Fever	120(77.4)	604(74.2)	0.42
Night sweat	72(46.4)	526(64.6)	0.0001*
Weight loss	108(69.7)	500(61.4)	0.03*
Sputum production	92(59.3)	510(62.6)	0.47
Dyspnea	95(61.3)	226(27.8)	0.0001*
Hemoptysis	17(10.9)	20(2.4)	0.0001*

Abbreviations: N=Number, figures in parentheses are percentage * Differences are statistically significant.

Table 2. Radiographic findings of studied patients at the time of pulmonary tuberculosis diagnosis.

Clinical presentation	65 years or more N=155	18-64 years N=814	P-value
Upper lobe infiltration	66(42.6)	381(46.8)	0.37
Cavitation	24(15.5)	232(28.5)	0.0001*
Upper lobe consolidation	22(14.2)	22(2.7)	0.0000*
Miliary	21(13.5)	99(12.2)	0.35
Lower lobe infiltration	21(13.5)	70(8.6)	0.04*
Nonspecific lesion	2(1.3)	10(1.2)	0.60

Abbreviations: N=Number, figures in parentheses are percentage, * Differences are statistically significant.

Table 3. Treatment outcome of smear positive and smear negative pulmonary tuberculosis among the studied groups

Age (years)	Treatment outcome	PTB+ N %	PTB- N %	Total N %	P value
65 years or more N=346	Successful	132(57.1)	58(50.4)	190(54.9)	0.14
	Unsuccessful	99 (42.9)	57(49.6)	156(45.1)	0.23
	Death	44(19.0)	27(23.5)	71(20.5)	
	Total	231(100)	115(100)	346(100)	
18-64 years N=2080	Successful	1439(87.2)	394(91.8)	1833(88.1)	0.32
	Unsuccessful	212(12.8)	35(8.2)	247(11.9)	0.35
	Death	85(5.1)	19(4.4)	104(5.0)	
	Total	1651(100)	429(100)	2080(100)	

Abbreviation: PTB+, Smear positive pulmonary tuberculosis; PTB-, Smear negative pulmonary tuberculosis.

Table 4. Comparison of successful treatment and death between the studied groups

Outcome	Sputum smear positivity	65 years or more N=346	18-64 years N=2080	P-value
Successful	Positive	132 (38.1)	1439(69.2)	0.003*
	Negative	58(16.8)	394(18.9)	
	Total	190(54.9)	1833(88.1)	<0.0001*
Death	Positive	44(12.7)	85(4.1)	0.003*
	Negative	27(7.8)	19(0.9)	
	Total	71(20.5)	104(5.0)	<0.0001*

Abbreviations; N=Number, figures in parentheses are percentage, * Differences are statistically significant

DISCUSSION

Epidemiological studies on tuberculosis suggest a recent declining trend in new TB cases worldwide. Despite the global drop in the incidence of new cases of PTB, the proportion of the elderly patients with PTB remains high and has even increased in some areas. According to the National Population and Housing Census of 2011, the percentage of the elderly in the total population of Khuzestan was 5.7% (10), therefore, the frequency of PTB was expected to be high among the elderly in this region (11, 12). In the current study, 54.9% of the elderly patients had been successfully treated. They had higher frequency of weight loss, dyspnea, and hemoptysis in comparison to younger patients. They were less likely to be sputum smear positive for AFB in comparison to younger PTB patients (66.8% vs. 77.4%). TB treatment failure and the mortality rate in the elderly patients were higher than in younger subjects. Radiographic markers of active PTB such as cavitations were less frequent in the elderly, but upper lobe consolidation and lower lobe infiltration were more commonly observed in this group.

In previous studies, response to anti-TB treatment in the elderly patients due to the high mortality in this group was poor (2, 13,14). The mortality rate from TB during treatment was reported to be 21% in a study by Pratt et al, in the United States (14) and 27% in a study in Taiwan by Wang et al. (2). The mortality rate in the elderly (aged 65 or more) PTB patients was higher than that in younger (20-64 years old at the time of diagnosis) TB patients in the United

States (21% vs. 7%, $P < 0.001$). In another study in Taiwan, the mortality rate in aged PTB cases was higher than that in younger PTB patients (27% vs. 4%, $P = 0.001$). In our study, the mortality rate was 20.5% (71/346) in the elderly PTB patients; which is compatible with the aforementioned studies. There was a statistically significant difference in mortality rate between the elderly patients and younger patients and the obtained value was higher than the mortality rate of aged TB patients in Iran (11.2%, 14/125) in 2008 (7), which could be explained by the fact that in the current study we excluded pediatric patients younger than 18 years, whereas in the previous study all TB cases in all age groups were included. Elderly patients, due to organ dysfunctions and immunological changes secondary to aging, are at an increased risk for severe PTB or death due to PTB. Treatment is complicated due to age-related problems such as renal and liver dysfunction. Because some of the aged people are under treatment with multiple medications for underlying illnesses, drug interactions and adverse events may be associated with higher frequency of death (11).

In our study, the prevalence of sputum positive for AFB in the elderly patients was lower than that in younger patients (66.7% vs. 77.9%). This finding is consistent with the results of previous studies (2,11-14). Elderly patients have difficulty obtaining adequate sputum for examination. This might be attributed to their inability to produce sputum because of their weakness in coughing. Quality of the delivered sputum by the elderly patients is poor and more saliva secretion than pulmonary secretion is obtained from these patients.

In our study, atypical imaging findings of PTB lesions in the elderly patients' chest X-ray suggest that pulmonary lesions occur more often in lower lung fields. These findings are similar with previous studies and medical literature (2, 5, 11, 13, 15). Our findings are in agreement with the results of a study from Iran (6). Towhidi et al. reported that upper lobe infiltrations were more common in the younger group (54.5% vs. 15%, $P < 0.05$), whereas lower lung field infiltrations had similar frequency in both

groups (35% vs. 24%, $P>0.05$) (6). Cavitation was significantly more common in the younger group compared to the elderly (63% vs. 25%, $P<0.05$). Since most cases of pulmonary TB in the elderly are resulted from reactivation of primary infection, classically, reactivation of TB is expected to involve the upper lobes of the lungs (11). This atypical finding in imaging should be kept in mind because misinterpretation of the images may delay timely detection and initiation of treatment.

In the current study, we found that dyspnea, hemoptysis, and weight loss were significantly more common in the elderly patients. There were no statistically significant differences between case and control groups in presence of cough, expectoration, and fever except for night sweat. There were controversial results about clinical presentation of PTB in previous studies (6, 11, 13, 16, 17). Some studies described that younger patients were more likely to have fever, night sweats and hemoptysis (16); while some others explained that there was no significant difference in most symptoms (except for dyspnea) between the elderly PTB patients and younger PTB patients (13).

Study strength and limitation: To the best of our knowledge, there is no similar study in the province, and there are limited studies in this field in Iran. Therefore, this study can be considered as a new work. The study design was retrospective and incomplete data caused some difficulties, but large number of studied patients enabled us to randomly choose patients with complete data. Future population-based studies are needed to generalize these results to the whole community in the region.

CONCLUSION

In summary, elderly patients with PTB showed higher frequency of dyspnea, weight loss and hemoptysis. Chest X-ray showed less frequent typical findings of active PTB such as cavities, and microscopic examination showed less frequency of sputum smears positive for AFB in the elderly patients. However, the treatment outcome was less favorable than that in younger TB patients.

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