

# Drug Resistance Pattern in Pulmonary Tuberculosis Patients Coming to Pulmonology Ward BVH Bahawalpur

MUHAMMAD WASEEM<sup>1</sup>, MARYAM RAFIQ<sup>2</sup>, MUHAMMAD RAUF UL HASSAN<sup>3</sup>

## ABSTRACT

**Aim:** To determine the frequency of drug resistance pattern of mycobacterium tuberculosis (MTB) among pulmonary tuberculosis patients coming to Pulmonology Department BVH Bahawalpur.

**Methods:** This descriptive cross sectional study was conducted in Department of pulmonology, Bahawal Victoria Hospital, Bahawalpur from October 2015 to April 2016. All required tests were carried out in Department of Pathology, Quaid-e-Azam medical college, Bahawalpur.

**Results:** Mean age of the patients was 46.71±12.25 years. Male patients were 170(66.40%) and female patients were 86(33.59%). Total 50(19.53%) patients were found with drug resistance and 206(80.43%) patient sensitive to anti TB drugs. No significant association of gender and age with drug resistance was found.

**Conclusion:** In the present study the most common pattern observed is TB with predominant resistance to INH. No significant association was of gender and age with drug resistance was observed.

**Keywords:** Tuberculosis; resistance patterns; susceptibility tests; multidrug resistance

---

## INTRODUCTION

Tuberculosis (TB) is an ancient disease which is playing havoc with human health and economy for a long time. TB remains a leading cause of morbidity and mortality despite all global efforts<sup>1</sup>. TB affects 10 million new cases every year and about 3 million die due to this disease all over the world<sup>2</sup>. Developing Countries bear more than 90% of TB disease burden<sup>1,2</sup>. In Eastern Mediterranean Region (EMR) of WHO, 43% of TB cases reside in Pakistan<sup>1,2</sup>. Pakistan is ranked 6<sup>th</sup> among 22 high TB burden countries<sup>1,2</sup>. Annual death rate due to TB is 39 per 100000 in Pakistan<sup>3,4</sup>.

Drug resistance in tuberculosis is an issue of great concern throughout the world<sup>5</sup>. Drug resistant TB has higher mortality rates as compared to drug sensitive TB<sup>6</sup>. Drug resistant TB poses great challenge in terms of treatment for program managers<sup>7</sup>. Incidence of MDR-TB (Mycobacterium tuberculosis resistant to at least Isoniazid and Rifampicin) in Pakistan in new and previously treated cases is 3.4% and 36% respectively according to WHO reports<sup>8</sup>. Epidemiological studies are necessary to optimize drug therapy and to prevent spread of resistant strains in a specified area<sup>9</sup>. There are small studies on drug resistance pattern from Pakistan specially southern Punjab<sup>7</sup>. A study conducted in Lahore showed that most of the patients of drug resistant TB have resistance to both Isoniazid and

Rifampicin (17%) and 25.9% patients were resistant to Rifampicin alone<sup>10</sup>. This study is performed to determine the drug resistance pattern in tuberculosis patients in Bahawalpur as number of drug resistant cases reporting is on the increase in Pakistan<sup>8</sup>. Determining the frequency and pattern of drug resistance in this region will prove very helpful in estimating and treating the growing threat of drug resistant TB. It will also help to compare frequency of drug resistant cases in this area with frequency of resistant cases in overall Pakistan<sup>8</sup>.

## MATERIAL AND METHODS

This descriptive cross sectional study was conducted in Department of pulmonology, Bahawal Victoria Hospital, Bahawalpur from October 2015 to April 2016. All required tests were carried out in Department of Pathology, Quaid-e-Azam medical college, Bahawalpur. Permission was taken from Ethical Review Committee before starting the study and written informed consent was taken from all the selected patients. Total 256 male and female patients aged 18-60 years having diagnosis of category I pulmonary tuberculosis (patients having one sputum sample positive for AFB) were recruited for the study.

A person whose sputum smear examination positive for acid-fast bacilli was labelled as Pulmonary TB case. Mycobacterium (MTB) is cultured by 1% proportion method on Lowenstein-Jensen (LJ) medium. MTB growth is checked after introduction of anti-tuberculosis drugs (Isoniazid, Rifampicin, Ethambutol, Pyrazinamide and

---

<sup>1,2</sup>Postgraduate Resident, Department of Pulmonology, BVH/ QAMC, Bahawalpur

<sup>3</sup>Assistant Professor Pulmonology, BVH, Bahawalpur  
Correspondence to Dr. Muhammad Waseem

Streptomycin) into culture media. If MTB growth is not halted after introduction of any of these drugs, then MTB is considered resistant to that particular drug. A patient of pulmonary tuberculosis who has never taken ATT or has taken ATT less than 1 month was labelled as category 1 case of TB<sup>11</sup>.

All patients who were receiving ATT currently, patients with extra-pulmonary TB, and those who cannot expectorate, patient suffering from severe systemic illness (i.e. sepsis, malignancy, trauma), unconscious, unable to spontaneously clear the airways or with other medical condition requiring immediate tracheal intubation and hemodynamically unstable patients were excluded from the study.

Demographic data of the patients was entered on a pre-designed Proforma. Early morning fasting sputum sample (at least 2ml) of all participants were collected in a sterile container. It was promptly transported to Microbiology section of Pathology department QAMC. Samples were refrigerated in laboratory till processing. All samples were subjected to culture and drug sensitivity testing by 1% proportion method on Lowenstein-Jensen (LJ) medium for 6 weeks by the same consultant microbiologist. Findings of the laboratory were entered on pre-designed proforma.

All the collected data was entered in SPSS version 17 and analyzed. Mean and SD was calculated for age and frequencies were calculated for categorical variables. P value ≤5% was considered as statistically significant.

## RESULTS

Total 256 patients with pulmonary tuberculosis were included. Mean age of the patients was 46.71±12.25 years. Total 50(19.53%) patients were found with MTB and 206(80.47%) patients without MTB (Fig. 1).

Among the patients of pulmonary tuberculosis, drug resistance was found in 50 (19.53%) patients followed by 22(8.59%) patients were resistant to Isoniazid and 14(5.47%) patients resistant to Rifampicin, 10(3.91%) patients resistant to Ethambutol, 4(1.56%) patients resistant to Pyrazinamide and no patient resistant to Streptomycin (Table 1).

All the 256 patients of pulmonary tuberculosis were divided into two age groups age group 18-40 years and age group 41-60 years. Total 64(25%) patients belonged to age group 18-40 years and MTB was found in 16(25%) patients and 192(75%) belonged to age group 41-60 years and MTB was found in 34(17.71%). No significant association was seen between the age of the patients and MTB (P value 0.207) (Table 2).

After the gender distribution of the patient, among the 170(66.40%) male patients with pulmonary tuberculosis MTB was observed in 34(20%) patients and among the 86(33.59%) female patients with pulmonary tuberculosis, MTB was seen in 16(18.6%) patients. Insignificant association was seen between gender and MTB (P value 0.868) (Table 3).

Fig. 1: Frequency of drug resistance

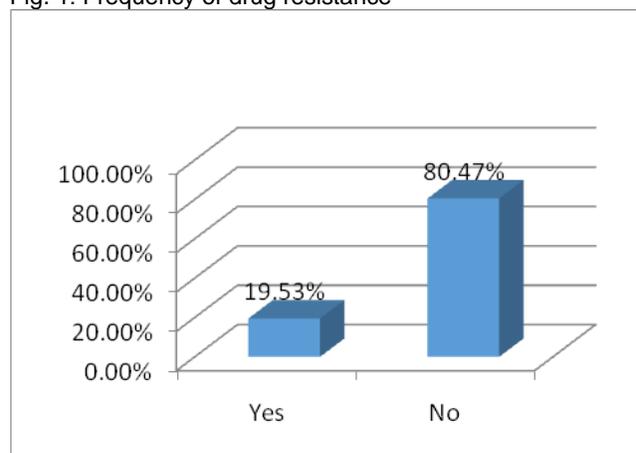


Table 1: Drug resistance pattern

Status	Frequency	%age
Drug Sensitive	206	80.47
<b>Drug resistance</b>	<b>50</b>	<b>19.53</b>
Isoniazid	22	8.59
Rifampicin	14	5.47
Ethambutol	10	3.91
Pyrazinamide	4	1.56
Streptomycin	0	0

Table 2: Age distribution of the patients.

Age group	Drug resistance		Total
	Yes	No	
18-40	16(25%)	48(75%)	64(25%)
41-60	34(17.71%)	158(82.29%)	192(75%)
Total	50(19.53%)	206(80.47%)	256

P value 0.207

Table 3: Gender distribution of the patients

Gender	Drug resistance		Total
	Yes	No	
Male	34(20%)	136(80%)	170(66.40%)
Female	16(18.6%)	70(81.4%)	86(33.59%)
Total	50(19.53%)	206(80.47%)	256

P value 0.868

## DISCUSSION

To estimate the drug resistance of MTB, it is extremely important to evaluate the epidemiology and control of tuberculosis. Like many developing countries, in Pakistan, drug resistant tuberculosis is increasing and is a significant threat to tuberculosis control because there are few drugs effective against TB<sup>9</sup>.

Pakistan ranks sixth among the list of 22 high TB burden countries with a TB related death rate of 43/100,000 population annually. Resistance to TB drugs has been widely reported from various parts of the country<sup>8,9,14-19</sup>, however, pertinent community based data that represents a national profile is lacking<sup>10,11</sup>. In the absence of community data, hospital based studies provide indication of the levels of drug resistance and particularly of resistance trends over the years. Our study showing an overall resistance rate of 19.53% to the anti-tuberculosis drugs. Githui et al<sup>12</sup> and Lee et al<sup>13</sup> reported in their studies drug resistance rate as 18.3% and 18.7% which is comparable with our study. Ndung'u et al<sup>14</sup> found TB drug resistance in 30.1% cases which is higher than our findings.

In present study there was a greater number (66.40%) of males was found with pulmonary TB than females (33.59%) and insignificant ( $P=0.868$ ) association was seen between drug resistance and gender. This differs with earlier studies in Kenya where more females were associated with drug resistance than males ( $P=0.008$ )<sup>12</sup>. Our findings also in contrast with studies in Pakistan, where drug resistance was associated with 70.9% males and 29.15% females, and also in Tanzania, where drug resistance was associated with 68% males and 32% females. Globally a 70% predominance of males over female patients was reported<sup>15,16</sup>. The WHO reported that 67.2% of the global male population was diagnosed with TB as compared to the female population.<sup>17</sup> The greater number of males compared to females could be attributed to behavioral factors such as smoking, which is a predisposing factor to TB with more males being smokers than females. Alcohol consumption, malnutrition and the delay in seeking medical treatment, especially by men, are other factors that have been associated with higher numbers of males than females with TB, with over 66.40% of the participants in the current study being male<sup>18,19</sup>.

In our study the drug resistance rates for individual drugs; Isoniazid, Rifampicin, Ethambutol, Pyrazinamide and Streptomycin were 8.59%, 5.47%, 3.91%, 1.56% and 0% respectively. The highest drug resistance rate was observed for Isoniazid. These results are comparable with one study by Ndung'u et al<sup>14</sup>.

In one study by Hussin et al<sup>20</sup> resistance rates for individual drugs were 27%, 11%, 0%, 14.5% and 13% for INH, RIF, PYR, ETH, STREP respectively. Rasul et al<sup>21</sup> reported individual drug resistance as 25%, 25%, 24%, 10% and 21% for INH, RIF, PYR, ETH, STREP respectively. Haq et al<sup>22</sup> reported the overall drug resistance was noted among the 36% patients out of 100 patients with individual drug

resistance for INH, RIF, PYR, ETH, STREP as 25%, 15%, 0%, 12% and 19% respectively. Iqbal et al<sup>7</sup> reported overall TB drug resistance as 53% and note resistance for INH, RIF, PYR, ETH, STREP as 26%, 28%, 29%, 15% and 24% respectively.

Resistance to INH in this study was 8.59%, which was in agreement with results obtained in earlier studies in Kenya<sup>12</sup> where resistance to INH was 10.2%. INH resistance in the present study was higher than earlier study in Ethiopia and Bangladesh.<sup>23-24</sup>

## CONCLUSION

In the present study the most common pattern observed is TB with predominant resistance to INH. No significant association was of gender and age with drug resistance was observed. There is a rise in the number of drug resistant tuberculosis cases, especially MDR. Hence close monitoring of drug resistant pattern is required to formulate designs of different regimens in the treatment of drug resistant tuberculosis; especially MDR-TB based on accredited laboratory reports, in a specialized center which is very much essential for the betterment of the patients and the community.

## REFERENCES

1. WHO. Global tuberculosis control: epidemiology, strategy, financing: WHO report 2011. Geneva: WHO; 2011.
2. World Health Organization. Global tuberculosis control. WHO report 2011. Geneva: WHO; 2011.
3. Sloan JP, Sloan MC. An assessment of default and non-compliance in tuberculosis control in Pakistan. *Trans Royal Soc Trop Med Hyg* 1981;75(5):717-8.
4. Vermund SH, Altaf A, Samo RN, et al. Tuberculosis in Pakistan: a decade of progress, a future of challenge. *J Pak Med Assoc* 2009;59[4(S-1)]:1-8.
5. Mohan A, Sharma SK. Epidemiology. In: Sharma SK, Mohan A, editors. *Tuberculosis*. New Dehli: Jaypee Brothers Medical Publishers; 2001. P. 14-29.
6. Sharam SK, Guleria R, Jain D, Ehawla TC, Saha P, Mohan A, et al. Effect of additional oral ofloxacin administration in the treatment of multi-drug resistant tuberculosis. *Indian J Chest Dis Allied Sci* 1996;38:73-9.
7. Iqbal R, Shabbir I, Mirza N, Hassan M. TB drug resistance an alarming challenge answer DOTS. *Pakistan J Med Res* 2003;42(3):134-8
8. World Health Organization. Global tuberculosis control: surveillance, planning, financing: WHO report Geneva 27, Switzerland; 2008.
9. Bengisun JS, Karnak D, Palabiyikoglu I, Saygun N. Mycobacterium tuberculosis drug resistance in Turkey, 1976-97. *Scand J Infect Dis* 2000; 32: 507-10.
10. Butt T, Ahmed RN, Kazmi SY, Rafi N. Multi-drug resistant tuberculosis in Northern Pakistan. *J Pak Med Assoc* 2004; 54: 469-72.

11. Rasul S, Shabbir I, Iqbal R, Haq M, Khan S, Saeed MS, et al. Trends in multidrug resistant tuberculosis. *Pak J Chest Medi* 2001; 7: 21-28.
12. Githui WA, Hawken MP, Juma ES, Godfrey-Faussett P, Swai OB, Kibuga DK, et al. Surveillance of drug-resistant tuberculosis and molecular evaluation of transmission of resistant strains in refugee and non-refugee populations in North-Eastern Kenya. *Int J Tuberc Lung Dis*. 2000 Oct;4(10):947–55.
13. Lee JH, Chang JH (2001) Drug resistance tuberculosis in tertiary referral teaching hospital in Korea. *Korean J Intern Med* 16: 173-179.
14. Ndung'u PW, Kariuki S, Ng'ang'a Z, Revathi G. Resistance patterns of *Mycobacterium tuberculosis* isolates from pulmonary tuberculosis patients in Nairobi. *J Infect Dev Ctries*. 2012 Jan;6(1):33–9.
15. Taha Nazir. Isoniazid resistance of *Mycobacterium tuberculosis* isolated from human patients. *African Journal of Microbiology Research* [Internet]. 2011 Nov 9 [cited 2015 Mar 11];5(25). Available from: <http://www.academicjournals.org/AJMR/abstracts/abstracts/abstract%202011/9Nov/Nazir%20et%20al.htm>
16. Willy U, Fernand M, Eduardo V, Gernard M, Candida M, Ronald B, Elma S, Wafaie F (2008) Primary antimicrobial resistance among *Mycobacterium tuberculosis* isolates from HIV seropositive and HIV seronegative patients in Dar es Salaam Tanzania. *BMC (Research Notes)* 1: 58.
17. WHO (2008) Antituberculosis drug resistance in the world report NO. 4 prevalence and trends Geneva. The WHO/IUATLD global project on anti-tuberculosis drug resistance surveillance. Available [http://whqlibdoc.who.int/hq/2008/WHO\\_HTM\\_TB\\_2008.394\\_eng.pdf](http://whqlibdoc.who.int/hq/2008/WHO_HTM_TB_2008.394_eng.pdf). Accessed 10 September 2010.
18. Lonroth K, Juramillo E, Williams B, Dye C, Raviglione M (2009) Drivers of tuberculosis epidemics. The role of risk factors and social determinants. *Social science and medicine* 68(: 2240-2246. Available <http://www.sciencedirect.com/science/article/pii/S02777953609002111>. Accessed 8 November 2011.
19. Rajeswari R, Chandrasekaran V, Suhedev M, Sivasubramaniam S, Sudha G, Rehu G (2002) Factors associated with patient and health system delays in diagnosis of tuberculosis in South India. *Int J Tub Lung Dis* 6: 789-795.
20. Hussain R, Hasan R, Khurshid M, Sturm AW, Ellner JJ, Dawood G. Pulmonary tuberculosis in a BCG vaccinated area: relationship of disease severity with immunological and hematological parameters and drug resistance patterns. *Southeast Asian J Trop Med Public Health*. 1996 Jun;27(2):257–62.
21. Rasul S, Shabbir I, Iqbal R, Haq M, Khan S, Saeed MS, et al. Trends in multidrug resistant tuberculosis. *Pak J Chest Medi* 2001; 7: 21-28.
22. Haq M U, Awan SR, Khan S U, Saeed S, Iqbal R, Shabbir I et al. Sensitivity pattern of *Mycobacterium tuberculosis* at Lahore (Pakistan). *Annals* 2002;8:190-3.
23. Kassu D, Daniel A, Eshatu L, Mekdes GM, Benium F (2008) Drug susceptibility of *Mycobacterium tuberculosis* isolates from smear negative pulmonary tuberculosis patients , Addis Ababa, Ethiopia. *Ethiop J Health Dev* 22: 212-215.
24. Van Deun A, Aung KJ, Chowdhury S, Saba S, Paukay A, Ashraf A, Rigout L, Fissette K, Portael F (1999) Drug susceptibility of *Mycobacterium tuberculosis* in rural area of Bangladesh and its relevance to the national treatment regimes. *Inter J Tuberc Lung Dis* 3: 143-148.