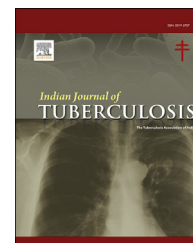


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Original article

Treatment outcome of tuberculosis treatment regimens in Kandahar, Afghanistan

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ABSTRACT

Background: Tuberculosis (TB) is a chronic disease that mostly affects low-income countries. TB is transmitted through droplet aerosolization from a person with active pulmonary TB. Afghanistan is one of the 22 high TB burden countries where 39,445 people develop this disease and 7840 people die each year. Treatment outcome is one of the best measurements that explain how the current regimen works.

Material and methods: This was a retrospective cohort study, conducted in Kandahar Province, to find out the treatment outcome of anti-TB drugs regimens in TB patients. Data of pulmonary and extra-pulmonary TB patients, who fulfilled the eligible criteria of the study and were treated from 2005 to 2015, was retrieved from their medical record forms.

Results: Among 1000 TB patients, 599 (59.9%) were females and 401 (40.1%) males; most of the patients (678/1000 [67.8%]) were from Kandahar city while 322/1000 (32.2%) were from the other districts of Kandahar. Mean age of the patients were 36.1 years with SD of 19.3 years. Main signs and symptoms of fever, cough, and weight loss were present in 949/1000 (94.9%), 880/1000 (88%), and 544/1000 (54.4%) of the patients, respectively. On first visit 459/1000 (45.9%) patients were sputum AFB (acid fast bacilli) positive. Majority (247/459 [53.8%]) of these patients were AFB 2+. After 2 months of intensive anti-TB treatment, 9/459 (1.9%) patients were still AFB positive (1+). Treatment outcome of these 1000 patients showed that 479 (47.9%) completed the treatment, 298 (29.8%) were cured, 35 (3.5%) failed the anti-TB treatment, while 5 (0.5%) patients died.

Conclusion: This clearly shows that TB is still one of the major threats to the people of Kandahar Province. There are cases of TB who do not respond to the first line regimens of anti-TB drugs advised by WHO and Afghan Ministry of Public Health (MoPH).

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1. Introduction

Tuberculosis is one of the world's deadliest diseases. During the last five years, TB is the leading cause of death from a single infectious agent, ranking above HIV/AIDS.¹ In 2016, worldwide the incidence of TB was 10.4 million people with the mortality of 1.7 million people. More than 95% of these deaths occurred in low- and middle-income countries.¹ Globally, this fatal disease has an enormous economic impact on many countries.² *Mycobacterium tuberculosis*, the causative agent of TB, infects one-fourth of the world's population.³

Although the incidence of tuberculosis declined greatly during the twentieth century in the industrially developed nations, these nations are now experiencing an upsurge of this disease. Multi-drug resistant tuberculosis (MDRTB) has become a major problem in several regions throughout the world and in some countries extensively resistant forms of the disease extensively drug-resistant tuberculosis (XDR-TB) have emerged and raise the very serious threat of untreatable disease.⁴

Due to the presence of several decades conflicts in the country, limited or even no studies have been performed in this field. According to 2014 tuberculosis report of World Health Organization (WHO), Afghanistan is included in the category of the world 22 high TB-burden countries. With a population of nearly 31 million, Afghanistan has about 39,445 new cases each year and an overall estimated TB prevalence of nearly 69,000 cases. In 2013, the estimated rate (per 100,000 population) of TB prevalence, incidence, and mortality were 340 (178–554), 189 (167–212), and 42 (27–53), respectively.⁵

Between 2000 and 2014, the estimates of TB incidence in Afghanistan have remained nearly stable as nearly 189 per 100,000 population. On the other hand, case detection rate has gradually increased from 19% (18–21%) in 2000 to 53% (47–60%) in 2014.⁶

WHO targeted treatment success rate was 85% for the year 2015. Some countries have already achieved this target but some are still behind.

There are studies done to identify the treatment outcome of TB treatment regimen and the associated factors that can influence the treatment outcomes in different countries. Among associated factors that were highlighted in the literature were old age,^{7–12} male sex,^{11–13} co-morbid diseases such as diabetes and HIV,^{11,14} advanced chest radiographic findings,^{11,13} history of previous TB treatment,^{8,15,16} unemployment,^{8,15} multi-drug resistance status,⁹ alcoholism^{15,17} and as well as drug abuse.¹⁵

WHO has estimated the treatment success rate around 86% in Afghanistan but there are not enough studies in the country to strongly support its reliability.⁵

Afghanistan is one of the 22 high TB burden countries where 39,445 people develop this disease and 7840 people die each year. Treatment outcome is one of the best measurements that explain how the current regimen works. Many studies about treatment outcome of TB in different period of time and several places out of Afghanistan have been carried out but due to the long-lasting conflict in Afghanistan limited studies in this field have been performed and no published study has been done in Kandahar, yet.¹⁸ Through this study,

we will be able to find the treatment outcome of TB treatment regimen in Kandahar Province.

2. Materials and methods

2.1. Study design

This was a retrospective cohort study. Data of patients, who fulfilled the eligible criteria of the study and were treated during the 11 years period (2005–2015), was retrieved from their medical record forms.

Medical record forms were screened in a backward order, starting from 2015 to 2005 and relevant information was collected with data collection sheet. Data collection sheets were prepared to pick up all essential data related to our study, including; demographics, symptoms, laboratory investigation plus other essential information.

2.2. Study population

The study population was comprised of all forms of TB patients who were treated in provincial hospital and TB centers of Kandahar Province. We screened medical record forms of tuberculosis patients who were treated during 2005–2015. As per the inclusion and exclusion criteria, 1000 patients were recorded.

2.3. Research question

What is the treatment outcome of current tuberculosis treatment regimen in Kandahar?

2.4. Primary objective

- To achieve the treatment outcome of anti-TB treatment regimen in patients.

2.5. Inclusion criteria

- All age groups
- Pulmonary and extrapulmonary TB patients treated with standard short course regimen (2Isoniazid, Rifampicin, Pyrazinamide, Ethambutol (HRZE)/4HR) or receiving the 8-month retreatment regimen (2HRZES/1HRZE/5Isoniazid, Rifampicin, Ethambutol (HRE))

2.6. Exclusion criteria

- Pregnant women
- Patients who changed regimens from 2HRZE/4HR or 2HRZES/1HRZE/5HRE due to any problems such as adverse events or drug resistance.

2.7. Sample size calculations

Sample size was determined using the formula: $n = Z^2pq/d^2$. Our sample size was 1000 patients.

2.8. Ethical considerations

Ethical approval was taken from Kandahar University Ethics Committee.

2.9. Data analysis

Data was analyzed with SPSS (version 22).

2.10. Operational definitions

- Sputum Smear Positive:** Patients were considered smear positive, if at least two sputum specimens were positive for AFB (acid fast bacilli) by microscopy, one sputum specimen positive for AFB with the presence of chest radiographic abnormalities suggestive of pulmonary tuberculosis (PTB) or at least one sputum smear positive with a culture positive conformity.¹⁷
- Sputum Smear Negative:** A case of pulmonary TB is considered to be smear-negative if at least two sputum specimens at the start of treatment are negative but culture positive for AFB. Or meet the following diagnostic criteria:
 - Decision by a clinician to treat with a full course of anti-TB therapy
 - Radiographic abnormalities consistent with active pulmonary TB
- New and previously treated patients with their treatment regimens:
 - New patients:** Who have never had treatment for TB, or have taken anti-TB drugs for less than 1 month. A total of six-month treatment (category-1) is given in two phases; intensive phase of two months with regimen consisting of isoniazid (H), rifampicin (R), pyrazinamide (Z) and ethambutol (E) {2HRZE} and the continuation phase of four months comprising isoniazid and rifampicin (4HR).¹⁷
 - Previously treated patients:** Default, failure or relapse cases with current TB disease are defined previously treated patients. They are taking the eight-month standard treatment regimen (category-2) containing HRZE for two months; HRZE for the third month and HRE for the continuous 5-month phase {2HRZES/1HRZE/5HRE}.¹⁷
- Treatment outcome:
 - Cure:** A patient whose sputum smear or culture was positive at the beginning of the treatment but who was smear- or culture-negative in the last month of treatment and on at least one previous occasion.
 - Treatment completed:** A patient who completed treatment but who does not have a negative sputum smear or culture result in the last month of treatment and on at least one previous occasion.
 - Treatment failure:** A patient whose sputum smear or culture is positive at 5 months or later during treatment. Also included in this definition are patients found to harbor a multidrug-resistant (MDR) strain at any point of time during the treatment, whether they are smear-negative or -positive.
 - Died:** A patient who dies for any reason during the course of treatment.

- Default:** A patient whose treatment was interrupted for 2 consecutive months or more.
- Transfer out:** A patient who has been transferred to another recording and reporting unit and whose treatment outcome is unknown.
- Treatment success:** The sum of cured and completed treatment.¹⁷

3. Results

This was a retrospective study conducted in Kandahar. Data were collected from the health clinics and district hospitals of all the 17 districts of Kandahar Province. For this study, medical records of 1000 TB patients were observed according to the inclusion and exclusion criteria.

3.1. Baseline characteristics

Among 1000 TB patients, 599 (59.9%) were females while 401 (40.1%) were males. The mean age was 36.1 years, with SD of 19.3 years (range 1–100 years). Majority of the patients (678 [67.8%]) were from Kandahar city, while 322 (32.2%) were from other districts of Kandahar province as well as surrounding provinces (Table 1).

3.2. Signs and symptoms

Percentage of each symptom based on available data was recorded. Among these patients, 880/1000 (88%) of the patients were complaining from cough while 103/1000 (10.3%) patients were not coughing. Fever was present in 949/1000 (94.9%) patients, weight loss in 544/1000 (54.4%), chest pain in 101/1000 (10.1%), 37/1000 (3.7%), while dyspnea in 108/1000 (10.8%) of the TB patients (Table 2).

3.3. Diagnostic findings

Among the TB patients, 984/1000 (98.4%) were new cases while 16/1000 (1.6%) were retreatment cases. Majority (670/1000

Table 1 – Distribution of the patients.

Address	Frequency, n	Percent, %
Kandahar City	678	67.8
Arghistan District	3	0.3
Daman District	8	0.8
Dand District	36	3.6
Ghorak District	1	0.1
Khak Rez District	23	2.3
Maiwand District	6	0.6
Mianashin District	4	0.4
Nesh District	4	0.4
Panjwai District	93	9.3
Shah Wali Kot District	47	4.7
Shorawak District	1	0.1
Spin Boldak District	4	0.4
Takhta Pul District	1	0.1
Zarai District	14	1.4
Surrounding Provinces	33	3.3
Total	1000	100

Table 2 – Main signs and symptoms present in TB patients.

Symptom/sign	Number (/1000)	Percentage, %
Fever	949	94.9
Cough	880	88.0
Weight loss	544	54.4
Chest pain	101	10.1
Dyspnea	108	10.8

[67%]) of the patients were having pulmonary tuberculosis while 330/1000 (33%) of the patients were diagnosed as extra-pulmonary tuberculosis. Contact with a TB patient was present in only 117/1000 (11.7%) patients, with 332/1000 (33.2%) patients not having any previous history of contact with TB patients.

On first visit, 459/1000 (45.9%) of the patients were sputum AFB (acid fast bacilli) positive. Majority (247/459 [53.8%]) of these patients were AFB 2+. After 2 months of intensive anti-TB treatment, 9/459 (1.9%) patients were still AFB positive (1+) (Table 3).

3.4. Treatment regimens

For all the patients, 6 months anti-TB drug regimens were used. For the first 2 months, 4 drugs were used, i.e., Isoniazid (INH), rifampicin, ethambutol, and pyrazinamide. For the last 4 months, 2 anti-TB drugs were used, i.e., INH and rifampicin.

3.5. Treatment outcome

Treatment outcome of all the TB patients are shown in Table 4. Eighty-seven patients in the study defaulted. Their main age was 36.1 years, with SD of 18.7 years (range 7–87) (Table 5).

In this study, 670/1000 (67%) patients were diagnosed as having pulmonary TB while 330/1000 (33%) were having extrapulmonary TB. The mean age of the pulmonary TB patients was 37 years, with SD of 19.3 (range 1–100) (Table 6).

4. Discussion

Worldwide, TB is more common among men than women.^{19–21} But in our study, 599/1000 (59.9%) of the TB patients were females while 401/1000 (40.1%) were males. Among our neighbor countries, exceptions to the global pattern of male preponderance of TB are found in Iran and Pakistan. In Iran, the rate is slightly higher in females than in males.^{22,23} In Pakistan, the relation between sex and TB rates varies between provinces. In Punjab and Sindh provinces, females

Table 3 – Status of sputum AFB at first visit.

AFB status at 1st visit	Frequency, n	Percent, %
AFB 1+	98	21.4
AFB 2+	247	53.8
AFB 3+	114	24.8
TOTAL	459	100

Table 4 – Treatment outcomes of the 1000 TB patients.

Treatment outcome	Frequency, n	Percent, %
Treatment completed	479	47.9
Cured	298	29.8
Transferred	96	9.6
Failed	35	3.5
Defaulted	87	8.7
Dead	5	0.5
Total	1000	100

Table 5 – Data of only defaulted cases of TB.

Variable	Frequency, n	Percent, %
Age (n = 87)		
<50 years	67	77.0
≥50years	20	23.0
Gender (n = 87)		
Male	39	44.8
Female	48	55.2
Site of disease (n = 87)		
Pulmonary	52	59.8
Extra-pulmonary	35	40.2
History of contact (n = 54)		
Yes	19	35.2
No	35	64.8
Fever (n = 76)		
Present	73	96.1
Absent	3	3.9
Cough (n = 76)		
Present	64	84.2
Absent	12	15.8
Weight loss (n = 87)		
Present	48	55.2
Absent	39	44.8
AFB status at first visit (n = 34)		
1+	12	35.3
2+	17	50.0
3+	5	14.7
Sputum smear at first visit (n = 72)		
Positive	34	47.2
Negative	38	52.8
Sputum smear after 2 months of intensive treatment (n = 23)		
Positive	0	0
Negative	23	100

account for less than half of the reported TB cases, but in Khyber-Pashtunkhwa and Balochistan provinces the percentage of females is about 60%.^{23,24} The two later provinces have common border with Afghanistan as well as have the people of similar ethnicity. The main causes of preponderance of TB case in female in Afghanistan have not been established. However cultural and religious issues may play a role. Due to cultural restrictions in most of the areas in the country, female cannot work outside home. Prolong TB contacts have been reported increasing the spread of the TB bacilli. It has been reported that TB bacilli are indoor infections and the chance of transmission in closed areas is quite common.^{24,4}

Treatment outcomes were assessed based on WHO guidelines.¹⁷ In this study, treatment success rate was 77.7% (cured were 29.80% while treatment completed were 47.9%). Our findings are under the figure of WHO report for

Table 6 – Data of only pulmonary TB patients.

Variable	Frequency, n	Percent, %
Age (n = 670)		
<50 years	456	68.1
≥50 years	214	31.9
Gender (n = 670)		
Male	281	41.9
Female	389	58.1
History of contact (n = 269)		
Yes	86	32.0
No	183	68.0
Fever (n = 666)		
Present	656	98.5
Absent	10	1.5
Cough (n = 667)		
Present	653	97.9
Absent	14	2.1
Weight loss (n = 670)		
Present	388	57.9
Absent	282	42.1
AFB status at first visit (n = 448)		
1+	97	21.7
2+	237	52.9
3+	114	25.4
Sputum smear at first visit (n = 640)		
Positive	448	70.0
Negative	192	30.0
Sputum smear after 2 months of intensive anti-TB treatment (n = 372)		
Positive	10	2.7
Negative	362	97.3
Treatment outcome (n = 559)		
Success	522	93.4
Failure	37	6.6

Afghanistan indicating the success rate of TB treatment regimen around 86%⁵ and also less than the figures reported from neighboring countries.⁵ The main cause could be the persistent insecurity, lack of health information, illiteracy,

and economic problems in this region. To find out the main reasons behind the low cure rate and treatment success, further studies should be conducted in different parts of Afghanistan.

Table 7 explains the outcome of tuberculosis treatment regimens in different countries with different settings.

Prevalence of pulmonary TB in the setting of lower HIV prevalence is around 60–70% while the prevalence of extra-pulmonary TB is high in HIV high prevalence countries (40–45%).²⁷ As the prevalence of HIV is lower in Afghanistan particularly in Kandahar Province, hence we found that majority (670/1000 [67%]) of the patients were having pulmonary tuberculosis while 330/1000 (33%) of the patients were diagnosed as extra-pulmonary tuberculosis. A recent study which was conducted in Bahawalpur, Pakistan by Atif Muhammad et al. is quite similar to our study found that 71.2% of the study populations were having pulmonary tuberculosis.²⁸ This figure is in correspondence to our study.

In this study around 10% of the patients were transferred to other health facilities. Transferring of the patients from one health center to other in the same or different districts or even provinces is not a favorable outcome. As the literacy and education level of the people in our country is not sufficient, they may not attend a newly introduced health facility for follow up. The achieved figure from our study is quite similar to other studies conducted in People's Democratic Republic of Laos,²⁹ Malawi³⁰ and Morocco³¹ with reported rates of 16.4%, 13%, and 8.4%, respectively.

In conclusion, the treatment success rate among PTB patients in this study were lower than the expected success target of 85%. Similarly, treatment success rates in new smear positive PTB cases were also less than targets set by the WHO.⁵ A large proportion of patients were lost to follow-up (defaulted) during treatment, which causes serious concern and warrants urgent action.

Table 7 – Outcome of TB treatment regimens in different countries with different settings.

Study	Population	Outcome	
		Success	Not success
Berhe et al., 2012 ^{25,8} (Northern Ethiopia)	<ul style="list-style-type: none"> • 407 • Sputum smear positive PTB patients • Rx. Regimen: 2HRZE/4HR 	89.2% <ul style="list-style-type: none"> • Cure 85.5% • Rx. complete 4.4% 	10.8% <ul style="list-style-type: none"> • Failure 3.7% • Death 3.9% • Default 3.2% • Transfer out 1.5%
Ige and Oladokun, 2011 ²⁶ (Ibadan, Nigeria)	<ul style="list-style-type: none"> • 857 • New sputum smear positive PTB patients • Rx. Regimen: 2HRZE/4HR 	74.4% <ul style="list-style-type: none"> • Cure 60.4% • Rx. complete 14% 	<ul style="list-style-type: none"> • Failure 2.6% • Death 5.6% • Default 2.1% • Transfer out 15.3%
Joseph et al., 2011 ¹⁹ (South India)	<ul style="list-style-type: none"> • 286 • Sputum smear positive PTB • Rx. Regimen: 2HRZE/4HR and 2HRZES/1HRZE/5HRE 	<ul style="list-style-type: none"> • New PTB 77.4% • Retreatment PTB 47.3% 	<ul style="list-style-type: none"> • New smear positive PTB • Failure 15.1% • Default 7.5% • Retreatment smear positive PTB • Failure 32.4% • Default 20.3%
This study, (Kandahar, Afghanistan)	<ul style="list-style-type: none"> • 1000 • All types of tuberculosis patients • Rx. regimen 2HRZE/4HR and 2HRZES/1HRZE/5HRE 	78% <ul style="list-style-type: none"> • Cure 30% • Rx. Complete 48% 	<ul style="list-style-type: none"> • Failure 4% • Death 1% • Default 9% • Transfer out 10%

Rx. = treatment, PTB = pulmonary tuberculosis.

5. Conclusion and recommendations

TB is prevalent in Kandahar Province. This devastating disease is still one of the major threats to these people and a major economic burden for Afghan MoPH. Effective tracing methods for patients lost to follow-up should be developed and implemented to minimize treatment interruptions. Moreover, patients with an increased risk of having unsuccessful treatment outcomes should be provided with enhanced supervision and treatment monitoring to improve outcomes. There were the cases of TB who did not respond to the first line regimens of anti-TB drugs advised by WHO and Afghan MoPH. Further studies are needed to find out the main reasons behind the low cure rate and treatment success.

Conflicts of interest

All authors have none to declare.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijtb.2018.10.008>.

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