

Pattern of Drug Resistance Among “Previously Treated Pulmonary Tuberculosis Cases” Attending Gulab Devi Hospital Lahore

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ABSTRACT:

Objective: To assess the prevalence of drug resistance in previously treated tuberculosis patients attending Gulab Devi Chest Hospital Lahore in 2007.

Materials and Methods: Drug susceptibility for first line anti-tuberculosis drugs was done for 214 previously treated pulmonary tuberculosis patients attending Gulab Devi Hospital Lahore.

Study period was one year (Jan 2007 – Dec 2007), done by conventional culturing on solid medium (Lowenstein-Jensen medium). Drug sensitivity was applied using the proportion method.

Results: A total of 214 isolates of *Mycobacterium tuberculosis* were obtained from treated patients of pulmonary tuberculosis. All of these patients had taken at least one month or more of first line anti tuberculosis drugs. 120 (56%) were male and 94 (44%) were female. Age distribution was 11-90yrs. 69 patients (32 %) had taken regular treatment while 145 patients (68 %) were having irregular treatment history. Out of 214 *Mycobacterium tuberculosis* isolates 78 (36.4 %) were resistant to both isoniazid and rifampicin (multi drug resistance). Overall resistance to isoniazid was observed in 99 patients (46.2%), to rifampicin in 125 patients (58.4%), streptomycin in 100 (46.7%) and to ethambutol in 40 patients (18.6%).

Conclusion: In this study, we found a high proportion of multi drug resistance (MDR) in addition to resistance to two or more drugs. This study also underlines the importance of continuous monitoring of trends in drug resistance, which would provide useful input for shaping future policies to prevent the emergence and dissemination of MDR tuberculosis.

INTRODUCTION

Despite all the advances made in the treatment and management, tuberculosis (TB) still remains as one of the main public health problem.¹ During the last one decade there has been increase in reported incidence of drug resistance in Category II cases, especially those treated with improper regimens, and also in an irregular fashion. The figures for MDR rates in such cases vary from area to area and overall 10% to 15% MDR rates have been estimated. This makes the drug susceptibility testing important for this category particularly in those showing poor response to Category II DOTS regimen.² The emergence of multidrug-resistant TB (MDR-TB), defined as resistance to isoniazid (INH, H) and rifampicin (RMP, R), the two most potent anti-tuberculosis drugs, has posed additional challenges in controlling TB.^{4,5}

Furthermore, the recent phenomenon of extensively drug-resistant TB (XDR-TB) is a cause for grave concern, in which treatment with existing anti-tuberculosis drugs is almost impossible.⁶ Therefore there is an urgent need to estimate the prevalence of MDR-TB among previously treated TB cases and monitor its trends.³

MATERIALS AND METHODS

Drug susceptibility testing for first line anti-tuberculosis drugs of 214 isolates of *Mycobacterium tuberculosis* was carried out in Gulab Devi Hospital Lahore. These isolates were recovered from sputa of patients suffering from pulmonary tuberculosis and had taken at least one month or more of treatment with first line anti tuberculosis drugs. All the treated patients who reported to our center from January 2007 to December 2007 were included in this study. All the patients were sputum smear positive for acid fast bacilli on Ziehl Neelsen staining. All Sputa were cultured on conventional solid medium (Lowenstein-Jensen medium) for isolation of *Mycobacterium tuberculosis*. Drug sensitivity was applied using the standard proportion method.

RESULTS

Total patients were 214 out of which 120(56%) were male and 94 (44%) were female. Age distribution of the patients (table 1) show that majority of the patients are in the most productive age group.

Table 1: Age distribution

Age(years)			Patient s	%age			
11-20			38	18%			
21-30			62	29 %			
31- 40			30	14%			
41-50			36	16.8%			
51-60			24	11%			
61-70			15	07%			
71-80			06	2.8%			
81-90			03	1.4%			

Table 2: Percentage of isolates resistant to one or more anti-tuberculosis drugs

Number of Drugs		Patients	All Patients N=214			
One Drugs		54	25%			
Two Drugs		62	29%			
Three Drugs		40	19%			
Four Drugs		33	16%			
Five Drugs		05	2%			
None		20	9%			

Table 3 Resistance to individual primary anti tuberculosis drugs

Drugs			Patient s (214)	%age			
Isoniazid + Rifampicin.(MDR)			78	36.4 %			
Rifampicin			125	58.4 %			
Isoniazid			99	46.2%			
Streptomycin			100	46.7%			
Ethambutol			40	18.6%			
Pyrazinamide			91	42.5%			

69 patients (32%) gave history of regular intake of drugs while 145 patients (68%) were taking anti tuberculosis drugs irregularly. Out of 214 cases 54 (25%) were resistant to a single drug, 62 (29%) were resistant to any two drugs, 40(19%) were resistant to any three drugs, 33 (16%) were resistant to any four drugs, 5(2%) were

resistant to any five drugs, 20 (9%) were sensitive to all drugs.(table 2)

Among the first-line drugs, overall resistance to INH was 46.2%, while resistance to RIF was 58.4%.100 patients (46.7%) showed resistance to streptomycin, while resistance to Ethambutol and Pyrazinamide was18.6% and 42.5% respectively.

Out of 214 isolates, 78 (36.4 %) showed multi-drug resistance (resistance to INH and RIF).(table 3)

DISCUSSION

In our study there is demonstration of high incidence of resistance to anti tuberculosis drugs.194 patients (91%) show resistance to one or more drugs while about 36% patients show resistance to isoniazid and rifampicin (multi drug resistance). Shah et al. (2002) from Gujrat, India studied 482 previously treated pulmonary tuberculosis patients and reported that resistance to isoniazid and rifampicin was 15.77 %.⁷ Another study conducted at Lahore by Rizwan Iqbal et al (2004-2006) of 894 patients multi drug resistance (MDR) was observed in 27% of treated cases.⁸ Hanif M et al. New Delhi, India (2006) studied 2880 Mycobacterium tuberculosis isolates from previously treated cases, 1498 (52%) were resistant to one or more anti-tuberculosis drugs, of which 47.1% were MDR.⁹

So there is a significant rise in resistance over the years, especially MDR that is resistance to isoniazid and rifampicin. This proportion was significantly higher among treatment failures compared to relapses and treatment after default cases, underlining the need for early identification of treatment failure by early referral for culture and drug susceptibility testing, and initiation of appropriate treatment. There is a need to establish centers with adequate facilities for susceptibility testing. Chronic interrupters/defaulters and relapse cases have a higher tendency to develop resistance than the normal or newly smear positive case.

CONCLUSION

In this study, a high proportion of drug-resistant cases had MDR in addition to resistance to two or more drugs. This study also underlines the importance of continuous monitoring of trends in drug resistance, which would provide useful input

for shaping future policies to prevent the emergence and dissemination of MDR.

REFERENCES

1. Parmasivan C N, Venkataraman P. Drug resistance in tuberculosis in India. Indian J Med Res 2004; 120: 377–386.
2. Hemvani, N., Chitnis, D. S., Bhatia, G. C. & Sharma, N. (2001). Drug resistance among tubercle bacilli from pulmonary tuberculosis cases in central India. Indian J Med Sci 55, 382–392.[Medline]
3. M. Hanif, S. Malik, V. K. Dhingra Acquired drug resistance pattern in tuberculosis cases at the State Tuberculosis Centre, Delhi, India New Delhi Tuberculosis Centre, State Tuberculosis Demonstration Centre, New Delhi, India
4. Parmasivan C N, Venkataraman P. Drug resistance in tuberculosis in India. Indian J Med Res 2004; 120: 377–386.
5. Migliori G B, Espinal M, Danilova I D, Punga V V, Grzemska M, Raviglione M C. Frequency of recurrence among MDR-TB cases successfully treated with standardised short course chemotherapy. Int J Tuberc Lung Dis 2002; 6: 858–864.
6. World Health Organization. Extensively drug-resistant tuberculosis (XDR-TB): recommendations for prevention and control. Wkly Epidemiol Record 2006; 81: 430– 432.
7. Shah, A. R., Agarwal, S. K. & Shah, K. V. (2002). Study of drug resistance in previously treated tuberculosis patients in Gujrat, India. Int J Tuberc Lung Dis 6, 1098–1101.[Medline]
8. Rizwan Iqbal, Iffat Shabbir, Saulat ullah Khan, M.Nazir Mirza, Shamshad Rasul Awan, Mumtaz Hasan Pakistan, Pak J Med Res 2008; Vol. 47, No. 1, Multidrug Resistance Tuberculosis in Lahore
9. Hanif M, Malik S, Dhingra VK Acquired drug resistance pattern in tuberculosis cases at the State Tuberculosis Centre, Delhi, India.