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STUDENTS' CORNER ORIGINAL ARTICLE

DISTRIBUTION OF DR-TB BY SEX, AGE GROUPS, OCCUPATION, PROVINCE, DIVISION, DISTRICT, TYPE OF DISEASE, TYPE OF DRUG RESISTANCE, TREATMENT REGIMEN AND OUTCOME OF TREATMENT IN DR-TB POPULATION IN D.I.KHAN DIVISION, PAKISTAN

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ABSTRACT

Background: Drug-resistant tuberculosis (DR-TB) is the major cause of mortality worldwide. Our objectives were to determine the distribution of DR-TB by sex, age groups, occupation, province, division, district, type of disease, type of drug resistance, treatment regimen and outcome of treatment in DR-TB population in D.I.Khan Division, Pakistan.

Materials & Methods: This cross-sectional study was conducted in Department of Community Medicine, Gomal Medical College, D.I.Khan, Pakistan. A sample of 286 DR-TB patients was selected consecutively from population at risk. Sex, age groups, occupation, province, division and district were demographic while type of disease, type of drug resistance, treatment regimen and outcome of treatment were research variables. All variables being nominal were described by count, percentage & cumulative percentage with 95% confidence interval for proportion. Distribution of DR-TB patients by all the ten variables were substantiated by chi-square goodness-of-fit test.

Results: Out of 286 DR-TB patients, 123 (43%) were men and 163 (57%) women. DR-TB cases were most prevalent in age group 15-44 years 172 (60.14%), housewife 140 (48.95%), Khyber Pakhtunkhwa 175 (61.19%), D.I.Khan Division 178 (62.24%) and district 121 (42.31%). Most common type of disease, drug resistance and treatment regimen was pulmonary TB 282 (98.60%), MDR 273 (95.45%) and longer treatment (n=273 MDR-TB) 246 (90.11%) respectively. Treatment success rate was 161 (56.29%). The observed prevalence by occupation, province, division, district and type of disease in our sample was similar to expected prevalence in population ($p>.05$ for all), while it was different from population by sex, age groups, type of drug resistance, regimen and treatment outcome ($p<.05$ for all).

Conclusion: The prevalence of DR-TB was higher in women, age group 15-44 years, housewife, Khyber Pakhtunkhwa and D.I.Khan Division and District. Most common type of disease, drug resistance and treatment regimen was pulmonary TB, MDR and longer treatment respectively. Treatment success rate was 56.29%. The observed prevalence by occupation, province, division, district and type of disease in sample was similar to population, while it was different by sex, age groups, type of drug resistance, regimen and treatment outcome.

KEY WORDS: Tuberculosis; Pulmonary Tuberculosis; Drug-Resistant Tuberculosis, Multidrug-Resistant Tuberculosis; MDR Tuberculosis; Extensively Drug-Resistant Tuberculosis; XDR-TB; Drug Resistance; Multidrug Resistance.

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1. INTRODUCTION

1.1 Background Tuberculosis (TB) is the 10th leading cause of mortality worldwide and the leading cause of death from a single infectious disease. Globally in 2018, about 10 million people suffered from TB. TB causes 1.2 million deaths in HIV non-infected patients and 251,000 deaths in HIV infected patients.

In 2018 the highest prevalence was in adult men 57%, followed by adult women 32% and children 11%. There was 8.6% prevalence of TB in HIV patients. Eight countries are responsible for two thirds of the global TB burden: India 27%, Indonesia 8%, China 9%, Philippines 6%, Pakistan 6%, Nigeria 4%, Bangladesh 4% and South Africa 3%. Globally in 2018, about 3.4% new TB cases and 18% previously treated cases had MDR/RR TB. In 2018, about 0.5 million incident cases were rifampicin-resistant (RR); out of which 78% were multidrug-resistant (MDR) TB. About 214,000 deaths occurred from MDR-TB in 2017.[1]

Pakistan is 5th high-prevalent country for TB and 5th for DR-TB. Estimated TB incidence, prevalence and mortality is 267/100,000, 341/100,000 and 27/100,000 population respectively with about 525,000 annual incident TB cases.[2]

Worku, et al.[3] from Addis Ababa, Ethiopia from November 2011 to December 2016 with 340 pulmonary MDR/RR-TB cases notified distribution as 180 (52.94%) men and 160 (47.06%) women, 5 (1.5%) in age group <15 years, 105 (30.9%) in 15-24, 199 (58.5%) in 25-44 and 31 (9.1%) in ≥45 years.

Johnston, et al.[4] from Canada reported successful treatment in 62% (95% CI 57-67), death in 11% (95% CI 9-13), failed therapy in 8% (95% CI 5-11), default rate 13% (95% CI 9-17) and 2% (95% CI 1-4) were not evaluated out of 4,959 MDR-TB patients for years 1973-2006.

He, et al.[5] from Shandong Province, China from January 2007 to December 2014 reported 13,486 culture-confirmed TB cases, of which 21.2% (2,855*100/13,486=21.2%) were resistant to at least one first line anti-TB drugs, 6.2% (838*100/13,486=6.2%) were MDR-TB patients and 1.2% (16*100/13,486=1.2%) were resistant to rifampicin.

Alene, et al.[6] from Changsha, Hunan, China from 2011 to 2014 reported 481 DR-TB, including 471 (98%) MDR-TB and 10 (2%) XDR-TB. Out of 481 DR-TB cases, 340 (70.7%) were men and 141 (29.3%) women, 380 (79.0%) farmer, 15 (3.1%) labourer, 16 (3.3%) employed, 19 (3.8%) unemployed and 51 (10.6%) other/unknown, 261 (54.3%) were cured, 14 (2.9%) completed, 13 (2.7%) died, 63 (13.1%) failure and 130 (27.0%) loss to follow up cases.

Venkatesh, et al.[7] from Gorakhpur, India from November 2015, to October 2016 reported 157 MDR-TB patients as 80 (51%, 95%CI 43.2-58.6) in age group 18-29 years, 45 (28.7%, 95%CI 22.1-36.1) in 30-40 and 32 (20.3% 95%CI 14.8-27.3) in >40 years, 108 (68.8%, 95%CI 61.1-75.5) in men and 49 (31.2%, 95%CI 24.4-38.8) in women and 153 (97.5%, 95%CI 93.6-99.0) had pulmonary TB, 2 (1.3%, 95%CI 0.3-4.5) had pulmonary & pleural TB and 2 (1.3 % 95% CI 0.3-4.5) had pulmonary & other system TB respectively.

Hasan, et al.[8] from Karachi, Pakistan from 2006 to 2009 notified frequency of MDR and XDR TB among 9,523 *mycobacterium tuberculosis* isolates as 38.66% (3,682*100/9,523=38.66%) and 1.19% (113*100/9,523=1.19%) respectively.

Akhter, et al.[9] from Lahore, Pakistan from Jan. 2010 to June 2014 distributed 1,250 retreatment DR-TB cases across MDR-TB and mono/ poly-resistant TB as 861(69%) and 389 (31%), across men and women as 664 (53.12%) and 586 (46.88%), across age groups of 0-14 years, 15-45 and >46 years as 31 (2.48%), 996 (79.68%) and 223 (17.84%) and across pulmonary and extra pulmonary TB as 1231 (98.48%) and 19 (1.52%) respectively.

Wahab, et al.[10] from Peshawar, Pakistan from December 2006 to October 2007 showed distribution of 30 MDR-TB cases as 17 (56.7%) men and 13 (43.3%) women, 4 (13.3%) in age group <20 years, 18 (60%) in 20-40, 8 (26.7%) in >40 years, 11 (36.67 %) labourer, 1 (3.33%) student, 2 (6.67 %) govt. employee, 13 (43.33%) housewife and 3 (10 %) others.

Ahmad, et al.[11] from Peshawar, Pakistan from Jan. 2012 to July 2013 reported 289 DR-TB cases. Out of 289 DR-TB cases, 17 (5.88%) were treated MDR-TB cases, 243 (84.08%) newly diagnosed MDR-TB cases (total MDR-TB cases 17+243=260 (89.96%), 10 (3.46%) were mono-resistant TB, six (2.08%) poly-resistant TB and 13 (4.50%) XDR-TB. Out of 243 newly diagnosed MDR-TB, 238 (97.9%) were pulmonary, two (0.8%) pulmonary & extra pulmonary (total pulmonary cases 238+2=240 [98.77%]) and three (1.23%) extra-pulmonary cases.

Arshad, et al.[12] from Peshawar, Pakistan from February 2011 to December 2012 reported 51.76% (132*100/255=51.76) MDR-TB cases out of 255 DR-TB cases. Out of 132 MDR-TB cases, 67 (67*100/132=50.76%) were eligible for shorter treatment regimen, while 65 (65*100/132=49.24%) were not eligible.

1.2 Research Problems (RPs), Knowledge Gaps (KGs) & Justification

Allocation of resources is planned on the basis of overall and group wise burden of the problem/ disease. Unawareness of distribution of drug resistant tuberculosis (DR-TB) by sex, age groups, occupation, province, division, district, type of disease, type of drug resistance, treatment regimen and outcome of treatment in DR-TB population in D.I.Khan Division, Pakistan are our ten RPs. Unavailability of data regarding these RPs on various databases like Google Scholar, PubMed, ScienceDirect, ProQuest and Pakistan Research Repository are our ten KGs. To fill these KGs is justification of our project.

1.3 Research Questions (RQs)

RQ 1-10: What is the distribution of DR-TB by sex, age groups, occupation, province, division, district, type of disease, type of drug resistance, treatment regimen and outcome of treatment respectively in DR-TB population in D.I.Khan Division, Pakistan?

RQ 11-20: Is there any difference between the observed and expected distribution of DR-TB by sex, age groups, occupation, province, division, district, type of disease, type of drug resistance, treatment regimen and outcome of treatment respectively in DR-TB population in D.I.Khan Division, Pakistan?

1.4 Research Objectives (ROs)

The objectives of our study were to determine the:

RO 1-10: distribution of DR-TB by sex, age groups, occupation, province, division, district, type of disease, type of drug resistance, treatment regimen and outcome of treatment respectively in DR-TB population in D.I.Khan Division, Pakistan.

RO 11-20: difference between the observed and expected distribution of DR-TB by sex, age groups, occupation, province, division, district, type of disease, type of drug resistance, treatment regimen and outcome of treatment respectively in DR-TB population in D.I.Khan Division, Pakistan.

1.5 Research Hypotheses (Null)

H_{01}: There is no difference between the observed and expected distribution of DR-TB by sex in DR-TB population in D.I.Khan Division, Pakistan. (RQ 11, RO 11)

H_{02}: There is no difference between the observed and expected distribution of DR-TB by age groups in DR-TB population in D.I.Khan Division, Pakistan. (RQ 12, RO 12)

H_{03}: There is no difference between the observed and expected distribution of DR-TB by occupation in DR-TB population in D.I.Khan Division, Pakistan. (RQ 13, RO 13)

H_{04}: There is no difference between the observed and expected distribution of DR-TB by province in DR-TB population in D.I.Khan Division, Pakistan. (RQ 14, RO 14)

H_{05}: There is no difference between the observed and expected distribution of DR-TB by division in DR-TB population in D.I.Khan Division, Pakistan. (RQ 15, RO 15)

H_{06}: There is no difference between the observed and expected distribution of DR-TB by district in DR-TB population in D.I.Khan Division, Pakistan. (RQ 16, RO 16)

H_{07}: There is no difference between the observed and expected distribution of DR-TB by type of disease in DR-TB population in D.I.Khan Division, Pakistan. (RQ 17, RO 17)

H_{08}: There is no difference between the observed and expected distribution of DR-TB by type of drug resistance in DR-TB population in D.I.Khan Division, Pakistan. (RQ 18, RO 18)

H_{09}: There is no difference between the observed and expected distribution of DR-TB by treatment regimen in DR-TB population in D.I.Khan Division, Pakistan. (RQ 19, RO 19)

H_{10}: There is no difference between the observed and expected distribution of DR-TB by outcome of treatment in DR-TB population in D.I.Khan Division, Pakistan. (RQ 20, RO 20)

1.6 Operational definitions[13]

Mono-resistance: "Resistance to any one first-line anti-TB drug only".

Poly-resistance: "Resistance to more than one first-line anti-TB drugs, other than both isoniazid and rifampicin".

Multidrug resistance (MDR): "Resistance to at least both isoniazid and rifampicin".

Extensive drug resistance (XDR): "Resistance to any fluoroquinolone, and at least one of three second-line injectable drugs (capreomycin, kanamycin and amikacin), in addition to multidrug resistance".

Rifampicin resistance (RR): "Resistance to rifampicin detected using phenotypic or genotypic methods, with or without resistance to other anti-TB drugs. It includes any resistance to rifampicin, in the form of mono-resistance, poly-resistance, MDR or XDR".

Multi drug-resistance TB (MDR-TB): "Resistance to at least both isoniazid and rifampicin".

Extensive drug-resistance TB (XDR-TB): "Resistance to any fluoroquinolone FQ and at least one of the injectable second-line drugs SLIs (amikacin or streptomycin) in addition to multidrug resistance".

Cured: "Treatment completed as recommended by the national policy (minimum 18 months past culture conversion) without evidence of failure and three or more consecutive cultures taken at least 30 days apart are negative after the intensive phase".

Treatment completed: "Treatment completed as recommended by the national policy (minimum 18 months past culture conversion) without evidence of failure but no record that three consecutive cultures taken at least 30 days apart are negative after the intensive phase".

Failure: "Treatment terminated or need for permanent regimen change of at least two anti-TB drugs because of:

- lack of conversion by the end of the intensive phase, or
- bacteriological reversion in the continuation phase after conversion to negative, or

- evidence of additional acquired resistance to fluoroquinolone or second-line injectable drugs, or
- adverse drug reactions (ADRS)"

Died: "A patient who dies for any reason during the course of treatment".

Lost to follow-up: "A patient whose treatment was interrupted for two consecutive months or more".

Not evaluated: "A patient for whom no treatment outcome is assigned (this included cases "transferred out" to another treatment unit and whose treatment outcome is unknown)".

2. MATERIALS AND METHODS

2.1 Design, Setting &Duration: This cross-sectional study was conducted at the Department of Community Medicine, Gomal Medical College, D.I.Khan, Pakistan from January 10, 2020 to February16, 2020. The proposal for this project was approved by the Institutional Research & Ethics Committee. The project was supervised by Dr. Muhammad Marwat.

2.2 Population, Sample Size, Technique and Selection: Programmatic Management Unit of Drug Resistant Tuberculosis (PMDT) Center of our hospital provides health services for DR-TB to D.I.Khan Division, which consists of D.I.Khan & Tank districts, South Waziristan Agency & Frontier Region of Darazinda. The population of the Division was 2,803,147 in 2017 Census. The prevalence of TB in Pakistan is estimated for the year 2017 as 341/100,000 population.[1] DR-TB would contribute its 5% (5*341/100=17.05) as 17.05/100,000 (17.05*100/100,000=0.017%).[2]

Using Raosoft®[14] online calculator, with margin of error 0.1511%, confidence level 95%, population size at risk for DR-TB 2,803,147 and assumed prevalence of 0.017% of DR-TB in this population, sample size of 286 was calculated.

All patients of DR-TB were eligible for inclusion with no exclusion criteria.

2.3 Procedure of Conduct

The data of 286 DR-TB patients was retrieved from ENRS (Electronic Nominal Registration System) maintained at PMDT Center, MMM Teaching Hospital, D.I.Khan, Pakistan. This PMDT Center was established on September 01, 2013 and first patient was registered on October 29, 2013. These 286 patients were registered till December 31, 2019, a data set for six years.

2.4 Data Collection Plan

Secondary was collected through literature search, while primary data was collected through observation. Primary data was collected for the following six demographic variables (attributes); sex (men, women), age group (0-14 years, 15-44 and ≥45 years), occupation (office worker, labourer & housewife), province (Khyber Pakhtunkhwa, Punjab, Baluchistan, Sindh & FATA), division (D.I.Khan, Bannu, Sargodha, Zhob and Others) and district (D.I.Khan, Tank, Lakki Marwat, Bannu, Bhakkar, Mianwali, Zhob, South Waziristan Agency, North Waziristan Agency & others).

Data was collected for the following four research variables (attributes); type of disease (pulmonary, extra-pulmonary), type of drug resistance (mono-resistance, poly-resistance, MDR & XDR), treatment regimen (shorter treatment regimen, longer treatment regimen) and outcome of treatment (cured, treatment completed, died, failed, lost to follow up, not evaluated & still under treatment). All these variables were measured on nominal scale except age groups on ordinal scale.

2.5 Data Analysis Plan

2.5.1 Descriptive Analysis and Estimation of Parameters

Descriptively all the ten variables were analyzed by count, percentage and cumulative percentage. Estimation of parameters for proportion for the population was given as confidence interval at confidence level of 95%, using Wilson score interval for the binomial distribution through an online statistical calculator.[15] It would mean that if the confidence interval is calculated for an infinite number of samples with a sample size of 286, 95% of the calculated confidence intervals will contain the true value of the proportion of the population.

2.5.2 Testing of Hypotheses

Distribution of DR-TB by sex, age groups, occupation, province, division, district, type of disease, type of drug resistance, treatment regimen and outcome of treatment were analyzed separately by chi-square goodness-of-fit test (H_{01}-H_{10}).[16-17] Observed counts, expected counts, their difference, chi-square value, degree of freedom and level of significance were given at alpha .05 by an online calculator.[18,19]

3. RESULTS

3.1 Descriptive Analysis and Estimation of Parameters

3.1.1 Distribution of DR-TB by sex (RQ 1)

Out of 286 patients with DR-TB, 123 (43%, 95%CI 37.39-48.80) were men and 163 (57%, 95% CI 51.19-62.60) women.

3.1.2 Distribution of DR-TB by age groups (RQ 2)

The highest prevalence was in age group 15-44 years 172 (60.14%, 95%CI 54.37-65.81) patients. (Table 3.1.2)

3.1.3 Distribution of DR-TB by occupation (RQ 3)

The housewife was the modal occupation category with 140 (48.95%) patients. (Table 3.1.3)

3.1.4 Distribution of DR-TB by province (RQ 4)

Khyber Pakhtunkhwa province had highest number of patients as 175 (61.19%). (Table 3.1.4)

3.1.5 Distribution of DR-TB by Division (RQ 5)

D.I.Khan Division has the highest prevalence of cases 178 (62.24%). Others included one each from Layyah, Chakwal and Larkana districts. (Table 3.1.5)

3.1.6 Distribution of DR-TB by district (RQ 6)

D.I.Khan district had highest number of patients as 121 (42.31%). Others included one each from

Table 3.1.2: Distribution of DR-TB by age groups in DR-TB population in D.I.Khan Division, Pakistan (n=286)

Variable	Attributes	Sample Statistics			95% CI for Proportion	
		Count	Percentage	Cumulative %	Lower	Upper
Age Group	0-14 years	8	2.80	2.80	1.40	5.42
	15-44 years	172	60.14	62.94	54.37	65.81
	≥45 years	106	37.06	100.00	31.67	42.79
Total		286	100%		Population Parameters	

Table 3.1.3: Distribution of DR-TB by occupation in DR-TB population in D.I.Khan Division, Pakistan (n=286)

Variables	Attributes	Sample Statistics			95% CI for Proportion	
		Count	Percentage	Cumulative %	Lower	Upper
Occupation	Office worker	33	11.54	11.54	08.33	15.76
	Labor	113	39.51	51.05	34.01	45.27
	House wife	140	48.95	100%	43.21	54.71
Total		286	100%		Population Parameters	

Table 3.1.4: Distribution of DR-TB by province in DR-TB population in D.I.Khan Division, Pakistan (n=286)

S. No.	Province	Sample Statistics			95% CI for Proportion	
		Count	Percentage	Cumulative %	Lower	Upper
1	Khyber Pakhtunkhwa	175	61.19	61.19	55.42	66.65
2	Punjab	56	19.58	80.77	15.39	24.56
3	Baluchistan	9	03.15	83.92	01.66	05.87
4	Sindh	1	00.35	84.27	00.06	01.95
5	FATA	45	15.73	100%	11.97	20.40
Total		286	100%		Population Parameters	

Table 3.1.5: Distribution of DR-TB by division in DR-TB population in D.I.Khan Division, Pakistan (n=286)

S. No.	Division	Sample Statistics			95% CI for Proportion	
		Count	Percentage	Cumulative %	Lower	Upper
1	D.I.Khan	178	62.24	62.24	56.49	67.66
2	Bannu	40	13.99	76.23	10.45	18.49
3	Sargodha	56	19.58	95.81	15.40	24.57
4	Zhob	9	3.15	98.96	1.67	5.88
5	Others	3	1.04	100.00%	0.35	3.02
Total		286	100.00%		Population Parameters	

Layyah, Chakwal and Larkana districts. (Table 3.1.6)

3.1.7 Distribution of DR-TB by type of disease (RQ 7)

There were 282 (98.60%, 95% CI 96.45-99.45%) patients of pulmonary and 4 (01.40%, 95% CI 0.54-3.54%) patients of extra-pulmonary tuberculosis.

3.1.8 Distribution of DR-TB by type of drug resistance (RQ 8)

MDR-TB was most prevalent 273 (95.45%). (Table 3.1.8)

3.1.9 Distribution of MDR-TB by treatment regimen (RQ 9)

Out of 273 MDR-TB cases (273 MDR-TB/286 DR-TB), 27 (9.89%, 95% CI 6.89-14.01) were on STR, while 246 (90.11%, 95% CI 85.99-93.11) on LTR.

3.1.10 Distribution of DR-TB by outcome of treatment (RQ 10)

The outcome of treatment in term of patients cured was 158 (55.24%). (Table 3.1.10)

Table 3.1.6: Distribution of DR-TB by district in DR-TB population in D.I.Khan Division, Pakistan (n=286)

S. No.	District	Sample Statistics			95% CI for Proportion	
		Count	Percentage	Cumulative %	Lower	Upper
1	D.I.Khan	121	42.31	42.31	36.70	48.10
2	Tank	18	06.29	48.60	04.01	09.72
3	Lakki Marwat	27	09.44	58.04	06.56	13.39
4	Bannu	9	03.15	61.19	01.66	05.87
5	Bhakkar	49	17.13	78.32	13.21	21.93
6	Mianwali	5	01.75	80.08	00.74	04.02
7	Zhob	9	03.15	83.22	01.66	05.87
8	South Waziristan Agency	41	14.33	97.55	10.74	18.86
9	North Waziristan Agency	4	1.40	98.95	00.55	03.54
10	Others	3	1.05	100.00%	00.36	3.04
Total		286	100.00%		Population Parameters	

Table 3.1.8: Distribution of DR-TB by type of drug resistance in DR-TB population in D.I.Khan Division, Pakistan (n=286)

S. No.	Type of drug resistance	Sample Statistics			95% CI for Proportion	
		Count	Percentage	Cumulative %	Lower	Upper
1	Mono-drug resistance	1	00.35	00.35	00.06	01.95
2	Poly-drug resistance	2	00.70	01.05	00.19	02.51
3	MDR	273	95.45	96.50	92.37	97.87
4	XDR	10	03.50	100.00 %	01.91	05.63
Total		286	100.00%		Population Parameters	

Table 3.1.10: Distribution of DR-TB by outcome of treatment in DR-TB population in D.I.Khan Division, Pakistan (n=286)

S. No.	Outcome of Treatment	Sample Statistics			95% CI for Proportion	
		Count	Percentage	Cumulative %	Lower	Upper
1	Cured	158	55.24	55.24	49.45	60.90
2	Treatment completed	3	01.05	56.29	00.35	03.03
3	Died	59	20.63	76.92	16.34	25.69
4	Failed	9	03.15	80.07	01.66	05.87
5	Lost to follow up	31	10.84	90.91	07.74	14.97
6	Not evaluated	6	02.09	93.00	00.96	04.50
7	Still under treatment	20	07.00	100.00	04.57	10.55
Total		286	100		Population Parameters	

3.2 Hypotheses Testing

3.2.1 Distribution of DR-TB by sex (RQ 1 & 11, H_{01}): Our observed distribution for men versus women was 123:163 from a sample of 286 against expected counts of 664:586 from 1,250 previously treated DR-TB cases by Akhter, et al.[9] These were not comparable due to different sample sizes/ denominators. Hence the expected counts and expected percentages were adjusted for a sample of 286. The expected counts of 664:586 were replaced by 151.92:134.08 (adjusted expected). Adjusted expected percentages came similar to expected percentages, so not changed. (Table 3.2.1.1)

The observed distribution of DR-TB by sex in sample was compared to the expected distribution in the population through chi-square goodness-of-fit test, which showed p-value <alpha. H_{01} was declared as false and therefore rejected, showing that the observations did not fit the statistical model of the population. In simple words, our observed prevalence of DR-TB in men 43% was statistically significantly lower to what we expected (adjusted) for men 53.12% & our observed prevalence of DR-TB in women 57% was higher to what we expected (adjusted) for women 46.88% from Akhter, et al.[9] (Table 3.2.1.2)

3.2.2 Distribution of DR-TB by age groups (RQ 2 & 12, H_{02}): Our observed distribution for age groups (in years) of 0-14:15-44: ≥45 was 8:172:106 from a sample of 286 against expected counts of 31:996:223 from 1,250 previously treated DR-TB cases by Akhter, et al.[9] These were not comparable due to different sample sizes/ denominators. Hence the expected counts and expected percentages were adjusted for a sample of 286. The expected counts of 31:996:223 were replaced by 7.09:227.89:51.02 (adjusted expected). Adjusted expected percentages came similar to expected percentages, so not changed. (Table 3.2.2.1)

The observed distribution of DR-TB by age groups in sample was compared to the expected distribution in the population through chi-square goodness-

Table 3.2.1.1:Observed, expected and adjusted expected counts and percentages for distribution of DR-TB population by sex in D.I.Khan Division, Pakistan (n=286)

Variable	Attributes	Observed counts	Observed %ages	Expected counts	Expected %ages	Adjusted expected counts	Adjusted expected %
Sex	Men	123	123*100/286 =43%	664	664*100/1250 =53.12%	664*286/1250 =151.92	151.92*100/286 =53.12%
	Women	163	163*100/286 =57%	586	586*100/1250 =46.88%	586*286/1250 =134.08	134.08*100/286 =46.88%
Total		286	100%	1250	100.00%	286.00	100.00%

Table 3.2.1.2: Comparison of observed (sample) to the expected (population) distribution of DR-TB population by sex in D.I.Khan Division, Pakistan (n=286)

Variable	Attributes	O	E	O-E	$(O-E)^2$	$(O-E)^2/E$	χ^2	d.f.	p-value
Sex	Men	123	151.92	-28.92	836.37	5.51	11.743	1	.00061
	Women	163	134.08	28.92	836.37	6.24	H_{01} rejected at alpha .05		
Total		286	286.00	Chi-square goodness of fit with Yates correction					

O= Observed count, E= Expected count, χ^2= Chi-square statistics, d.f.= degree of freedom

Table 3.2.2.1:Observed, expected and adjusted expected counts and percentages for distribution of DR-TB population by age groups in D.I.Khan Division, Pakistan (n=286)

Variable	Attributes	Observed counts	Observed %ages	Expected counts	Expected %ages	Adjusted expected counts	Adjusted expected %
Age groups	0-14 years	8	2.80	31	31*100/1250 =2.48%	31*286/1250 =7.09	7.09*100/286 =2.48%
	15-44 years	172	60.14	996	996*100/1250 =79.68%	996*286/1250 =227.89	227.89*100/286 =79.68%
	≥ 45 years	106	37.06	223	223*100/1250 =17.84%	223*286/1250 =51.02	51.02*100/286 =17.84%
Total		286	100.00%		100.00%	286.00	100.00%

of-fit test, which showed p-value <alpha. H_{02} was declared as false and therefore rejected, showing that the observations did not fit the statistical model of the population. In simple words, our observed prevalence (distribution by age groups) of DR-TB in different age groups was not similar to expected prevalence by Akhter, et al.[9] (Table 3.2.2.2)

3.2.3 Distribution of DR-TB by occupation (RQ 3 & 13, H_{03}): The observed distribution of DR-TB by occupation in sample was compared to the assumed expected distribution in the population through chi-square goodness-of-fit test. The assumed expected distribution was estimated from Wahab, et al.[10] which showed distribution of 30 MDR-TB cases as 11 (36.67 %) labourer, 01 (3.33%) student, 02 (6.67%) govt. employee, 13 (43.33%) housewife and 03 (10 %) others. H_{03} proved to be true, hence accepted, showing that the observed distribution of DR-TB by occupation in sample is similar to expected for population. (Tables 3.2.3.1 & 3.2.3.2)

Table 3.2.2.2: Comparison of observed (sample) to the expected (population) distribution of DR-TB population by age groups in D.I.Khan Division, Pakistan (n=286)

Variable	Attributes	O	E	O-E	$(O-E)^2$	$(O-E)^2/E$	χ^2	d.f.	p-value
Age groups	0-14 years	8	7.09	0.91	0.83	0.12	73.071	2	<.00001
	15-44 years	172	227.89	-55.89	3123.69	13.71			
	≥ 45 years	106	51.02	54.98	3022.80	59.25	H_{02} rejected at alpha .05		
Total		286	286.00	Chi-square goodness of fit with Yates correction					

O= Observed count, E= Expected count, χ^2= Chi-square statistics, d.f.= degree of freedom

Table 3.2.3.1: Observed and expected counts and percentages for distribution of DR-TB population by occupation in D.I.Khan Division, Pakistan (n=286)

Variable	Attributes	Observed counts	Observed %ages	Expected counts	Expected %ages
Occupation	Office worker	33	33*100/286 =11.54%	29	29*100/286= 10.14%
	Labor	113	113*100/286 =39.51%	115	115*100/286=40.21%
	House wife	140	140*100/286 =48.95%	142	142*100/286=49.65%
Total		286	100.00%	286	100.00%

Table 3.2.3.2: Comparison of observed (sample) to the expected (population) distribution of DR-TB population by occupation in D.I.Khan Division, Pakistan (n=286)

S. No.	Occupation	O	E	O-E	$(O-E)^2$	$(O-E)^2/E$	χ^2	d.f	p-value
1	Office worker	33	29	4	16	0.55	0.615	2	.7354
2	Labor	113	115	-2	4	0.03			
3	House wife	140	142	-2	4	0.03	H_{03} accepted at alpha 0.05		
Total		286	286	Chi-square goodness of fit with Yates correction					

O= Observed count, E= Expected count, χ^2 = Chi-square value, d.f.= degree of freedom

Table 3.2.4.1: Observed and expected counts and percentages for distribution of DR-TB population by province in D.I.Khan Division, Pakistan (n=286)

S. No.	Provinces	Observed counts	Observed %ages	Expected counts	Expected %ages
1	Khyber Pakhtunkhwa	175	175*100/286 =61.19 %	177	177*100/286 =61.89 %
2	Punjab	56	56*100/286 =19.58%	46	46*100/286 =16.08%
3	Baluchistan	9	9*100/286 =03.15%	12	12*100/286 =4.20 %
4	Sindh	1	1*100/286 =00.35%	1	1*100/286 =0.35%
5	FATA	45	45*100/286 =15.73%	50	50*100/286 =17.48%
Total		286	100.00%	286	100.00%

3.2.4 Distribution of DR-TB by province (RQ 4 & 14, H_{04}): The observed distribution of DR-TB by province in sample was compared to the hypothetical expected distribution in the population through chi-square goodness-of-fit test. H_{04} proved to be true, hence accepted showing that the observed distribution of DR-TB by province in sample is similar to hypothetical expected distribution for population. (Tables 3.2.4.1 & 3.2.4.2)

3.2.5 Distribution of DR-TB by Division (RQ 5 & 15, H_{05}): The observed distribution of DR-TB by Division in sample was compared to the hypothetical expected distribution in the population through chi-square goodness-of-fit test. H_{05} proved to be true, hence accepted showing that the observed distribution of DR-TB by division in sample is similar to hypothetical expected distribution for population. (Tables 3.2.5.1 & 3.2.5.2)

3.2.6 Distribution of DR-TB by district (RQ 6 & 16, H_{06}): The observed distribution of DR-TB by district in sample was compared to the hypothetical expected distribution in the population through chi-square goodness-of-fit test. H_{06} proved to be true, hence

Table 3.2.4.2: Comparison of observed (sample) to the expected (population) distribution of DR-TB population by province in D.I.Khan Division, Pakistan (n=286)

S. No.	Provinces	O	E	O-E	$(O-E)^2$	$(O-E)^2/E$	χ^2	d.f	p-value
1	Khyber Pakhtunkhwa	175	177	-2	4	0.02	3.447	4	.48606
2	Punjab	56	46	10	100	2.17	H_{04} accepted at alpha 0.05		
3	Baluchistan	9	12	-3	9	0.75			
4	Sindh	1	1	0	0	0.00			
5	FATA	45	50	-5	25	0.50			
Total		286	286	Chi-square goodness of fit with Yates correction					

Table 3.2.5.1: Observed and expected counts and percentages for distribution of DR-TB population by division in D.I.Khan Division, Pakistan (n=286)

S. No.	Division	Observed counts	Observed %ages	Expected counts	Expected %ages
1	D.I.Khan	178	178*100/286= 62.24%	181	181*100/286= 63.29%
2	Bannu	40	40*100/286=13.99 %	43	43*100/286= 15.03%
3	Sargodha	56	56*100/286=19.58 %	50	50*100/286=17.48 %
4	Zhob	9	9*100/286= 3.15%	11	11*100/286= 3.85%
5	Others	3	3*100/286=1.04 %	1	1*100/286=0.35 %
Total		286	100.00%	286	100.00%

Table 3.2.5.2: Comparison of observed (sample) to the expected (population) distribution of DR-TB population by division in D.I.Khan Division, Pakistan (n=286)

S. No.	Division	O	E	O-E	$(O-E)^2$	$(O-E)^2/E$	χ^2	d.f	p-value
1	D.I.Khan	178	181	-3	9	0.05	5.343	4	.25391
2	Bannu	40	43	-3	9	0.21			
3	Sargodha	56	50	6	36	0.72			
4	Zhob	9	11	-2	4	0.36			
5	Others	3	1	2	4	4.00	H_{05} accepted at alpha .05		
Total		286	286	Chi-square goodness of fit with Yates correction					

O= Observed count, E= Expected count, χ^2 = Chi-square value, d.f.= degree of freedom

accepted showing that the observed distribution of DR-TB by district in sample is similar to hypothetical expected distribution for population. (Tables 3.2.6.1 & 3.2.6.2)

3.2.7 Distribution of DR-TB by type of disease (RQ 7 & 17, H_{07}): Our observed distribution for pulmonary versus extra-pulmonary TB was 282:4 from a sample of 286 against expected counts of 1231:19 from 1,250 previously treated DR-TB cases by Akhter, et al.[9] These were not comparable due to different sample sizes/ denominators. Hence the expected counts and expected percentages were adjusted for a sample of 286. The expected counts of 1231:19 were replaced by 281.65:4.35 (adjusted expected). Adjusted expected percentages came similar to expected percentages, so not changed. (Table 3.2.7.1)

The observed distribution of DR-TB by type of disease in sample was compared to the expected distribution in the population through chi-square goodness-of-fit test, which showed p-value >alpha. H_{07} was declared as true and therefore accepted, showing that the observations fit the statistical model of the population. In simple words, our observed prevalence of DR-TB for pulmonary TB 98.60% was statistically similar to what we expected (adjusted) for

Table 3.2.6.1: Observed and expected counts and percentages for distribution of DR-TB population by districts in D.I.Khan Division, Pakistan (n=286)

S. No.	Districts	Observed counts	Observed %ages	Expected counts	Expected %ages
1	D.I.Khan	121	121*100/286=42.31%	125	125*100/286= 43.71%
2	Tank	18	18*100/286= 06.29%	22	22*100/286= 7.69%
3	Lakki Marwat	27	27*100/286= 09.44%	19	19*100/286= 6.64%
4	Bannu	9	9*100/286= 03.15%	8	8*100/286= 2.80%
5	Bhakkar	49	49*100/286= 17.13%	50	50*100/286= 17.48%
6	Mianwali	5	5*100/286= 01.75%	4	4*100/286= 1.40%
7	Zhob	9	9*100/286= 03.15%	10	10*100/286= 3.50%
8	South Waziristan Agency	41	41*100/286= 14.33%	42	42*100/286= 14.68%
9	North Waziristan Agency	4	4*100/286= 1.40%	5	5*100/286= 1.75%
10	Others	3	3*100/286= 1.05%	1	1*100/286= 0.35%
Total		286	100.00%	286	100.00%

Table 3.2.6.2: Comparison of observed (sample) to the expected (population) distribution of DR-TB population by district in D.I.Khan Division, Pakistan (n=286)

S. No.	Districts	O	E	O-E	$(O-E)^2$	$(O-E)^2/E$	χ^2	d.f	p-value
1	D.I.Khan	121	125	-4	16	0.13			
2	Tank	18	22	-4	16	0.73			
3	Lakki Marwat	27	19	8	64	3.37			
4	Bannu	9	8	1	1	0.13			
5	Bhakkar	49	50	-1	1	0.02	8.943	9	.4426
6	Mianwali	5	4	1	1	0.25			
7	Zhob	9	10	-1	1	0.10			
8	South Waziristan Agency	41	42	-1	1	0.02			
9	North Waziristan Agency	4	5	-1	1	0.20			
10	Others	3	1	2	4	4.00	H_{06} accepted at alpha .05		
Total		286	286	Chi-square goodness of fit with Yates correction					

O= Observed count, E= Expected count, χ^2 = Chi-square value, d.f.= degree of freedom

pulmonary TB 98.48% & our observed prevalence of DR-TB for extra-pulmonary TB 1.40% was also similar to what we expected (adjusted) for extra-pulmonary TB 1.52% from Akhter, et al[9]. (Table 3.2.7.2)

3.2.8 Distribution of DR-TB by type of drug resistance (RQ 8 & 18, H_{08}): Our observed distribution for mono-resistant: poly-resistant: MDR: XDR-TB was 1:2:273:10 from a sample of 286 against expected counts of 10:6:260:13 from 289 DR-TB cases by Ahmad, et al.[11]. These were not comparable due to different sample sizes/ denominators. Hence the expected counts and expected percentages were adjusted for a sample of 286. The expected counts of 10:6:260:13 were replaced by 9.90:5.94:257.30:12.86 (adjusted expected). Adjusted expected percentages came similar to expected percentages, so not changed. (Table 3.2.8.1)

The observed distribution of DR-TB by type of drug resistance in sample was compared to the expected distribution in the population through chi-square goodness-of-fit test, which showed p-value < alpha. H_{08} was declared as false and therefore rejected, showing that the observations not fit the statistical model of the population. In simple words, our ob-

Table 3.2.7.1: Observed, expected and adjusted expected counts and percentages for distribution of DR-TB population by type of disease in D.I.Khan Division, Pakistan (n=286)

Variable	Attributes	Observed counts	Observed %ages	Expected counts	Expected %ages	Adjusted expected counts	Adjusted expected %
Type of disease	Pulmonary TB	282	282*100/286 =98.60%	1231	1231*100/1250 =98.48%	1231*286/1250 =281.65	281.65*100/286 =98.48%
	Extra pulmonary TB	4	4*100/286 =1.40%	19	19*100/1250 =1.52%	19*286/1250 =4.35	4.35*100/286 =1.52%
Total		286	100.00%	1250	100.00%	286.00	100.00%

Table 3.2.7.2: Comparison of observed (sample) to the expected (population) distribution of DR-TB population by type of disease in D.I.Khan Division, Pakistan (n=286)

Variable	Attributes	O	E	O-E	$(O-E)^2$	$(O-E)^2/E$	χ^2	d.f	p-value
Type of disease	Pulmonary	282	281.65	0.35	0.1225	0.00	0.028	1	.86572
	Extra-pulmonary	4	4.35	-0.35	0.1225	0.028	H_{07} accepted at alpha .05		
Total		286	286.00	Chi-square goodness of fit with Yates correction					

O= Observed count, E= Expected count, χ^2 = Chi-square value, d.f.= degree of freedom

Table 3.2.8.1: Observed, expected and adjusted expected counts and percentages for distribution of DR-TB population by drug resistance in D.I.Khan Division, Pakistan (n=286)

Variable	Attributes	Observed counts	Observed %ages	Expected counts	Expected %ages	Adjusted expected counts	Adjusted expected %
Type of drug resistance	Mono-resistant	1	1*100/286 =0.35%	10	10*100/289 =3.46%	10*286/289 =9.90	9.90*100/286 =3.46%
	Poly-resistant	2	2*100/286 =0.70%	6	6*100/289 =2.08%	6*286/289 =5.94	5.94*100/286 =2.08%
	MDR	273	273*100/286 =95.45%	260	260*100/289 =89.96%	260*286/289 =257.30	257.30*100/286 =89.96%
	XDR	10	10*100/286 =3.50%	13	13*100/289 =4.50%	13*286/289= 12.86	12.86*100/286 =4.50%
Total		286	100.00%	289	100.00%	286.00	100.00%

served prevalence of DR-TB in different attributes of drug resistance was not matching to the expected prevalence for population by Ahmad, et al.[11] (Table 3.2.8.2)

3.2.9 Distribution of MDR-TB by treatment regimen (RQ 9 & 19, H_{09}): Our observed distribution for STR versus LTR was 27:246 from a sample of 273 MDR-TB cases against expected counts of 67:65 from 132 MDR-TB cases by Arshad, et al.[12] These were not comparable due to different sample sizes/ denominators. Hence the expected counts and expected percentages were adjusted for a sample of 273. The expected counts of 67:65 were replaced by 138.57:134.43 (adjusted expected). Adjusted expected percentages came similar to expected percentages, so not changed. (Table 3.2.9.1)

The observed distribution of DR-TB by treatment regimen in sample was compared to the expected distribution in the population through chi-square goodness-of-fit test, which showed p-value <alpha. H_{09} was declared as false and therefore rejected, showing that the observations did not fit the statistical model of the population. In simple words, our observed prevalence of MDR-TB patients on STR 9.89%% was significantly lower to what we expected (adjusted) for MDR-TB patients on STR 50.76% & our observed prevalence of MDR-TB patients on LTR 90.11% was higher to what we expected (adjusted) for MDR-TB patients on LTR 49.24% as compared to the prevalence by Arshad , et al.[12] (Table 3.2.9.2)

3.2.10 Distribution of DR-TB by type of outcome of treatment (RQ 10 & 20, H_{10}): The observed distribution of DR-TB by outcome of treatment in sample was compared to the expected distribution in the population through chi-square goodness-of-fit test. The expected counts for outcome were estimated from a systematic review and meta-analysis by Johnston, et al.[4] from Canada and Alene, et al.[6]

Table 3.2.8.2: Comparison of observed (sample) to the expected (population) distribution of DR-TB population by type of drug resistance in D.I.Khan Division, Pakistan (n=286)

S. No.	Type of drug resistance	O	E	O-E	$(O-E)^2$	$(O-E)^2/E$	χ^2	d.f	p-value
1	Mono-resistant	1	9.90	-8.90	79.21	8.00	12.208	3	.0067
2	Poly-resistant	2	5.94	-3.94	15.52	2.61			
3	MDR	273	257.30	15.70	246.49	0.96			
4	XDR	10	12.86	-2.86	8.18	0.64	H_{08} rejected at alpha 0.05		
Total		286	286.00	Chi-square goodness of fit with Yates correction					

Table 3.2.9.1: Observed, expected and adjusted expected counts and percentages for distribution of MDR-TB population by type of regimen in D.I.Khan Division, Pakistan (n=273)

Variable	Attributes	Observed counts	Observed %ages	Expected counts	Expected %ages	Adjusted expected counts	Adjusted expected %ages
Sex	STR	27	27*100/273 =9.89%	67	67*100/132 =50.76%	67*273/132 =138.57	138.57*100/273 =50.76%
	LTR	246	246*100/273 =90.11%	65	65*100/132 =49.24%	65*273/132 =134.43	134.43*100/273 =49.24%
Total		273	100%	132	100.00%	273.00	100.00%

Table 3.2.9.2: Comparison of observed (sample) to the expected (population) distribution of MDR-TB population by treatment regimen in D.I.Khan Division, Pakistan (n=273)

Variable	Attributes	O	E	O-E	$(O-E)^2$	$(O-E)^2/E$	χ^2	d.f	p-value
Treatment Regimen	STR	27	138.57	-111.57	12447.86	89.83	182.428	2	<.00001
	LTR	246	134.43	111.57	12447.86	92.60	H_{09} rejected at alpha 0.05		
Total		273	273.00	Chi-square goodness of fit with Yates correction					

O= Observed count, E= Expected count, χ^2 = Chi-square value, d.f.= degree of freedom

from Changsha from Hunan Province of China. H_{010} proved to be false, hence rejected showing that the observed prevalence of DR-TB by outcome of treatment in sample was different from the expected prevalence obtained from the above two studies.[4,6] (Tables 3.2.10.1 & 3.2.10.2)

4. DISCUSSION

4.1 Distribution of DR-TB by sex (RQ 1 & 11, H_{01}): In our study (n=286) prevalence of DR-TB was lower in men 43% (95% CI 37.39-48.80) than women 57% (95% CI 51.19-62.60). In contrast to our study, the following five studies showed higher prevalence in men than women.[3,6,7,9,10] Akhter, et al.[9] from Lahore, Pakistan distributed 1,250 retreatment DR-TB cases across men and women as 53.12% and 46.88% respectively. Wahab, et al.[10] from Peshawar, Pakistan showed distribution of 30 MDR-TB cases as 56.7% men and 43.3% women. Alene, et al.[6] from Changsha, China reported 480 DR-TB cases with 70.7% men and 29.3% women. Venkatesh, et al.[7] from Gorakhpur, India reported distribution of 157 MDR-TB patients as 68.8% (95% CI 61.1-75.5) in men and 31.2 % (95% CI 24.4-38.8) in women. Worku, et al.[3] from Addis Ababa, Ethiopia with 340 pulmonary MDR/RR-TB cases notified distribution as 52.94% men and 47.06% women.

No study similar to ours could be obtained from literature. Similarly no studies showing similar prevalence of DR-TB cases in men and women could be obtained.

Our observed prevalence in men 43% was lower to what we expected (adjusted) for men 53.12% & in women 57% it was higher to what we expected (adjusted) for women 46.88% from Akhter, et al[9]. (Table 3.2.1.2)

4.2 Distribution of DR-TB by age groups (RQ 2 &12, H_{02}):

In our study DR-TB was most prevalent in age group 15-44 years 60.14%, (95% CI 54.37-65.81) (Table 3.1.2). Almost similar results were reported by Wa-

Table 3.2.10.1: Observed and expected counts and percentages for distribution of DR-TB population by outcome of treatment in D.I.Khan Division, Pakistan (n=286)

S. No.	Outcome of Treatment	Observed counts	Observed %ages	Expected counts	Expected %ages
1	Cured	158	158*100/286 =55.24%	156	156*100/286 =54.54%
2	Treatment completed	3	3*100/286 =1.05%	8	8*100/286 =2.80%
3	Died	59	59*100/286 =20.63%	8	8*100/286 =2.80%
4	Failed	9	9*100/286 =3.15%	38	38*100/286 =13.29%
5	Lost to follow up	31	31*100/286 =10.84%	50	50*100/286 =17.48%
6	Not evaluated	6	6*100/286 =2.09%	6	6*100/286 =2.09%
7	Still under treatment	20	20*100/286 =7.00%	20	20*100/286 =7.00%
Total		286	100.00%	286	100.00%

Table 3.2.10.2: Comparison of observed (sample) to the expected (population) distribution of DR-TB population by outcome of treatment in D.I.Khan Division, Pakistan (n=286)

S. No.	Outcome of Treatment	O	E	O-E	$(O-E)^2$	$(O-E)^2/E$	χ^2	d.f	p-value
1	Cured	158	156	2	4	0.03	357.627	6	<.00001
2	Treatment completed	3	8	-5	25	3.13			
3	Died	59	8	51	2601	325.13			
4	Failed	9	38	-29	841	22.13			
5	Lost to follow up	31	50	-19	361	7.22			
6	Not evaluated	6	6	0	0	0.00			
7	Still under treatment	20	20	0	0	0.00	H_{10} rejected at alpha .05		
Total		286	286	Chi-square goodness of fit with Yates correction					

O= Observed count, E= Expected count, χ^2 = Chi-square value, d.f.= degree of freedom

hab, et al.[10] (n=30 MDR cases) 60% in 20-40 years, Akhter, et al.[9] (n=1,250 retreatment DR-TB cases) 79.68% in 15-45 years, Venkatesh, et al.[7] (n=157 MDR–TB cases) 79.7% in 18-40 years and Worku, et al.[3] (n=340 pulmonary MDR/RR-TB cases) 89.4% in 15-44 years age group.

Our observed prevalence (distribution by age groups) in different age groups was different from expected prevalence by Akhter, et al.[9] (Table 3.2.2.2)

4.3 Distribution of DR-TB by occupation (RQ 3 & 13, H_{03}): Our study showed highest prevalence in housewife 48.95%, followed by labourer 39.51% and office worker 11.54% (Table 3.1.2). Almost similar results were by Wahab, et al.[10] from Peshawar. On contrary Alene, et al.[6] from Changsha, China reported highest prevalence in farmers 79.0%.

Our observed distribution by occupation was similar to assumed expected distribution estimated from Wahab, et al.[10] (Table 3.2.3.2)

4.4 Distribution of DR-TB by province (RQ 4 & 14, H_{04}): In our study Khyber Pakhtunkhwa province had highest number of DR-TB patients 61.19% (95% CI 55.42-66.65) (Table 3.1.4). No study could be retrieved for comparison. Our observed prevalence across different provinces of Pakistan in sample was similar to hypothetical expected distribution for population. (Table 3.2.4.2)

4.5 Distribution of DR-TB by Division (RQ 5 & 15, H_{05}): In our study D.I.Khan Division had highest number of DR-TB patients 62.24% (95% CI 56.49 -67.66) (Table 3.1.5). No study could be retrieved from literature for comparison. Our observed prevalence across different divisions of Pakistan in sample was similar to hypothetical expected distribution for population. (Table 3.2.5.2)

4.6 Distribution of DR-TB by district (RQ 6 & 16, H_{06}): In our study D.I.Khan district had highest number of DR-TB patients 42.31% (95% CI 36.70-48.10) (Table 3.1.6). No study could be retrieved for comparison. Our observed prevalence across different districts of Pakistan in sample was similar to hypothetical expected distribution for population. (Table 3.2.6.2)

4.7 Distribution of DR-TB by type of disease (RQ 7 & 17, H_{07}): Our study reported higher prevalence of DR-TB in pulmonary 98.60% (95%CI 96.45-99.45%) than extra-pulmonary cases 1.40% (95% CI 0.54-3.54%). Similar results were reported by Akhter, et al.[9],Venkatesh, et al.[7] and Ahmad, et al.[11]

Our observed prevalence for pulmonary TB 98.60% was similar to what we expected (adjusted) for pulmonary TB 98.48% & our observed prevalence of extra-pulmonary TB 1.40% was also similar to what we expected (adjusted) for extra-pulmonary TB 1.52% from Akhter, et al.[9] (Table 3.2.7.2)

4.8 Distribution of DR-TB by type of drug resistance (RQ 8 & 18, H_{08}):

In our study prevalence of MDR-TB was highest 273 (95.45%) (Table 3.1.8). Ahmad, et al.[11] from Peshawar reported 260 (89.96%) total MDR-TB out of 289 DR-TB cases. Alene, et al.[6] from Changsha, China reported 481 DR-TB cases of which 471 (98%) were MDR-TB. He, et al.[5] from Shandong Province, China reported 29.35% (838*100/2,855=29.35%) MDR-TB out of 2,855 DR-TB cases.

Our observed prevalence of DR-TB in different attributes of drug resistance did not match to the expected prevalence for population by Ahmad, et al.[11] (Table 3.2.8.2)

4.9 Distribution of MDR-TB by treatment regimen (RQ 9 & 19, H_{09}): In our study out of 273 MDR-TB patients, 9.89% received STR while 90.11% LTR. Contrary to ours was study by Arshad, et al.[12] from Peshawar who reported higher prevalence of 132 MDR-TB patients on STR 50.76% and lower prevalence of MDR-TB patients on LTR 49.24%.

In simple words, our observed prevalence of MDR-TB patients on STR 9.89% was lower to what we expected (adjusted) for MDR-TB patients on STR 50.76% & our observed prevalence of MDR-TB patients on LTR 90.11% was higher to what we expected (adjusted) for MDR-TB patients on LTR 49.24% by Arshad, et al.[12] (Table 3.2.9.2)

4.10 Distribution of DR-TB by outcome of treatment (RQ 10 & 20, H_{20}): Our study showed 56.29% (95%CI 50.50-61.92) completed treatment successfully (cured+ completed), 20.63% (95%CI 16.34-25.69) died, 3.15% (95%CI 1.66-5.87) failed treatment, 10.84% (95%CI 7.74-14.97) loss to follow up/defaulted, 2.09% (95%CI 0.96-4,50) not evaluated and 7% (95%CI 4.57-10.55) still under treatment (Table 3.1.10). Johnston, et al.[4] from Canada (n=4,959 MDR-TB patients) reported 62% (95% CI 57–67) successful treatment, 11% (95% CI 9-13) died and 8% (95%CI 5-11) failed therapy, default rate 13% (95%CI 9-17) and not evaluated 2% (95%CI 1-4). Alene, et al.[6] from Changsha, China reported (n=481 DR-TB) 57.2% completed treatment successfully (cured +completed), 2.7% died, 13.1% failure and 27.0% loss to follow up. The proportion of successful treatment and not evaluated was similar in ours and the above mentioned studies. The proportion of death was higher while treatment failure and loss to follow up were lower in our sample than the above mentioned studies. 7% patients were still under treatment in our study, while other studies did not mention it.

The observed distribution of DR-TB by outcome of treatment in sample was different from the expected distribution, estimated from the above two studies.[4,6] (Table 3.2.10.2)

4.11 Innovative strengths of our study: Research is problem solving process for a defined population through a sample. We have drawn sample from our

population at risk. Data of this sample was analyzed (descriptive statistics) and the population parameters were inferred from the analyzed data (estimation of parameter; inferential statistics). In this way population characteristics were inferred from sample, the ultimate purpose of research. Most global literature has no mention of their populations. Finally observed data of the sample was compared to the expected data from the population to see whether this sample is similar/ dissimilar to the population (hypothesis testing-inferential statistics).

We have arranged our research/ study as per design of "Marwat's Logical Trajectory for Research Process",[20-27] giving this effort a rational flow and including to sort out our research problems, knowledge gaps, converting research problems into research questions and research objectives, making research hypotheses and doing collection, analysis and interpretation of relevant data.

5. CONCLUSIONS

The prevalence of DR-TB was higher in women, age group 15-44 years, housewife, Khyber Pakhtunkhwa and D.I.Khan Division and District. Most common type of disease, drug resistance and treatment regimen was pulmonary TB, MDR and longer treatment respectively. Treatment success rate was 56.29%. The observed prevalence by occupation, province, division, district and type of disease in sample was similar to population, while it was different by sex, age groups, type of drug resistance, regimen and treatment outcome.

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CONFLICT OF INTEREST
Authors declare no conflict of interest.
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AUTHORS' CONTRIBUTION

The following authors have made substantial contributions to the manuscript as under:

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All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.