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The tuberculosis case fatality rate and the treatment results of the young adult male patients of the last 9 years (2002-2010)

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ÖZET

Tüberkülozlu genç erkek hastaların son 9 yıllık tedavi sonuçları ve tüberküloz olgu fatalite hızı

Ülkemizde tüberküloz (TB) açısından bir risk grubu olarak kabul edilen asker popülasyondan çıkan ve hastanemizde takip edilen 2002-2010 yılları arasındaki TB'li olgu serisinin tedavi sonuçları ve olgu fatalite hızı araştırılmıştır. Bu çalışma, 1 Ocak 2002 ile 31 Aralık 2010 tarihleri arasında tanı konulan akciğer TB'li hastalarda, geriye dönük veri araştırmasıyla yapılmıştır. Kliniğimize TB tanısıyla 2002-2010 yılları arasında 1871 asker hasta takip edilmiştir. Son 9 yıllık TB'li asker hasta verileri incelendiğinde; yıllar içerisinde kliniğimizde takip edilen hasta sayısında azalma olduğu görülmektedir. TB tanısıyla yıllık ortalama yatan hasta sayısı 208±125'dir. Akciğer TB'li hasta oranı % 81,7, akciğer dışı TB oranı ise % 18,3'dür. Dokuz yıllık dönemdeki toplam tedavi başarı oranı, ortalama % 91,3'tür. Tüberküloz hastalarının yaş ortalaması 21,5±2,2 yıldır. Tüm hastaların ortalama yatış süresi; 32,06±15,3 gündür. 2002 ile 2010 yılları içerisinde 6 hasta, TB nedeniyle hayatını kaybetmiştir. Son dokuz yıllık (2002-2010) TB olgu fatalite hızı; % 0,32 olarak hesaplanmıştır. Ölen hastaların yaş ortalaması; 26±6,6 yıldır. Hepsi erkek hasta olup, ortalama yatış süresi; 53,5±47,2 gündür. Tüm ölen hastaların tanısı, yeni olgu yayma pozitif akciğer tüberkülozu idi ve hepsine dörtlü antiTB tedavi verildi. Toplam tüberküloz tedavi başarı oranımız % 91,3 gibi yüksek ve tüberküloz olgu fatalite hızımız % 0,32 gibi oldukça düşük bir oran saptanmıştır. Ölen hastaların yaş ortalamasının yüksek, radyolojik yaygınlığının fazla ve hastanede yatış sürelerinin uzun olduğu görülmüştür.

Anahtar Kelimeler: *akciğer; tüberküloz; olgu fatalite hızı*

SUMMARY

Tuberculosis (TB) case fatality rate and treatment results in soldiers, a population that is accepted as a risk group for TB in our country, in our hospital between 2002 and 2010 were investigated. Data of patients diagnosed with pulmonary TB between January 01, 2002 and December 31, 2010 were retrospectively analyzed. Totally, 1871 patients were followed-up in our clinic with the diagnosis of TB between 2002 and 2010. The 9-year data of soldier patients with TB revealed a reduction in the number of patients hospitalized in our clinic. The rates of patients with pulmonary and extra-pulmonary TB were 81.7% and 18.3%, respectively. The mean treatment success rate in the 9-year period was 91.3%. The TB case fatality rate in the 9-year period was found to be 0.32%. Total TB treatment success was high as 91.3% and TB case fatality rate was low as 0.32%. Our data indicated that the mean age was high, radiological involvement was severe and hospital stay was longer in patients who died.

Key words: *pulmonary; tuberculosis; case fatality rate*

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Introduction

Tuberculosis (TB) remains as the second leading infectious disease causing death following human immunodeficiency virus (HIV) worldwide (1). In 2010, 8.8 million (range, 8.5-9.2 million) new TB cases have been defined. According to the 2011 Global Tuberculosis Control Report of the World Health Organization (WHO), the incidence and prevalence of TB were 128/100,000 and 178/100,000, respectively, and the mortality associated with TB was 20/100,000 worldwide (1). In 2010, TB-related death was determined in 1.1 million (range, 0.9-1.2 million) HIV-negative patients and in 0.35 million (range, 0.32-0.39 million) HIV-positive patients worldwide (1). The incidence of TB has been decreasing since 2002 and the number of definite TB cases has been decreasing since 2006. Within the frame of global TB control strategy of WHO, namely "The Stop TB Strategy", one of the aims is to reduce the prevalence and mortality rates of TB in 1990 by 50% until 2015 (2). This goal was achieved in America and was nearly achieved in the Western Pacific Region.

In the 2011 Report of Tuberculosis Fight in Turkey, the TB incidence was 22/100,000, the TB prevalence was 24/100,000, and mortality due to TB (pulmonary and extrapulmonary TB) was 3.0% (3).

Along with the effective TB control programs, a reduction has been observed in the prevalence and incidence of TB in Turkey in the recent years. For the last 5 years, the Turkish Ministry of Health has been releasing the number of patients died of TB; however, in Turkey, the number of studies about TB-related fatality rate remains inadequate.

Males aged between 15 and 35 years account for the great majority of TB patients in Turkey (3). We, therefore, think that the results of the present study obtained from young adult patients, who were evaluated in terms of TB fatality rate, would be a good sample for our country. In the present study, the fatality rate among patients hospitalized with the diagnosis of TB between 2002 and 2012 and received anti-TB therapy in our clinic was investigated and TB case fatality rate was calculated. The results of this study were compared with previous data from our clinic, as well as with the results of the studies from other countries. Moreover, we presented treatment outcomes of soldier patients with TB followed in our hospital between 2002 and 2010, which are considered as a risk group for TB in our country.

Materials and Methods

In the present retrospective study, data of patients diagnosed with TB in a chest diseases clinic in Istanbul between 1 January 2002 and 31 December 2010 were reviewed. Approval of the Ethical Committee was obtained. In all patients, bacteriological sampling (sputum and/or gastric lavage) was observed to be performed for at least three times prior to the treatment. All patients with pleurisy underwent pleural puncture and biopsy, and treatment was commenced based on clinical and radiological consistency and pleural adenosine deaminase values in the patients in whom diagnosis could not be established by histopathological or microbiological examination. The patients underwent chest x-ray, complete blood count, routine biochemical analyses, and tuberculin skin test at the beginning of the treatment. Radiological involvement on the chest x-rays of the patients, which were taken at the time of hospitalization, were evaluated by modifying the scale used in the study of Somoskovi et al (4). (Table 1).

Table 1: Modified Somoskovi scale used for radiological evaluation.

Groups	Involved Pulmonary Area
Mild	Radiological involvement accounts for 1/6 of both pulmonary areas
Moderate	Radiological involvement accounts for 2/6 of both pulmonary areas
Severe	Radiological involvement accounts for 3/6 of both pulmonary areas or more

Data regarding age, smoking status, duration of hospital stay, presence of Bacillus Calmette–Guérin (BCG) vaccination, state of TB contact, diagnoses, received treatments, concomitant diseases and sputum conversion time were recorded. Terms used in the present study are defined below and in accordance with the definitions in "Tuberculosis Diagnosis and Treatment Guideline" published in 2011 by Turkish Republic Ministry of Health Department of Tuberculosis Control (5).

Pulmonary Tuberculosis: TB that involves lung parenchyma.

Extrapulmonary tuberculosis: Acid-resistant bacilli (ARB) positive samples that are obtained from organs other than lung parenchyma, or patients with histological and clinical findings consistent with TB.

Pulmonary + extrapulmonary tuberculosis: They are considered in the pulmonary TB indicating that patients have both involvements.

Smear-positive pulmonary tuberculosis: Patients with at least two sputum smears (or in fasting gastric juice, induced sputum, bronchoscopic lavage) positive for ARB; or patients with only one sputum smear positive for ARB and having radiological findings consistent with pulmonary TB and in whom treatment of TB was determined by a physician; or patients with one sputum smear positive for ARB and with positive TB culture.

Smear-negative pulmonary tuberculosis: Patients with negative sputum smear but positive culture; or patients with clinical and radiological findings consistent with TB and three negative sputum smear and without clinical response despite receiving broad-spectrum antibiotic (not containing quinolone) therapy for at least one week and who were determined to receive treatment for TB in a hospital where differential diagnosis could be performed.

New case: Patients not receiving treatment for TB previously or receiving treatment for less than one month.

Cure: A patient with positive sputum smear at the beginning of the treatment whose sputum smear then converted to negative and with negative sputum smear once more at the end of the treatment.

Treatment completion: Either the patient was smear-negative or smear-positive at the beginning, completion of the treatment considering the patient being improved both clinically and radiologically despite the absence of sputum examination at the end of the treatment.

Treatment success: Cure + treatment completion.

Case with unsuccessful treatment: Newly diagnosed cases in whom sputum smears or cultures are positive for bacillus 5 months or more after the treatment.

Death: Death of the patients in the course of treatment due to any reason.

Statistical Analysis

Continuous variables were described as mean±standard deviation and range. Percentile values were described without decimals. Tuberculosis case fatality rate was defined as the ratio of patients died due to TB to all patients with TB. Patients who died of other causes during TB treatment were excluded.

Results

A total of 1,871 soldier patients were hospitalized in our clinic with the diagnosis of TB between 2002 and 2010. Soldier patients admitted to our hospital with the pre-diagnosis of TB were hospitalized, their diagnoses were confirmed, and the treatment was commenced. Since non-military patients were not included in the study, the study group consisted of males. Review of the 9-year (2002-2010) data of military patients with TB revealed a reduction in the number of patients with TB admitted to our clinic. In the 9-year period, the mean annual number of inpatients with the diagnosis of TB was 208±125. The mean age of all TB patients was 21.5±2.2 years, and their mean duration of hospital stay was 32.06±15.3 days. The mean conversion time was 27.6±15.1 days. The rates of patients with pulmonary and extrapulmonary TB were 81.7% and 18.3%, respectively (Table 2). The mean treatment success rate was 91.3% within the 9-year period.

Six patients died due to TB between the years 2002 and 2010; they were HIV negative and had no comorbid disease. All of them died in the hospital during antituberculosis treatment. The 9-year TB case fatality rate was 0.32%. Annual fatality rates for TB were 0.25% in 2002, 0.24% in 2003, 1.27%

Table 2: Case fatality rates and treatment outcomes between 2002 and 2010.

Year	Mean	2010	2009	2008	2007	2006	2005	2004	2003	2002
Number of cases	208	65	92	89	168	191	232	236	404	394
Rate of EPTB (%)	18.3	23.1	20.5	16.1	21.6	18.1	25.6	16.7	12.6	10.9
Rate of PTB (%)	81.7	76.9	79.5	83.9	78.4	81.9	74.4	83.3	87.4	89.1
Total treatment success (%)	91.3	89.2	93	92	89.9	94.3	92.7	89.8	90.8	90.6
Fatality rate (%)	0.32	0.0	0.0	1.12	0.0	0.0	0.0	1.27	0.24	0.25

EPTB: extrapulmonary tuberculosis, **PTB:** pulmonary tuberculosis.

in 2004, 0% in 2005, 2006 and 2007, 1.12% in 2008, and 0% in 2009 and 2010. The mean age of the patients who died was 26±6.6 years (Table 3).

All of these patients were male and the mean duration of hospital stay was 53.5±47.2 days. Of the patients who died, 83% had BCG scar and 33% had history of TB contact. The diagnosis of the patients who died was new case, smear-positive pulmonary TB; one patient had additional empyema. All patients received quartet of anti-TB treatment. The mean conversion time of patients who died was 29.7±54.1 days and their mean duration of military service was 8.2±3.2 months. We used sputum smear examination for conversion. The mean pack-years of smoking was 8±11.4. Of the patients, four were primary school graduates, whereas two were high school graduates. Two of them had history of narcotic usage and one of them had history of alcohol usage. None of the patients had any resistance of antituberculosis drugs. Evaluation of radiological involvement revealed that five patients had severe and one patient had moderate radiological involvement. Died patients did not any adverse drug reactions with antituberculosis treatment.

Discussion

Tuberculosis remains as the second leading infectious disease causing death following HIV worldwide (1). If not treated, approximately 70% of smear-positive, HIV negative patients die in 10 years within the natural course of the disease. Mortality rates have dramatically reduced along with the combined use of anti-TB drugs, which were found in 1940s. The TB incidence and TB-related death rate have been decreasing worldwide. The global TB control strategy of WHO, named as 'The Stop TB Strategy', aimed at reducing the prevalence and mortality rates of TB by 50% until 2015 (2).

Tuberculosis fatality rate is the ratio of patients died due to TB to all patients with TB; in other words, it indicates how many TB patients died due to this disease. TB mortality indicates the frequency of death due to TB in the population (including patients and healthy individuals). Although mortality and fatality rate are different epidemiologic definitions, they are confused with each other. TB mortality is indirectly calculated by formulas using TB incidence and case fatality rates in the countries where recording systems are inadequate (6,7).

According to the Global Tuberculosis Control Report of the WHO, the incidence and prevalence of TB in Turkey in 2010 were 28/100,000 and 24/100,000, respectively, and the mortality associated with TB was 3.1/100,000 (1). TB-related mortality rates in Turkey were 262/100,000 in 1935 and 204/100,000 in 1950, and along with the combined use of anti-TB drugs, TB-related mortality rates were reported to be 20/100,000 in 1970 and 8.2/100,000 in 1982 (8). There are not any studies or data about case fatality rate of pulmonary tuberculosis of Turkish patients in the current literature. Evaluation of the data from Turkey revealed a reduction in TB mortality. A remarkable reduction has been observed

Table 3: Demographic and clinical characteristics of the patients who died.

Patient	1	2	3	4	5	6	Mean±SD
Age	21	35	34	22	21	23	26±6.6
Duration of hospital stay	79	135	44	4	38	21	53.5±47.2
Diagnosis	PTB + Empyema	PTB	PTB	PTB	PTB	PTB	-
Number of BCG scars	2	1	1	0	2	1	-
Tuberculosis Contact	Absent	Absent	Present	Absent	Present	Absent	-
Educational status	Primary school	High school	Primary school	Primary school	Primary school	High school	-
Smoking (pack/year)	4	30	0	0	10	4	8±11.4
Treatment	HRZE	HRZS	HRZS	HRZE	HRZS	HRZE	-
Radiology	Severe	Severe	Moderate	Severe	Severe	Severe	-
Duration of military service (months)	6	10	9	12	9	3	8.2±3.2

PTB: pulmonary tuberculosis, **SD:** standard deviation, **H:** isoniasid, **R:** rifampicin, **Z:** pirazinamid, **E:** ethambutol, **S:** streptomycin, **BCG:** bacillus calmetto guerin.

in mortality in years with the establishment of TB control organizations, widespread use of anti-TB drugs, and with directly supervised treatment applications initiated in 2000s.

In the 2011 Report of Tuberculosis Fight in Turkey, treatment success rates were reported to be 90.4% for pulmonary TB, 92.4% for extrapulmonary TB, and 91% for all cases (3). In the present study, the mean treatment success rate was determined to be 91.3% in the 9-year period. The treatment success rate of the present study was in line with that of Turkey. A decrease was observed in years in the number of patients followed and treated for TB. While the number of patients who were followed and treated was 394 in 2002, it was 65 in 2010. Therefore, the high standard deviations of the mean values of parameters reported in the present study might be attributed to the decrease in the number of patients in years. According to the 2011 Report of Tuberculosis Fight in Turkey, the pulmonary TB-related mortality rate was 3.1%, the extrapulmonary TB-related mortality rate was 2.5%, and the mortality rate for all cases (including both old and new cases) was 3.0% in 2008. The TB-related mortality rates were 2.8% in new cases and 4.4% in old cases, and it was 13.4% for patients aged ≥65 years. TB-related mortality rates were 2.7% in 2005, 3.0% in 2006 and 2.9% in 2007. In the present study, TB-related fatality rate was found to be 0.32%. This fatality rate is lower than that reported for Turkey. We think one of the explanation for low TB-fatality rate is that our patients were young and the other is that all patients were treated in the hospital until sputum conversion and treated with Directly Observed Treatment (DOT).

Tuberculosis-related fatality rates have been calculated for different countries. Shen et al. found total fatality rate to be 5.5% in culture-positive pulmonary TB patients; however, 50.5% of deaths occurred due to causes other than TB (9). They reported risk factors for mortality as advanced age, male gender, sputum smear positivity, and comorbidity (9). In the study conducted in Spain, Cayla et al. found fatality rate to be 1.8% (10). In their study, Kourbatova et al. found fatality rate to be 3.6% (11). A study from India found TB case fatality rate to be higher (12%) in patients previously received treatment for TB and to be lower (2%) in patients with extrapulmonary TB (12). A study conducted in Brazil found TB case fatality rate to be 7.2% in all TB patients between 2000 and 2004 (13). In a study conducted in our clinic, Kartaloğlu et al. reported that 133 of 22,651 patients died due to TB in a 23-year period (1977-1999) and that fatality rate was 0.587% (14). As compared with this 30-year period, the fatality rate was observed to be decreased in the 9-year period in the present study.

None of the patients who died had concomitant disease and all were HIV negative. Of the dead patients, 33% had a history of TB contact and 66% were smokers. The mean age of all TB patients was 21.5±2.2 years, and their mean duration of hospital stay was 32.06±15.3 days. The mean age and the mean duration of hospital stay of patients who died were 26.6±6.6 years and 53.5±47.2 days, respectively. Evaluation of characteristics of patients who died revealed that their mean age was high and that they had severe radiological involvement and a long duration of hospital stay. The high standard deviation of duration of hospital stay in patients who died resulted from death of a patient due to TB on the 4th day of hospitalization. It was remarkable that 83.3% of the patients were immunized with BCG vaccine. In a study conducted in our clinic, BCG scar was determined in 70.5% of 404 TB patients (15).

Conclusion

We are in the opinion that, the present study is of importance as it highly represents young male population of Turkey and exposes the TB data of a risk group in detail. The total success rate was found to be high as 91.3% and TB case fatality rate was found to be quite low as 0.32%. Improvement is being observed and maintained in almost all parameters in our TB series in years due to directly observed treatment, which is resolutely implemented in our hospital. We think that, aspects of the TB problem in Turkey would be exposed in detail by means of case series in populations at high risk for TB, as our population, as well as cross-sectional epidemiological studies and treatment outcomes that would be reported.

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