Treatment outcomes of patients with tuberculosis in war affected region of Khyber Pakhtunkhwa, Pakistan

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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 program. This study aimed to assess treatment outcomes 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, from January 2011 to December 2014. A binary logistic regression models were used to identify factors associated with successful TB treatment outcomes defined as the sum of cure and completed treatment.
Results: A total of 515 TB patients were registered, of which 237 (46%) were males and 278 (53.98%) females. Of all patients, 234 (45.44%) were cured and 210 (40.77%) completed treatment. The overall treatment success rate was 444 (86.21%). Age 0-20 years (adjusted odds ratio, AOR= 3.47; 95% confidence interval, CI)= 1.54-7.81; P= 0.003), smear-positive pulmonary TB (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. Type of TB, age, treatment category, and year of enrollment were significantly associated with successful treatment outcomes.

Background
Globally, tuberculosis (TB) remains the leading cause of death from a single infectious agent (Mycobacterium tuberculosis), ranking above human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) [1-2]. In 2018, an estimated 10 million incident TB cases and 1.6 million deaths due to TB were reported globally [1]. The magnitude of the disease varies from country to country with more prevalent in low-income countries [1-2].
Increasing the rate of successful treatment outcome is one of the strategies for effective control of TB in the community. The End TB Strategy defines targets for 2030; to decrease the incidence rate by 80% (new cases per 100,000 population per year) and 90% reduction in the number of TB deaths
compared with levels in 2015 [3]. However, successful treatment outcome has increased in several countries following the implementation of Directly Observed Treatment Short-Course (DOTS) program [4]. TB is still a major health problem in Pakistan, with an estimated 510,000 new TB cases and approximately 15,000 drug resistant TB cases reported every year [5]. Recently, a standardized TB prevention and control program that regularly monitors the incidence of TB and as well as drug susceptibility testing in the population has been launched at Hayatabad Medical Complex Peshawar, Khyber Pakhtunkhwa province [6]. In Khyber Pakhtunkhwa province of Pakistan several studies have been conducted on the prevalence of TB [7-12]. Monitoring treatment outcomes among war affected countries such as Pakistan provides evidence to assess the effectiveness of TB control programs. There are few epidemiological studies conducted in Pakistan on TB treatment outcomes [13-17]. However, data are limited between 2011 and 2014 in Khyber Pakhtunkhwa for the analysis of trends. Therefore, the aim of this study was to assess the TB treatment outcomes and its determinants in Batkhela, Khyber Pakhtunkhwa, Pakistan, between 2011 and 2014.

Methods

Study design

A retrospective cohort study was conducted among TB patients who enrolled at District Head Quarter (DHQ) Hospital Batkhela, Pakistan, from January 2011 to December 2014.

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) [18]. The DHQ Hospital Batkhela, providing health care facilities to the local residence of Batkhela and district Malakand. 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. At the hospital, TB treatment is prescribed based on the recommendations of the national TB guidelines, which is based on recommendations from WHO guidelines. All newly diagnosed TB patients receive a standardized regimen of first-line TB drugs that consists of an 2-month intensive phase with a combination of pyrazinamide (Z), isoniazid (INH),
ethambutol (E), and rifampicin (R) a 2-month continuation phase with a combination of rifampicin (R) and ethambutol (E). However, certain groups of TB patients (such as MDR-TB patients) cannot receive the first-line regimen, requiring second-line regimens [19-20].

**Participants**

All TB patients who were enrolled at DHQ Hospital between 1\textsuperscript{st} January 2011 and 31\textsuperscript{st} December 2014 were included.

**Data sources**

Data were extracted from patients’ TB registration books and medical records by trained data collectors. The registration books contained basic information such as socio-demographic and clinical characteristics of the patients.

**Variables**

Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers.

**Laboratory procedure**

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. Smear microscopy with Ziehl-Neelsen staining and fluorescence microscopy are used in the Hospital for both the diagnosis and monitoring of TB [21].

**Standard definition**

TB treatment outcomes and clinical cases were defined according to the standard World Health Organization (WHO) definitions (Table 1). In this study, treatment success was defined as a sum of cured and treatment completed; and poor treatment was defined as the sum of treatment failure, death or lost to follow up.

Table 1 Standard definition modified from WHO definitions [22]
### Treatment outcomes and clinical case definitions

| Category                                      | Definition                                                                                           |
|-----------------------------------------------|------------------------------------------------------------------------------------------------------|
| **Cured**                                     | A patient who was initially sputum smear-positive and who finished treatment with bacteriology result at the end of treatment or was sputum smear negative on two occasions. |
| **Treatment completed**                       | A patient who completed treatment but did not meet the criteria for cure or failure; this applies to sputum smear-positive and sputum smear-negative patients with pulmonary TB. |
| **Treatment failure**                         | A patient who was initially sputum smear-positive and remained bacteriology or sputum smear-positive at month five or later during treatment. |
| **Death**                                     | A patient who died from any cause during the course of treatment.                                   |
| **Lost to follow-up**                         | A patient who has been on treatment for at least four weeks and whose treatment was for eight or more consecutive weeks. |
| **Transfer out**                              | A patient who has been transferred to another recording and reporting unit and whose treatment outcome is unknown. |
| **Successful treatment outcome**              | A patient who was cured or completed treatment                                                    |
| **Unsuccessful treatment outcome**            | A patient who had treatment failure, lost to follow up, or death.                                   |
| **Smear-positive pulmonary TB**               | A patient with at least two sputum specimens which were positive for acid fast bacilli 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**     | 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 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, genital tract, skin, joints and bones, the meninges and others. |

### Statistical analysis

The collected data were checked for completeness by principal investigator. Data were entered, cleared and descriptive analyses were carried out using Statistical Package for Social Sciences (SPSS) version 20. Binary 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.

### Results

**Demographic characteristics of the patients**

A total of 515 TB patients, registered and treated for TB at DHQ Hospital between January 2011 to December 2014, were included in this study. Of these, 278 (53.98%) were female and 185 (35.92%)
were age less than 20 years (Table 2).

**Clinical characteristics of the patients**

Of the total patients, 252 (48.93%) were smear positive PTB, 82 (15.92%) were smear negative PTB and 181 (35.15%) were EPTB as shown in Table 2. Majority of the patients 493 (95.72%) were new TB cases, and 503 (97.7%) were treatment category I (CAT-I). The number of cases diagnosed with TB in the hospital was increased from 116 (22.52%) in 2011 to 161 (31.26%) in 2014.

**Table 2** Characteristics of TB patients attending the DOTS services

| Characteristics          | Type of TB n (%) |
|--------------------------|------------------|
|                          | Smear positive PTB | Smear negative PTB | 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               | 243 (48.31)      | 79 (15.70)        | 181 (36.51) | 503 (97.66) |
| Category-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 (23.30) |
| 2014                     | 79 (49.11)       | 20 (12.42)        | 62 (38.5)  | 161 (31.26) |
| **Total**                | 252 (48.93)      | 82 (15.92)        | 181 (35.14) | 515          |

Abbreviations: PTB: Pulmonary TB; EPTB: Extra-pulmonary TB

**Treatment outcomes**

The overall TB treatment success rate (i.e. cured and treatment completed) in Batkhela was 444/515 (86.21%). Of all patients, 234 (45.44%) were cured, 210 (40.77%) completed treatment, 14 (2.72%) died, 20 (3.88%) lost to follow-up, and 3 (0.58%) were transferred out (Table 3). The treatment success rate was higher among female 243/278 (87.41%) than male 201/237 (84.81%) and increased over time.

**Table 3** Trends of TB treatment outcome among TB patients attending the DOTS services
Factors associated with treatment success

Table 4 shows factors associated with successful TB treatment outcomes. Type of TB, age, and year of treatment commencement were significantly associated with successful treatment outcomes. The odds of successful treatment outcomes was higher among patients with age group 0-20 years (AOR=3.47; 95% CI: 1.54-4.7.81), 21-40 years (AOR=2.76; 95% CI: 1.26-6.03), and 41-60 years (AOR=2.82; 95% CI: 1.08-7.35) compared to patients with age group >=61 years. The study also found that the odds of successful treatment outcomes was three times higher among smear positive pulmonary TB patients than extra pulmonary TB patients (AOR= 3.58; 95% CI: 1.89-6.78). The odds of successful treatment outcomes was higher among patients with treatment CAT-I than patients with treatment category II (CAT-II) (AOR = 4.71, 95% CI: 1.17- 18.97).

| Treatment outcome/year | Year of treatment, n (%) | Overall outcome, n (%) |
|------------------------|--------------------------|------------------------|
|                        | 2011                     | 2012                   | 2013                   | 2014                   |
| Cured                  | 46 (39.65)               | 57 (48.30)             | 60 (50)                | 71 (44.09)             | 234 (45.44)           |
| Completed              | 55 (47.42)               | 55 (46.61)             | 52 (43.33)             | 48 (29.81)             | 210 (40.77)           |
| Total success          | 101 (87.07)              | 112 (94.91)            | 112 (93.33)            | 119 (73.91)            | 444 (86.21)           |
| Died                   | 2 (1.72)                 | 1 (0.85)               | 2 (1.67)               | 9 (5.59)               | 14 (2.72)             |
| Defaulted              | 0 (0.0)                  | 2 (1.69)               | 3 (2.5)                | 15 (9.32)              | 20 (3.88)             |
| Transfer out           | 0 (0.0)                  | 2 (1.67)               | 1 (0.62)               | 3 (0.58)               |                      |
| Unrecorded             | 13 (11.21)               | 3 (2.54)               | 1 (0.83)               | 17 (10.56)             | 34 (6.60)             |
| Unsuccessful           | 15 (12.93)               | 6 (5.08)               | 8 (6.67)               | 42 (26.08)             | 71 (13.78)            |
| 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 (0.53-1.63) |
| Female    | 278 (53.99)         | 243 (87.41)               | 1.00         |         | 1.00         |
| Age       |                     |                           |              |         |              |
| 0-20      | 185 (35.92)         | 165 (89.19)               | 3.34 (1.61-6.93) | 0.001   | 3.47 (1.54-7.81) |
| 21-40     | 189 (36.69)         | 165 (87.30)               | 2.78 (1.37-5.65) | 0.005   | 2.76 (1.26-6.03) |
| 41-60     | 82 (15.92)          | 72 (87.80)                | 2.91 (1.22-6.95) | 0.016   | 2.82 (1.08-7.35) |
| ≥61       | 59 (11.45)          | 42 (71.18)                | 1.00         |         | 1.00         |
| TB form   |                     |                           |              |         |              |
| Smear positive PTB | 252 (48.93) | 232 (92.06)               | 2.88 (1.60-5.16) | 0.000   | 3.58 (1.89-6.78) |
| Smear negative PTB | 82 (15.92) | 67 (81.70)                | 1.11 (0.57-2.16) | 0.762   | 1.18 (0.56-2.48) |
| EPTB      | 181 (35.15)         | 145 (80.11)               | 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         |
| Treatment category |        |                           |              |         |              |
| Category I | 503 (97.66)         | 437 (86.87)               | 0.21 (0.06-0.68) | 0.01    | 4.71 (1.17-18.97) |
| Category II| 12 (2.33)           | 7 (58.33)                 | 1.00         |         | 1.00         |
| Year of treatment |          |                           |              |         |              |
| 2011      | 116 (22.52)         | 101 (87.06)               | 2.37 (1.24-4.54) | 0.009   | 2.42 (1.22-4.82) |
| 2012      | 118 (22.91)         | 112 (94.91)               | 6.58 (2.69-16.09) | 0.000   | 6.26 (2.52-15.59) |
| 2013      | 120 (23.30)         | 112 (93.33)               | 4.94 (2.22-10.98) | 0.000   | 4.31 (1.88-9.86) |
| 2014      | 161 (31.26)         | 119 (73.91)               | 1.00         |         | 1.00         |

Abbreviations: PTB: Pulmonary tuberculosis; EPTB: extra-pulmonary TB; COR: Crude odds ratio; AOR: Adjusted odds ratio.

Discussion

In this study, the overall TB treatment success rate is higher from previous published studies in different countries; studies from India reported the overall treatment success rates were (81%) [23], (83%) [24], (84.21%) [25], and (86%) [26], in Thailand the success rate was (78.5%) for patients in the TB Case Management cohort, while the success rate is high (87.5%) for patients in the National Health Security Office cohort [27], Iran (83.1%) [28], Uzbekistan (83%) [29], Denmark (80.5%) [30], Malaysia (67.26%) [31], Ethiopia (85.6%) [32], Somalia (81.8%) [33], Nigeria (83.1%) [34], in Afghanistan the treatment success rates were (77.5%) in male and (84.4%) in female patients [35], and (77.7%) [36]. However, the treatment success rate was lower than that reported in the previous studies in Pakistan [13, 37]. Type of TB, age, and year of treatment commencement were significantly associated with successful treatment outcomes.

In this study, patients with age less than 60 years were nearly three times more likely to get successful treatment outcome as compared to patients with age greater than 61 years. These results
are consistent with previous studies conducted in Ethiopia [32]. This may be due to the fact that older age patients are at a higher risk of death due to ageing. Another reason for low treatment outcome in older age patients could be because older age patients might be at higher risk of having chronic comorbidities such as cardiovascular diseases, hypertensions, and cancers. Low socio-economic status, poor adherence to treatment, and difficulty of traveling and arriving early at health facilities for DOTS could be also other reasons for low treatment outcomes in older age patients. These findings highlight the importance of providing close follow up for older age patients to increase their successful treatment outcome.

The other important finding is that smear positive pulmonary TB patients were more likely to have a successful treatment outcome than other types of TB patients. This result is consistent with previous studies conducted in Ethiopia [32]. This could be explained by the fact that smear positive pulmonary TB patients might be diagnosed easily and started the treatment promptly and may have close follow by health professionals. All TB diagnosed patients were treated at DOTS clinics using regimens recommended by WHO. Two types of treatment category were set CAT-I and CAT-II. Results of the current study show that patients with treatment CAT-I was more likely to have successful treatment outcomes than patients with treatment CAT-II.

Our study also showed that patients who started treatment before 2014 were more likely to have successful treatment outcomes than patients who started treatment in 2014. The finding indicated that successful treatment outcomes were decreased overtime from (87.0%) in 2011 and (94.9%) in 2012 to (73.9%) in 2014. This may be related to the desaturation of health care systems and TB treatment services of country because of the war. It could be also due to increased number of multidrug-resistant tuberculosis (MDR-TB) which is defined as TB that is resistant to the two most powerful first-line TB drugs (i.e. isoniazid and rifampicin). We also found that the overall prevalence of smear positive PTB was high among reported cases, which concurs with previous studies showing that majority of patients taking TB treatment were smear positive PTB [37]. The smear positive PTB 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
overall case fatality rate was (2.72%) which is high from previous published studies [38]. The high rate of mortality among TB patients 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, and poor nutritional status in our society.

This study has several limitations. Firstly, since the study was based on secondary data, some important clinical variables such as HIV, diabetes mellitus, and other co-morbidities as well as behavioral factors such as alcohol drinking and smoking were not available in the registers and therefore were not included in our study. Secondly, in this study those patients who had documented evidence of completion were counted as having a successful treatment outcome, whereas they may have undetected failure of therapy. This may lead to overestimation of the treatment outcome rate in our study. Third, as the study used data reported between 2011 and 2014, we have not assessed recent treatment outcomes, and a longer follow-up period will be required to assess longer-term trends in treatment outcomes.

Conclusions
The overall treatment success rate is satisfactory but still need to be improved to achieve the international targeted End TB Strategy milestones. Type of TB, age, treatment category, and year of enrollment were significantly associated with successful treatment outcomes. Successful treatment outcomes were decreased over time which is an alarming signal for MDR-TB.

Abbreviations
TB: Tuberculosis; DHQ: District Head Quarter; AOR: Adjusted Odds Ratio; CI: Confidence Interval; HIV: Human Immunodeficiency Virus; AIDS: Acquired Immunodeficiency Syndrome; DOTS: Directly Observed Treatment Short-Course; WHO: World Health Organization; AFB: Acid Fast Bacilli; PTB: Pulmonary Tuberculosis; EPTB: Extra-pulmonary Tuberculosis; SPSS: Statistical Package for Social Sciences; CAT-I: Category-I; CAT- II: Category-II; COR: Crude Odds Ratio; MDR-TB: Multidrug-resistant Tuberculosis.

Declarations
Ethics approval and consent to participate

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. To ensure confidentiality of the information collected from TB registration books, name or identification number of TB patient was not included in the data collection sheet.

**Consent for publication**

Not required.

**Availability of data and materials**

The datasets used, generated and/or analyzed in this study are available free of cost from the principal author/corresponding author on reasonable request.

**Competing interests**

The authors declare no competing interests.

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**Authors’ contributions**

TA: Study design, data collection and extraction, paper writing and analysis; MAJ: Study design and critical review; MK, H: Help in data collection and paper writing; MMK, AH, THM, MW: Technical assistance and literature search; EE: Help in statistical analysis. MAJ, MK, H, MK, KAA, HJ: Critical reviewed and edited the final manuscript. HJ: Funding acquisition. All authors have read and approved the final manuscript for publication.

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References

1. Global Tuberculosis Report 2019. Geneva: World Health Organization; 2019. Licence: CC BY-NC-SA 3.0 IGO.

2. MacNeil A, Glaziou P, Sismanidis C, Maloney S, Floyd K. Global epidemiology of tuberculosis and progress toward achieving global targets-2017. Morbidity and Mortality Weekly Report. 2019; 68(11): 263-266. DOI: http://dx.doi.org/10.15585/mmwr.mm6811a3external icon.

3. World Health Organization (WHO). Global tuberculosis report 2018. Geneva: World Health Organization; 2018. Licence: CC BY-NC-SA 3.0. IGO.

4. Otu AA. Is the directly observed therapy short course (DOTS) an effective strategy for tuberculosis control in a developing country?. Asian Pacific Journal of Tropical Disease. 2013; 3(3): 227-231. DOI: https://doi.org/10.1016/S2222-1808(13)60045-6.

5. WHO EMRO. Tuberculosis: Pakistan. (http://www.emro.who.int/pak/programmes/stop-tuberculosis.html, accessed 22 November, 2019).

6. Khan MT, Malik SI, Ali S, Masood N, Nadeem T, Khan AS, Afzal MT. Pyrazinamide resistance and mutations in pncA among isolates of Mycobacterium tuberculosis from Khyber Pakhtunkhwa, Pakistan. BMC Infectious Diseases, 2019; 19: 116. DOI:10.1186/s12879-019-3764-2.

7. Ayaz S, Tahira N, Khan S, Khan SN, Rubab L, Akhtar M. Pulmonary Tuberculosis: Still Prevalent in Human in Peshawar, Khyber Pakhtunkhwa. Pakistan Journal of Life and Social Sciences. 2012; 10(1): 39-41.

8. Ahmad TA. Epidemiology of tuberculosis: current status in district Dir (Lower) Pakistan. International Journal of Scientific and Engineering Research. 2013; 4(11):755-63.
9. Ahmad T, Ahmad K, Rehman MM, Khan A, Jadoon MA, Rehman MN, Akif FA, Naz BS, Khan S, Ullah A. Tuberculosis is still a prevalent disease in population of District Dir (Lower) Khyber Pakhtunkhwa Pakistan. Global Veterinaria. 2014; 12(1):125-8. DOI: 10.5829/idosi.gv.2014.12.01.82277.

10. Ahmad T, Zohaib, Daud M, Zaman Q, Saifullah, Jadoon MA, Ismail M, Tariq M, Hussain A, Haroon, Murtaza BN, Aryal S, Pandey S, Muhammad F, Muhammad R. Prevalence of tuberculosis infection in general population of district Dir (lower) Pakistan. Middle-East Journal of Scientific Research. 2015; 23(1):14-7. DOI: 10.5829/idosi.mejsr.2015.23.01.91145.

11. Ahmad T, Jadoon MA, Khattak MN. Prevalence of sputum smear positive pulmonary tuberculosis at Dargai, District Malakand, Pakistan: A four year retrospective study. Egyptian Journal of Chest Diseases and Tuberculosis. 2016; 65(2):461-4. DOI: https://doi.org/10.1016/j.ejcdt.2015.12.004.

12. Lalokhil MS, Khan A, Adnan M, Khan MI. Prevalence of pulmonary tuberculosis in district Mardan Khyber Pakhtunkhwa, Pakistan. Microbiology: Current Research. 2019; 3(1):1-7.

13. Ahmad T, Haroon, Khan M, Khan MM, Ejeta E, Karami M, Ohia C. Treatment outcome of tuberculosis patients under directly observed treatment short course and its determinants in Shangla, Khyber-Pakhtunkhwa, Pakistan: A Retrospective study. International Journal of Mycobacteriology. 2017; 6: 360-364. DOI: 4103/ijmy.ijmy_69_17.

14. Atif M, Anwar Z, Fatima RK, Malik I, Asghar S, Scahill S. Analysis of tuberculosis treatment outcomes among pulmonary tuberculosis patients in Bahawalpur, Pakistan. BMC Research Notes. 2018; 11(1):370. DOI: 1186/s13104-018-3473-8.

15. Akhtar S, Rozi S, White F, Hasan R. Cohort analysis of directly observed treatment
outcomes for tuberculosis patients in urban Pakistan. The International Journal of Tuberculosis and Lung Disease. 2011; 15(1):90-96.

16. Syed MA. Treatment outcome of tuberculosis patients registered at DOTs centre in a tertiary care hospital. International Journal of Infectious Diseases. 2014; 21. DOI: http://dx.doi.org/10.1016/j.ijid.2014.03.953.

17. Abbasi S, Tahir M. Effectiveness of Directly Observed Therapy Short Course (DOTS) in Patients with Tuberculosis Registered at Federal General Hospital, Islamabad. International Journal of Infectious Diseases. 2018; 73. DOI: https://doi.org/10.1016/j.ijid.2018.04.4194.

18. Block Wise Provisional Summary Results of 6th Population & Housing Census-2017 [Retrieved on 06-02-2019]. Available from: http://www.pbscensus.gov.pk/sites/default/files/bwpsr/kp/malakand%20protected%20area_blockwise.pdf.

19. World Health Organization. Treatment of tuberculosis: guidelines for national programmes, third edition. Revision approved by STAG, June 2004. WHO/CDS/TB/2003.313. [Retrieved on 06-02-2019]. Available from: https://www.who.int/tb/publications/tb_2003_313_chap4_rev.pdf.

20. Centers for Disease Control and Prevention. (2003). Treatment of tuberculosis, American Thoracic society, CDC, and Infection Diseases Society of America: Treatment of Tuberculosis. MMWR. 2003; 52:1-77. [Retrieved on 06-02-2019]. Available from: https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5211a1.htm.

21. Pai M, Behr MA, Dowdy D, Dheda K, Divangahi M, Boehme CC, Ginsberg A, Swaminathan S, Spigelman M, Getahun H. Tuberculosis. Nature Reviews Disease Primers. 2016; 2: 16076. DOI: https://doi.org/10.1038/nrdp.2016.76.

22. Definitions and reporting framework for tuberculosis – 2013 revision (Updated 2014)
Geneva, Switzerland 2013.

23. Ramya VH, Gayathri G, Gangadharan V. A study of treatment outcomes of pulmonary tuberculosis and extrapulmonary tuberculosis patients in a tertiary care centre. International Journal of Advances in Medicine. 2017; 4(4):1133-1137. DOI: http://dx.doi.org/10.18203/2349-3933.ijam20173246.

24. Akarkar NS, Pradhan SS, Ferreira AM. Treatment outcomes among tuberculosis patients at an urban health centre, Goa, India- eight year retrospective record based study. International Journal of Community Medicine and Public Health. 2017; 4(3):831-834. DOI: http://dx.doi.org/10.18203/2394-6040.ijcmph20170767.

25. Trivedi PR, Khakhkhar TM. Treatment outcome of tuberculosis patients under directly observed treatment short-course and factors affecting the outcome in tertiary care hospital. International Journal of Basic & Clinical Pharmacology. 2019; 8(5):981-986. DOI: http://dx.doi.org/10.18203/2319-2003.ijbcp20191588.

26. Ramachandran G, Kupparam HKA, Vedhachalam C, Thiruvengadam K, Rajagandhi V, Dushthackeer A, Karunaianantham R, Jayapal L, Swaminathana S. Factors Influencing Tuberculosis Treatment Outcome in Adult Patients Treated with Thrice-Weekly Regimens in India. Antimicrobial Agents and Chemotherapy. 2017; 61(5): e02464-16. DOI: 10.1128/AAC.02464-16.

27. Somsong W, Lawpoolsri S, Kasetjaroen Y, Manosuthi W, Kaewkungwal J. Treatment outcomes for elderly patients in Thailand with pulmonary tuberculosis. Asian Biomed (Res Rev News). 2018; 12(2):75-82. DOI: 10.1515/abm-2019-0004.

28. Khazaei S, Hassanzadeh J, Rezaeian S, Ghaderi E, Khazaei S, Hafshejani AM, Salehiniya H, Zahiri A. Treatment outcome of new smear positive pulmonary tuberculosis patients in Hamadan, Iran: A registry-based cross-sectional study. Egyptian Journal of Chest Diseases and Tuberculosis. 2016; 65:825-830. DOI:
http://dx.doi.org/10.1016/j.ejcdt.2016.05.007.

29. Gadoev J, Asadov D, Tillashaykhov M, Tayler-Smith K, Isaakidis P, Dadu A, de Colombani P, Hinderaker SG, Parpieva N, Ulmasova D, Jalolov A, Hamraev A, Ali E, van den Boom M, Hammerich A, Gozalov O, Dara M. Factors Associated with Unfavorable Treatment Outcomes in New and Previously Treated TB Patients in Uzbekistan: A Five Year Countrywide Study. PLoS ONE 2015; 10(6): e0128907. DOI: 10.1371/journal.pone.0128907.

30. Holden IK, Lillebaek T, Seersholm N, Andersen PH, Wejse C, Johansen IS. Predictors for Pulmonary Tuberculosis Treatment Outcome in Denmark 2009–2014. Scientific Report. 2019; 9: DOI:10.1038/s41598-019-49439-9.

31. Atif M, Sulaiman SA, Shafie AA, Ali I, Asif M, Babar ZU. Treatment outcome of new smear positive pulmonary tuberculosis patients in Penang, Malaysia. BMC Infectious Disease. 2014; 14:399. DOI: http://dx.doi.org/10.1186/1471-2334-14-399.

32. Beza MG, Wubie MT, Teferi MD, Getahun YS, Bogale SM, Tefera SB. A Five Years Tuberculosis Treatment Outcome at Kolla Diba Health Center, Dembia District, Northwest Ethiopia: A Retrospective Cross-sectional Analysis. Journal of Infectious Diseases and Therapy. 2013; 1(1): 1-6. DOI: 10.4172/2332-0877.1000101.

33. Ali MK, Karanja S, Karama M. Factors associated with tuberculosis treatment outcomes among tuberculosis patients attending tuberculosis treatment centres in 2016–2017 in Mogadishu, Somalia. Pan African Medical Journal. 2017; 28:197. DOI: 10.11604/pamj.2017.28.197.13439.

34. Sakajiki MA, Garba B, Ibrahim Y, Mohammed BA, Abdullahi U, Sada KB, Ibrahim TM. Treatment outcome of Tuberculosis at a specialist hospital in North Western Nigeria - A 30 months retrospective study. Pakistan Journal of Chest Medicine 2018; 24(1):04-9.
35. Zhuben M, Delawer FM, Andar AH, Salimi F, Ngamvithayapong-Yanai J. High tuberculosis treatment success in Kabul, Afghanistan despite high patient transfers out. Eastern Mediterranean Health Journal. 2013; 19(8):694-697. DOI: 10.26719/2013.19.8.694.

36. Rahimi BA, Rahimy N, Ahmadi Q, Hayat MS, Wasiq AW. Treatment outcome of tuberculosis treatment regimens in Kandahar, Afghanistan. Indian Journal of Tuberculosis. In Press, Corrected Proof, Available online 7 November 2018. DOI: https://doi.org/10.1016/j.ijtb.2018.10.008.

37. Ahmad T, Jadoon MA. Cross sectional study of pulmonary tuberculosis at Civil Hospital Thana, District Malakand Khyber Pakhtunkhwa Pakistan. World Journal of Zoology. 2015; 10(3):161-167. DOI: 10.5829/idosi.wjz.2015.10.3.9578.

38. Saleem M, Ahmad W, Jamshed F, Sarwar J, Gul N. Prevalence of Tuberculosis in Kotli, Azad Kashmir. Journal of Ayub Medical Collage Abbottabad. 2013: 25(1-2): 175-178.

Figures
Figure 1
Map of study area (highlighted as green)

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