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Antibiotic Susceptibility Pattern of Mycobacterium tuberculosis

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ABSTRACT

Background: The emergence and spread of DR and MDR-TB threat global TB control. The susceptibility patterns of *M. tuberculosis* isolates against anti-tuberculosis drugs informs an important aspect of TB controls and surveillance and analysis of local rates of TB drug resistance helps in the detection and monitoring of the extent of DR and MDR strains, indicating the quality of TB control in the country.

Methods: A cross sectional study was conducted to find out antibiotic susceptibility pattern of *Mycobacterium tuberculosis* in pulmonary tuberculosis patients at national tuberculosis center. All the samples were stained by auramine fluorochrome method; processed by NaOH Ogawa Method; primary cultured; subcultured in 2% Ogawa media; cultured in drug LJ media and finally results observed and interpreted. Here Drug susceptibility test was done on *M. tuberculosis* isolate from each patient by Proportion method as standard protocol.

Results: Ethambutol (66.10%) was found to be the most effective anti-TB drug according to the susceptibility test followed by RMP (60.33%), SM (59.66%) and INH (41.69%) against *M. tuberculosis*. Among 45 isolated untreated patients, primary drug resistance was observed in 20%, to two drugs in 17.77%, to three drugs in 11.11%, to four drugs in 6.66% and primary Multi-drug resistant in 22.22%. Among 250 isolated from previous treated patients, acquired resistance to one drug was found in 23.60%, to two drugs in 12.40%, to three drugs in 16.40%, to four drugs in 18.80% an acquired Multi-drug resistant in 37.20%. Among 250 treated 68.40% (n=171) were relapse,18% (n=45) were chronic, 7.6% (n=19) were follow-up, 3.2% (n=8) were defaulter, and 2.8% (n=7) were treatment failure. MDR-TB was found the highest in chronic cases (64.44%) followed by follow-up case (47.36%), treatment failure cases (42.85%), relapse cases (27.48%) and default cases (12.5%). A statistical analysis reveals significant relationship between prior history of treatment and the development of drug resistance. However, no significant relationship between age and sex with the emergence of drug resistance isolates.

Conclusion: MDR-TB was found the highest in chronic cases (64.44%) followed by follow-up case (47.36%), treatment failure cases (42.85%), relapse cases (27.48%) and Default cases (12.5%).

Key words: multi drug, relapse, resistant, sensitivity, tuberculosis

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INTRODUCTION

Tuberculosis (TB) is a treatable and preventable disease.[1] It is an infectious bacterial disease caused by Mycobacterium an acid fast bacilli.[2] The SAARC region accounts more than 29% of global burden of tuberculosis with 0.6 million deaths every year and 2 million new cases annually.[3] Tuberculosis is a socio-medical problem.[4] Ziehl-Neelson Staining or by Fluoro-chrome staining allows highly accurate diagnosis widely available, simple and multi-purpose equipment.[5] Culture increases the number of tuberculosis cases found, often by 30-50% and detects cases earlier, often before they become infectious.[6] Most of the recent advances in the laboratory diagnosis of TB BY rapid culture, identification, and susceptibility systems.[7]

Drug resistant tuberculosis is a case of tuberculosis (usually pulmonary) excreting bacilli resistant to one or more anti-tuberculosis drugs. MDR-TB is resistant to at least Isoniazide and Rifampicin, the main anti-tuberculosis drugs.[8]

DOTS strategy as one of the most cost effective health interaction and recommends that effective TB treatment be a part of the essential clinical service package available in primary health care. In Nepal, DOTS strategy has been implemented since 1996 and has already reduced the number of deaths.[9]

METHODS

A cross sectional study conducted to find out antibiotic susceptibility pattern of Mycobacterium tuberculosis in pulmonary tuberculosis patients was at National Tuberculosis Centre from September 2005 to May 2006. A total of 295 clinically suspected patients having sputum positive diagnosed by fluorescent microscopy were included in the study. The microscopy produced bright yellowish bacteria against a dark background. The sputum samples were decontaminated and cultured on 2% modified Ogawa media and smear examination was done from pellet. The M. tuberculosis bacteria were confirmed by different biochemical tests. The culture positive isolates were tested for anti-TB drug susceptibility testing by Proportional Method as standard protocol.

Each strain was tested against four antibiotics at the following concentrations: Isoniazid (INH) at 0.25µm/ml and 8µm/ml; Ethambutol (EMB) at 1µm/ml and 2µm/ml; Streptomycin(SM) at 4µm/ml and 8µm/ml and Rifampicin (RMP) at 20µm/ml and 40µm/ml.

The LJ medium is used for all the resistance tests. Working drug dilutions was prepared on the day of use; 1 ml of working solution added to 500 ml of LJ medium will yield final drug concentrations equivalent to the different critical concentrations. The medium is distributed in volumes of 6–8 ml in sterile 17 mm x 170 mm screw-capped test tubes, coagulated at 85 °C for 45 minutes, and allowed to cool at room temperature for 24 hours; the screw caps are then tightened and the tubes stored at 4 °C. The control medium without drugs is prepared at the same time as the drug-containing media. The period of validity of the media stored at 4 °C is 2 months.

RESULTS

A total of 295 suspected PTB cases attending at NTC was included in the study. The sputum samples from patients under study were subjected to test for Fluorochrome staining, culture and antibiotic susceptibility testing for culture positive isolates.

Among the studied 295 cases, 73.89% (n=218) were male and 26.10% (n=77) were female in the age group from 11 year to 88 year. The study showed that the highest number was seen in the age group 21-30, followed by 31-40 (Table 1).

Among 295 *M. tuberculosis* isolates, 41.69% (n=123) were sensitive to INH; 59.66% (n=176) were sensitive to SM; 60.33% (n=178) were sensitive to RMP; and 66.10% (n=195) were sensitive to EMB (Table 2).

Similarly, 58.30% (n=172) were resistant to INH: 40.33% (n=119) were resistant to SM; 9.66% (n=117) were resistant to RMP; and 33.89% (n=100) were resistant to EMB.

Among 295 cultures positive *M. tuberculosis* isolates studied from drug susceptibility testing, resistance to one or more anti-drugs were exhibited.

Out of 295 isolates, 45 isolates were from untreated patients and 250 isolates were from treated patients.

Among the untreated patients, 35.55 %(n=16) were sensitive to all the 4 drugs whereas the remaining were resistant to two or more drugs. Resistant to only one drug was shown by 20% (n=9) of the isolates. Resistant to two drugs was shown by 17.77% (n=8), three drugs to 11.11% (n=5) and four drugs to 6.66% (n=3) of the isolates (Table 3).

Out of the 250 treated TB patients, 25.20% (n=63) were sensitive to all the four anti-TB drugs and the remaining187 isolates were resistant to one or more drugs. Resistant to one drug was found in 23.6 % (n=59); two drugs to 12.4 % (n=31) and three drugs to 16.4% (n=41).

Multi Drug Resistance (MDR) in untreated TB patients were found in 22.22% (n=10) and in treated TB patients was 37.20 % (n=93).

Among 250 treated cases, 68.4 % (n=171) were relapses; 18% (n=45) were chronic; 7.6% (n=19) were follow-up; 3.2% (n=8) were defaulters; and 2.8% (n=7) were Treatment failure PTB cases (Table 4).

The highest percentage of MDR TB was from chronic (64.44%) followed by follow-up (47.36%), Treatment failure (42.85%), relapse (27.48%) and defaulter (12.5%).

The primary drug resistance (PDR) to one drug was 20%, to two drugs was 17.77%, to 3 drugs was 11.11% to four drugs was 6.66% and primary MDR was in 22.22% of the isolates (Table 5). Similarly, acquired drug resistance to one drug was 23.60%,to two drugs was 12.40%, to three rugs was 16.40% , to four drugs was 18.80% and acquired MDR was in 37.20% of the isolates.

The highest number of Mycobacterium spp was found to be maximum in age group above 71 i.e. (100%, n=7) followed by 80% (n=36) in 31-40 age group,78.94% (n=15) in age group 11-20, 74.19% (n=46) in 21-30 age group, 69.23% (n=27) in 41-50 age group, 61.90% (n=13) in 51-61 age group and 8.33% (n=2) in age group 61-70 in case of male (Table 6).

In case of female patients, the highest number of resistant was found in age group 41-50 76.92% (n=10) followed by 73.91% (n=17) in 21-30 age group, 66.66% (n=12) in age group11-20, 31-40 and 61-70, 40% (n=2) in 51-60 age group (Table 7). The study demonstrated that age and sex were not significantly related to drug resistance ($P<0.05$).

The study demonstrated that age and sex were not significantly related to drug resistance. Among 79 drug sensitive strains isolated from PTB patients, 40.50% (n=32) were isolated from those patients who had previous cases of TB in his/her family and 59.50% (n=47) had no previous cases of PTB in his/her family.

DISCUSSION

Tuberculosis has become a grave concern in all part of the world because of recent resurgence of TB. Reasons of this resurgence have been identified by WHO as mainly due to HIV pandemic, less health priority given to the disease and significant increase of multidrug resistant tubercle bacilli as a result of inadequate treatment. The causative agent was discovered more than 100 years ago and highly effective drugs and vaccines are available making TB a preventable and curable disease. It remains as the most significant cause of morbidity and mortality due to a single infectious agent in the world.

Tuberculosis is one of the major public health problems in the third world countries with approximately estimated 60% of the adult population being infected with TB. In Nepal, about 45% of the total population is infected with TB. Every year 40,000 people develop active TB of whom 20,000 have infectious pulmonary disease. Nepal, by estimated number of cases, is ranked at 27 globally. Despite the expansion and implementation of a much improved National Tuberculosis Programme (NTP) through DOTS Strategy throughout the country,6000-7000 people still die from TB each year in Nepal.[9]

The main objective of this study is to know the resistance pattern of the anti-TB drugs in PTB patients. A total 295 cases were included in this study carried out from September 2005 to May 2006. Out of 295 cases, 250 cases were previously treated cases and 45 were untreated cases. During this study, among the 295 cases of TB, 73.89 %(n=218) males were found higher in number than female 26.10% (n=77) in age group discussion from 11 to above 80 year. The highest number of cases belonged to the age group 21-30 (29.81%).This finding was concordant with similar studies in other countries. In a similar study in Italy, Ponticiella et al. (1997) reported 82.2% males and 17.8% of females among 90 active PTB cases; Blumberg et al (1991-1997) in Atlanta, USA reported 74% of the male and 26%of the female TB cases among 1536 cases. Likewise, in Archangeh, Russia, Toungoussova et al in Korea reported 66.49% if the male and 34.31% of the female TB cases among 2486 cases. Kuban et al in Cameroon, Yaunde, reported 65.76% of male and 34.25% of the female TB cases among 111 cases; Riantawan et al in Thailand reported 77% male and 23% of the female cases among 1441 cases.[10-15] Tuberculosis Control Programme, Nepal reported 66.77% male and 33.23% female of TB cases among 14,384 newly diagnosed TB cases during 2002/2003.All above findings are consistent with this study. Shrestha et al reported 47% males and 3.05% of female TB cases in histopathological specimens at Tribhuvan University Teaching Hospital.[12] Smith reported that as in most countries of the world, in Nepal, the reported incidence of TB is higher in man than women. Rijal reported that the study conducted at NTC, among the 325 cases, 75.69% were male and 24.30% were female.[12-19] Thus the incidence of TB was found higher in male than female patients; male patients are affected more than female patients. According to the significance test, the prevalence of TB in male and female was found to be statistically significant. These possible factors explain the gender differences observed, the most commonly accepted being that women are less exposed to infection than men. The second might be the biological difference, such as an increased susceptibility

in male. Finally, infected women may progress more frequently to disease and die more rapidly, leaving a cohort with a low prevalence of infection.

In this study, out of 295 culture positive isolates, 15.25% (n=45) isolates from the untreated TB cases and 84.74% (n=250) isolates from the treated TB cases. The study showed that 26.77 %(n=79) were sensitive to all the four drugs and 68.81 %(n=203) cases were drug resistant to one or more drugs. Monoresistance to INH, SM, RMP and EMB was detected in 41(13.89%), 19(6.44%), 1(0.33%) and 7(2.37%) strains respectively; and 23.05% to a total single drug resistance. Similarly, resistance to two drugs was detected in 39 strains(13.22%);resistant to three drugs was detected in 46 strains (16.94%).The level of Multi-drug resistant cases were found to be 34.91% (22.22% Primary MDR and 37.20% Acquired MDR).

The highest rates of drug resistance were discovered for isoniazid and streptomycin. In both new and treated cases, 13.33% and 14% of the strains isolated were resistant to isoniazid respectively; whereas 6.66% and 6.40% of the strains isolated from new and previously treated patients were resistant to streptomycin respectively.

The initial drug resistance case was found in 8.47% to one or more of the four anti-TB drugs was found to be 60.33%.In addition, the primary drug resistance(PDR) to one drug was 20%, to two drugs was 17.77%,to 3 drugs was 11.11% and to four drugs was 6.66%.And the acquired drug resistant to one drug was 23.60%, to two drugs was 12.40%, to three drugs was 16.40% and to four drugs was 18.80%.The primary MDR was found to 22.22% of the isolates and the acquired MDR was in 37.20% of isolates. This finding of this study is similar with the latest third surveillance report of WHO 2004 in Nepal. The report revealed that 1.3% and 20.5% of the new and old cases had MDR in Nepal. The rate of acquired MDR-TB was higher (19.25%) than the rate of primary MDR-TB (2.63%).

Out of 295 culture positives isolates obtained from the PTB patients,171 isolates were from relapse cases,45 isolates from chronic cases,19 isolates from follow-up cases,8 isolates from default cases and 7 isolates from treatment failure cases. The highest percentage of MDR was obtained from the chronic cases (64.44%) followed by follow-up cases (47.36%), treatment failure cases (42.85%), relapse cases (27.48%) and default cases (12.5%).

The finding of this study is in agreement with other studies conducted at different places. Al Marri in the state of Qatar reported that 85% of the cases were sensitive to anti-TB drugs and 15% cases were resistant to one or more anti-TB drugs among 406 cases of PTB.[14] In West Province of Cameroon, the level of initial drug resistance was found in 14.28% and acquired drug resistance was found in 0.74%,the rate of MDR was found 0.98% (0.49%initial MDR and 1% for acquired MDR); Kuban et al. reported 4.1%MDR case among 566 isolates, 15.2% initial drug resistance and 11.6% acquired drug resistance and 1.06% and acquired MDR cases 3%).[15] Indian studies showed that 3.4% of the new cases and 25% of the old cases had MDR-TB (WHO,2000).[23] The anti-TB drug sensitivity test conducted in Nepal 1987-1990 revealed that 1.6% and 9.6% of the new and old cases respectively had MDR-TB.GC et al.(2001) found 8.57% of initial MDR cases and 100% of acquired MDR cases; Bhattarai et al. (2003) obtained 4.16% of primary MDR cases and 5% of acquired MDR cases. Similarly, Rijal et al. (2003) found primary MDR in 2.63% of the isolates and acquired MDR in 19.25% of isolates.[17-23] The alarming increment in MDR-TB cases may be owing to late identification of suspected MDR-TB cases. Identification of all cases of MDR-TB would require culture and susceptibility testing of tuberculosis suspects, an ideal that is unachievable in developing countries like Nepal. The culture and sensitivity facilities for *M. tuberculosis* in our country are country are only in National Tuberculosis Centre (NTC) and Germany-Nepal Tuberculosis. Project (GENETUP).Other reasons for increase in MDR-TB may have smear negative TB and hence may even remain undiagnosed with tuberculosis. Even among those with smear positive disease, initial response to treatment may be good, and MDR-TB may not be suspected in some cases.

Our study revealed that there were high rates of initial drug resistance against isoniazid and streptomycin among both new and treated cases .This may be due to low cost and widespread use in the treatment of TB. The most significant finding of our study was the low frequency of primary resistance to rifampicin which is a good indicator for success of DOTS. Mono resistance to Rifampicin was not observed at all in new cases. Resistance to Rifampicin predicted resistance to isoniazid and streptomycin and served as marker of MDR.

The high rates of resistance among new cases indicated that drug resistant strains are circulating and are being transmitted from patient to patient in our country Nepal. Transmission of already resistant strains as a serious problem and threat, as it is different to treat patients infected with drug resistance, it is important for a TB control programme to have reliable laboratory facilities for susceptibility testing of *M .tuberculosis* isolates.

This study showed there were no any relation of age and sex, with drug resistance. The result of the present study was in agreement with the study of Al-Marri in Qatar; Warndroff et al in Karongo District, Malavi also supports

our study that neither nor acquired drug resistance were associated with sex or age.[14,18]

Likewise, the family history of TB cases, smoking and alcoholic habit of the patients did not show any significant relation with drug resistance. This study was similar to the study of Leung in Hong Kong; and Toungoussova et al., 2002; Archangels in Russia.[10,20]

Increase cases of MDR-TB are a global problem. MDR-TB can be cured by the effective implementation of DOTS strategy. Regular monitoring of MDR-TB and policy in accordance with the operational research finding enables the controls and drug quality assessment is helpful for emerging MDR-TB.

In 1997 the World Health Organization (WHO), the International Union Against Tuberculosis and Lung Disease (IUATLD) and partners world-wide released the first report of the global project on anti-tuberculosis drug resistance.[22] The data generated in this report were reinforced in a recently published second report. Directly observed treatment short-course (DOTS), the WHO strategy for TB control cures virtually all patients with drug-susceptible TB and some drug resistant TB through the administration of short-course chemotherapy with first-line drugs.

However, patients with multidrug-resistant (MDR) tuberculosis (TB) to at least isoniazid and rifampicin are more likely to fail short-course chemotherapy. In recent years there has been encouraging evidence that patients with MDR TB can be cured with appropriate management based on second-line drugs. Unfortunately, second-line drugs are inherently more toxic and less effective than first-line drugs and reliable assessment of drug resistance is an essential prerequisite for appropriate use. Treatment is prolonged and significantly more expensive. Accurate laboratory drug susceptibility testing (DST) data to second-line drugs will support clinical decision making and help to prevent the emergence of further drug resistance in patients with MDR TB. In order to meet the challenges posed by MDR TB, the WHO established the DOTS-Plus initiative to assess the feasibility and cost-effectiveness of using second-line drugs to manage patients with MDR TB primarily in middle and low-income countries.

DOTS-Plus is needed in areas where MDR-TB has emerged due to previous inadequate TB control programmes. Therefore, DOTS-Plus pilot projects are only recommended in settings where the standard DOTS strategy is fully in place to protect against the creation of further drug resistance. DOTS-Plus is designed to cure MDR-TB using second-line TB drugs. These drugs should be stored and dispensed at specialized health centers with appropriate facilities and well-trained staff. It is vital that DOTS-Plus pilot projects follow WHO recommendations in order to minimize the risk of creating drug resistance to second line TB drugs. DOTS-Plus works as a supplement to standard DOTS-based TB programmes already in place.

If patients failing DOTS are presumed to have MDR-TB, and if drug-susceptibility testing is limited, they might be placed on an empirical treatment regimen consisting of second-line TB drugs. Under DOTS Plus, they must endure an additional two years of daily, observed combination therapy, including injectable antibiotics, which can produce unpleasant side-effects. As of July 2002, the Green Light Committee (GLC) had approved seven pilot projects to implement the DOTS-Plus strategy, and is currently reviewing five further applications. Preliminary results from those programmes already under way show percentages of culture negativization to be between 46 and 79 percent. Continued support for these projects – together with the implementation of new programmes in other countries – will contribute to the building of a sound policy for the control of MDR-TB.

Estonia's country-wide DOTS-Plus programme began in March 2001, and allows for the enrolment of 200 patients over a two-year period. Preliminary results show a sputum negativization of 46 percent of patients after six months of treatment. The pilot project has become a leverage tool to promote the expansion of the DOTS strategy in Estonia.

Latvia began to implement DOTS fully in 1997. However, poor case management in the past and the overcrowded conditions of TB wards still helped to make Latvia the country with the second highest MDR-TB rate in the world. The proportion of MDR-TB among new TB patients in this country is 9.5 percent. On February 2001, the GLC approved a countrywide DOTS-Plus pilot project.

Strengthening MDR-TB control now through DOTS-Plus will help to reduce morbidity, mortality and transmission due to MDR-TB. By directing MDR-TB patients to effective treatment protocols now, we are saving direct costs. And by controlling the primary cycle of MDR-TB transmission now, we are saving future funds and indirect costs that would otherwise have to be diverted into treatment for both sick individuals and those that they infect.

CONCLUSION

MDR-TB was found the highest in chronic cases (64.44%) followed by follow-up case (47.36%), treatment failure cases (42.85%), relapse cases (27.48%) and Default cases (12.5%). A statistical analysis reveals no significant relationship between age and sex with the emergence of drug resistant isolates.

Table 1. Age and sexwise distribution of PTB patients

S.N.	Age group	Male		Female		Total	
		No.	%	No.	%	No.	%
1	11-20	19	6.44	18	6.10	37	12.54
2	21-30	62	21.02	23	7.79	85	28.81
3	31-40	45	15.25	16	5.42	61	20.68
4	41-50	39	13.22	13	4.41	52	17.63
5	51-60	21	7.12	5	1.69	26	8.81
6	61-70	24	8.14	3	1.02	27	9.15
7	71-80	6	2.03	0	0.00	6	2.03
8	Above 80	1	0.34	0	0.00	1	0.34

Table 2. Pattern of antibiotic sensitivity of isolates

S.N.	Antibiotics	No. of isolates	Sensitive		Resistant	
			No.	%	No.	%
1	INH	295	123	41.69	172	58.30
2	SM	295	176	59.66	119	40.33
3	RMP	295	178	60.33	117	39.66
4	EMB	295	195	66.10	100	33.89

Table 3. Antibiotic susceptibility pattern in patients with or without past history of treatment

SN	Drug susceptibility testing result	Untreated TB patients		Treated TB patients		Total	Total in Percent
		No.	%	No.	%		
1	Total tested	45	15.25	250	84.74	295	
2	Sensitive to all 4 Drugs	16	35.55	63	25.20	79	26.77%
3	Resistant to 1 Drug						
	INH	6	13.33	35	14.00	41	13.89%
	SM	3	6.66	16	6.40	19	6.44%
	RMP	0	0	1	0.40	1	0.33%
	EMB	0	0	7	2.80	7	2.37%
4	Resistant to 2 Drugs						
	INH+RMP	2	4.44	9	3.60	11	3.72%
	INH+SM	1	2.22	5	2.00	6	2.03%
	RMP+SM	3	6.66	3	1.20	6	2.03%
	INH+EMB	2	4.44	14	5.60	16	5.42%
	SM+EMB	0	0	0	0	0	0%
5	Resistant to 3 Drugs						
	INH+RMP+SM	3	6.66	24	9.60	27	9.15%
	RMP+SM+EMB	0	0	0	0	0	0%
	RMP+INH+EMB	2	4.44	11	4.40	13	4.40%
	INH+SM+EMB	0	0	6	2.40	6	2.03%
6	Resistant to all Drugs	3	6.66	47	18.80	50	16.94%
7	Multi-Drug Resistance (MDR) at least INH + RMP	10	22.22	93	37.20	103	34.91%

Table 4. Antibiotic susceptibility pattern in patients with past treatment

S.N.	Drug susceptibility testing result	Relapse		Chronic		Follow-Up		Default		Treatment failure	
		No.	%	No.	%	No.	%	No.	%	No.	%
1	Total tested	171	68.4	45	18	19	7.6	8	3.2	7	2.8
2	Sensitive to all 4 Drugs	45	26.31	5	11.11	6	31.57	4	5	2	28.57
3	Resistant to 1 Drug										
	INH	28	16.37	3	6.66	2	10.52	1	12.5	1	14.28
	SM	13	7.60	2	4.44	0	0	1	12.5	0	0
	RMP	1	0.58	0	0	0	0	0	0	0	0
	EMB	9	5.26	1	2.22	0	0	0	0	0	0
4	Resistant to 2 Drugs										
	INH+RMP	5	2.92	0	0	1	5.26	0	0	1	14.28
	INH+SM	3	1.75	0	0	0	0	1	12.5	0	0
	RMP+SM	3	1.75	1	2.22	0	0	0	0	0	0
	INH+EMB	12	7.01	1	2.22	0	0	0	0	0	0
	SM+EMB	0	0	0	0	0	0	0	0	0	0
5	Resistant to 3 Drugs										
	INH+RMP+SM	12	7.01	10	22.22	1	5.26	0	0	1	14.28
	RMP+SM+EMB	1	0.58	0	0	0	0	0	0	0	0
	RMP+INH+EMB	5	2.92	6	13.33	0	0	0	0	0	0
	INH+SM+EMB	2	1.16	2	4.44	1	5.26	0	0	0	0
6	Resistant to all Drugs	25	14.61	13	28.88	7	36.84	1	12.5	1	14.28
7	Multi-Drug Resistance (MDR) at least INH+RMP	47	27.48	29	64.44	9	47.36	1	12.5	3	42.85

The highest percentage of MDR TB was from chronic (64.44%) followed by follow-up (47.36%), treatment failure (42.85%), relapse (27.48%) and defaulter (12.5%).

Table 5. Comparison of primary and acquired anti-TB drug resistance.

Drug resistance	1 Drug	2 Drugs	3 Drugs	4 Drugs	MDR
Primary drug resistance (n=45)	20.00	17.77	11.11	6.66	22.22
Acquired drug resistance (n=250)	23.60	12.40	16.40	18.80	37.20

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Table 6. Age wise distribution of resistant *M. tuberculosis* in male

S.N.	Age group	No. of isolates	Sensitive		Resistant	
			No.	%	No.	%
1	11-20	19	4	21.05	15	78.94
2	21-30	62	16	25.80	46	74.19
3	31-40	45	9	20.00	36	80.00
4	41-50	39	12	30.76	27	69.23
5	51-60	21	8	38.09	13	61.90
6	61-70	24	22	91.66	2	8.33
7	Above 71	7	0	0.00	7	100
Total		217	71		146	

Table 7. Age wise distribution of resistant *M. tuberculosis* in female

S.N.	Age group	No. of isolates	Sensitive		Resistant	
			No.	%	No.	%
1	11-20	18	6	33.33	12	66.66
2	21-30	23	6	26.08	17	73.91
3	31-40	16	4	25.00	12	66.66
4	41-50	13	3	23.07	10	76.92
5	51-60	5	3	60.00	2	40.00
6	61-70	3	1	33.33	2	66.66
Total		78	23		55	

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