RESEARCH ARTICLE

Factors associated with loss to follow-up and death in patients with extensively drug-resistant tuberculosis

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Abstract

Objective: : To identify the factors associated with loss to follow-up and death during drug-resistant tuberculosis treatment.

Method: The retrospective study was conducted in Punjab, Pakistan, and comprised data from January 1, 2020, to December 31, 2022, of extensively drug resistant tuberculosis patients enrolled for treatment at four major Programmed Management Drug-resistant Tuberculosis sites. Socio-demographic, microbiological, clinical data along with treatment outcomes was extracted in December 2022 from the relevant database. The association of treatment success was explored with patient characteristics, and independent factors associated with loss to follow-up and death during the treatment were identified. Data was analysed using SPSS 21.

Results: Of the 680 patients with mean age 35±15 years, 374(55%) were males and 306(45%) were females. There were 305(44.9%) cases of treatment success, 162(23.8%) were lost to follow-up, and 213(31.3%) died. Factors related to loss to follow-up were age >35 years, previous history of second-line anti-tuberculosis drugs, adverse events of treatment, employed status, and resistance to all first-line anti-tuberculosis drugs ($p<0.05$). Factors associated with death were previous history of second-line anti-tuberculosis drugs, adverse events of treatment and employed status ($p<0.05$).

Conclusion: Employed status, previous history of second-line drugs, and adverse events of treatment were associated with loss follow-up and death in extensively drug resistant tuberculosis.

Keywords: Drug-resistant tuberculosis, Lost to follow-up, Risk factors, Mortality, Management. (JPMA 75: 1702; 2025)

DOI: https://doi.org/10.47391/JPMA.21347

Introduction

Drug-resistant tuberculosis (TB) has become a health issue as it contributes to significant loss to follow-up and death globally. Multidrug-resistant (MDR) TB is described resistance to at least both isoniazid (H) and rifampicin (R), while extensively drug-resistant (XDR) TB is defined as MDR-TB with added resistance to at least one additional Group A drug and any fluoroquinolones (FQs).[1,2] The World Health Organisation in 2021 reported that 20% (95% confidence interval [CI]: 16-26%) of MDR-TB cases have converted to XDR-TB globally.[3] The treatment success rate for MDR-TB patients who started their treatment in 2019 was 73% and it was 67% for XDR-TB patients.[1]

In 2020, there were 5.8 million confirmed new TB cases and 1.3 million deaths, which had increased from 1.2 million in 2019. Of these deaths, 191,000 (range: 191,000-264,000) occurred among MDR-TB/XDR-TB patients, the proportion of previously treated cases was 18% (95% unit interval [UI]: 11-26%) in 2021.[3] Pakistan is fourth on the list of 30 high-burden countries, with an estimated 15,000 MDR-TB infections.[4] The National TB Control Programme, Pakistan (NTP) in 2019 reported the highest frequency of MDR-TB cases (46%) in Punjab, followed by Sindh (39%), Khyber Pakhtunkhwa (KP) (10%) and Balochistan (2.7%).[2]

Drug resistance usually occurs due to inadequate treatment, like inappropriate treatment regimens, poor drug quality, use of lower than recommended doses, and poor adherence to treatment.[2] TB treatment outcomes are categorised according to the National TB guidelines in conformity with the WHO.[2,5] Cure is considered treatment completed (minimum 18 months with 16 months past culture conversion) without evidence of failure, and the last three consecutive cultures taken at least 30 days apart are negative during the continuous phase of treatment. Treatment completed means the treatment of at least 18 months with 16 months past culture conversion without evidence of failure, but no record that the last three consecutive cultures taken at least 30 days apart are negative. Lost to follow-up is defined as a patient whose treatment was interrupted for two consecutive months or more. The status 'died' is described as a patient who dies for any reason during the duration of treatment.[2,5]

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Submission complete: 16-08-2024 **1st Revision received:** 31-12-2024
Acceptance: 02-08-2025 **Last Revision received:** 01-08-2025

The current study was planned to measure the treatment outcomes of XDR-TB at in the Punjab province of Pakistan.

Materials and Methods

The retrospective study was conducted in Punjab, Pakistan, and comprised data from January 1, 2020, to December 31, 2022, of XDR-TB patients enrolled for treatment at four major Programmed Management Drug-resistant Tuberculosis (PMDT) sites. Punjab is the biggest province with respect to population in Pakistan[6] and the NTP established 11 PMDT sites for the management of DR-TB at different public hospitals of Punjab through The Global Fund support. These PMDT sites have their own teams of physicians, laboratory technicians, psychiatrists, treatment coordinators, pharmacists and other clerical staff. XDR-TB patients are sent to their respective PMDT sites for routine examination and treatment. The current study focussed on XDR-TB patients registered with PMDT sites Bahwal Victoria Hospital, Bahawalpur, District Headquarter (DHQ) Hospital, Sialkot, Gulab Devi Chest Hospital, Lahore, and Nishtar Hospital, Multan. All XDR-TB patients were treated at PMDT facilities under NTP standards, with therapy extending 20-24 months, including 18 months after culture conversion. Data of MDR-TB patients aged <15 years was excluded.

After approval from the Provincial Bioethics Committee of Punjab, socio-demographic, microbiological and clinical data along with treatment outcomes was extracted in December 2022 from the Electronic Nominal Recording Reporting System (ENRS) of PMDT sites using convenience sampling technique. The socio-demographic data included gender, age, and employment status. Microbiological data included resistance to first-line drug (FLD), second-line drug (SLD) anti-TB drugs, and sputum culture test. The clinical data included body weight at the time of registration, comorbidity, previous history of FLD, history of SLD, registration group, and adverse events due to treatment. The treatment outcomes data included treatment success (treatment completed and cured), loss to follow-up, and death due to TB.

Data was analysed using SPSS 21. Categorical variables were expressed as frequencies and percentages, and they were subjected to Pearson's chi-square test. Continuous variables were expressed as mean±standard deviation and significant differences were assessed using the *t*-test. P<0.05 was considered statistically significant. Univariable logistic regression analysis was used to investigate the relationship between treatment success and patient characteristics. Variables with $p<0.05$ in univariable analysis were added to the multivariate logistic regression model. Adjusted odds ratio (AOR) with 95% CI was computed.

Results

Of the 680 patients, 177(26.03%) were from Bahawal Victoria Hospital, Bahawalpur, 72(10.59%) were from DHQ Hospital, Sialkot, 141(20.74%) were from Gulab Devi Chest Hospital, Lahore, and 290(42.64%) were Nishtar Hospital, Multan. The overall mean of the patients was 35±15 years. There were 374(55%) males and 306(45%) females. Of the total, 305(44.9%) cases of treatment success, 162(23.8%)

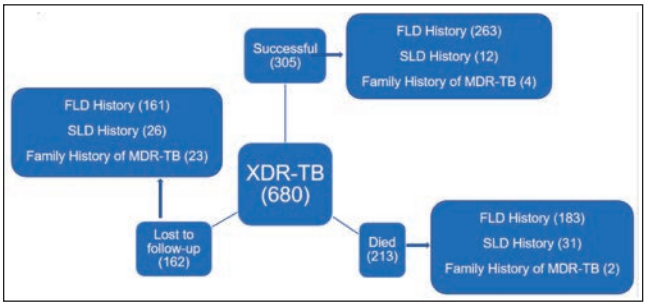

Figure-1: Flow diagram of the data.

XDR-TB: Extensively drug resistant tuberculosis, SLD: Second-line drug, FLD: First-line drug, MDR-TB: Multidrug resistant tuberculosis.

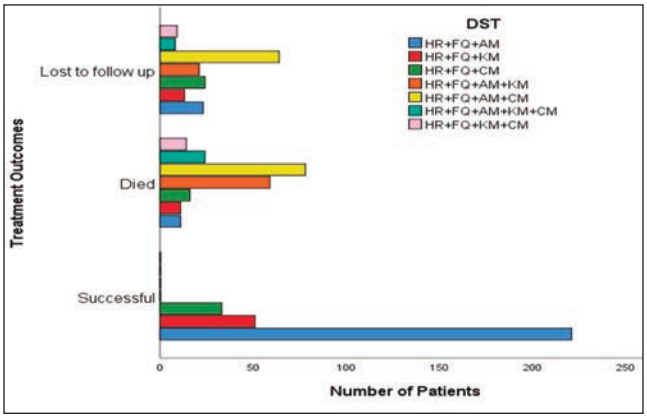

Figure-2: Treatment outcomes for the resistance pattern.

DST: Drug susceptibility testing, R: Rifampicin, H: Isoniazid, FQ: Fluoroquinolone, AM: Amikacin, CM: Capreomycin, KM:

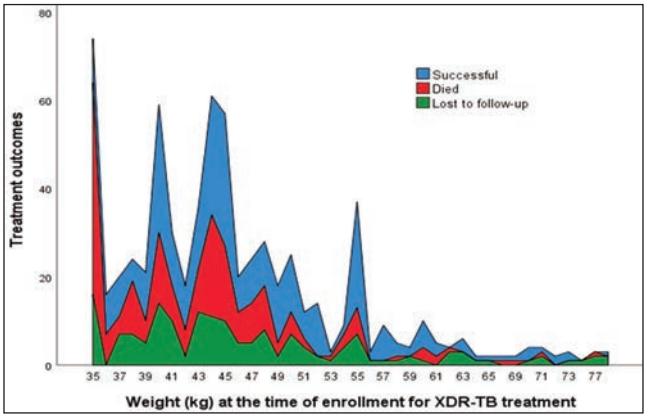

Figure-3: Distribution of treatment outcomes with respect to body weight of the patients. *XDR-TB: Extensively drug resistant tuberculosis.*

Table-1: Socio-demographic and clinical characteristics for treatment outcomes.

Characteristics	Total n (column %)	XDR-TB treatment outcomes			*p*-value
		Successful n (row %)	Died n (row %)	Lost to follow -up n (row %)	
Mean Age (years)	35±15	32±13	38±17	36±15	<0.001
Gender					0.128
Male	374(55.0)	164(43.9)	110(29.4)	100(26.7)	
Female	306(45.0)	141(46.1)	103(33.7)	62(20.3)	
Employment status					0.001
Employed	222(32.6)	104(46.8)	62(27.9)	56(25.2)	
Unemployed	87(12.8)	20(23.0)	41(47.1)	26(29.9)	
Self- employed	269(39.6)	126(46.8)	83(30.9)	60(22.3)	
Student	102(15.0)	55(53.9)	27(26.5)	20(19.6)	
Weight (kg) at the start of treatment, mean±SD	44±10	45±10	40±9	46±11	<0.001
Previous TB History					0.681
No	99(14.6)	42(42.4)	30(30.3)	27(27.3)	
Yes	581(85.4)	263(45.3)	183(31.5)	135(23.2)	
Previously SLD use					<0.001
No	609(89.6)	292(47.9)	181(29.7)	136(22.3)	
Yes	71(10.4)	13(18.3)	32(45.1)	26(36.6)	
Comorbidity					0.666
No	572(84.1)	255(44.6)	183(32.0)	134(23.4)	
Yes	108(15.9)	50(46.3)	30(27.8)	28(25.9)	
Resistance to FLD					0.027
HR	21.2(31.2)	83(39.2)	59(27.8)	70(33.0)	
HRE	47(6.9)	20(42.6)	18(38.3)	09(19.1)	
HRS	34(5.0)	20(58.8)	08(23.5)	06(17.6)	
HRZ	81(11.9)	32(39.5)	27(33.3)	22(27.2)	
HRES	53(7.8)	26(49.1)	18(34.0)	09(17.0)	
HREZ	84(12.4)	36(42.9)	28(33.3)	20(23.8)	
HRZS	50(7.4)	22(44.0)	17(34.0)	11(22.0)	
HREZS	119(17.5	66(55.5)	38(31.9)	15(12.6)	
Registration Group					0.010
New	84(12.4)	35(41.7)	26(31.0)	23(27.4)	
Previous treated	355(52.2)	160(45.1)	109(30.7)	86(24.2)	
After lost to follow up	40(5.9)	08(20.0)	16(40.0)	16(40.0)	
After failure	169(24.9)	84(49.7)	57(33.7)	28(16.6)	
Relapse	32(4.7)	18(56.3)	05(15.6)	09(28.1)	
Adverse events					<0.001
No	585(86.0)	243(41.5)	190(32.5)	152(26.0)	
Yes	95(14.0)	62(65.3)	23(24.2)	10(10.5)	

Successful: Cured + treatment completed, H: Isoniazid, R: Rifampicin, E: Ethambutol, S: Streptomycin, Z: Pyrazinamide, SD: Standard deviation, XDR-TB: Extensively drug resistant tuberculosis, SLD: Second-line drug, FLD: First-line drug.

were lost to follow-up, and 213(31.3%) died (Figure 1). Age, employment status, body weight, history of SLD and FLD use, registration group and adverse events were significantly associated with treatment outcome (Table 1).

Based on the resistance pattern, all patients had resistance to R, H and FQs, while the patients who either died or were lost to follow-up had the highest frequency of resistance to R, H, amikacin (AM) and capreomycin (CM) (Figure 2).

Of the 467 patients with XDR-TB, 162(34.7%) were lost to follow-up. A significant association was found between age >35 years, previous history of SLD (p=0.002; AOR=1.85; 95%CI=1.25-2.75) and loss to follow-up (p=0.001; AOR=4.32; 95%CI=1.87-9.98). Similarly, adverse events of treatment showed a decrease in the odds of being lost to follow-up among XDR-TB patients (p<0.001; AOR=0.27; 95%CI=0.13-0.52), and employed status was significantly associated with loss to follow-up (p=0.005; AOR=3.03; 9%%CI=1.40-6.54) compared to unemployment status, while resistance to FLDs was significantly associated with loss to follow-up (p=0.001; AOR=0.30; 95%CI=0.15-0.59). Gender, previous TB history, comorbidity and registration group were not significantly associated with treatment outcomes (Table 2).

Table-2: The factors associated with loss to follow-up among patients with XDR-TB.

Variables	Total (n=467)	XDR-TB treatment outcomes		Univariable Analysis Unadjusted Odds Ratio [95% CI, *p*-value]	Multivariable Analysis Adjusted Odds Ratio [95% CI, *p*-value]
		Successful n (%) 305(65.3%)	Lost to follow-up [n (%)] 162(34.7)		
Age (years)					
≤ 35	281	198(42.4)	83(17.8)	Ref.	Ref.
> 35	186	107(22.9)	79(16.9)	1.76[1.20-2.60, 0.004]	1.85[1.25-2.75,0.002]
Gender					
Female	203	141(30.2)	62(13.3)	Ref.	-
Male	264	164(35.1)	100(21.4)	1.39[0.94-2.05,0.099]	
Employment status					
Employed	160	104(22.3)	56(12.0)	Ref.	
Unemployed	46	20(4.3)	26(5.6)	2.41[1.24-4.71,0.010]	-
Self- employed	186	126(27.0)	60(12.8)	0.88[0.57-1.38,0.590]	
Student	75	55(11.8)	20.4.3)	0.68[0.37-1.24,0.204]	
Weight					
>44 kg	281	198(42.4)	83(17.8)	Ref.	-
≤44 kg	186	107(22.9)	79(16.9)	0.85[9,57-1.25,0.403]	
Previous TB History					
No	69	42(9.0)	27(5.8)	Ref.	-
Yes	398	263(56.3)	135(28.9)	0.80[0.47-1.35,0.402]	
Previously SLD use					
No	428	292(62.5)	136(29.1)	Ref.	Ref.
Yes	39	13(2.8)	26(5.6)	4.29[2.14-8.61,<0.001]	4.32[1.87-9.98,0.001]
Comorbidity					
No	389	255(54.6)	134(28.7)	Ref.	-
Yes	78	50(10.7)	28(6.0)	1.07[0.64-1.77,0.806]	
Resistance to FLD					
HR	153	83(27.2)	70(43.2)	Ref.	Ref.
HRE	29	20(6.6)	09(5.6)	0.53[0.23-1.25,0.147]	-
HRS	26	20(6.6)	06(3.7)	0.36[0.14-0.94,0.036]	-
HRZ	54	32(10.5)	22(13.6)	0.82[0.44-1.53,0.524]	-
HRES	35	26(8.5)	09(5.6)	0.41[0.18-0.93,0.034]	-
HREZ	56	36(11.8)	20(12.3)	0.66[0.35-1.24,0.196]	-
HRZS	33	22(7.2)	11(6.8)	0.59[0.27-1.31,0.195]	-
HREZS	81	66(21.6)	15(9.3)	0.27[0.14-0.51,<0.001]	0.30[0.15-0.59,0.001]
Registration Group					
New	58	35(11.5)	23(14.2)	Ref.	Ref.
Previous treated	246	160(52.5)	86(53.1)	0.82[0.45-1.47,0.503]	-
After lost to follow-up	24	08(2.6)	16(9.9)	3.04[1.12-8.26,0.029]	1.08[0.24-4.84,0.925]
After failure	112	84(27.5)	28(17.3)	0.51[0.26-0.99,0.050]	0.30[0.08-1.10,0.069]
Relapse	27	18(5.9)	09(5.6)	0.76[0.29-1.98,0.576]	-
Adverse events					
No	394	243(79.7)	151(93.8)	Ref.	Ref.
Yes	72	62(20.3)	10(6.2)	0.26[0.13-0.52, <0.001]	0.27[0.13-0.55,<0.001]

*Ref.=Reference ; XDR-TB: Extensively drug resistant tuberculosis, H: Isoniazid, R: Rifampicin, E: Ethambutol, S: Streptomycin, Z: Pyrazinamide, SLD: Second-line drug, CI: Confidence interval.

There was a significant association of weight <40kg with death and loss to follow-up (Figure 3).

Of the 518 patients with XDR-TB, 213(41.1%) died. A significant association was for death with age, weight at the time of registration, and previous history of SLD (Table 3). Adverse events of treatment showed a decrease in the odds of death among XDR-TB patients (p=0.010; AOR=0.49; 95%CI=0.29-0.85), and employed status was significantly associated with death (p=0.001; AOR=3.07; 95%CI=1.56-6.02). Gender, previous TB history, comorbidity, resistance to FLDs and registration group were not significantly associated with death (p>0.05).

Discussion

Globally, the success rate of treatment among XDR-TB patients is 44.2%, far below the WHO's target rate of 75%.[7]

Table-3: The factors associated with death during treatment among XDR-TB patients.

Variables	Total (n=518)	XDR-TB treatment outcomes		Univariable Analysis Unadjusted Odds Ratio [95% CI, *p*-value]	Multivariable Analysis Adjusted Odds Ratio [95% CI, *p*-value]
		Successful n(%) 305(58.9)	Died n(%) 213(41.1)		
Age (years)					
≤ 35	307	198(38.2)	109(21.0)	Ref.	Ref.
> 35	211	107(20.7)	104(20.1)	1.77[1.24-2.52, 0.002]	2.32[1.57-3.41,<0.001]
Gender					
Female	244	141(27.2)	103(19.9)	Ref.	-
Male	274	164(31.7	110(21.2)	0.91[0.65-1.30, 0.633]	
Employment status					
Employed	166	104(20.1)	62(12.0)	Ref.	Ref.
Unemployed	61	20(3.9)	41(7.9)	3.44[1.85-6.39,<0.001]	3.07[1.56-6.02,0.001]
Self-employed	209	126(24.3)	83(16.0)	1.11[0.73-1.68,0.641]	-
Student	82	55(10.6)	27(5.2)	0.82[0.47-1.44,0.495]	-
Weight					
>44 kg	351	178(34.4)	173(33.4)	Ref.	Ref.
≤44 kg	167	127(24.5)	40(7.7)	0.32[0.22-0.49,<0.001]	0.26[0.17-0.43,<0.001]
Previous TB History					
No	72	42(8.1)	30(5.8)	Ref.	-
Yes	446	263(50.8)	183(35.3)	0.97[0.59-1.61,0.919]	
Previously SLD use					
No	473	292(56.4)	181(34.9)	Ref.	Ref.
Yes	45	13(2.5)	32(6.2)	3.97[2.03-7.77,<0.001]	3.41[1.64-7.07,0.001]
Comorbidity					
No	438	255(49.2)	183(35.3)	Ref.	-
Yes	80	50(9.7)	30(5.8)	0.84[0.51-1.37,0.475]	
Resistance to FLD					
HR	142	83(16.0)	59(11.4)	Ref.	-
HRE	38	20(3.9)	18(3.5)	1.27[0.62-2.60,0.520]	
HRS	28	20(3.9)	08(1.5)	0.56[0.23-1.36,0.203]	
HRZ	59	32(6.2)	27(5.2)	1.19[0.64-2.19,0.583]	
HRES	44	26(5.0)	18(3.5)	0.97[0.49-1.94,0.940]	
HREZ	64	36(6.9)	28(5.4)	1.09[0.60-1.99,0.767]	
HRZS	39	22(4.2)	17(3.3)	1.09[0.53-2.22,0.819]	
HREZS	104	66(12.7)	38(7.3)	0.81[0.48-1.36,0.810]	
Registration Group					
New	61	35(6.8)	26(5.0)	Ref.	Ref.
Previous treated	269	160(30.9)	109(21.0)	0.92[0.52-1.61,0.763]	-
After lost to follow-up	24	08(1.5)	16(3.1)	2.69[1.00-7.23,0.050]	1.25[0.30-5.26,0.759]
After failure	141	84(3.5)	57(11.0)	0.91[0.50-1.68,0.771]	-
Replapse	23	18(3.5)	05(1.0)	0.37[0.12-1.14,0.083]	-
Adverse events					
No	433	243(46.9)	190(36.7)	Ref.	Ref.
Yes	85	62(12.0)	23(4.4)	0.47[0.28-0.79,0.005]	0.49[0.29-0.85,0.010]

*Ref.=Reference; XDR-TB: Extensively drug resistant tuberculosis, H: Isoniazid, R: Rifampicin, E: Ethambutol, S: Streptomycin; Z: Pyrazinamide, SLD: Second-line drug, CI: Confidence interval.

The treatment success rate of 44.9% in the current study is inferior to reports from China (76%),[8] India (81.6%)[9] and Uganda (77.3%).[10]

The loss to follow-up rate (162/467) in the current study (34.7%) is relatively high rate compared to the global estimate of 6%[3] but is lower than the rates reported from Georgia (37.7%),[11] Indonesia (47.1%),[12] India (87%)[13] and New Guinea 39%.[14] As the XDR-TB patients who are employed are highly infective and potential sources of XDR-TB transmission, loss to follow-up of patients aged >35 years and having a history of SLD is a serious threat to the public health. Resistance to FLDs and SLDs has been widely reported as a factor of unsuccessful treatment outcomes among DR-TB patients.[15,16]

In the current study, 213(41.1%) patients died during the study period due to XDR-TB. Similar results have been from the same province of Pakistan have been reported by other studies.[17,18]

Additionally, the current study's death rate is higher than that of a study conducted in Punjab (30%) by Abdul Majeed et al. using programmed data, and by Wahid et al. in Pakistan (9.9%) which used multicentre data.[19,20]

In the multivariate analysis, XDR-TB patients with employed status were significantly more likely to die. The XDR-TB patients are more likely to die due to a combination of risk factors, including age, weight, history of SLD treatment, and adverse treatment events. Other studies in Pakistan found a similar correlation between unsuccessful therapy and adverse events in patients with MDR-TB and XDR-TB.[11,21]

The current study has limitations. First, due to the retrospective design, some important factors were missing in the record of the patients at PMDT sites, and it was not possible to include the level of education, baseline lung cavitation, body mass index (BMI) and behaviour status that have all been previously reported as important predictors of unsuccessful treatment outcome in XDR-TB.[22,23] Second, the findings may not be generalised because the sample was drawn using convenience sampling technique from four PMDT sites in a single province of Pakistan.

Conclusions

Among XDR-TB patients, those aged >35 years, having employed status, SLD history, patients facing adverse reactions of treatment, and those with all FLD antibiotic resistance at diagnosis were at the highest risk of an unsuccessful treatment outcome.

Disclaimer: None.

Conflict of Interest: None.

Source of Funding: None.

References

1. World Health Organization. Global tuberculosis report. Geneva: WHO; 2021. [Online] [Cited 2021 Feb 19]. Available from: URL: https://apps.who.int/iris/bitstream/handle/10665/336069/9789240013131-eng.pdf
2. National TB Control Program, Pakistan. Annual report. Islamabad: NTP; 2019. [Online] [Cited 2019 Feb 23]. Available from: URL: https://ptp.gkp.pk/ptp-admin/admin/pdf/Annual_Report_TB_Pakistan_2019.pdf
3. World Health Organization. Global Task Force on TB Impact Measurement: report of a subgroup meeting on methods used by WHO to estimate TB disease burden, 11–12 May 2022, Geneva, Switzerland. Geneva: WHO; 2022. [Online] [Cited 2022 Oct 10]. Available from: URL: https://apps.who.int/iris/bitstream/handle/10665/363428/9789240057647-eng.pdf
4. Ali S, Khan MT, Khan AS. Prevalence of multidrug-resistant Mycobacterium tuberculosis in Khyber Pakhtunkhwa – a high tuberculosis endemic area of Pakistan. Pol J Microbiol. 2020;69:133-7. doi:10.33073/PJM-2020-005.
5. Sattar A, Biomedical Sci J Res T. Rising trends of multidrug-resistant tuberculosis in Pakistan. Biomed J Sci Tech Res. 2018;12:1-4. doi:10.26717/BJSTR.2018.12.002254.
6. Punjab Bureau of Statistics. Punjab in figures. Lahore: Planning and Development Board; 2020. [Online] [Cited 2020 December 10]. Available from: URL: https://bos.punjab.gov.pk/system/files/PIF-2022.pdf
7. Pedersen OS, Holmgaard FB, Mikkelsen MKD, Lange C, Sotgiu G, Lilleaek T, et al. Global treatment outcomes of extensively drug-resistant tuberculosis in adults: a systematic review and meta-analysis. J Infect. 2023;87:177-89. doi:10.1016/j.jinf.2023.06.014.
8. Li Q, Shi CX, Lu M, Wu L, Wu Y, Wang M, et al. Treatment outcomes of multidrug-resistant tuberculosis in Hangzhou, China, 2011 to 2015. Medicine (Baltimore). 2020;99:e21296. doi:10.1097/MD.0000000000021296.
9. Desai U, Joshi JM. Extrapulmonary drug-resistant tuberculosis at a drug-resistant tuberculosis center, Mumbai: our experience – hope in the midst of despair. Lung India. 2019;36:3-7. doi:10.4103/lungindia.lungindia_192_18.
10. Kintu TM, Mwanahamisi BS, Muwanguzi M, Kyagambiddwa T, Miiro E, Tishekwa N, et al. Unfavorable treatment outcomes among patients with drug-resistant TB in Uganda. Int J Tuberc Lung Dis. 2023;27:291-7. doi:10.5588/ijtld.22.0638.
11. Frank M, Adamashvili N, Lomtadze N, Kokhreidze E, Avaliani Z, Blumberg H. Long-term follow-up reveals high posttreatment mortality rate among patients with extensively drug-resistant tuberculosis in the country of Georgia. Open Forum Infect Dis. 2019;6:ofz152. doi:10.1093/ofid/ofz152.
12. Soedarsono S, Mertaniasih NM, Kusmiati T, Permatasari A, Alfian IN. Determinant factors for loss to follow-up in drug-resistant tuberculosis patients: the importance of psycho-social and economic aspects. BMC Pulm Med. 2021;21:360. doi:10.1186/s12890-021-01735-9.
13. Shringarpure KS, Isaakidis P, Sagili KD, Baxi RK. Loss-to-follow-up on multidrug-resistant tuberculosis treatment in Gujarat, India: the when and who of it. PLoS One. 2015;10:e0132543. doi:10.1371/journal.pone.0132543.
14. Foster J, Mendez D, Marais BJ, Peniyamina D, McBryde ES. Predictors of unfavourable treatment outcome in patients diagnosed with drug-resistant tuberculosis in the Torres Strait/Papua New Guinea border region. PLoS One. 2022;17:e0266436. doi:10.1371/journal.pone.0266436.
15. Kanwal S, Akhtar A. Risk factors associated with loss to follow-up among multidrug-resistant tuberculosis patients registered for treatment in programmatic management of drug-resistant tuberculosis sites of Punjab, Pakistan. J Biostat Epidemiol. 2020;6:162-9.
16. Faye LM, Hosu MC, Iruedo J, Vasaikar S, Nokoyo KA, Tsuro U, et al. Treatment outcomes and associated factors among tuberculosis patients from selected rural Eastern Cape hospitals: an ambidirectional study. Trop Med Infect Dis. 2023;8:315. doi:10.3390/tropicalmed8060315.
17. Kanwal S, Akhtar AM, Ahmed A. Factors associated with mortality to drug-resistant tuberculosis and their programmatic management in treatment centres of Punjab, Pakistan. J Pak Med Assoc. 2017;67:858-62.
18. Atif M, Mukhtar S, Sarwar S, Naseem M, Malik I, Mushtaq A, et al. Drug resistance patterns, treatment outcomes and factors affecting unfavourable treatment outcomes among extensively drug-resistant tuberculosis patients in Pakistan: a multicentre record review. Saudi Pharm J. 2022;30:462-9. doi:10.1016/j.jsps.2022.01.015.
19. Akhtar AM, Kanwal S, Majeed S, Majeed W. Weight variation increases the risk of death during the intensive phase of treatment among MDR-TB patients: a retrospective study. Pak J Med Sci. 2023;39:1080-5. doi:10.12669/pjms.39.4.7025.

20. Wahid A, Ahmad N, Ghafoor A, Latif A, Saleem F, Khan S, et al. Effectiveness of shorter treatment regimen in multidrug-resistant tuberculosis patients in Pakistan: a multicenter retrospective record review. Am J Trop Med Hyg. 2021;104:1784-91. doi:10.4269/ajtmh.20-1134.
21. Khan I, Ahmad N, Khan S, Muhammad S, Ahmad Khan S, Ahmad I, et al. Evaluation of treatment outcomes and factors associated with unsuccessful outcomes in multidrug-resistant tuberculosis patients in Baluchistan province of Pakistan. J Infect Public Health. 2019;12:809-15. doi:10.1016/j.jiph.2019.04.009.
22. Saifullah A, Mallhi TH, Khan YH, Iqbal MS, Alotaibi NH, Alzarea AI, et al. Evaluation of risk factors associated with the development of MDR- and XDR-TB in a tertiary care hospital: a retrospective cohort study. PeerJ. 2021;9:e10826. doi:10.7717/peerj.10826.
23. Abubakar M, Ahmad N, Ghafoor A, Latif A, Ahmad I, Atif M, et al. Treatment outcomes of extensively drug-resistant tuberculosis in Pakistan: a countrywide retrospective record review. Front Pharmacol. 2021;12:640555. doi:10.3389/fphar.2021.640555.

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SK: Design, statistical analysis, data interpretation and final approval.
AH: Data entering and drafting.
AMA: Review and provide the data.