Analysis of Treatment Outcome in Patients with Tuberculosis in War Affected Region of Khyber Paktunkhwa, Pakistan

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TAUSEEF AHMAD
School of Public Health, Southeast University, Nanjing, China
Tauseef.ahmad@hu.edu.pk Corresponding Author

Muhammad Ayub Jadoon
AUST

Muhammad Khan
Hazara University

Muhammad Mumtaz Khan
University of Haripur

Akbar Hussain
Dalian Medical University

Taha Hussain Musa
Southeast University

Muhammad Waqar
GCMBDR

Eyasu Ejeta
Wollega University

Manoochehr Karami
Hamdan University of Medical Sciences

Kefyalew Addis Alene
The Australian National University

Hui Jin
Southeast University
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**SUBJECT AREAS**

*Internal Medicine Specialties*

**KEYWORDS**

*Tuberculosis, Treatment outcome, Pakistan*
Abstract

Background

Globally, tuberculosis (TB) remains the leading cause of death from a single infectious disease. TB treatment outcome is an indicator for the effectiveness of a national TB control programs. This study aimed to assess treatment outcome of TB patients and its determinants in Batkhela, Khyber Pakhtunkhwa, Pakistan.

Methods

A retrospective cohort study was designed using all TB patients who were enrolled at District Head Quarter (DHQ) Hospital Batkhela, Pakistan. Distribution of TB types, treatment outcome and associated factor with successful treatment was computed using SPSS version 20.0 software for windows.

Results

A total of 515 TB patients were registered, of which 237 (46%) were males and 278 (53.98%) females. Of the total, 234 (45.44%) were cured and 210 (40.77%) completed treatment with overall treatment success rate was 444 (86.21%). Age 0-20 years (AOR = 3.47; 95% CI= 1.54-7.81; P= 0.003), smear-positive pulmonary TB (SPPTB) (AOR = 3.58; 95% CI= 1.89-6.78; P= <0.001), treatment category (AOR = 4.71; 95% CI= 1.17-18.97; P= 0.029), and year of enrollment 2012 (AOR= 6.26; 95% CI= 2.52-15.59; P= <0.001) were significantly associated with successful treatment outcome.

Conclusions

The overall treatment success rate is satisfactory but still need to be improved to achieve the international targeted treatment outcome. An increase was observed in overall case-fatality rate during the study duration which is an alarming signal for public health.

Introduction

Globally, Tuberculosis (TB) remains the leading cause of death from a single infectious disease and more prevalent in low-income countries. However, the magnitude of the disease is varying from country to country. In 2016, an estimated 10.4 million people were infected with TB worldwide. In the
same year, maximum number of incident cases were reported in the World Health Organization (WHO) South-East Asia Region (45%), followed by African Region (25%), Western Pacific Region (17%), Eastern Mediterranean Region (7%), European Region (3%) and the WHO Region of the Americas (3%). Of the 30 high burden countries India, Indonesia, China, the Philippines and Pakistan (in descending order) contributed 56% of estimated cases [1].

In Pakistan, an estimated 510,000 new TB cases and approximately 15,000 developing drug resistant TB cases reported every year. Pakistan ranked fifth among the 30 high burden TB countries. To control TB disease, the tracing and treatment of active or latent TB are important. National Tuberculosis Control Program (NTP) of Pakistan needs to review their strategies and focus on those areas where the disease is prevalent [2]. In Khyber Pakhtunkhwa province of Pakistan several studies have been conducted on the prevalence of TB [3-7], however, there are limited studies on the treatment outcome of TB [8]. Therefore, this study was undertaken to assess TB treatment outcome and its determinants in Batkhela, Khyber Pakhtunkhwa, Pakistan.

Methods

Study setting

Batkhela is the capital city of Malakand district and it is one of the popular business city in Khyber Pakhtunkhwa province. Malakand district is situated in Khyber Pakhtunkhwa province. The total population of the district is 720,295 (2017 census). The area is surrounded by district Dir (Lower) in the north, Swat district in the east, Mardan andCharsadda districts in the south east and south west respectively, Mohmand and Bajaur agencies are in the west [9]. The DHQ Hospital Batkhela, providing health care facilities to the local residence of Batkhela and district Malakand (Figure 1). The area has been providing humanitarian protection and shelter for a large number of refugees from different districts of Malakand division during flood and war.

Study population

Study population was all registered TB patients attending DOTS services in TB centre, DHQ Hospital Batkhela from 1st January 2011 to 31st December 2014.
**Study design and data collection**
A hospital based retrospective study was conducted. The data were retrieved from the TB clinic registration books. The unit registers reviewed contained basic information such as socio-demography and clinical profile of the patients, date of TB diagnosis and treatment outcome. The data was collected by trained unit healthcare personnel under supervision of principal investigator by using self-designed performa and entered in to Excel sheet.

**Laboratory procedure**
Diagnosis of all the registered TB patients was done in the entire hospital. According to the standard protocol the sputum was collected from the suspected patients having symptom of TB in 5ml sterile bottle, after collection of sputum the bottle were kept in 15 ml sterile bottle to avoid the leakage of the infectious samples. The samples were labeled and further process by the laboratory technician of the hospitals. The Zheil-Neelsen stain/sputum smear microscopy was performed for all the suspected PTB cases.

**Standard definition**
According to the standard definitions of the WHO, the following clinical case and treatment outcome operational terms were used [10].

**Smear-positive pulmonary TB (SPPTB)**
A patient with at least two sputum specimens which were positive for acid fast bacilli (AFB) by microscopy, or a patient with only one sputum specimen which was positive for AFB by microscopy, and chest radiographic abnormalities consistent with active pulmonary tuberculosis (PTB).

**Smear-negative pulmonary tuberculosis (SNPTB)**
A patient with symptoms suggestive of TB, with at least two sputum specimens which were negative
for AFB by microscopy, and with chest radiographic abnormalities consistent with active PTB, or a patient with two sets of at least two sputum specimens taken at least two weeks apart, and which were negative for AFB by microscopy and radiographic abnormalities consistent with PTB and lack of clinical response to one week of broad spectrum antibiotic therapy.

**Extra-pulmonary tuberculosis (EPTB)**

This included TB of organs other than the lungs, such as lymph nodes, abdomen, genitourinary tract, skin, joints and bones, the meninges and others.

Treatment outcomes were categorized into: (a) cured, a patient who was initially sputum smear-positive and who finished treatment with a negative bacteriology result at the end of treatment or was sputum smear negative on two occasions at the end of treatment; (b) treatment completed, a patient who completed treatment but did not meet the criteria for cure or failure; this definition applies to sputum smear-positive and sputum smear-negative patients with pulmonary TB and to patients with EPTB; (c) died, a patient who died from any cause during treatment time; (d) failed, a patient who was initially sputum smear-positive and remained bacteriology or sputum smear-positive at month five or later during treatment; (e) defaulted, a patient whose treatment was interrupted for two consecutive months or more; (f) transferred out, a patient who was referred to another health facility for treatment from whom information on treatment outcome could not be obtained; (g) successfully treated, a patient who was cured and/or completed treatment; and (h) unsuccessful outcome: If treatment resulted in treatment failure, defaulted, or died.

**Statistical analysis**

The collected data were checked for completeness by principal investor. Data were entered, cleared and descriptive analyses were carried out using Statistical Package for Social Sciences (SPSS) version 20. Multivariable logistic regression model was used to analyze the association between treatment outcome and potential determinate variables at 95% confidence interval. *P*-value of less than 0.05 was considered as statistically significant.
Ethical consideration

The study protocol was reviewed and approved by the Advanced Studies and Research Board (ASRB) of Hazara University Mansehra, Pakistan (Reference No. HU/R&P/ASRB/2015/1995). Official permission was also sought from District Health Officer (DHO) and District Tuberculosis Officer (DTO), Malakand district. The written informed consent was obtained from the patients. To ensure confidentiality of the information collected from TB registration books, names or identification numbers of TB patients were not included in the data collection sheet.

Results

A total of 515 suspected TB registered cases were studied. Majority of the study participants were females 278 (53.98%). The study participants were divided into four age groups 0-20 years 185 (35.92%), 21-40 years 189 (36.69%), 41-60 years 82 (15.92%) and ≥ 61 years 59 (11.45%). The treatment category CAT-I was the most dominant and commonly used 503 (97.7%). In term of patient category 493 (95.72%) were diagnosed as new cases and 10 (1.94%) were relapse TB patients. The clinical profile of the study participants shows in total, 252 (48.93%) were SPPTB, 82 (15.92%) were SNPTB and 181 (35.15%) were EPTB (Table 1). The overall results revealed that the treatment success rate (cured and treatment completed) of TB patients in Batkhela was 444/515 (86.21%). The treatment success rate was recorded high among the female as compared to male. Only 210 (40.77%) of TB patients had completed their treatment while 234 (45.44%) patients were cured, in addition 14 (2.72%) were died, and 20 (3.88%) were defaulted cases (Table 2). Predictor factors for successful treatment outcome among registered TB cases (Table 3).

Discussion

Many studies and research have been carried out on TB but still the disease remains an important health problem especially in low income countries where majority of the peoples living below the line of poverty. The overall treatment success rate was (86.21%). The treatment success rate was recorded high among the female subjects 243/278 (87.41%) as compared to male 201/237 (84.81%) (AOR= 0.93; 95% CI= 0.53-1.63; P= 0.81). The overall case fatality (CF) rate was observed 14/515
A study conducted by Saleem et al. [11] at District Kotli, Azad Kashmir reported the mortality due to TB was (1.04%).

In our study, treatment success rate was lower from previous published studies [8, 12]. High treatment success rate was observed in age between 0-20 years and reported statistically significant (AOR=3.47; 95% CI= 1.54-7.81; P= 0.003). Type of TB (SPPTB) was significantly associated with successful treatment outcome (AOR=3.58; 95% CI= 1.89-6.78; P= <0.001). All the suspected patients were treated with DOTS regimen prescribed by WHO. Two types of treatment category were set CAT-I and CAT-II. Results of the current study show that majority of PTB suspected patients (97.66%) were put under CAT-I category. The treatment success rate was significantly associated with CAT-I (AOR=4.71; 95% CI= 1.17-18.97; P= 0.029). In addition, year of treatment 2012 was also observed statistically significant with treatment outcome (AOR=6.26; 95% CI= 2.52-15.59; P= <0.001).

In our study among the total registered TB patients (48.93%) were SPPTB, (15.92 %) NPTB and (35.15%) EPTB. The overall prevalence of SPPTB was reported high. Our results corroborate with other studies reported high prevalence of SPPTB [13]. The SPPTB patients are dangerous and can easily spread the infection in the community. Early diagnosis and treatment of such cases are very important and necessary to reduce the progression of TB. The gender disparity is a key indicator which brings the attention to male and female. Of the total studied cases, SPPTB were reported (48.93%), of which the prevalence of SPPTB was reported high in female 132/252 (52.38%). Our finding is similar with other studies [3, 4, 6, 13]. The high rate of disease in the female could be attributed to less access to hospitals, at door step availability of least health diagnostic facilities, no early diagnosis and treatment of the disease, poverty, poor hygienic condition, joint family system, social exclusion, poor nutritional status and illiteracy in female population in our society.

Conclusions
The overall treatment success rate was reported (86.21%) which is below the national targeted treatment outcome. Age, type of TB, treatment category and year of enrollment were significantly associated with successful treatment outcome. An increase was observed in overall CF rate in the
study area which is an alarming signal. In our study, SPPTB was reported high with high cases among
the productive age group between 21-40 years. The accurate information as well as the data required
on the incidence and prevalence of TB to implement an effective TB control initiative to control CF
and achieved target treatment outcome. This study will add data TB prevalence and treatment
outcome to provide the baseline information for population and health and government authorities.

Abbreviations

TB: Tuberculosis; DHQ: District Head Quarter; DOTS: Directly Observed Treatment Short course; PTB:
Pulmonary Tuberculosis; EPTB: Extra-pulmonary Tuberculosis; WHO: World Health Organization; NLCP:
National Leprosy Control Program; AFB: Acid Fast Bacilli; SPSS: Statistical Package for Social Sciences;
ASRB: Advanced Studies and Research Board; DHO: District Health Officer; DTO: District Tuberculosis
Officer; NTP: National Tuberculosis Program; MDR-TB: Multidrug-resistant Tuberculosis.

Declarations

Ethical approval and consent form

This study was reviewed and approved by the ethical research committee (Advanced Studies and
Research Board) of Hazara University Mansehra, Khyber Pakhtunkhwa Pakistan [No.
HU/R&P/ASRB/2015/1995]. The study was conducted in accordance with approval guideline and prior
permission was granted by the higher authority of DHQ Hospital Batkhela. The written informed
consent was obtained from the patients.

Consent for publication

Not applicable.

Availability of data materials

During the study the data generated and analyzed are available free of cost. Before using of data for
any kind of purpose the permission must be taken from the principal author.

Competing interest
All the authors declared that, they have no competing interest regarding publication of the study.

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None.

**Author’s contribution**

TA: Study design, Data collection, Paper writing and analysis; MAJ: Study design and critical review; MK: Paper writing and critical review; H: Help in data collection; MMK, AH, MW, HJ: Technical assistance and literature search; EE: Help in statistical analysis and critical review. MK, KAA: Critical review.

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**Author’s detail**

1. Department of Epidemiology and Health Statistics, School of Public Health, Southeast University, Nanjing (210009), China
2. Department of Microbiology, Hazara University Mansehra 21300, Khyber Pakhtunkhwa, Islamic Republic of Pakistan
3. Department of Microbiology, Abbottabad University of Science and Technology Abbottabad, Khyber Pakhtunkhwa, Islamic Republic of Pakistan
4. Centre for Human Genetics, Hazara University Mansehra, KhyberPakhtunkhwa, Islamic Republic of Pakistan
5. College of Life Sciences, Northwest University, Xian (710069), China
6. Department of Public Health, University of Haripur, Khyber Pakhtunkhwa, Islamic
Republic of Pakistan

7. Department of Medical Microbiology, Dalian Medical University, 9 Western Section Lvshun South Road, Lvshunkou District, Dalian, Liaoning, China

8. Genome Centre for Molecular Based Diagnostics and Research Centre, CI-25 Block B Al-Sudais Plaza Abdalian Cooperative Society, Lahore, Islamic Republic of Pakistan

9. Department of Medical Laboratory Sciences, College of Health Sciences, Wollega University, Nekemte, Ethiopia

10. Modeling of Noncommunicable Diseases Research Center, Department of Epidemiology, School of Public Health, Hamadan University of Medical Sciences, Hamadan, Iran

11. Institute of Public Health, College of Medicine and Health Sciences, University of Gondar, Gondar, Ethiopia

12. Research School of Population Health, College of Medicine, Biology and Environment, The Australian National University, Canberra, ACT, Australia

*Correspondence to:* Tauseef Ahmad (Ph.D Scholar); Department of Epidemiology and Health Statistics, School of Public Health, Southeast University, Nanjing (210009), China

E-mail: Tauseef.ahmad@hu.edu.pk; ayubjadoon@hotmail.com (MAJ)

jinhui_hld@163.com (HJ)

ORCID

Tauseef Ahmad  https://orcid.org/0000-0001-8793-273X

Authors E-mails ID’s

Tauseef.ahmad@hu.edu.pk (TA)

ayubjadoon@hotmail.com (MAJ)

muhammadkhan1985@gmail.com (MK)
Mumtaz.muhmmadee@gmail.com (MMK)
akbarhussain135@gmail.com (AK)
taha.hm99@yahoo.com (THM)
waqarkhan96@gmail.com (MW)
eyasu.ejeta@gmail.com (EJ)
man.karami@yahoo.com (MK)
kefyalew.alene@anu.edu.au (KAA)
jinhui_hld@163.com (HJ)

References
1. Department of Epidemiology and Health Statistics, School of Public Health, Southeast University, Nanjing (210009), China
2. Department of Microbiology, Hazara University Mansehra 21300, Khyber Pakhtunkhwa, Islamic Republic of Pakistan
3. Department of Microbiology, Abbottabad University of Science and Technology Abbottabad, Khyber Pakhtunkhwa, Islamic Republic of Pakistan
4. Centre for Human Genetics, Hazara University Mansehra, Khyber Pakhtunkhwa, Islamic Republic of Pakistan
5. College of Life Sciences, Northwest University, Xian (710069), China
6. Department of Public Health, University of Haripur, Khyber Pakhtunkhwa, Islamic Republic of Pakistan
7. Department of Medical Microbiology, Dalian Medical University, 9 Western Section Lvshun South Road, Lvshunkou District, Dalian, Liaoning, China
8. Genome Centre for Molecular Based Diagnostics and Research Centre, Cl-25 Block B Al-Sudais Plaza Abdalian Cooperative Society, Lahore, Islamic Republic of Pakistan
9. Department of Medical Laboratory Sciences, College of Health Sciences, Wollega
Tables

Table 1: Characteristics of TB patients attending the DOTS services in Batkhela, Pakistan

| Characteristics          | Type of TB n (%) |
|--------------------------|------------------|
|                          | SPPTB | SNPTB | EPTB | Total n (%) |
| **Sex**                  |        |       |      |             |
| Male                     | 120 (50.63) | 39 (16.45) | 78 (32.91) | 237 (46.01) |
| Female                   | 132 (47.47) | 43 (15.46) | 103 (37.05) | 278 (53.98) |
| **Age**                  |        |       |      |             |
| 0-20                     | 74 (40.00)  | 39 (21.01) | 72 (38.91) | 185 (35.92) |
| 21-40                    | 100 (52.91) | 23 (12.16) | 66 (34.92) | 189 (36.69) |
| 41-60                    | 46 (56.09)  | 8 (9.15)   | 28 (34.14) | 82 (15.92)  |
| ≥61                      | 32 (54.23)  | 12 (20.33) | 15 (25.42) | 59 (11.45)  |
| **TB patient category**  |        |       |      |             |
| New                      | 234 (47.46) | 79 (16.02) | 180 (36.51) | 493 (95.72) |
| Relapse                  | 8 (80.03)   | 2 (20.00)  | 0 (0.00)    | 10 (1.94)   |
| Other                    | 10 (83.33)  | 1 (8.33)   | 1 (8.33)    | 12 (2.33)   |
| **Treatment category**   |        |       |      |             |
| Category-I (CAT-I)       | 243 (48.31) | 79 (15.70) | 181 (36.51) | 503 (97.66) |
| Category-II (CAT-II)     | 9 (75.00)   | 3 (25.00)  | 0 (0.00)    | 12 (2.33)   |
| **Treatment year**       |        |       |      |             |
| 2011                     | 50 (43.10)  | 26 (22.41) | 40 (34.48)  | 116 (22.52) |
| 2012                     | 59 (50.00)  | 17 (14.40) | 42 (35.59)  | 118 (22.91) |
| 2013                     | 64 (53.33)  | 19 (15.83) | 37 (30.83)  | 120 (23.3 0) |
| 2014                     | 79 (49.11)  | 20 (12.42) | 62 (38.5)   | 161 (31.26) |
| **Total**                | 252 (48.93) | 82 (15.92) | 181 (35.14) | 515          |

SPPTB: smear-positive pulmonary TB; SNPTB: smear-negative pulmonary TB; EPTB: extra-pulmonary TB; CAT-I: Category-I; CAT-II: Category-II.

Table 2: Trends of TB treatment outcome among TB patients attending the DOTS services in Batkhela, Pakistan
### Table 3: Predictor factors for successful treatment outcome among registered TB cases in Batkhela, Pakistan

| Character                | No. (%) of TB cases | Successful outcome, n (%) | COR (95% CI)  | P-value | AOR (95% CI)  |
|--------------------------|---------------------|---------------------------|---------------|---------|---------------|
| **Sex**                  |                     |                           |               |         |               |
| Male                     | 237 (46.01)         | 201 (84.81)               | 0.08 (0.48 -1.32) | 0.39    | 0.93 (0.93 - 1.93) |
| Female                   | 278 (53.99)         | 243 (87.41)               | 1.00          | 1.00    | 1.00          |
| **Age**                  |                     |                           |               |         |               |
| 0-20                     | 185 (35.92)         | 165 (89.19)               | 3.34 (1.61 -6.93) | 0.001   | 3.47 (1.58 - 7.60) |
| 21-40                    | 189 (36.69)         | 165 (87.30)               | 2.78 (1.37 -5.65) | 0.005   | 2.76 (1.37 - 5.65) |
| 41-60                    | 82 (15.92)          | 72 (87.80)                | 2.91 (1.22-6.95) | 0.016   | 2.82 (1.22 - 6.95) |
| ≥61                      | 59 (11.45)          | 42 (71.18)                | 1.00          | 1.00    | 1.00          |
| **TB form**              |                     |                           |               |         |               |
| SPPTB                    | 252 (48.93)         | 232 (92.06)               | 2.88 (1.605-5.16) | 0.000   | 3.58 (1.59 - 7.99) |
| SNPTB                    | 82 (15.92)          | 67 (81.70)                | 1.11 (0.57-2.16) | 0.762   | 1.18 (0.67 - 2.06) |
| EPTB                     | 181 (35.15)         | 145 (80.11)               | 1.00          | 1.00    | 1.00          |
| **Patient category**     |                     |                           |               |         |               |
| New                      | 493 (95.72)         | 426 (86.40)               | 0.57 (0.07-4.55) | 0.603   | 0.57 (0.07 - 4.55) |
| Relapse                  | 10 (1.94)           | 7 (70.00)                 | 0.21 (0.02-2.46) | 0.215   | 0.21 (0.02 - 2.46) |
| Other                    | 12 (2.33)           | 11 (91.67)                | 1.00          | 1.00    | 1.00          |
| **Treatment category**   |                     |                           |               |         |               |
| Category I               | 503 (97.66)         | 437 (86.87)               | 0.21 (0.06-0.68) | 0.01    | 4.71 (1.00 - 21.16) |
| Category II              | 12 (2.33)           | 7 (58.33)                 | 1.00          | 1.00    | 1.00          |
| **Year of treatment**    |                     |                           |               |         |               |
| 2011                     | 116 (22.52)         | 101 (87.06)               | 2.37 (1.24-4.54) | 0.009   | 2.42 (1.22 - 4.83) |
| 2012                     | 118 (22.91)         | 112 (94.91)               | 6.58 (2.69-16.09) | 0.000   | 6.26 (2.69 - 16.09) |
| 2013                     | 120 (23.30)         | 112 (93.33)               | 4.94 (2.22-10.98) | 0.000   | 4.31 (2.22 - 10.98) |
| 2014                     | 161 (31.26)         | 119 (73.91)               | 1.00          | 1.00    | 1.00          |

SPPTB: smear-positive pulmonary TB; SNPTB: smear-negative pulmonary TB; EPTB: extra-pulmonary TB; COR: Crude odds ratio; AOR: Adjusted odds ratio.

Figures
Figure 1

Map of study area (highlighted as green).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.
Supplementary data.xlsx