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Original Research Article

"A STUDY ON ANTI-TUBERCULAR DRUG RESISTANCE PATTERN IN A TERTIARY CARE HOSPITAL"

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ABSTRACT:

Background: Tuberculosis is one of the oldest infectious diseases known to mankind. Archaeological evidences from ancient civilizations have shown the existence of tuberculosis in the prehistoric era. Even though effective chemotherapy for tuberculosis has been available for decades, tuberculosis still remains as a public health challenge all over the world. Over the years not only the medical implications but also the social and economic impact of tuberculosis has been enormous.

AIM: To measure anti-tubercular drug resistance pattern at S.V.S. MEDICAL COLLEGE AND HOSPITAL, MAHABUBNAGAR DISTRICT.

MATERIAL & METHODS: Study Design: Prospective hospital based observational study. **Study area:** The study was carried out in the Department of Pulmonary Medicine, S.V.S Medical College and Hospital, Enugonda, Mahbubnagar. **Study Period:** Mar. 2021 – Feb. 2022. **Study population:** Patients with both Pulmonary and Extra pulmonary tuberculosis who were attending to the study facility. **Sample size:** study consisted of 50 subjects. 1.Collection of samples (sputum, bronchial wash, pleural fluid, synovial fluid & lymph node tissue). 2. Staining method was done by Fluorescence microscopy staining procedure. 3.Grading of the slide as per WHO. 4. Culture & DST was done on L-J medium and Proportionate method.

Results: Among the resistant cases, isolated R resistance was observed in 10 cases (33.3%), R with H was observed in 12 cases (40%), R with S was observed in 2 cases (6.66%), R with H, S & Lfx was observed in 2 cases (6.66%) and R with H & S was observed in 1 case (3.33%).

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CONCLUSION: The study demonstrates that levels of R, MDR & XDR are more than expected levels when compared with other studies conducted in India as per global DRS guidelines. In view of these results, Multidrug resistance continues to be a serious problem in Mahbubnagar District of TELANGANA. R resistance can be considered as a surrogate marker for MDR-TB. On the basis of these results, it is now necessary to conduct more DRS in much larger population.

Keywords: Anti-tubercular drug resistance**,** Mahbubnagar District, DOTS-Plus programmes

INTRODUCTION:

Tuberculosis is one of the oldest infectious diseases known to mankind. Archaeological evidences from ancient civilizations have shown the existence of tuberculosis in the prehistoric era. Even though effective chemotherapy for tuberculosis has been available for decades, tuberculosis still remains as a public health challenge all over the world. Over the years not only the medical implications but also the social and economic impact of tuberculosis has been enormous.

In 1993, the World Health Organisation (WHO) declared Tuberculosis as a global emergency because of the scale of the Tuberculosis epidemic and the HIV pandemic. There was a need for improving the global Tuberculosis control programme. The persistence of TB has been chiefly due to failure of the NTCP. Poverty, overcrowding and migration, prevalence of diabetes, malignancy has contributed for significant rise of TB cases in HIV endemic areas. To help and address the situation, a global strategy called DOTS was introduced. WHO has been promoting the incorporation of the DOTS strategy into the national tuberculosis control programmes all over the world since then.

National Tuberculosis Programme stated in 1962 when reviewed in 1992 after three decades of operation; it was found that it has not made much of an epidemiological impact on the disease. The reviewed resulted in the genesis of Revised National Tuberculosis Control Programme (RNTCP). The programme tested as a pilot project in 1993 was found to be effective. The programme tested as a pilot project in 1993 was found to be effective. The expansion of the programme was started in 1998. The programme is based on the WHO strategy of Directly Observed Treatment Short course (DOTS).

The first WHO endorsed DOTS-Plus programmes began in 2000. At that time, the Green Light Committee (GLC) was established to promote access to high quality second-line drugs for appropriate use in TB control programmes. DOTS-Plus pilot projects have demonstrated the feasibility and effectiveness of MDR-TB treatment in less affluent countries. In 2002, the Global Fund to fight AIDS, TB, and Malaria (GFATM) started financing TB control programmes, including MDR-TB, thus greatly reducing the economic barrier to MDR3 TB control. Since then, DOTS-Plus projects have multiplied rapidly. By the end of 2007, 67 projects in 52 countries approved by the GLC, with a cumulative total of over 30,000 MDR-TB patients, had been launched worldwide, many of them with financial support from the GFATM. Based on data and experience from these projects, practices and further scientific evidence have emerged regarding services for MDR-TB. DOTS-Plus programmes can and should strengthen the basic DOTS strategy.

It is envisioned that by the year 2010 the DOTS Plus services will be introduced in all the states across the country. By 2012, it is aimed to extend these services to all smear

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positive retreatment cases and new cases who have failed an initial first line drug treatment. And by 2015, these services will be made available to all smear positive pulmonary TB cases registered under the programme. It is intended to treat at least 30,000 MDR cases annually by 2012-13.

HISTORY OF THE PROJECT

In 1994, the Global Project on Anti-Tuberculosis Drug Resistance Surveillance was initiated by the WHO and the International Union against Tuberculosis and Lung Diseases, aiming to measure the magnitude of drug resistant tuberculosis and to monitor trends [1]. At this time, a first set of guidelines was developed to assist national tuberculosis control programs in conducting anti tuberculosis drug resistant surveys [2].

The present study was undertaken to know the antitubercular drug resistance surveillance in S.V.S Medical College and Hospital in Mahbubnagar.

AIM: To measure anti-tubercular drug resistance pattern at S.V.S. MEDICAL COLLEGE AND HOSPITAL, MAHABUBNAGAR DISTRICT.

MATERIAL & METHODS:

Study Design: Prospective hospital based observational study.

Study area: The study was carried out in the Department of Pulmonary Medicine, S.V.S Medical College and Hospital, Enugonda, Mahbubnagar.

Study Period: Mar. 2021 – Feb. 2022.

Study population: Patients with both Pulmonary and Extra pulmonary tuberculosis who were attending to the study facility.

Sample size: study consisted of 50 subjects.

Sampling method: Simple random Sampling Technique.

Inclusion criteria:

1. Patients of either sex are included in the study.
2. Patients of age greater than 14 years are included in the study.
3. Patients with both Pulmonary and Extra pulmonary tuberculosis are included in the study.
4. Both New and Retreated cases are included in the study.
5. Relapse, Default & Failure PTB cases are included in the study.
6. Contacts of MDR TB patients are included in the study.

Exclusion criteria:

1. Children less than 14 years are excluded from the study.
2. New cases without contact history of Resistant TB are excluded from the study.

Ethical consideration: Institutional Ethical committee permission was taken prior to the commencement of the study.

Study tools and Data collection procedure:

1. Collection of samples (sputum, bronchial wash, pleural fluid, synovial fluid & lymph node tissue).
2. Staining method was done by Fluorescence microscopy staining procedure.
3. Grading of the slide as per WHO.
4. Culture & DST was done on L-J medium and Proportionate method.

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Statistical analysis:

For statistical calculations, data is spread in excel sheet descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean□SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance. Chi-square/Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. A p value ≤ 0.05 was considered statistically significant. The Statistical software namely SPSS 21.0 was used for the analysis of the data.

OBSERVATIONS & RESULTS:

Table 1: DRUG RESISTANCE TO ANTITUBERCULOSIS DRUGS

TOTAL SUSPECTS	CULTURE NEGATIVE	CULTURE POSITIVE	SENSITIVE	RESISTANT
50 (100%)	10 (20%)	40 (80%)	10 (20%)	30 (60%)

Total suspects observed in my study were 50 cases. Among these, culture negative were 10cases (20%) and culture positive were 40 (80%). Among the culture positive cases, sensitive cases were 10 (20%) and resistant cases were 30 (60%).

Table 2: DRUG RESISTANCE AMONG CULTURE POSTIVE PATIENTS

H	R	Z	E	S	SR	HRS	MDR	XDR
2 6.66%	10 33.3%	0 0%	0 0%	1 3.3%	2 6.6%	1 3.3%	12 40%	2 6.6%

Among the resistant cases, R resistance was observed in 10 cases (33.3%) & H resistance was 2 cases (6.66%). Among the resistant cases, MDR TB was observed in 12 cases (40%) and XDR TB cases were observed in 2cases (6.66%).

Table 3: PATTERN OF DRUG RESISTANCE

1 DRUG	2 DRUGS	3 DRUGS	4 DRUGS
H 2	HR 12	HRS 1	HRSLfx 2
R 10	RS 2		
S 1			
TOTAL 13	TOTAL 14	TOTAL 1	TOTAL 2

Among the resistant cases, mono drug resistance was observed in 13 cases (43.3%), resistance to 2 drugs was observed in 14 cases (46.6%), resistance to 3 drugs was observed in 1 case (3.33%) and resistance to 4 drugs was observed in 2 cases (6.66%).

Table 4: ANALYSIS RIFAMPICIN RESISTANT CASES

R	RS	HRS	HRE	HRSLfx
10 (33.3%)	2 (6.66%)	1 (3.33%)	12 (40%)	2 (6.66%)

Among the resistant cases, isolated R resistance was observed in 10 cases (33.3%), R with H was observed in 12 cases (40%), R with S was observed in 2 cases (6.66%), R with H, S & Lfx was observed in 2 cases (6.66%) and R with H & S was observed in 1 case (3.33%).

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Table 5: DRUG RESISTACE PATTERN AMONG NEW AND RETREATED CASES

	TOTAL	CULTURE NEGATIVE	CULTURE POSITIVE	SENSITIVE	RESISTANT
NEW	**12**	**6**	**6**	**3**	**3**
RETREATED	**38**	**4**	**34**	**7**	**27**

Among 50 cases 12 cases were new and 38 were retreated, among the new 6 were culture positive and 3 were found to be resistant & among the retreated 34 were positive and 27 were resistant.

Table 6: RESISTANCE PATTERN IN AGE GROUPS

AGE GROUP	TOTAL NO OF CASES	NO OF RESISTANT CASES
5 - 15	**1**	**1**
16 - 25	**0**	**0**
26 - 35	**1**	**0**
36 - 45	**12**	**6**
46 - 55	**20**	**13**
56 - 65	**14**	**9**
66 - 75	**2**	**1**

Among the resistance cases highest no of suspects (20 & 40%), resistant cases (13 & 43.3&) were observed in the age group of 46-55, followed by more no of suspects (14 & 28%), resistant cases (9 & 30%).

Table.7: RESISTANCE PATTERN IN SEX GROUPS

SEX GROUP	TOTAL NO OF CASES	NO OF RESISTANT CASES
MALE	**40 (80%)**	**25 (83.3%)**
FEMALE	**10 (20%)**	**5 (50%)**

Among the 50 suspects males were 40 (80%) and females were 10 (20%). Among the males, resistant cases were 25 (83.3%) and among females were 5 (50%).

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Table 8: RESISTANCE PATTERN IN PULMONARY AND EXTRAPULMONARY TUBERCULOSIS

	TOTAL NO OF CASES	NO OF RESISTANT CASES
PULMONARY	**47**	**27**
EXTRAPULMONARY	**3**	**3**

Among the 50 suspects Pulmonary TB suspects were 47 (94%) and EPTB were 3 (6%). Among the PTB suspects resistance was observed 27 cases (90%) and of EPTB resistance cases was observed in 3 cases (100%).

DISCUSSION:

In the present study conducted in Mahbubnagar district among 50 suspects the male and female sex ratio was found to be 4:1. B. Mahadev, P. Kumar, S.P. Agarwal[5] L.S. Chauhan and N. Srikantaramu et al[3], conducted study of 693 sputum positive cases in Hoogli and Mayyurbhanj districts. The male and female sex ratio in both districts was 3:1.

In the present study conducted in 50 suspects, 40 (80%) were found to be culture positive. Sujatha Chandrasekaran et al[4], among 880 culture positive cases 657 (74.65%) were found to be sensitive and 223 (25.34%) were found to be resistant. B. Mahadev, P. Kumar, S.P. Agarwal, L.S. Chauhan and N. Srikantaramu et al, among 545 (89.17%) culture positive cases 486 (10.82%) were found to be sensitive and 59 were found to be resistant.

In the present study among 30 resistant cases isolated resistance to H, R & S are 6.66%, 33.33% & 3.33% respectively. Cases with MDR TB are 3.38% and XDR TB ar. 6.66%. Sujatha Chandrasekaran et al[4], among 223 resistant cases isolated resistance to H, R & S are 68.8%, 5.38% & 5.82% respectively. Cases with MDR TB are 6.27% and no XDR TB cases. B. Mahadev et al[3], among 59 resistant cases isolated resistance to H, R & S are 15.25%, 0% & 42.37% respectively. Cases with MDR TB are 3.38% and no XDR TB cases.

In the present study among 30 resistant cases resistance to Rifampicin is most common with Isoniazid resistance followed by Rifampicin alone. In present study resistant pattern was observed in PTB & EPTB cases. In this study out of 50 patients' total cases of PTB were 47. Out of 47, 27 were found to be resistant and all the 3 EPTB cases were found to be resistant. In present study highest number of culture positive cases and resistant cases were found in the age group of 46-55years. In this age group 20 cases were found to be culture positive and 13 were found to be resistant. In the present study among 50 cases 12 cases were new and 38 were retreated, among the new 6 were culture positive and 3 were found to be resistant & among the retreated 34 were positive and 27 were resistant.

Sujatha Chandrasekaran et al[4], among 223 resistant cases resistance to Rifampicin is most common with Isoniazid resistance followed by Rifampicin alone. B. Mahadev et al[3], among 59 resistant cases resistance to Rifampicin is most common with Isoniazid & Streptomycin resistance.

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India has the highest global burden of MTB and MDR-TB. Nearly half of the world's MDR-TB patients are from three countries, namely, India (27%), China (14%), and Russia (9%)[5]. Indian survey of TB drug resistance in 2016 reports a lower incidence of MDR in treated (11.6% vs. 18%) and new cases (2.84% vs. 3.4%) in comparison with the global WHO 2019 report[6].

Traditionally, the etiopathogenesis of MDR-TB is attributed to poor compliance and programmatic failure. We do not find any significant difference in the MDR-TB prevalence between previously treated and new cases. Although isoniazid mono-resistance had a small positive association with previous treatment, rifampicin mono-resistance was not associated with earlier treatment. Our results support the observation by Dheda et al.[7] claiming that factors other than poor compliance and program failure are strongly implicated in the prevalence of MDR-TB, and they need to be identified.

TB drug resistance may be sub-classified as true resistance, heteroresistance and Inferred resistance. In true resistance, only the mutant strain is present. Detection of both the mutant and the wild type strains is known as heteroresistance, while the absence of both mutant and wild type strain is considered as Inferred resistance. Heteroresistance is considered to be the early stage in the development of drug-resistant TB.

Inadequate treatment can be defined as direct or indirect mono-therapy, and this can be related to the health professional, to the drug, or to the patient himself. If the treatment is irregular, the number of bacterial death and bacterial growth cycles will be greater, giving more opportunities for individual mutations of different independent genes to accumulate.

CONCLUSION:

The study demonstrates that levels of R, MDR & XDR are more than expected levels when compared with other studies conducted in India as per global DRS guidelines. In view of these results, Multidrug resistance continues to be a serious problem in Mahbubnagar District of TELANGANA. R resistance can be considered as a surrogate marker for MDR-TB. On the basis of these results, it is now necessary to conduct more DRS in much larger population. Measures to manage Multidrug resistant tuberculosis are urgently needed and immediately programmes of tuberculosis are adopted or expanded. Mainly a DST laboratory should be established in Mahbubnagar district as the incidences of MDR TB & XDR TB are high.

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