Research Paper Medical Science

Primary Drug Resistant Pulmonary Tuberculosis in Tertiary Care Center

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ABSTRACT

Introduction:Drug-resistant tuberculosis is a major problem worldwide & is a crucial issue in the control of Tuberculosis. This study is the analysis on the drug resistance profile of M. tuberculosis isolated from patients newly diagnosed with pulmonary TB.

Methods:All new cases of Pulmonary Tuberculosis were subjected to sputum smear examination and sputum culture for AFB followed by drug-susceptibility testing by proportion method.

Results:Resistance to any drug was seen in 17.49% and multidrug-resistant tuberculosis(MDR-TB) was observed in 3.28%.Primary drug re¬sistance to Isoniazid, Streptomycin Rifampicin and ethambutol was 13.66%, 8.74%, 4.92% and 2.73% respectively.

Conclusions:This study suggests that all newly diagnosed cases of Pulmonary Tuberculosis, with AFB smear negativity should also be subjected for AFB culture so as to ascertain active disease. There is a need of continuous monitoring of drug resistance trends, in order to assess the efficacy of current interventions and their impact on the TB epidemic.

KEYWORDS : Drug resistant Tuberculosis, Isoniazid, Rifampicin, ethambutol

Introduction

Tuberculosis is an ancient disease and has long been a major public health challenge in the world particularly in the developing countries like India where it continues to be one of the leading causes of morbidity and mortality.

Easy availability of Anti-TB drugs has led to their indiscriminate use with emergence of Drug resistance. An estimate of drug resistance is extremely important in the epidemiology and control of tuberculosis.

An assessment of the magnitude of Multi-drug Resistant Tuberculosis is not very well described globally & data remains scantier for India. In view of this, we present here data on the incidence of primary drug resistance pulmonary Tuberculosis analysed at Department of Pulmonary Medicine, Grant Medical College and Sir JJ group of Hospitals, Mumbai, Maharashtra, India over a period of 2 years.

Materials and Methods

The study was carried out in a Grant Medical college and Sir JJ Group of Hospitals over a period of 2 years.

All self-reporting chest symptomatic patients with no past history of pulmonary Tuberculosis, above 12 years, with cough of two weeks or more, with or without other symptoms suggestive of TB and patients with radiological evidence suggestive of Pulmonary Tuberculosis, were subjected to sputum smear examinations by Ziehl - Neelsen Staining Method and sputum culture for AFB.

All Sputum Samples were subjected to Mycobacterium Tuberculosis culture on Lowenstein Jensens (LJ) Media, after concentration by N-acetyl-L- cysteine(NALC) – NaOH Concentration method. The positive growths were characterized using standard array of biochemical tests.

All Mycobacterium tuberculosis cultures were subjected for drug susceptibility test (DST) by proportion method.

After culture and identification of Mycobacterium Tuberculosis Drug Susceptibility testing was done by proportion method with drug concentration of 4 microgram/ml for streptomycin, 0.2 microgm/ml for Isoniazid, 40 microgm/ml for Rifampicin and 2 microgm/ml for Ethambutol. The critical proportion for declaring a strain as resistant to the drugs was 1%.

Observations and Discussion

204 patients initially eligible for the study, subjected to sputum microscopy by Ziehl - Neelsen Staining Methodand sputum culture for AFB.On Microscopy 110 (53.92%) were Smear positive and 94 (46.08%) patients were Smear negative. Among 204 patients on culture, 11 (5.39%) were contaminated and were excluded from the study. Of the 193 remaining cultures, 10 (4.90%) were negative and 183 (89.71%) were positive. Thus 183 (89.71%) constituted the final study sample. In our study, culture negativity and contamination rates were 4.90 % and 5.39 % respectively which is in accordance to the DRS guidelines which prescribes 5 to 20 % loss[1].

Table-1

	Sputum AFB Culture positive	Sputum AFB Culture Negative	Contamination grown
Sputum AFB Smear Positive	97	6	7
Sputum AFB Smear Negative	86	4	4
Total	183	10	11

On applying One-way ANOVA test we conclude that the results of test Sputum AFB culture matches with the true state of the patient where as the result of test Sputum AFB Smear is significantly different from the true state of the patient.

Out of the 183 patients included in the study, 104(56.83 %) were males and 79 (43.17 %) were females . Mean age of the study population was 35.98 years.

The gender distribution in the group of patients having primary drug resistance was unequal. 11.48% of females as compared to 6.01% of males had Primary drug resistant Tuberculosis.

All the patients of the study i.e. 100 % presented with Cough followed by fever (91.8 %) and loss of appetite (67.76%)

Cough, fever, breathlessness along with loss of appetite and weight loss were the commonest presenting symptoms in patients of primary drug resistance pulmonary Tuberculosis

Right upper zone followed by left upper zone was the most common radiological involvement in Drug resistant patients.

Table-2

Drug Susceptibility pattern	Number	Percentage
Total Culture Positive	183	100
Sensitive to all drugs	151	82.51
Resistant to any drug	32	17.49
Mono-resistance	16	8.74
Streptomycin (S)	3	1.64
Isoniazid (H)	13	7.10
Rifampicin (R)	-	-
Ethambutol (E)	-	-
Multidrug resistance	6	3.28
H+R	1	0.55
H+R+S	3	1.63
H+R+E	1	0.55
H+R+S+E	1	0.55
Other patterns	10	5.46
S+H	5	2.73
S+R	2	1.09
S+E	1	0.55
H+E	1	0.55
R+E	-	-
S+R+E	1	0.55
S+H+E	-	-

Out of the 183 patient included in the study, 32(17.49%) patients had resistant pattern. The remaining 151(82.51%) patients had a sensitive strain.

Thus the occurrence of primary drug resistance in our study was 17.49%.

Of the 32 patients, only 16 patients (8.74%) of the study populations had monodrug resistance. Isolated resistance to streptomycin was seen in 3 (1.64 %) patients and to INH was seen in 13(7.10 %) patients. No isolated resistance to Rifampicin and Ethambutol was observed.

In poly drug resistance, exclusive multi drug resistance (i.e. only resistance to isoniazid and rifampicin) was seen in 1 (0.55%) patients, multi drug resistance in other patterns i.e. HRS, HRE and HRSE were seen in 5 patients. Thus resistance To H and R is usually accompanied with resistance to other Drugs as well.

The occurrence of primary multi drug resistance in our study was 3.28%.

The Comparative Data is given in Table 3.

Table-3 :Comparison of our results with results of other National Studies[6]

Location	Period	No. of isolates	Any resistance (%) to				
			S	H	R	SH	HR
9 centers-ICMR I	1964-65	1838	14.7	12.5	ND	6.5	ND
9 centers-ICMR II	1965-67	851	13.8	15.5		NA	ND
GCI-SH, Chennai	1976	254	14.2	12.5	ND	6.5	ND
Bangalore	1980's	436	5.7	17.4	3.0	3.9	1.1
Wardha	1882-89	323	14.9	21.4	8.0	8.0	5.3
Gujarat	1983-86	570	7.4	13.8	0.0	4.2	0.0
Bangalore	1985-86	588	4.8	17.3	2.9	3.0	1.4
North Arcot	1989-90	2779	11.6	21.3	1.7	8.0	1.6
Pondicherry	1985-91	1841	8.1	10.8	1.0	3.7	0.8
Kolar	1987-89	292	5.1	32.9	4.4	4.1	3.4
Raichur	1988-89	244	11.4	19.3	3.3	6.6	3.3
North Arcot*	1988-90	241		12.9	2.5		1.7
North Arcot*	1989-98	747		19.0	11.8		4.4
Jaipur	1989-91	1009	7.6	10.1	3.0	1.7	0.9
New Delhi	1990-91	324	ND	18.5	0.6	ND	0.6
Military Hospital Pune	1992-93	473	8.2	3.2	4.0	2.1	1.0
Tamilnadu	1997	384	6.8	15.4	4.4	4.4	3.4
North Arcot	1999	282	12.4	23.4	2.8	8.5	2.8
Raichur	1999	278	7.2	18.7	2.5	4.0	2.5
Wardha*	2000	197	7.6	15.0	0.5	3.0	0.5
Jabalpur*	2002	273	7.0	16.5	1.8	2.6	1.1
Model Dots Area**	1999-03	1610	-	11.8	-	-	1.6
HIV/TB**	2000-02	168	13.7	13.0	-	-	4.3
Hoogly	2000-01	263	13.7	10.3	3.0	4.1	3.0
Mayhurbhanj	2000-01	282	3.9	2.5	0.7	0.7	0.7
Ernakulum[19]	2004	305	23.6	8.8	3.6	3.3	2
Gujarat[20]	2005-06	1571	15.0	11.0	0.2	2.9	2.4
Present Study	2008-10	183	8.74	13.66	4.92	2.73	3.28

*** TRC, Chennai, unpublished findings ** TRC, Chennai, interim findings, unpublished**

Table-4 :Comparison of our results with global data[7]

	Our Study	Global	AFR	AMR	EMR	EEUR	Non EUR	SEAR	WPR
Any H	13.66	10.3	6.7	7.9	6.3	6.3	5.2	10.3	13.3
Any R	4.92	3.7	1.9	3.2	3.3	3.3	1.1	3.4	5.0
Any S	8.74	10.9	6.9	9.0	10.1	10.1	4.0	8.9	14.6

Any E	2.73	2.5	1.3	1.5	1.9	1.9	0.7	3.0	3.0
Any resistance	17.49	17	11.4	14.9	13.7	13.7	7.9	15.8	22.0
MDR	3.28	2.9	1.5	2.2	2.0	2.0	0.9	2.8	3.9

We can state that results of our study are very much comparable to the date from various Regions of the world, more with Western Pacific Region and South East Asian Region.

Conclusion

The levels of H, R, S, E and MDR are within the expected levels, when compared with other Indian studies and global data. Resistance to H and R is usually accompanied with resistance to other Drugs as well. Primary monoresistance to Rifampicin which is a potent anti TB drug has not been seen in our study. Also mono resistance to Ethambutol was not seen. Most common in economically productive age group of 30-40 yrs(mean age-35yrs). There was almost equal distribution of male and female populations screened for the study but higher percentage of females in the study populations showed primary drug resistance. The sputum smear status did not indicate the presence of active Tuberculous infection when compared to Culture report which was positive in a majority of sputum smear negative patients i.e. Sputum smear result did not represent the true status of the patient. An estimate of drug resistance is extremely important in the epidemiology and control of tuberculosis. This study suggests that in all newly diagnosed cases of Pulmonary Tuberculosis, patients with AFB smear negativity should also be subjected for AFB culture study so as to ascertain active disease and there is a need of continuous monitoring of drug resistance trends, in order to assess the efficacy of current interventions and their impact on the TB epidemic.

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