Original Article

DRUG RESISTANCE PATTERN AMONG AFB SMEAR POSITIVE RETREATMENT COMPLETED CASES

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Abstract

Background: Worldwide, multidrug resistance (MDR TB) is a serious issue. It has increased over the last decade. Re-treatment completed sputum smear positive cases have much higher incidence of MDR-TB as compared to primary MDR – TB.

Objective: To estimate the incidence of drug resistance pattern among AFB smear positive re-treatment completed cases.

Study Design: Evidence based prospective study.

Study Setting: Institute of Chest Medicine, Mayo Hospital Lahore, Tertiary care hospital affiliated with King Edward Medical University, Lahore, Pakistan.

Pakistan Medical Research Council

Methodology: A total 50 (Male 22, Female 28) pulmonary TB patients who had completed Re- treatment regimen in the past and are still sputum smear positive for acid fast Bacilli were included in the study. Three consecutive sputum specimens were collected at Aga Khan University collection center at Lahore. The specimen were sent to Agha Khan University Lab Karachi for AFB smear, culture and drug sensitivity both for essential and reserve drugs. Reports for AFB smear were received within a week, while culture and drug sensitivity reports after 6 weeks. Reports data was analyzed for essential and reserve anti tuberculous drug sensitivity for mycobacterium tuberculosis.

Results: Data Analysis revealed MDR TB in 31(62%) patients which include 11 males and 23 females. Individual drug resistance to essential drugs was INH – 62%, Rifampicin – 68%, Ethambutol – 24%, PZA – 25% and Streptomycin – 21%. Poly drug resistance was determined in 38% cases. Individual drug resistance to reserve drugs – kanamycin, Amikacin, ofloxacin, Ethionamide and PAS was 4%, 4%, 36%, 10% and 2% respectively.

Conclusion: There is a very high proportion of MDR TB in sputum smear AFB positive retreatment cases.

Suggestion: Comprehensive measures including DOTS PLUS are needed to control MDR TB in Pakistan.

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Key words: MDR TB, XDR TB, Re-treatment regimen, Essential drugs, Reserve drugs, AFB – acid fast bacilli.

Introduction

Tuberculosis (TB) is a major global health problem. Each year millions of people suffer with TB. Worldwide tuberculosis is the commonest cause of death from an infectious disease only super ceded by human immunodeficiency virus (HIV).[1]

Multidrug – resistant TB (MDR-TB) has become a serious threat to TB control and the emergence of extensively drug – resistant TB (XDR – TB) has further heightened this threat. Multi – drug Resistant Tuberculosis defined as resistance to isoniazid and rifampicin, with or without resistance to other first line anti-TB drugs. MDR-TB is a classic example of a disease which has spread due to our own fault. It results from improper supplies of drug, inappropriate ATT regimens, poorly handled cases, inadequate follow up and very poor compliance by patients.[2]

About 440,000 cases of MDR tuberculosis reported in 2008 worldwide. India and China had the greatest number of patients of MDR tuberculosis, combining to make almost half of the total cases of the world. More than three quarters of the estimated cases of MDR tuberculosis occurs in previously treated Patients.[3]

Among the countries which have high burden of TB Pakistan is at number 6 position. In the EMRO region Pakistan has the highest prevalence of MDR cases. WHO survey conducted in Pakistan showed that, 3.4% patients are suffering from primary MDR and the prevalence of MDR in treated patients is 36%.[4]

Persons at risk of development of MDR Tuberculosis are those who were previously treated for tuberculosis, contacts of patients previously treated and/or known to have MDR – TB, living in developing countries and those patients which remains smear positive after taking ATT for 3 months.[5]

Amongst previously treated patients transmission of drug – resistant tuberculosis occurs in the community. In countries like Pakistan, the patients who are diagnosed with MDR TB have mostly taken at least two incomplete courses of treatment with anti tuberculous drugs. Moreover, in many countries, conventional methods are used to diagnose MDR tuberculosis which takes months to confirm the diagnosis of MDR tuberculosis and during this period of time infectious patient remained in the community and spread the disease in the community.[6]

In-appropriate anti-tuberculous drug therapy allows selectively the multiplication of resistant organisms and these resistant organisms leads to failure of the therapy and development of the MDR tuberculosis. These resistant strains may be transmitted to the normal persons.[7]

Early diagnosis and appropriate management of MDR patients are the most effective measures for the control of MDR TB. Regional patterns of drug susceptibility are necessary to design an appropriate treatment regimen; this will prevent the treatment failure and reduces the number of secondary MDR tuberculosis patients.

Objective

To estimate the incidence of drug resistance pattern among AFB smear positive re-treatment completed cases.

Study Design

Evidence based prospective study.

Study Setting

Institute of Chest Medicine, Mayo Hospital Lahore, tertiary care hospital affiliated with King Edward Medical University Lahore, Pakistan**.**

Methodology

A total of 50(Male 22, Females 28) patients, who had completed Retreatment regimen and they were still acid fast bacilli sputum smear positive were included in the study. The registered patients have age range between 15 – 76 year with median age for men 38.2 years and for females 25.2 years. The patients were admitted in the ward with their consent to include them in the study. Three more samples of sputum on three next consecutive days were sent to Agha Khan Lab at Karachi through their collection centers at Lahore for acid fast bacilli smear, culture and drug sensitivity both for essential and reserve drugs sensitivity. The inclusion criteria for the study pattern was:

1. Patients who had completed WHO retreatment regimen.

2. Patients still AFB Smear positive.
3. No gender discrimination.
4. Adult age.

Table 1:

Drug	Male		Female		Total		Significance of Resistance	
	N = 22		N = 28		N = 50		Overall Presence	Comparison between Genders
	n	%	n	%	n	%	p-value(*)	p-value($)
NIH	12	54.5	19	67.9	31	62.0	< 0.001	0.503
Rifampicin	14	63.6	20	71.4	34	68.0	< 0.001	0.779
INH + Rifampicin	12	54.5	19	67.9	31	62.0	< 0.001	0.503
Ethambutol	7	31.8	17	60.7	24	48.0	< 0.001	0.081
PZA	5	22.7	20	71.4	25	50.0	< 0.001	0.002
Streptomycin	10	45.5	17	60.7	27	54.0	< 0.001	0.43

*P value calculated for hypothesis (H1: $P \neq 0$)

$ P value calculated for difference between proportions with continuity correction (H1: $P1 - P2 \neq 0$)

Results

Data analysis of study patients include.

Total No. of Patients: 50.

Gender Distribution

Male: 22.

Females: 28.

Age Distribution

Age range 15 – 76 years.

Median age for men – 38.2 years.

Median age for women – 25.2 years.

Drug Sensitivity Pattern

Essential Drugs (Table 1).

Reserve Drugs (Table 2).

Data cited in the table 1 indicates MDR – TB in 62% and poly – drug resistance in 38% cases. Individual drug resistance to INH , Rifampicin , Ethambutol, Pyrazinamide and streptomycin is 62%, 68%, 42%, 50% and 54% respectively.

Table 2:

Drug	Subjects			% of Drug Resistance
	Total	Male	Female	
1. Amikacin	2	1	1	4
2. Kanamycin	2	1	1	4
3. Ofloxacin	18	5	13	36
4. Ethionamide	5	2	3	10
5. PAS	1	0	1	2

Among reserve drugs resistance to kanamycin , Amikacin, ofloxacin, Etionamide is 4%, 36%, 10% and 2% respectively. Drug sensitivity to reserve drugs detects XDR in 4% of study patients.

Discussion

Worldwide an increase in the incidence and prevalence of multidrug resistance (MDR) tuberculosis has created an alarming situation.[8] WHO declared TB as a global emergency in 1993[9] and Pakistan declared it as national emergency in 2001.[10] Multidrug resistance tuberculosis has been documented in nearly 90 countries worldwide.[11] Persons who are at greater risk to MDR – TB include previously treated cases, dwellers

of high incidence MDR TB countries, close contacts of MDR TB patients and AFB smear positive patients after 3 months of therapy.

In our study. The individual resistance to INH, Rifampicin, Ethambutol, PZA, Streptomycin is 62%, 68%, 42%, 50% and 54% respectively. MDR proportion was high up to 62% and poly – drug resistance is detected in 38% of the study cases. Resistance to reserve drugs Amikacin, Kanamycin, Ofloxacin, Ethionamide and PAS was 4%, 4%, 36%, 10% and 2%, respectively. So the incidence of XDR-TB is 4%. Amongst reserve drugs ofloxacin has the highest rate of resistance (36%) and PAS has the lowest resistance (2%) cases.

Incidence of MDR TB is increasing in Pakistan. Different regions in the world have MDR TB between 24 – 28%.[12,13] A decade ago WHO / IUALTD Global surveillance project between 1994 to 1997 revealed drug resistance between 2.3% to 42.4%. The resistance rate for INH was from 2.3% to 39.0%, Streptomycin 9% to 35.1%, Rifampicin 0% to 23%, Ethambutol 0 to 9.4% and multidrug resistance was 0 to 22.1%.[14] According to Danish K et al, study the individual resistance to INH and Rifampicin was 67% and 76% respectively and to both INH and Rifampicin (MDR TB) was 43.47%.[15] Individual resistance to INH and Rifampicin matches to our study results but MDR is low as compared to our study.

Considering the above mentioned studies results and our study results indicate high proportion of multi drug resistance and poly drug resistance in treated TB cases.

Conclusion

There is a very high proportion of MDR TB in sputum smear AFB positive retreatment cases.

Suggestions

1. In order to control MDR TB, we must try to address the issues for MDR TB development.

   Comprehensive measures including DOTS Plus strategy must be adopted to treat and control the multi-drug resistance tuberculosis.

2. Mega studies should be conducted for real estimation of MDR and XDR in Pakistan.

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