World Journal of Pharmaceutical and Life Sciences <u>WJPLS</u>

www.wjpls.org

SJIF Impact Factor: 5.008

MYCOBACTERIUM TUBERCULOSIS (MTB) RESISTANCE PATTERN TO FIRST LINE ATT

Dr. Salman Sarwar*, Sumera Zia and Bakhtawar Jabeen

Sheikh Zayed Hospital, Rahim Yar Khan.

*Corresponding Author: Dr. Salman Sarwar Sheikh Zayed Hospital, Rahim Yar Khan.

Article Received on 22/09/2018

Article Revised on 12/09/2018

Article Accepted on 02/10/2018

ABSTRACT

Objective: To determine the Mycobacterium Tuberculosis (MTB) resistance pattern to first line Anti tuberculosis therapy (ATT). **Methodology:** This cross sectional study was done at Department of Pulmonology, Sheikh Zayed Hospital, Rahim Yar Khan during July to December 2017. The diagnosed cases of pulmonary TB were selected irrespective of the gender and with age range of 12 to 60 years. Sputum sample of these cases was processed at solid Lowenstein Jensen (LJ) media for at least 6 weeks, MTB isolated from these sample were then tested for their susceptibility to first line ATT. The MIC of the studied drugs per ml of LJ medium for resistance testing were 0.2 mcg for isoniazid, 02 mcg for streptomycin, , 05 mcg for Ethambutol, 100 mcg for pyrazinamide and 01 mcg for rifampicin. **Results:** In the present study, 50 cases were sleeted. The mean age of the cases was 43.34 ± 8.21 years. There were 68% males and 32% females. Over all drug resistance was seen in 16 (32%) of the cases. Drug resistance was seen in 7 (14%) of the cases. One drug resistance was seen in 12 (24%) of the cases while all 4 drug resistance was seen in 1 (2%) of the cases only. **Conclusion:** Drug resistance is common to first line ATT and the most resistant drug is Streptomycin.

KEYWORDS: MTB, ATT, LJ media.

INTRODUCTION

Tuberculosis (tb) is the disease of the ancient times and was once considered as untreatable caused by Mycobacterium Tuberculosis (MTB). The advent of effective chemotherapy was the major achievement in the context of this resistant organism. The two important concerns regarding TB management were the length of the treatment and side effect profile which lead to an interrupted treatment and emergence of drug resistance.^[1-2]

First line anti-tuberculosis is the most effective regimen and include Rifampicin, Isoniazid, Ethambutol, Pyrazinamide and Streptomycin. The second and the third line ATT drugs are less efficacious and have more side effective profile, that's why the steps are always taken to conserve these drugs to avoid resistance development.^[3-5] Chest X ray is the first investigation to suspect TB, however, sputum examination is still considered the investigation of choice to label the diagnosis of pulmonary TBt.^[6-8] There are multiple tests to diagnose it accurately an among them Gene xpert is considered as the most useful and cheaper one as compared to cultures.⁹⁻¹¹ Standard Anti tuberculosis therapy is started initially comprising and then changes are made accordingly according to the sensitivity pattern on cultures.^[12-15]

MATERIAL AND METHODS

Objective

To determine the Mycobacterium Tuberculosis (MTB) resistance pattern to first line Anti tuberculosis therapy (ATT).

Study design

Cross sectional.

Study Setting

Department of Pulmonology, Sheikh Zayed Hospital, Rahim Yar Khan.

Study Duration

July to December 2017.

Sampling techniques

Non probability consecutive sampling

In the present study the diagnosed cases of pulmonary TB were selected irrespective of the gender and with age range of 12 to 60 years. The cases with ATT defaulter and re treatment cases were excluded from the study.

Sputum sample of these cases was processed at solid Lowenstein Jensen (LJ) media for at least 6 weeks, MTB isolated from these sample were then tested for their susceptibility to first line ATT. The MIC of the studied drugs per ml of LJ medium for resistance testing were 0.2 mcg for isoniazid, 02 mcg for streptomycin, , 05 mcg for Ethambutol, 100 mcg for pyrazinamide and 01 mcg for rifampicin.

Statistical analysis

The data was processed with the help of SPSS-23. Mean and standard deviations were calculated for numerical while frequency and percentages for nominal data.

RESULTS

In the present study, 50 cases were sleeted. The mean age of the cases was 43.34 ± 8.21 years. There were 68% males and 32% females as shown in table I. Over all drug resistance was seen in 16 (32%) of the cases. Drug resistance was seen most commonly against streptomycin which was observed in 9 (18%) of the cases followed by Isoniazid seen in 7 (14%) of the cases (table II). One drug resistance was seen in 12 (24%) of the cases while all 4 drug resistance was seen in 1 (2%) of the cases only as in table III.

	Table I:	Demographics	of subjects	(n=50).
--	-----------------	---------------------	-------------	---------

Variable	Number	Percentage
Male	34	68%
Female	16	32%
Variable	Mean ± SD	Range
Age (years)	43.34±8.21	13-60
BMI (Kg/m ²)	26.27±3.88	14-32

Table II: Resistance pattern of MTB (n= 50).

Drugs	Number	Percentage
Streptomycin	9	18%
Isoniazid	7	14%
Pyrazinamide	2	4%
Rifampicin	2	4%
Ethambutol	2	4%

Table III: Number of drugs and resistance pattern (n= 50).

Drugs	Number	Percentage
1-drug	12	24%
2-drug	2	4%
3-drug	1	2%
4-drug	1	2%
None	16	32%

DISCUSSION

Tuberculosis is a great mimicker and can present as any clinical manifestation and vitally can involve any part of the body and that's why lead to immense delay in the diagnosis sometimes. Along with this long course of chemotherapy and irrational use of these drugs lead to a higher degree of resistance pattern.^[16-18]

Over all drug resistance was seen in 16 (32%) out of 50 cases tested for sputum culture. The results were slightly higher as compared to the previous studies done in the past. by Haq MU et al, found this prevalence in 23% of the cases, furthermore they also found that streptomycin was the one with highest degree of resistance and was seen in 19.05% of cases; which was closer to the resistance pattern of the present study where streptomycin resistance was observed in 9 (18%) of the cases. Resistance to INH was seen in 7 (14%) of the cases in the present study and was also to be 14.9% with similar study, then Ethambutol seen in 3.4%, Pyrazinamide in 2.3% and least was seen in terms of Rifampicin affecting 2.3% of cases.^[6]

One drug resistance pattern was seen in 12 (24%) of the cases in this study. The results were closer to the studies done in the past.¹⁶⁻¹⁷ According to analysis done by World Health Organization where they found that 4.8% (95% Cl 4.6-6.0) of all TB cases are resistant to one or more drugs. The highest burden of these is seen in India and china where it was seen in around 50% of the whole resistant bug and 7% of these drug resistant cases are found in Russian Federation. Pakistan is the fourth highest among high-burden drug-resistant-TB countries.^[19-20]

CONCLUSION

Drug resistance is common to first line ATT and the most resistant drug is Streptomycin.

REFERENCES

- World Health Organization. Global Tuberculosis Report 2016. Geneva, Switzerland: World Health Organization; Available from: http://www.who.int/tb/publications/global_report/en/ . [Last accessed 2017 Mar 02], 2016.
- 2. Rahman M, Kamal SM, Mohammed FR, Alam B, Ahasan HN. Anti-tuberculosis drug resistance pattern among different category of tuberculosis patients. J med, 2009; 10(2): 45-47.
- NTP. Programmatic management of drug resistant tuberculosis (PMDT) [internet], 2014. [cited 2016 Jul 20]. Available from: http://www.who.int/ tb/dots/mdr_tb_guidelines_ppt.pdf.
- Mahmoudi A, Iseman MD. Pitfalls in the care of patients with tuberculosis. J Am Med Assoc, 1993; 270: 65-68.
- 5. Kandi S, Prasad SV, Sagar Reddy PN, Reddy VC, Laxmi R, Kopuu D, et al. Prevalence of multidrug resistance among re-treatment pulmonary tuberculosis cases in a tertiary care hospital, Hyderabad, India. Lung India, 2013; 30: 277–9.
- Haq M, Salam A, Bashir I. Prevalance of resistance to 1st line anti tubrerculosis drugs at Rahim yar khan. JSZMC, 2016; 7(3): 988-92.

- Nathavitharana RR, Cudahy PG, Schumacher SG, Steingart KR, Pai M, Denkinger CM, *et al.* Accuracy of line probe assays for the diagnosis of pulmonary and multidrug-resistant tuberculosis: A systematic review and meta-analysis. Eur Respir J, 2017; 49. pii: 1601075.
- Bablishvili N, Tukvadze N, Avaliani Z, Blumberg HM, Kempker RR. A comparison of the Xpert [®] MTB/RIF and GenoType [®]MTBDRplus assays in Georgia. Int J Tuberc Lung Dis., 2015; 19: 676-8.
- Theron G, Peter J, Meldau R, Khalfey H, Gina P, Matinyena B, *et al.* Accuracy and impact of Xpert MTB/RIF for the diagnosis of smear-negative or sputum-scarce tuberculosis using bronchoalveolar lavage fluid. Thorax, 2013; 68: 1043-51.
- World Health Organizaton. Treatment of tuberculosis guidelines for national programmes. 4th et. Geneva; WHO, 2009.
- 11. Raveendran, R, Oberoi JK, Wattal C. Multidrugresistant pulmonary and extra- pulmonary tuberculosis: a 13 years retrospective hospital-based analysis. Indian. J Med Res, 2015; 142: 575–582.
- Dusthackeer A, Sekar G, Chidambaram S, Kumar V, Mehta P, Swaminathan S. Drug resistance among extrapulmonary TB patients: Six years' experience from a supranational reference laboratory. Indian. J Med Res., 2015; 142: 568- 574.
- Lönnroth K, Migliori GB, Abubakar I, et al. Towards tuberculosis elimination: an action framework for low incidence countries. Eur Respir J, 2015; 45: 928-52.
- Gupta K, Nair D, Sharma P, Gupta A, Sen MK. Changing Trends in the Susceptibility Pattern of Mycobacterium tuberculosis Over a Decade from a Tertiary Care DOTS Centre Delhi. Mycobact Dis., 2016; 6: 211.
- Diacon AH, van der Merwe L, Barnard M, et al. β-Lactams against Tuberculosis--New Trick for an Old Dog? N Engl J Med, 2016; 375: 393-4.
- 16. Mohammad AB, Iliyasu G, Habib AG. Prevalence and genetic determinant of drug-resistant tuberculosis among patients completing intensive phase of treatment in a tertiary referral center in Nigeria. Int J Mycobacteriol, 2017; 6: 47-51.
- Maurya AK, Singh AK, Kumar M, Umrao J, Kant S, Nag VL, et al. Changing patterns and trends of multidrug-resistant tubeculosis at referral centre in Northern India: A 4-year experience. Ind J Med Microbiol, 2013; 31: 40–6.
- Caminero JA, Scardigli A. Classification of antituberculosis drugs: a new proposal based on the most recent evidence. Eur Respir J, 2015; 46: 887-93.
- Khalid M, Hassan S, Saeed MS. Drug resistance p[attern among AFB smear positive retreatment completed cases. Pak Med Res Council, 2015; 21(1): 5-8.

20. Almani SA, Memon NM, Qureshi AF. Drug resistant tuberculosis in Sindh. J Coll Physician Surg Pak, 2002; 12: 136-39.