NTI Bulletin 2003, 39 / 3&4, 5-10

SURVEILLANCE OF DRUG RESISTANCE IN MYSORE DISTRICT, KARNATAKA

B Mahadev[1], P Jagota[2], N Srikantaramu[3] & M Gnaneshwaran[4]

SUMMARY

Surveillance of Drug Resistance (SDR) was carried out in Mysore district of Karnataka with the objective of determining the proportion of Initial Drug Resistance among self-reporting new smear positive cases. The procedures prescribed by WHO/IUATLD were followed to carry out the study.

A total of 205 patients were taken into the study. One sputum specimen was collected from each patient selected for the study attending the health facilities. Susceptibility testing could not be done for two patients as the specimens were dried up. Out of the 203 patients, results were available for 179 patients for whom drug susceptibility to Streptomycin, INH, Rifampicin and Ethambutol was carried out. Among the 179 culture positive patients, 15 patients were excluded for the purpose of analysis (eight because of history of anti-TB treatment in the past and seven being patients from outside the district). Therefore, the core group included for the analysis were 164 of which 137 (83.5%) were sensitive to all drugs. The proportion of initial resistance in this group worked out to 11.6% for INH, 1.8% for Rifampicin and 1.2% for both INH & Rifampicin (MDR).

Key words : Self-reporting chest symptomatics, Anti-TB Treatment, Smear positive TB patients, Standardized procedure, Initial Drug Resistance, Multi Drug Resistance

INTRODUCTION

There has been a growing concern among the tuberculosis programme managers about the inadequacies of information on the prevalence of Multi Drug Resistance (MDR) both at global and national levels. The existing information was found to be very sketchy with lot of limitations regarding the sample size, elicitation of history of previous Anti-TB Treatment (ATT) and the procedures adopted for carrying out Drug Susceptibility testing[1]. In order to bridge the existing gaps, World Health Organization (WHO) and International Union Against Tuberculosis and Lung Disease (IUATLD) came out with a proposal for a global surveillance project. It has identified supranational reference laboratories on a regional basis to monitor the quality control for Institutions carrying out Surveillance of Drug Resistance (SDR) in different parts of the world[2].

In our country, an expert group meeting on SDR in Tuberculosis (TB) was organized by the Central TB Division, Ministry of Health & Family Welfare, Government of India at Tuberculosis Research Centre (TRC), Chennai in September 1997 to review the available data on the proportion of IDR. The group opined that there was no study available which was recent, representative of population and standard procedure adopted for carrying out drug susceptibility tests. The committee recommended to carry out systematic ongoing SDR among the new patients reporting to health facilities using standardized protocol with the broad framework meeting the three principles[2] enunciated below:

a) The samples collected should represent newly registered sputum positive TB patients from the area under study and the sample size being adequate.

b) The patient's history of previous ATT being elicited carefully for distinguishing primary from acquired drug resistance.

c) Standardized procedure followed by laboratories while carrying out susceptibility testing of anti-TB drugs.

The present study was taken up in Mysore district of Karnataka which has been covered under Short Course Chemotherapy (SCC) since 1990. The

1. Chief Medical Officer, 2. Former Director, 3. Statistical Assistant, National Tuberculosis Institute, 8, Bellary Road, Bangalore - 560 003. 4. Former District Tuberculosis Officer, Mysore District.

intake of patients for the study was for a period of one year commencing from January 1999. This was undertaken as a fore-runner for initiating SDR in 3 districts of eastern part of India viz., Hoogli (West Bengal), Mayurbhanj (Orissa) and Nagaon (Assam) by National Tuberculosis Institute (NTI), Bangalore.

OBJECTIVE

To determine the proportion of IDR among new cases of pulmonary TB detected in Mysore district.

MATERIAL & METHODS

The following procedures were adopted for the study:

a. **Intake criteria :** All self-reporting chest symptomatics including children having cough for three weeks or more with or without other cardinal symptoms of TB were subjected for smear examination. Those found smear positive and who had not had any Anti-TB Treatment [ATT) were taken into the study based on the information collected by the Medical Officer (MO) of the health facility using structured questionnaire.

b. A total of 205* smear positive patients who fulfilled the intake criteria were taken into the study from District Tuberculosis Centre (DTC) and 10 functioning Microscopy Centres (MCs) selected from the district. A day's training was imparted in the district head quarters for the personnel involved in the study with regard to selection criteria and other procedures.

c. One spot specimen was collected from each of the eligible smear positive TB patients. The specimens were treated with equal volume of 1% Cetyl Pyridium Chloride (CPC) with 2% Sodium Chloride as transport media[4]. This was transported to the NTI, Bangalore for Acid Fast Bacilli (AFB) culture.

d. The isolation of AFB was done using Lowenstein Jensen (LJ) media.

e. The positive cultures were subjected for sensitivity testing by economic version of proportion method as per IUATLD manual for national laboratory network with the critical drug concentration for INH (H) (0.2mg/ml), Rifampicin (R) (40 mg/ml), Streptomycin (S) (4mg/ml) and Ethambutol (E) (2mg/ml)[5]. The critical proportion for declaring resistance to each of the drug being 1%. Niacin & Para Nitro Benzoic acid tests procedure were carried out for identification tests[6&7]

f. Health Visitor of NTI using structured questionnaire cross-verified the history of past ATT of all patients taken into the study. Laboratory Technician of NTI confirmed the smear positivity at the centre after receiving the information from the respective centres.

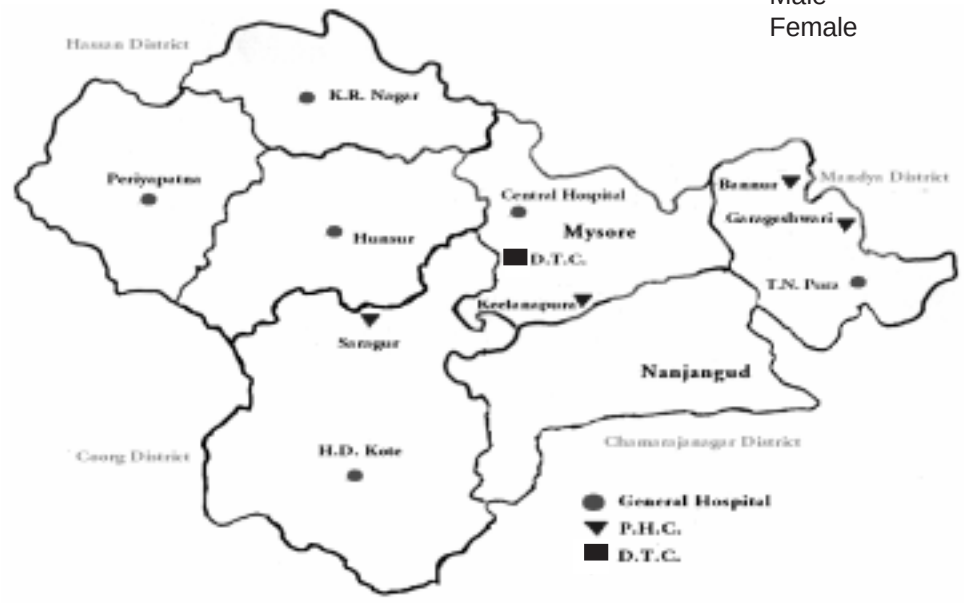
g. External Quality Control assessment of NTI laboratory was carried out by WHO recognized supranational reference laboratory of Brisbane, Australia validating the results of susceptibility testing by carrying out blind testing and confirmatory testing.

* It was estimated that a sample size of about 200 would be needed for the overall survey in order to detect resistance level of 15% to H expected in this area with a confidence interval of 10% to 20% and the level of confidence being 95%.

Fig. 1

MYSORE DISTRICT
SCC - 1990

Total Population : 26241911
Male : 1335841
Female : 1289070



RESULTS

Two hundred and five (205) patients were selected for the study from DTC and 10 functioning MCs of the district (Fig. 1), 150 (73.2%) were males and 55 (26.8%) were females.

Two sputum samples got dried up during transit and hence drug susceptibility testing could not be carried out. Out of the 203 patients subjected for primary isolation, 179 (88.2%) were positive to culture, 23 (11.3%) negative and 1 (0.5%) contaminated. There were 5 (2.4%) cases in the children aged less than 15 years (table 1).

Table 1. Distribution of patients by age

Age group (Yrs)	Number	Percentage (%)
< 15 Yrs.	5*	2.4
15-24	42	20.5
25-34	47	22.9
35-44	38	18.5
45-54	43	21.0
55-64	18	8.8
65 & above	10	4.9
Age not stated	2	1.0
Total	**205**	**100.0**

* 3 aged 12 yrs. & 2 aged 13 Yrs.

History of past treatment by culture result as elicited during the house visit by the Health Visitors of NTI is shown in table 2.

Table 2. Culture results by history of previous Anti-TB Treatment

Culture Result	No history of previous treatment	Patient not traced	Patient expired	History of previous treatment	Patient outside district	Total
Positive	140*	21*	3*	8	7	179
Negative	20	1	-	2	-	23
Contaminated	1	-	-	-	-	1
Total	161	22	3	10	7	203

*Core group = 164

For MDR analysis, 8 culture positive patients with history of previous treatment and 7 residing outside the district have been excluded. The susceptibility pattern for the core group of 164 is shown in table 3.

Table 3. Drug Susceptibility pattern of patients

Susceptibility pattern	No history of past ATT	
	Number	Percentage (%)
Sensitive to all drugs	137	83.5
Resistant to any drug	27	16.5
Total Tested	164	100.0
Resistant to one or more drugs		
R only	-	-
S only	7	4.3
H & S	6	3.7
H & R	1	0.6
H & E	1	0.6
R & E	1	0.6
H, S & E	10	0.6
H, R & E	-	-
Resistant to all drugs	1	0.6

83.5% were sensitive to all drugs. The proportion of Resistance in this group works out to 11.6% (19 / 164) for H, 1.8% (3 / 164) for R and 1.2% (2 / 164) for HR (MDR).

Of 8 patients with history of previous ATT, 4 had resistance to H, none was resistant to R or HR.

EXTERNAL QUALITY CONTROL ASSESSMENT

The results of blind testing under external quality control assessment during the period of the study showed a reproducibility of 80% for Streptomycin & 100% for the other three drugs. Confirmatory testing showed efficiency of 100% for Streptomycin, Rifampicin and Ethambutol and 78% for INH.

DISCUSSION

The study was carried out as per the guidelines recommended by WHO/IUATLD. The data on the sex distribution of TB patients taken into the study shows a preponderance of male patients attending the health facility. The ratio of male to female works out to 1:0.3 This is probably the reflection of the accessibility and utilisation pattern of health facilities in the study area.

In the present study (table 3), the level of resistance to H works out to 11.6% , 1.8% for R and 1.2% MDR-TB. Though 21 (11.7%) of the 179 culture positive patients could not be traced by the Health Visitors of NTI for collecting the information on the history of previous treatment, they have been included for the main analysis as they were classified as new cases by the MO of the health facility based on filled up questionnaire. Of them, 14 isolates were sensitive to all drugs and others showed resistance to one or more drug, but none to HR.

Very few similar studies using the rigid intake criteria have been carried out in the recent past. It is worth mentioning the study of Paramasivan et al carried out in the state of Tamilnadu from among 400 patients having the resistance level of 15.4% to H and 4.4% to R[8].

In another similar study carried out recently by Tuberculosis Research Centre (TRC), Chennai in North Arcot district of Tamilnadu, out of 282 patients, the resistance to H was 23.4% and 2.8% for R and in Raichur district of Karnataka, out of 278 patients, the resistance to H was 18.7% and 2.5% for R[9]. Probably, higher levels of resistance may partly be attributed to the longer duration of SCC being in operation in North Arcot and Raichur districts since 1980s as compared to Mysore district since 1990s.

The study carried out by Sujatha et al in 1990 from an urban DTC in Bangalore has also reported higher level of resistance to H (17.4%) and 21.1% to any drugs[10]. In another study carried out by the same author in 1992 in Kolar District TB Programme, the resistance to H has been shown to be 17.3% and 34.9% to any drugs[10]. As stated by the author, the levels of resistance are high as it happens to be a clinical situation and does not reflect the epidemiological situation[11].

CONCLUSION

The present study shows level of MDR-TB as 1.2% as against 3.4% from Tamilnadu[8], 2.8% from North Arcot and 2.5% from Raichur[9]. This indicates that it is not a major problem in the SCC district of Mysore. These type of studies should be carried out in other parts of the country to get a baseline information on IDR.

Such studies, if repeated after a period of 3 to 5 years in the same area would facilitate the programme planners to ascertain the trend of MDR. This also helps in taking decisions on modulating treatment regimens besides evaluating programme performance. The decline in the rate of prevalence of drug resistance has been demonstrated in high prevalent countries like Tanzania & China where programme performance have improved over a period of time using DOTS strategy[12,13].

ACKNOWLEDGEMENT

The authors thank the Director of Health & Family Welfare, Govt. of Karnataka; Jt. Director (TB); District TB Officer & staff of DTC; Medical Officers & Staff of the participating health centres of Mysore districts for extending their co-operation & services. The authors also appreciate the members of Technical Co-ordination Committee for their valuable suggestions besides acknowledging the sincere co-operation and field work carried out by Mrs VN Saroja, Sr PHN, Mrs Aleyamma Korah,

Mr B A Eswara, & Mr B A Shivashankar, Health Visitors, Mr H D Surendra, Mr D Narayana & Ms N Shivashankari, Lab. Technicians & all the staff of Bacteriology Section in conducting the study and Mr R Ravi, Stenographer for Secretarial Assistance.

LIST OF REFERENCES

1. The WHO/IUATLD working group on anti-tuberculosis drug resistance surveillance: Anti-tuberculosis drug resistance: is it worth measuring? **Monaldi Arch Chest Dis. 1996, 51, 299, 32.**

2. WHO Global tuberculosis programme and IUATLD: Guidelines for surveillance of drug resistance in tuberculosis. **1997, WHO/ TB 96, 216. WHO, Geneva.**

3. Central TB Division, New Delhi: Summary and recommendations of the expert group meeting on drug resistance surveillance in TB held at TB Research Centre, Chennai, 25-26th September 1997. DGHS, Ministry of Health & Family Welfare, Govt. of India, New Delhi:

4. Smithwick RW, Stratigos CB & David HL: Use of cetylpyridinium chloride and sodium chloride for the decontamination of sputum specimens that are transported to the laboratory for the isolation of M.tuberculosis. **J Clin Microbiol 1975, 1, 411-3.**

5. International Union Against Tuberculosis and Lung Diseases: Minimum Requirements, Role and Operation in a low income country. The Public Health Service National Tuberculosis Reference Laboratory and the National Laboratory network. 1998, 72 -76.

6. Allen B & Baker RJ In: Mycobacteria: Isolation, Identification and Sensitivity testing. Butterworth, London 1968, 17.

7. Kubica GP: Differential identification of mycobacteria: VII - key to features for identification of clinically significant mycobacteria, **Am Rev Resp Dis, 1973, 107, 9-21.**

8. Paramasivan CN et al: Surveillance of Drug Resistance in Tuberculosis in the state of Tamilnadu. **Ind J Tub 2000, 47, 27-33.**

9. Tuberculosis Research Centre, Chennai: Surveillance of drug resistance in two districts in south India, **TRC Annual Report 1999-2000, 58-59.**

10. Sujatha C et al: Initial Drug Resistance to Anti-Tuberculosis drugs in-patients attending an urban District Tuberculosis Centre, **Ind J Tub 1990, 37, 215-216.**

11. Sujatha C, Jagota P & Chaudhuri K: Initial Drug Resistance to Anti-Tuberculosis drugs in urban District Tuberculosis Programme, **Ind J Tub 1992, 39, 171-175.**

12. International Union Against Tuberculosis and Lung Diseases: The National Tuberculosis Leprosy Programme - United Republic of Tanzania. **Progress Report No.28. Paris; IUATLD, October 1992.**

13. Zhang LX et al: Trend of initial drug resistance of tubercle bacilli isolated from new patients with pulmonary tuberculosis and its correlation with the tuberculosis programme in Beijing. **Tubercle & Lung Dis. 1995, 76, 100-103.**