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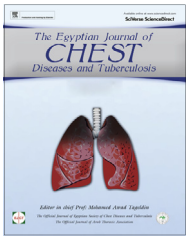

ORIGINAL ARTICLE

Pattern of pulmonary tuberculosis in elderly patients in Sohag Governorate: Hospital based study

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KEYWORDS

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Abstract *Background:* Tuberculosis (TB) in elderly is a worldwide problem.

Objective: To evaluate differences in clinical, radiological, laboratory features, adverse antituberculosis drug reactions and TB-related mortality in elderly and young pulmonary TB patients.

Results: The study included analysis of the medical history, chest radiographic and laboratory findings in 124 elderly and 124 young pulmonary TB patients, with mean age of 60.5 ± 9.1 and 31.6 ± 10.8 years, respectively ($p < 0.0001$), and comparable male predominance. There were higher frequencies of dyspnea, anorexia, weight loss, weakness and mental changes in elderly than young ($p = 0.001$, 0.004, < 0.0001, < 0.0001, 0.002, respectively) while there were higher frequencies of cough and sputum production, hemoptysis, and fever in young than elderly ($p = 0.008$, 0.01, 0.04, respectively) patients. Elderly had higher frequency of comorbidities ($p < 0.0001$). Elderly had higher frequency of atypical radiological findings for pulmonary tuberculosis and initial misdiagnosis as pneumonia and lung cancer ($p < 0.0001$, 0.001, 0.01, respectively). Elderly had a higher level of erythrocytic sedimentation rate ($p = .01$). Young had a higher frequency of positive sputum direct smear for acid fast bacilli ($p = 0.04$). Elderly had a higher role for fiberoptic bronchoscope

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in diagnosis of pulmonary TB ($p = 0.001$). There was a delay in the diagnosis of pulmonary TB in elderly ($p < 0.0001$) patients. Anti-tuberculosis drug side effects and TB-related mortality were more frequent in elderly ($p < 0.0001$, 0.03, respectively)patients.

Conclusion: This study showed that elderly pulmonary TB patients had higher frequencies of atypically clinical, radiological presentations, co-morbidities, anti-tuberculosis drug adverse reactions and TB related mortality.

Introduction

Along with the elderly populations' growth in numbers, there has been an increase in the number of TB cases among elderly populations [1]. The loss of cellular immune reactivity (i.e., negative tuberculin skin test) to *Mycobacterium tuberculosis* occurs in some elderly population who were previously infected with this organism, thereby rendering them vulnerable to re-infection. Also, the elderly are at a greater risk for reactivation of latent TB. In elderly, approximately three-quarters of all TB cases occur in the respiratory tract [2,3]. Although, the mortality rate of TB in elderly is six times higher, TB is a preventable cause of death in elderly patients [3]. An active approach to diagnose, treat and prevent TB in the elderly is indicated [3–6]. Elderly TB patients should remain under observation until adherence with their treatment regimen [7,8].

Age classification varied between countries and over time. Definitions fell into three main categories: (1) chronological; (2) change in capabilities (i.e., invalid status, senility and change in physical characteristics); and (3) change in social role (i.e., change in work patterns, adult status of children and menopause). Most developed world countries have accepted the chronological age of 60/or 65 as a definition of elderly person, but like many westernized concepts, this does not adapt well to the situation in Africa. According to WHO (2011), it seems more appropriate in Africa to use a combination of the three definitions. It was felt that by using age of 50 years, this project will be indirectly incorporating these other definitions [9].

Patients and methods

This study was conducted in Sohag University Hospital during the period between January 2010 and December 2012. Ethics committee approved the study. Written informed consents were obtained from the entire patients. This study included only patients with active pulmonary TB who were diagnosed and treated at our hospital. Exclusion criteria were all other forms of TB, like hilar and/or mediastinal lymphadenopathy, TB pleural effusion, pulmonary TB with co-existing extra-pulmonary TB and miliary TB to allow better data comparison, relapsed or multi-drug resistant cases. According to WHO (2011), we used age of 50 years as a definition of elderly [9]. All patients were human immunodeficiency virus negative.

Collected data included the following: demographic characteristics, presenting symptoms and body temperature, underlying illnesses, laboratory investigations including (1) complete blood count (was done by Coulter counter), (2) erythrocytic sedimentation rate (ESR) by westergreen methods, (3) microbiological investigation: specimen: morning sputum or bronchoalveolar lavage samples submitted for diagnosis of tuberculosis, samples were collected from each patient in 50 ml sterile plastic containers. Decontamination of sputum samples was carried out using the N-acetyl-L-cysteine (NALC/NaOH) method. (A) Microscopy: smears were stained with the ZN technique. (B) Culture: inoculation was done onto slants of Lowenstein Jensen medium. (4) Liver function tests were performed on a Boehringer Mannheim (BM)/autoanalyzer Cobas Integra 400 (checked before beginning of anti-TB treatment).

Radiological features were recorded according to interpretation of the initial chest radiography taken when the patient visited the hospital before a definite diagnosis had been made. That included the location and lesion appearance. The radiological appearance of pulmonary TB lesion was classified as typical fibrous nodular infiltrates and/or a cavitary lesion, consolidation, large opacity mimicking a mass or as others. Location of TB lesion was categorized as upper lobe involvement (upper lobe alone or upper with middle or lower lobe) or isolated middle and/or lower lobe involvement. Initial clinical diagnosis (before definite diagnosis) was classified as pulmonary TB, bacterial pneumonia, lung cancer, or others (such as sarcoidosis, etc).

Fiberoptic bronchoscope, bronchoalveolar lavage (BAL), brush and/or biopsy were performed only in selected cases such as patients who cannot expectorate or other diagnosis was expected such as lung cancer. Active pulmonary TB was diagnosed in the presence of at least one of the following criteria; (1) a positive sputum or BAL smear and/or positive culture for AFB regardless of sputum or BAL smear results; (2) biopsy based histopathological confirmation of the lung lesion; (3) clinical and chest radiographic findings that are highly suggestive of TB and a favorable response to anti-TB treatment even in absence of bacteriologic or histopathological confirmation. Diagnosis time was calculated from onset of symptoms till final diagnosis was obtained

After diagnosis of active pulmonary TB had been made and anti- TB medications started, patients were seen 1 week after medications and every 2 weeks thereafter, and at these visits were questioned about drug side effects. Chest radiograph and microbiological study were performed monthly. Liver function tests were carried out 1 week after beginning of medication and monthly thereafter. Patients were treated initially using the following regimen: isoniazed, rifampicin, ethambutol and pyrazinamid or streptomycin. Pyrazinamid was not prescribed for patients with liver diseases e.g., liver cirrhosis or active hepatitis. Treatment duration was at least 6 months. Anti-TB drug adverse reactions included mild gastrointestinal disturbances, severe gastrointestinal disturbances, mild transient liver transaminases [alanine transaminase (ALT) and aspartate transaminase (AST)] raise, and drug induced hepatitis was de-

fined as: (1) liver transaminase increase to $\geqslant 5$ times the normal upper limit, (2) any elevation of ALT and AST above basal levels in the presence of ictric hepatitis. If drug induced hepatitis was suspected, anti-TB drugs were stopped, when liver function tests returned to normal the anti-TB drugs were sequentially reintroduced. Pyrazinamid was not reintroduced [10,11]. Mortality during treatment was recorded.

Statistics

Statistical analysis was performed using the SPSS Version 11.0 soft ware package. Statistical differences between the clinical features of the two groups were determined with chi-square test. All values are reported as mean ± standard deviation (SD). A p value (2-tailed) $\leqslant 0.05$ was considered statistically significant. The student's t test was used when indicated for independent means.

Results

According to inclusion and exclusion criteria, the study included 124 elderly ($\geqslant 50$ year) and 124 young patients (< 50 year) with active pulmonary TB.

Table 1 showed that mean ages of the elderly group and young group were 60.5 ± 9.1 years and 31.6 ± 10.8 years, respectively ($p < 0.0001$). There was a comparable male predominance in both groups ($p = 0.2$). Co-morbid diseases were frequent in elderly patients ($p < 0.0001$). Diabetes mellitus was the most frequent co-morbidity in both groups, without statistically significant difference. An initial diagnosis of active pulmonary TB was made correctly in 86.3% ($n = 107$) of the young but only in 65.3% ($n = 81$) of elderly patients ($p < 0.0001$). 25% ($n = 31$) of elderly were misdiagnosed as bacterial pneumonia compared to 12.1% ($n = 15$) of young patients ($p = 0.008$). 8.9% ($n = 11$) of elderly but only 1.6% ($n = 2$) of young patients were misdiagnosed as lung cancer ($p = 0.01$).

As regards clinical and radiological criteria of the patients (Table 2), cough and sputum production were more common in young than in the elderly group ($p = 0.008$). Dyspnea was significantly frequent in the elderly ($p = 0.001$). Non specific general symptoms like anorexia, weight loss, weakness and mental changes were significantly frequent in the elderly patients ($p = 0.004$, < 0.0001, < 0.0001, 0.002, respectively). Hemoptysis was significantly frequent in the young ($p = 0.01$). Febrile sense, night sweat and elevated body temperature were significantly frequent in young patients ($p = 0.0006$, 0.002, 0.04, respectively). There was a significant delay in the diagnosis of pulmonary TB in the elderly group. The mean diagnosis time was 6.2 ± 2.3 weeks in elderly compared to 4.3 ± 2.1 weeks in the young group ($p < 0.0001$).

Radiological evaluation showed that, upper lobe involvement was more common in the young group. It was 87.9% and 70.2% for elderly and young groups respectively but isolate mid or lower lobe involvement was more common in the elderly group it was 29.8% for elderly compared to 12.1% for young. The lobar predilection was significant ($p = 0.0006$). Typical fibrous nodular type with or without a cavity lesion was significantly more frequent in the young than elderly patients ($p < 0.0001$), whereas consolidation or large opacity mimic a mass was significantly more frequent in the elderly than in young patients. P values were 0.001, 0.01, respectively.

As regards the laboratory findings of the patients (Table 3), positive sputum direct smear for AFB was the most common method of pulmonary TB diagnosis in the both groups, but significantly more frequent in young than elderly patients ($p = 0.04$). Positive sputum culture was significantly frequent in elderly patients ($p = 0.02$). Fiberoptic bronchoscope had a higher role in the diagnosis of pulmonary TB in elderly than young patients (16.2% elderly vs. 3.9% young patients,

Table 1 Demographic data, co-morbid diseases and initial diagnosis of active pulmonary TB in elderly and young patients.

	Elderly ($\geqslant 50$ year, %) ($n = 124$)	Young (< 50 year, %) ($n = 124$)	P value
Age (mean ± SD)	60.5 ± 9.1	31.6 ± 10.8	< 0.0001
(range, year)	50–90	16–49	
Gender			
Male	78 (62.9)	72 (58.1)	0.2
Female	46 (37.1)	52 (41.9)	0.4
Co-morbid diseases			
Diabetes mellitus	27 (21.8)	25 (20.2)	0.4
Chronic lung disease	22 (17.7)	10 (8.1)	0.02
Liver disease	16 (12.9)	7 (5.6)	0.04
Cardiovascular disease[a]	21 (16.9)	5 (4)	0.0008
Renal disease	3 (2.4)	2 (1.6)	0.7
Malignancy	1 (0.8)	1 (0.8)	0.9
Total	75 (60.5)	37 (29.8)	< 0.0001
Initial diagnosis			
Tuberculosis	81 (65.3)	107 (86.3)	< 0.0001
Pneumonia	31 (25)	15 (12.1)	0.008
Lung cancer	11 (8.9)	2 (1.6)	0.01
Others	1 (.8)	0 (0)	0.3

SD, standard deviation.

[a] Hypertension, ischemic heart disease, cerebrovascular accident were included.

Table 2 Clinical and radiological findings of active pulmonary TB in elderly and young patients.

	Elderly (⩾50 year, %) (n = 124)	Young (<50 year, %) (n = 124)	P value
Clinical manifestations			
Cough and sputum production	101 (81.5)	115 (92.7)	0.008
Hemoptysis	20 (16.1)	36 (29)	0.01
Dyspnea	43 (34.7)	21 (16.9)	0.001
Chest pain	14 (11.3)	9 (7.3)	0.3
Febrile sense	51 (41.1)	78 (62.9)	0.0006
Night sweat	46 (37.1)	70 (56.5)	0.002
Weakness	61 (49.2)	27 (21.8)	<0.0001
Weight loss	57 (46)	25 (20.2)	<0.0001
Anorexia	79 (63.7)	57 (46)	0.004
Mental changes	12 (9.7)	1 (.8)	0.002
↑Body temperature	69 (55.6)	85 (68.5)	0.04
Symptom duration (mean ± SD)	6.2 ± 2.3	4.3 ± 2.1	<0.0001
(range, weeks)	4–12	3–10	
Radiological finding			
Location of the lesion			
Upper*	87 (70.2)	109 (87.9)	0.0006
Lower¥	37 (29.8)	15 (12.1)	
Appearance of the lesion			
Typical feature×	81 (65.3)	110 (88.7)	<0.0001
Consolidation	28 (22.6)	10 (8.1)	0.001
Large opacity-Mass like	14 (11.3)	4 (3.2)	0.01
Others	1(.8)	0 (0)	0.3

↑: elevation; *: lesion on the upper lobe only or upper lobe plus other lobe; ¥: lesion in isolated middle and/or lower lobe; ×: fibrous nodular and/or cavitary.

Table 3 Laboratory findings of active pulmonary TB in the elderly and young patients.

	Elderly (⩾50 year, %) (n = 124)	Young (<50 year, %) (n = 124)	P value
Sputum			
Direct smear for AFB	77 (62.1)	92 (74.2)	0.04
Culture for TB	17 (13.7)	6 (4.8)	0.02
Bronchoscope (total)®	20(16.2)	5 (3.9)	0.001
Bronchoalveolar lavage (BAL)×	11 (8.9)	3 (2.3)	0.03
Histopathology¥	9 (7.3)	2 (1.6)	0.03
Diagnosis on radiological and clinical feature only∞	10 (8)	21 (17)	0.04
Hematologic findings			
Leukocytic count(mean ± SD)	7 ± 3.2	7.7 ± 3.1	0.08
range × 10^9/L)	3–14.2	3.2–14.4	
Leukocytosis (>11 × 10^9/L)	20 (16.1)	23 (18.5)	0.6
ESR (mean ± SD)*	91 ± 12	86 ± 19	0.01
(range, mm/hr)	65–130	60–125	

®: fiberoptic bronchoscope ;×: smear for AFB, culture for TB; ¥: for bronchoscopic biopsy; *:erythrocytic sedimentation rate; ∞: in absence of bacteriological or histopathological confirmation for TB.

p = 0.001). Direct smear of bronchoalveolar lavage or culture for AFB and histopathology for fiberoptic bronchoscope biopsy for TB were significantly more frequent in elderly than in young patients (p = 0.03, 0.03). Diagnosis of pulmonary TB on clinical and radiological findings without bacteriological or histopathological confirmation was significantly higher in young patients (p = 0.04). ESR level was significantly higher in elderly than in young patients (p = .01).

Table 4 showed details of anti-TB drug adverse reactions, the total number of patients who experienced adverse drug reactions was significantly higher in elderly than in young patients (41.1% elderly vs. 17.7% young, p < 0.0001). In the elderly group, the mortalities related to TB were higher in elderly than in the young group (7 elderly patients (5.6%) deceased because of TB vs. single young patient (0.03%)). The difference in both groups was statistically significant (p = 0.03).

Table 4 Adverse anti-TB drug reactions and treatment result of active pulmonary TB in elderly and young patients.

	Elderly (⩾50 year, %) (n = 124)	Young (<50 year, %) (n = 124)	P value
Adverse drug reaction			
Mild GIT trouble	26 (21)	14 (11.3)	0.04
Severe GIT trouble	10 (8.1)	2 (1.6)	0.02
Mild liver enzyme raise	18 (14.5)	8 (6.5)	0.04
Hepatitis	7 (5.6)	1 (0.8)	0.03
Total	51 (41.1)	22 (17.7)	<0.0001
Treatment result			
Completed treatment	110 (88.8)	122 (98.4)	
Death	14 (11.2)	2 (1.6)	<0.002
TB related death	7 (5.6)	1 (.8)	0.03
Other disease	7 (5.6)	1(.8)	0.03

GIT, gastrointestinal.

Discussion

Co-morbid diseases, malnutrition and the biological changes that are associated with aging can disrupt protective barriers, impair microbial clearance mechanisms, and contribute to the expected age-related decrease in cellular immune responses to microbes such as *M. tuberculosis*. These factors may lead to delay in the healing process and increase morbidity and mortality in elderly TB patients [4,6].

In our study we defined elderly by the age >50 years and this is consistent with Nirmal Chand et al. (2007) who studied TB in elderly and treatment outcome [1]. The male predominance among both elderly and young patients could be explained by their higher social and labor activities than females, thus favoring the transmission of TB. This result was consistently described by most of the studies [4,6–8].

The higher frequency of chronic lung, cardiovascular diseases in elderly patients was not supersizing because these diseases increase with aging. This result was consistent with the results of other studies [8,12–15]. The higher frequency of liver diseases in elderly group can be explained by the high prevalence of hepatitis C infection and liver cirrhosis probably due to use of non disposable syringe in treatment of prevalent schistosomiasis in Egypt early in the twentieth century [16–18]. Diabetes mellitus was the most common co-morbid disease in both groups which was explained by its immunosuppressive effect and increased susceptibility to TB infection. These results agreed with those of other investigators [7,11,14]. Malignancy was not frequent co-morbid disease in elderly patients in our study, in contrast to other studies which recorded that malignancy was a frequent co-morbid disease in elderly TB patients [11,14]. This could be explained by the lower cutting edge of elderly at 50 years compared to 60/65 years for these studies.

Febrile sense and elevated body temperature were less frequently recorded in elderly patients than in young. This can be explained by the decreased pyrogenic response with aging and reduced perception of fever in elderly. The lower frequency of sweating in older patients is likely related to the lower frequency of fever in them. The elderly TB patients commonly presented with non specific general symptoms such as anorexia, weight loss, weakness and mental changes because many elderly patients visit physicians after the disease had progressed to advanced stage due to lower awareness of the disease among them, and poor socioeconomic status in our society. These results were in agreement with those of other studies [1,7,12,19]. Although cough and sputum production were common symptoms in both young and elderly patients, they were statistically significant in young patients. This result was in agreement with other authors [7,11,19,20]. In our study, the higher frequency of hemoptysis in young patients was probably related to the higher frequency of lung cavitations in them. This was in agreement with other authors [4,8]. Korzeniewska-Kosela et al. (1994), Umeki (1989), and Lee et al. (2005) recorded that, no difference between elderly and young patients as regards cough, sputum production and hemoptysis, inconsistent with our study which recorded higher frequency of presentation of elderly by non specific manifestations which could be explained by earlier pulmonary TB detection by mass survey in the former studies [21,22,11].

The higher frequency of dyspnea in elderly patients can be explained by the decrease in pulmonary function with aging, higher frequency of chronic lung and cardiovascular diseases in elderly. These results was consistent with other studies [4,7,23]. The delayed diagnosis of pulmonary TB in elderly may be due to the higher frequency of unusual clinical presentation (which may be confused with age-related illness) and X-ray image showing atypical radiological presentation and/or to the lower awareness of the disease among them. This result was in agreement with many authors [1,4,8,11,15]. While, Pérez-Guzmán et al. (1999) recorded that no difference between elderly and young patients in duration of diagnosis which could be explained by earlier pulmonary TB detection by mass survey in this study [13].

In our study atypical radiological presentation of pulmonary TB in elderly led to misdiagnosis as pneumonia or lung cancer initially and this consistent with the results of Nirmal Chand et al. (2007), Mori and Leung (2010) who recorded increase frequency of TB lower lobe involvement with age and the frequency of cavitations steadily decrease with age [1,4]. Only selected patients received a fiberoptic bronchoscope examination, BAL, brush and/or biopsy. This role was more

prominent among elderly due to higher un-ability to expectorate sputum, atypical clinical and radiological findings and initial misdiagnosis as lung cancer. This was in agreement with different studies [4,5,11,24,25]. Higher frequency of diagnosis of pulmonary TB on clinical and radiological picture (in absence of bacteriological or histopathological confirmation) in young than elderly patients could be explained by the higher atypical clinical and radiological presentation of pulmonary TB in elderly. This was in agreement with other authors [1,6,8].

In our study, ESR level of elderly TB patients was significantly higher than that of young patients and this is probably due to normal increase of ESR with age [3,26]. This was in agreement with Lee et al. 2005 [11]. No significant difference in leukocytic count was observed between elderly and young patients, in our study. This result was in agreement with other authors [1,11] while, Cruz-Hervert et al. (2012) recorded that elderly patients had a lower leukocytic count which could be explained by the age related immunosuppression (the lower cutting edge of elderly at 65 years for this study compared to 50 years for our study) [6].

The higher frequency of anti-TB drugs adverse reactions in elderly was in agreement with different Egyptian and worldwide studies [6,10,15,27,28]. It is not surprising the TB related mortality was higher in elderly than young patients and this could be explained by age-related immunosuppression, malnutrition, co-morbid diseases, delayed diagnosis and initiation of treatment in them. This was in agreement with different authors [1,4,6–8,15].

Recommendation

A high index of suspicion and prompt investigations in elderly patients are mandatory for early diagnosis and treatment of TB hoping for decreasing TB related morbidity and mortality. Careful monitoring of elderly patients for adverse effects of anti-TB drugs is indicated.

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