Treatment results of tuberculous patients in Assiut Chest Hospital

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Aims
The improvement of the quality of TB treatment is essential to control of TB. The aims of this study were to identify the outcomes of TB treatment in patient recorded in Assiut Chest Hospital during the period from 2011 to 2015 and factors associated with undesirable treatment outcome and to estimate proportion of drug resistance among TB patients and identify factors associated with it.

Patients and methods
This study was a descriptive retrospective review of TB patients' registry. All tuberculous patients notified to the TB registry in Assiut Chest Hospital in the period from 1 January 2011 to 31 December 2015 and completed at least 6 months of treatment management were included in the study. Patients' records were reviewed for the following data: personal data, presenting symptoms, pattern of TB, regimen of treatment, and drug-resistant TB.

Results
The percentage patients with drug resistance were 60.9%. A total 75.1% of patients were cured and 5.1% of patients died. Cure rate was significantly higher in patients with extrapulmonary TB compared with 63.5% in pulmonary TB patients. The predictors for undesirable treatment outcomes were male sex, positive family history, pulmonary TB patients.

Conclusion
The success rate of all registered patients was satisfactory but, below WHO target, one-fifth showed failure of treatment was associated with male sex, illiterate, and drug-resistance *Mycobacterium tuberculosis*, success treatment was highest in extrapulmonary TB patients, cure rate was highest in nonresistant TB patients, drug resistance represented about two-thirds of all studied TB patients, and ~ 65% of pulmonary TB patients had drug resistance.

Keywords:
outcome, regimen, resistance, tuberculosis

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Introduction

Tuberculosis (TB) is a growing international health concern. It is a big killer among the infectious diseases in the world, after years of decline, TB has re-emerged as a serious public health problem worldwide, especially with increased *Mycobacterium tuberculosis* (MTB) strains which hinder the success of TB control programs [1].

The WHO proclaims TB as a worldwide public health emergency since 1993 and, since then it has set a target treatment success rate of 85% for annually detected smear positive cases and advocate strategy known as directly observed treatment, short course (DOTS) for TB control and from that time DOTS is considered the main tool to improve the case detection rate and integration of DOTS service with other health care [2].

In Egypt, TB is a major public health problem. It is estimated that ~19 000 new cases of TB develop annually. The primary strategy to expand the coverage of DOTS is to integrate TB treatment in primary health care centers. TB patients can go to any primary health care center near to their home for treatment and will only be required to visit the chest facility once a month for follow-up until their treatment is completed [3].

TB disease caused by organisms resistant to at least the two most potent first-line drugs (isoniazid and rifampicin) is called multi-drug-resistant TB (MDR-TB) and its treatment takes longer and requires drugs that are more toxic and more expensive [4].

The global plan to stop TB 2006–2015 (the Global Plan), was launched in January 2006 to prevent new

cases of MDR-TB and extensive drug resistance tuberculosis (XDR-TB) as well as accelerate the treatment of drug-resistant cases and that plan included the treatment of 1.6 million MDR-TB and XDR-TB patients by 2015 [5].

The number of people diagnosed with MDR-TB tripled between 2009 and 2013, and reached 136 000 worldwide. This was equivalent to 45% of the estimated MDR-TB cases among notified TB patients [1].

The aims of the study were to identify the outcomes of TB treatment in Assiut Chest Hospital during the period from 2011 to 2015, to clarify factors associated with undesirable treatment outcome and to estimate proportion and risk factors of drug resistance among TB patients.

Patients and methods

Patients

This study was a descriptive retrospective review of TB patients' registry. All tuberculous patients notified to the TB registry in Assiut Chest Hospital in the period from 1 January 2011 to 31 December 2015 and completed at least 6 months of treatment management were included in the study.

This study was approved by the Institutional Ethics and Research Committee of the Faculty of Medicine, Assiut University, Assiut, Egypt.

Ethical consideration

(1) Researcher got the proposal before starting data collection via the Ethics Committee of Assiut Faculty of Medicine.
(2) Privacy and confidentiality of all the information were assured following approval.
(3) Acceptance of Assiut Directorate of Health has been granted.
(4) Official approval from Assiut Chest Hospital to take review of all files.

Methodology

TB patients' records were reviewed for the following data:

(1) Personal data (age, sex, residence, occupation, educational level, marital status, and special habits).
(2) Presenting symptoms including: chest symptom, weight loss, fever, chronic diarrhea, etc.
(3) Pattern of TB: pulmonary involving lungs/extrapulmonary (which refer to a case of TB involving organs other lungs, e.g. pleural, lymph node, bone, gastrointestinal tract, skin, genital tract, and other).
(4) Regimen of treatment: either regimen 1 or regimen 2.

Regimen 1: treatment regimens have an initial (or intensive) phase lasting 2 months and a continuation phase usually lasting 4 or 6 months. Initial phase, consists of isoniazid, rifampicin, pyrazinamide, and ethambutol or streptomycin. Continuation phase consisting of isoniazid and rifampicin [1].

Regimen 2: treatment regimen consists of five drugs in the initial phase (2 months) and three drugs in the continuation phase (4–6 months). Three of the drugs isoniazid, rifampicin, and ethambutol are given throughout the treatment (Egyptian National Tuberculosis Control Programme, 2012) [4].

(5) Treatment outcome: according to National Tuberculosis Program 2014, outcomes were classified to cure, death, failure, or defaulted.

Working operational definition:

The cure was defined as: a patient who is smear negative in the last month of treatment and on at least one previous occasion.

Treatment failure was defined as: a patient with sputum smear or sputum culture positive at 5 months or later after the initiation of anti-TB treatment.

Treatment default was defined as: interruption of treatment for more than 2 months.

(6) Drug-resistant TB:

MDR-TB is resistant to isoniazid and rifampin [3].

Extensively drug-resistant TB is a form of MDR-TB that is not only resistant to isoniazid and rifampin, but also resistant to Fluor quinolones and one of the second-line treatment drugs [3].

Data collection

All data registered in patient's records were retrieved, organized, and computerized and prepared for analysis.

Statistical analysis

Analysis of data were done using Statistical Package for the Social Science program, version 16 (International Business Machines Corporation (IBM), Armonk, New York, USA) under Windows 10. Statistical methods were applied including: descriptive statistics as mean, SD, frequencies, and percentages were

calculated. Test of significance, χ^2 was used to compare the difference in distribution of frequencies among different groups. Multivariate logistic regression was used to detect predictors of undesirable outcome.

Ethical considerations

(1) Approval of the Ethics Committee of Assiut Faculty of Medicine was obtained before starting data collection.
(2) Acceptance of Assiut Directorate of Health has been granted.
(3) Official approval from Assiut Chest Hospital to take review of all files.
(4) Privacy and confidentiality of all the information were assured.

Results

The total number of recorded TB patients during the period of the study was 530 patients.

Age of the studied patients ranged from 1.0 to 85.0 years (34.05 ± 18.79). Male patients represented 49.2% and about 66% of patients came from rural areas. Approximately one-third of the patients were illiterate and 11.1% had a higher level of education (more than secondary and university). About 60% of male patients were smokers. Family history of TB was reported (7.5%) of the patients.

Table 1 shows that 50.8% of the patients had pulmonary TB. TB of gastrointestinal tract comprised 31% of the extrapulmonary TB. The regimen of treatment in the studied TB cases was about 88% were managed by regimen 1, whereas 12% were managed by regimen 2.

Table 2 shows the percentage patients with drug resistance were 60.9%.

A total of 26.3% of the patients developed resistance to ethambutol and 14.2% of the patients had resistance to pyrazinamide.

Table 3 shows that 64.7% of pulmonary TB patients had resistance to TB treatment.

Table 4 shows that 75.1% of patients were cured and 5.1% of patients died. The table also shows that the percentage of defaulted cases was 10.4% and failure rate was 9.4%.

Table 5 shows that patients with extrapulmonary TB type had a higher cure rate (86.7%) in compared with those with pulmonary TB (63.5%). Patients under treatment by regimen 1 had a higher cure rate (76.3%) in compared with those who under treatment by regimen 2 had (66.1%).

Table 1 Pattern and type of regimen in tuberculosis in the studied cases, Assiut Chest Hospital, 2011-2015

Types of TB	*n* (%) (*n*=530)
Pulmonary	266 (50.2)
Extrapulmonary	264 (49.8)
Type of extrapulmonary	
Gastrointestinal	82 (31.1)
Lymphatic	61 (23.1)
Meninges	16 (6.1)
Pleural	56 (21.2)
Pott's	38 (14.4)
Skin	11 (4.2)
Regimen	
Regimen I	468 (88.3)
Regimen II	62 (11.7)

TB, tuberculosis.

Table 2 Drug resistance among the studied tuberculosis patients, Assiut Chest Hospital, 2011-2015

Drug resistance	*n* (%) (*n*=530)	%
Nonresistant	207 (39.1)	39.1
Resistant	323 (60.9)	60.9
Type of drug resistance		
INZ resistance	77 (23.8)	23.8
RIF resistance	64 (19.8)	19.8
PYR resistance	46 (14.2)	14.2
ETM resistance	85 (26.3)	26.3
Multi-drug resistance	51 (15.8)	15.8

ETM, ethambutol; INZ, isoniazid; PYR, pyrazinamide; RIF, rifampicin.

Table 3 Drug resistance according to type of tuberculosis, Assiut Chest Hospital, 2011-2015

	Resistance [*n* (%)]		*P*
	Resistant (*n*=323)	Nonresistant (*n*=207)	
Type of TB			
Pulmonary	172 (64.7)	94 (35.3)	0.078
Extrapulmonary	151 (57.2)	113 (42.8)	

TB, tuberculosis.

Table 4 Treatment outcomes of the studied tuberculosis patients, Assiut Chest Hospital, 2011-2015

Outcome	*n* (%) (*n*=530)
Cure	398 (75.1)
Failure	50 (9.4)
Defaulted	55 (10.4)
Died	27 (5.1)

Table 5 Outcome of tuberculosis treatment according to type of tuberculosis and regimen of treatment, Assiut Chest Hospital, 2011-2015

	Outcome [*n* (%)]			
	Cure	Failure	Defaulted	Died
Type of TB				
Pulmonary	169 (63.5)	48 (18.0)	32 (12.0)	17 (6.4)
Extrapulmonary	229 (86.7)	2 (0.8)	23 (8.7)	10 (3.8)
Regimen				
Regimen I	357 (76.3)	43 (9.2)	46 (9.8)	22 (4.7)
Regimen II	41 (66.1)	7 (11.3)	9 (14.5)	5 (8.1)

TB, tuberculosis.

Table 6 Outcome of tuberculosis treatment according to type of tuberculosis, regimen, and drug resistance, Assiut Chest Hospital, 2011-2015

	Outcome [*n* (%)]		*P*
	Cure	Other outcomes	
Type of TB			
Pulmonary	169 (63.5)	97 (36.5)	0.000*
Extrapulmonary	229 (86.7)	35 (13.3)	
Regimen			
Regimen I	357 (76.3)	111 (23.7)	0.082
Regimen II	41 (66.1)	21 (33.9)	
Drug resistance			
Resistant	227 (70.3)	96 (29.7)	0.001*
Nonresistant	171 (82.6)	36 (17.4)	

TB, tuberculosis. *Significant difference (*P*<0.05)

Table 7 Multiple logistic regression predicting factors associated with undesirable treatment outcome, Assiut Chest Hospital, 2011-2015

	B	SE	*P*	OR	95% CI	
					Lower	Upper
Male sex	0.534	0.217	0.014*	1.706	1.115	2.611
Positive family history	0.760	0.355	0.032*	2.139	1.066	4.290
Pulmonary type of TB	1.204	0.227	0.000*	3.333	2.136	5.200
Drug resistance	0.618	0.230	0.007*	1.855	1.182	2.913
Constant	–2.569	0.267	0.000*	0.077		

CI, confidence interval; OR, odds ratio; TB, tuberculosis.
*Significant difference (*P*<0.05)

Table 6 shows that cure rate was significantly higher in patients with extrapulmonary TB compared with 63.5% in pulmonary TB patients.

Table 7 shows that by multivariate analysis, male sex, positive family history, pulmonary TB patients were the predictors for undesirable treatment outcomes.

Discussion

Despite the availability of effective drugs, TB is still a global emergency and one of the major public health problems in the 21st century. It is not only a public health problem, but also a socioeconomic issue [6].

In Egypt, in the early 1990s TB control faced many problems were: refusal by tuberculous patients to be hospitalized for their treatment, high defaulter rate, increasing levels of resistance against antituberculous drugs and insufficient and deficient health education to both community and health staff [7].

This study was a retrospective review of 530 records of TB patients attending Assiut Chest Hospital during the period from 2011 to 2015.

In the present study, TB was more common among female patients (50.8%) than male patients (49.2%).

Different results were obtained by Makhlouf in a retrospective study done in Assiut University Hospitals during the period from 1990 to 1993. They revealed that male cases were 58.2% of all cases and females were 41.8%. The difference between the two studies may be due to change in community habits with time as increase female employment, movement, and more exposure to infection [8].

In the present study, the total number of extrapulmonary TB cases was 264 (49.8%) of all TB cases and pulmonary cases were 266 (50.2%).

Percentage of extrapulmonary TB cases in our results was higher compared with results in El-Menia that found that 66.4% of cases were pulmonary cases and 33.58% of cases were extrapulmonary cases. In Dakahlia, it was also found that 66.9% were pulmonary TB and 33.1% were extrapulmonary TB cases [9,10].

Regarding the cure rate in our study, it was generally as high as 75.1%. However, the treatment success rate was below the recommended global target of 85% (WHO, 2015). In the study of El-Shabrawy and El-Shafei, the cure rate was slightly higher 80%.Other study in El-Behira Governorate reported (81.5%) cure rate of TB patients [11].

This study revealed that the overall unsuccessful TB treatment outcome rate was 24.9% (default, treatment failure, and death). This finding is against another study which reported 16.7% of unsuccessful outcome. A similar finding was found in Sharkia Governorate as 25.5% of tuberculous patients had unsuccessful treatment outcome.

The percentage of defaulters which constitutes a great problem during TB treatment was 10.4%. In El-Behira Governorate the default rate was 20.4% and El-Minia Governorate was 10.57% [10,11].

TB treatment failure in Egypt is a serious problem facing national TB control programs due to different risk factors regarding the disease. In this study, failure rate was 9.4% of TB patients lower than that reported in the study of El-Shabrawy and El-Shafei [12].

Our results showed that treatment failure was found higher in patients under regimen II than regimen I (33.9 vs. 23.7%); however in other studies the outcome was not affected by the regimen used. Dooley *et al.* [13], found that treatment failure among patients with regimen II was 30.1 and 69.9%. The current study found that the treatment regimen had significant predictive effect on the outcome in contrary with other previous studies which reported that the outcome was not affected by the regimen used [14,15].

In multivariable logistic regression the unsuccessful treatment outcomes of our finding were significantly higher in male sex; pulmonary TB, negative family history, and drug resistance. In comparison Albuquerque and colleagues, found that a history of prior TB treatment was significantly associated with unsuccessful treatment outcomes [16]. Similarly, Anunnatsiri and colleagues, found that a history of previous TB treatment was associated with treatment failure and death [17,18]. Before TB treatment, association with treatment failure is a clear indication of the importance of properly completing treatment and monitoring patients [19].

Therefore, careful monitoring of transmission trends of drug-resistant strains should be considered a priority to ensure a successful TB control program. This should be done through increased awareness, early case detection, rapid drug susceptibility testing, a full course of effective anti-TB treatment, continuous community-based surveillance of anti-TB drug resistance, and control of drug-resistant TB at the border entry points with neighboring TB high-burden countries.

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Conflicts of interest
There are no conflicts of interest.

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