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Original Research Article

A study on multi drug resistant tuberculosis at Sree Mookambika Institute of Medical Sciences

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ABSTRACT

Background: Tuberculosis (TB) is one of the major causes of morbidity and mortality worldwide. Resistance to antitubercular drugs has been noted since the drugs were first introduced, and occasionally outbreaks of drug-resistant tuberculosis have been reported worldwide. WHO emphasizes that good TB control prevents the emergence of drug resistance in the first place and that the proper treatment of multi-drug resistant tuberculosis prevents the emergence of XDR-TB. The objectives of the study were to examine the sputum samples regarding MDR-TB, to study the grading regarding sputum positive and to study the multi-drug resistance tuberculosis in Sree Mookambika Institute of Medical sciences.
Methods: Study design was cross-sectional, Study duration was January 2016-March 2017. Study place was Sree Mookambika Institute of Medical Sciences Hospital, Kulasekharam. Sample size was 400. Data entered in MS-Office Word- 2016. Institutional ethical committee clearance was obtained.
Results: In present study 54.86% patient had sputum AFB positive, 45.13% had sputum AFB negative smears. 75% of the sputum AFB positive pulmonary TB came under the age group between 20-60 and 25% above 60 yrs. 78.24% males, 21.75% females had sputum AFB smear positive pulmonary tuberculosis and 43.73% patients had positive sputum culture, 56.26% patients had negative sputum culture and the most common strain found was Mycobacterium tuberculosis.
Conclusions: So from our study we found that Mycobacterium tuberculosis is the major strain isolated from sputum samples. The resistance is more to Isoniazid and Rifampicin and is more in the rural parts of India. Early screening and drug susceptibility test of culture positive and MTB cases will help in initiating treatment of MDR-TB.

Keywords: Sputum, Multi-drug resistance tuberculosis, Sputum AFB positive

INTRODUCTION

Tuberculosis (TB) is one of the major causes of morbidity and mortality worldwide. In India, about 1.8 million new cases of TB are reported annually, which accounts for a fifth of new cases in the world—a greater numberthan in any other country.[1] In a study by Sharma et al total of 218 cases of sputum positive pulmonary tuberculosis were enrolled between 2008 and 2009 of which only 177 were carried in DST and two cases of MDR-TB were detected. The prevalence of MDR-TB among newly diagnosed pulmonary tuberculosis patients was 1.1 percent.[2]

In a study by Vijayalakshmi among 241 clinically suspected pulmonary tuberculosis patients**,** 61 (22.50%) patients were smear positive for AFB, among which

43(70.49%) were male and 18 (29.51%) were female.[3] In a study by Paramasivan a total of 1375 sputum specimens was received during February-March 1997 among which, 76.7% showed grade 1+, 16.3% showed grade 2+, 7.0% showed grade 3+. Although the phenomenon of drug resistance in M. tuberculosis was observed even in the early days of chemotherapy nearly 50 years ago, the current threat is due to the emergence of strains resistant to the two most potent anti-TB drugs viz., isoniazid (H) and rifampicin (R).[4]

In a study by Kumar 50 cultural isolates of M. tuberculosis isolated from 257 sputum samples from June 2010 to October 2012, Forty one (41) isolates were sensitive to both INH and RIF (82%).[5]

In a study by Vasanthakumari of the 782 sputum samples collected only 162 were AFB positive.[6] In this 33 cases had MDR TB among them 84.8% had irregular treatment/ interrupted treatment and 15.2% had taken drugs regularly. To overcome the problems of drug resistant TB there needs to be development of true point of care drug susceptibility tests, and their widespread implementation at affordable cost.[7]

Resistance to antituberculosis drugs has been noted since the drugs were first introduced, and occasionally outbreaks of drug-resistant tuberculosis have been reported worldwide. But recent outbreaks of XDR-TB have differed considerably from the previous outbreaks of drug-resistant tuberculosis and even multi-drug resistant tuberculosis outbreaks.[8]

Objectives

1) To examine the sputum samples regarding MDR-TB.
2) To study the grading regarding sputum positive.
3) To study the multi drug resistance tuberculosis in Sree Mookambika Institute of Medical sciences.

METHODS

Study design was cross-sectional; Study duration was January 2016 - March 2017. Study place was Sree Mookambika Institute of Medical Sciences Hospital, Kulasekharam, Kanyakumari district, Tamil Nadu. Sample size was calculated by $(Z_x)^2P$ (1-p) $/d^2$.[4] Sample size was 400. Inclusion criteria was MDR-TB patients of both sexes of age >20 years and exclusion criteria was those who are not willing. Sampling technique was Convenient. Predesigned questionnaire was used to collect the data. Data entered in MS-Office Word- 2016. Institutional ethical committee clearance was obtained.

Statistical analysis

For demographic and DST data, frequencies, percentages, means, medians, ranges, and confidence intervals (CI) were calculated as appropriate. The differences in groups were analysed by χ^2 test. The association of MDR-TB with HIV was analysed by multivariable regression analysis. A two-sided p-value of less than 0.05 was considered as statistically significant. The data was analyzed using the SPSS version 20.0 software.

RESULTS

In present the mean (median, range) age of the patients was 36.6 years (35, 20–60), and 32.7 years (35, 20-60) for males and females respectively (p>0.05). In our study of the all patients, 66.9% were from a lower socioeconomic background while 33.04% were of upper socioeconomic status, however, the prevalence of MDR-TB was found to be 19.5% and 23.7% in lower and upper socioeconomic groups, respectively the difference between MDR TB and socio economic status was not statistically significant (p>0.05).

Table 1: Age of AFB positive pulmonary TB.

Age in years	Percentage
20-60	75
>60	25

In present study 54.86% patient had sputum AFB positive and 45.13% had sputum AFB negative smears. 78.24% male patients and 21.75% females had sputum AFB smear positive pulmonary tuberculosis. We found that 76.7% patients are grade 1+ for smear positive, 16.3% are grade 2+ and 7.0% are grade 3+ for smear positive. In present study 43.73% patients had positive sputum culture and 56.26% patients had negative sputum culture and in our study the most common strain found was Mycobacterium tuberculosis.

Our results shows around 58% patients who had no previous h/o treatment/ initial resistance were sensitive to all anti tubercular therapy and 42% patients who had h/o previously treated/acquired resistance/contact were sensitive to all anti tubercular therapy. In present study we found that 76.36% of the patients showed resistance to any one anti tubercular drug. In our study 12.23% patients who had no previous h/o treatment/ initial resistance showed resistance to ISONIAZID and 13.86% patients who had h/o previously treated/acquired resistance/contact showed resistance to isoniazid.

In present study 0.96% patients who had no previous h/o treatment/ initial resistance showed resistance to rifampicin and 0.79% patients who had h/o previously treated/acquired resistance/contact showed resistance to rifampicin. In our study 4.75% patients who had no previous h/o treatment/ initial resistance showed resistance to ethambutol and 4.5% patients who had h/o previously treated/acquired resistance/contact showed resistance to ethambutol. In this study 1.49% patients who had no previous h/o treatment/ initial resistance showed resistance to streptomycin and 0.59% patients who had h/o previously treated/acquired resistance/ contact showed resistance to streptomycin.

We found that 5.24% patients who had no previous h/o treatment/ initial resistance showed resistance to isoniazid and rifampicin and 6.67% patients who had h/o previously treated/acquired resistance/contact showed resistance to isoniazid and rifampicin. Our results shows 1.0% patients who had no previous h/o treatment/ initial resistance showed resistance to HRE and 12.5% patients who had h/o previously treated/acquired resistance/ contact showed resistance to HRE.

In this study 6.25% patients who had no previous h/o treatment/ initial resistance showed resistance to HRSE and 8.45% patients who had h/o previously treated/acquired resistance/contact showed resistance to HRSE. We found that 1.8% patients who had no previous h/o treatment/ initial resistance showed resistance to HE and 6.2% patients who had h/o previously treated/ acquired resistance/contact showed resistance to HE.

In present study 1.3% patients who had no previous h/o treatment/ initial resistance showed resistance to HES and 6.2% patients who had h/o previously treated/acquired resistance/contact showed resistance to HES. Our results shows 3.4% patients who had no previous h/o treatment/ initial resistance showed resistance to any HR combination and 25% patients who had h/o previously treated/acquired resistance/contact showed resistance to any HR combination.

Table 2: Medications.

Regular	84.8%
Irregular	15.2%

In this study 8.33% patients showed resistance to HRS combination. In present study 60.4% residence from rural area showed resistance and 39.6% from urban area showed resistance. Our results shows of the all patients, 66.9% were from a lower socioeconomic background while 33.04% were of upper socioeconomic status, however, the prevalence of MDR-TB was found to be 19.5% and 23.7% in lower and upper socioeconomic groups, respectively, and the difference was not statistically significant (p>0.05).

Antimicrobial resistance

The drug resistance observed to any of the first line drugs in new and previously treated patients was 24.4% (95% CI, 16.4–33.4) and 44.9% (95% CI, 35.1–54.8) to isoniazid, 8.9% (95% CI, 4.8–14.5) and 25.6% (95% CI, 17.7–35.4) to rifampicin, 13.9% (95% CI, 10.6–25.3) and 30.7% (95% CI, 26.3–45.0) to ethambutol, and 26.1% (95% CI, 19.9–34.7) and 32.7% (95% CI, 24.3–42.1) to streptomycin, respectively. The total mono-resistance in new and previously treated patients was found to be 22.7% (95% CI, 15.4–29.9) and 30.6% (95% CI, 25.4–44.9), respectively.

DISCUSSION

In our study smear positive is 54.86%, smear negative is 45.13%. In Paramasivam study smear positive was 93.5%, smear negative was 6.5% and in Vijayalakshmi study smear positive was 22.5%, smear negative was 77.5%.[3,4] In Giridhakumar study smear positive was 19.45%, smear negative was 80.54% and in Kandi study smear positive was 84%, smear negative was 16%.[5,9]

Age group distribution of sputum AFB smear positive pulmonary tuberculosis patients in our study is 75% between 20-60 yrs, 25%>60 yrs. In Vijayalakshmi study it was 62% between 20-60 yrs, 24%>60 yrs. In Giridhakumar study it was 88% between 20-60yrs, 26%>60 yrs.[3,5]

Table 3: Smear positive grades.

Smear positive grades			
Author	Grade 1+	Grade 2+	Grade 3+
Paramasivam[4]	76.7	16.3	7.0
Our study	76.7	16.3	7.0

Gender distribution of sputum AFB smear positive pulmonary tuberculosis patients in our study is 78.24% in males, 21.75% in females. In Vijayalakshmi study it was 70.49% in males and 29.51% in females and in Giridhakumar study it was 86% in males, 14% in females.[3,5]

Sputum culture is 43.73% positive in our study,56.26% negative in our study and was 50% positive and 50% negative in Paramasivam study, in Vasanthakumari study 21.48% positive and 78.52% negative and in Giridhakumar study sputum culture was 19.45% positive, 80.54% negative.[4-6] In Kandi sputum culture was 84% positive, 16% negative.[9]

Strains isolated in our study is Mycobacterium Tuberculosis, in Paramasivam study was Mycobacterium tuberculosis, in Vijayalakshmi study it was Mycobacterium tuberculosis, in Vasanthakumari study it was Mycobacterium tuberculosis, In Giridhakumar study it was Mycobacterium tuberculosis.[3-6]

From drug susceptibility test in our study,58% with no history of treatment or initial resistance, 48% who was with previous treated or acquired resistance or contact and in Paramasivam study 70% was with no h/o treatment/initial resistance, 50% with h/o previous h/o treated/acquired resistance/contact.[4] In Giridhakumar study 75% with no h/o treatment /initial resistance, 30% with previous h/o treated/acquired resistance/contact.[5] In Kandi study it was 50% with no h/o treatment /initial resistance, 48% with previous h/o treated/acquired resistance/contact.[9]

Drug susceptibility test (any resistance) in our study is 34.28% with no h/o treatment /initial resistance, 42.08%

with previous h/o treated/acquired resistance/contact. In Paramasivam study it was 18.8 with no h/o treatment /initial resistance % and 50% with previous h/o treated/acquired resistance/contact.[4] In Vasanthakumari study it was 67% with no h/o treatment /initial resistance and 67% with previous h/o treated/acquired resistance/contact.[6] In Giridhakumar study it was 18% with no h/o treatment /initial resistance and 18% with previous h/o treated/acquired resistance/contact.[5] In Kandi study it was 34.28%with no h/o treatment /initial resistance and 42.08 with previous h/o treated/acquired resistance/contact.[9]

Table 4: Drug susceptibility test (resistance to isoniazid).

Drug susceptibility test (resistance to isoniazid)			
S. no.	**Author**	**Patients with no history of treatment/initial resistance**	**Patients with history of previously treated/acquired resistance**
1	Paramasivam[4]	7.6	12.5
2	Giridharkumar[5]	16	16
3	Subhakar Kandi[9]	13.09	13.09
4	Our study	12.23	13.86

Drug susceptibility test (resistance to rifampicin) in our study is 0.96% with no h/o treatment /initial resistance and 0.79% with previous h/o treated/acquired resistance/contact. In Paramasivam study it was 0.5% with no h/o treatment /initial resistance and 0.0% with previous h/o treated/acquired resistance/contact and in Giridhakumar study it was 0.0% with no h/o treatment /initial resistance and 0.0% with previous h/o treated/acquired resistance/contact.[4,5] In Kandi study it was 2.38% with no h/o treatment /initial resistance and 0.79% with previous h/o treated/acquired resistance/contact.[9]

Drug susceptibility test (resistance to ethambutol) in our study is 4.75% with no h/o treatment /initial resistance and 4.5% with previous h/o treated/acquired resistance/contact. In Paramasivam study it was 0.5% with no h/o treatment /initial resistance and 0.0% with previous h/o treated/acquired resistance/contact and in Kandi study it was 9% with no h/o treatment /initial resistance and 9% with previous h/o treated/acquired resistance/contact.[4,9]

Drug susceptibility test (resistance to Streptomycin) in our study it is 1.49% with no h/o treatment /initial resistance and 0.59% with previous h/o treated/acquired resistance/contact. In Paramasivam study it is 1.8% with no h/o treatment /initial resistance and 0.0% with previous h/o treated/acquired resistance/contact and in Kandi study it was 1.19% with no h/o treatment /initial resistance and 1.19% with previous h/o treated/acquired resistance/contact.[4,9]

Drug susceptibility test (resistance to HR) in our study it is 5.24% with no h/o treatment /initial resistance and 6.67% with previous h/o treated/acquired resistance/contact. In Paramasivam study it was 0.5% with no h/o treatment /initial resistance and 6.2% with previous h/o treated/acquired resistance/contact and in Vasanthakumari study it was 4.21% with no h/o treatment /initial resistance and 4.21% with previous h/o treated/acquired resistance/contact.[4,6] In Giridhakumar study it was 2% with no h/o treatment /initial resistance and 2% with previous h/o treated/acquired resistance/contact and in Kandi study it was 14.28%with no h/o treatment /initial resistance and 14.28% with previous h/o treated/acquired resistance/contact.[5,9]

Drug susceptibility test (resistance to HRE) in our study it is 1% with no h/o treatment /initial resistance and 12.5% with previous h/o treated/acquired resistance/contact and in Paramasivam studies it was 1.0% with no h/o treatment /initial resistance and 12.5% with previous h/o treated/acquired resistance/contact.[4]

Drug susceptibility test (resistance to HRSE) in our study is 6.25% with no h/o treatment /initial resistance and 8.45% with previous h/o treated/acquired resistance/contact. In Paramasivam study it was 1.8% with no h/o treatment /initial resistance and 6.2% with previous h/o treated/acquired resistance/contact and in Kandi study it was 10.71% with no h/o treatment /initial resistance and 10.71% with previous h/o treated/acquired resistance/contact.[4,9]

Drug susceptibility test (resistance to HE) in our study it is 1.8% with no h/o treatment /initial resistance and 6.2% with previous h/o treated/acquired resistance/contact and In Paramasivam study it was 1.8% with no h/o treatment /initial resistance and 6.2% with previous h/o treated/acquired resistance/contact.[4]

Drug susceptibility test (resistance to HES) in our study it is 1.3% who had not treated /initial resistance and 6.2% with previous h/o treated/acquired resistance/contact and in Paramasivam study it was 1.3% with no h/o treatment /initial resistance and 6.2% with previous h/o treated/acquired resistance/contact.[4]

Drug susceptibility test (any HR combination resistance) in our study it is 3.4% who had not treated /initial resistance and 25% with previous h/o treated/acquired resistance/contact and in Paramasivam study it was 3.4% with no h/o treatment /initial resistance and 25% with previous h/o treated/acquired resistance/contact.[4]

Drug susceptibility test (resistance to HRS) in our study it is 8.33% with no h/o treatment /initial resistance and 8.33% with previous h/o treated/acquired resistance/ contact and in Kandi study it was 8.33% with no h/o treatment /initial resistance and 8.33% with previous h/o treated/acquired resistance/contact.[9]

Regularity of drug intake among MDR-TB patients in our study is 84.8% regular and 15.2% irregular. In Vasanthakumari study it was 84.8% regular and 15.2% irregular.[6]

Distribution of MDR cases according to residence in our study it is 60.04% rural and 39.6% urban and in Kumar study it was 60.04% rural and 39.6% urban.[10]

CONCLUSION

In view of the results so far observed there is clear evidence of increase in the prevalence of drug resistance TB in India over the years. In our study we found that Mycobacterium tuberculosis is the major strain isolated from sputum samples. About 73.36% of the patients showed resistance to any one anti tubercular drug. The resistance is more to Isoniazid and Rifampicin and is more in the rural parts of India, of which 66.9% comes under lower socio economical background. Lack of knowledge, irregular treatment, and poor quality of drugs are major concerns for the drug resistance. Early screening of patients and drug susceptibility test of culture positive and MTB cases will help in initiating treatment of MDR-TB.

Recommendation

Awareness program should be conducted by the government regarding the facts about TB. Ensure the quality of drugs provided for the public. Studies about MDR TB should be conducted in other regions of India periodically.

Limitation

Done only in Medical collages and so can't be generalised.

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Conflict of interest: None declared
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