ISSN: 0975-3583,0976-2833 VOL15, ISSUE 08, 2024

To evaluate the clinical and demographic characteristics of multi drug-resistant tuberculosis in a tertiary care health centre in South India

Dr Srilatha sivuni [1], Dr. Chowdam shashi Kumar [2], Dr. Kategar Lakshmi Narayana[3*]

Dr. Gopaldas Vinay Kumar[4]

1. Associate professor, Dept of Paediatrics, Kurnool medical College, Kurnool.

2. Assistant professor, Dept of Paediatrics, Kurnool medical College, Kurnool.

3*. Assistant professor, Dept of Paediatrics, Kurnool medical College, Kurnool

4. Third year post graduate, Dept of Paediatrics, Kurnool medical College, Kurnool

*Corresponding Author

Background: Multidrug-Resistant Tuberculosis (MDR-TB) in children is a significant public health concern, mirroring the burden seen in adults. This study aims to evaluate the clinical and demographic characteristics of pediatric MDR-TB cases at a tertiary care center in South India, highlighting the need for improved diagnostic and treatment strategies.

Methods: A combined prospective and retrospective cross-sectional study was conducted on 40 pediatric MDR-TB cases from September 2022 to August 2024. Data were collected from case sheets and the district tuberculosis center in Kurnool. Statistical analysis was performed using SPSS version 20.0 to identify key clinical and demographic characteristics.

Results: The study included 40 children with MDR-TB, with a mean age of 16.63±2.13 years and a median age of 17 years. There was a noticeable female preponderance, with a female- to-male ratio of 13:7. Most patients belonged to the upper-lower socio-economic class. The predominant symptoms were fever (100%) and cough (100%). Additionally, 87.5% of the children knew their BCG vaccination status, and 22.5% had a history of contact with TB patients. A significant proportion of the children, 77.5%, were malnourished, and 55% had abnormal chest X-rays. Furthermore, 82.5% tested positive in the Mantoux test, and 12.5% were positive for Acid-Fast Bacilli (AFB).

Conclusion: The prevalence of MDR-TB among the pediatric population in the study was 10.92%. The findings underscore the critical need for enhanced diagnostic and treatment strategies for pediatric MDR-TB in India. The high rates of malnutrition and abnormal chest X-rays among affected children highlight the importance of comprehensive care approaches that address both the disease and associated comorbidities.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 08, 2024

Keywords: MDR-TB, children, clinical characteristics, demographic characteristics, South India, tertiary care center, malnutrition, chest X-ray abnormalities, BCG vaccination, tuberculosis contact.

Introduction

Background: MDR-TB is caused by Mycobacterium tuberculosis strains resistant to rifampicin and isoniazid.[1,2] Children with TB are often neglected, and the presence of MDR-TB in children indicates a high burden of the disease in adults. Factors influencing disease development include age, malnutrition, immune status, and exposure. [3,4]Only 3-4% of childhood MDR-TB cases are diagnosed globally, leading to higher mortality rates compared to drug- sensitive TB.[5,6]

MDR-TB, caused by Mycobacterium tuberculosis resistant to rifampicin and isoniazid, was first identified in 1956. TB spreads via droplets, and the BCG vaccine was developed in 1906. Drug-resistant strains complicate treatment and control efforts. Globally, 3.4% of new TB patients and 20% of previously treated patients have MDR-TB. Approximately 3% of pediatric TB cases are MDR-TB, with only 3-4% diagnosed annually. In India, children represent a significant portion of the TB burden, highlighting the need for targeted interventions.

Drug resistance arises from random mutations in large bacterial populations. Key genes involved include rpoB for rifampicin resistance and katG and inhA for isoniazid resistance. Improper treatment and transmission of resistant strains contribute to the spread. Children with MDR-TB are identified through exposure or symptoms like persistent cough, fever, and weight loss. Diagnosis involves history, examination, radiology, and microbiological tests. Universal Drug Sensitivity Testing (UDST) is crucial for accurate diagnosis.

MDR-TB regimens are longer, more toxic, and less adhered to than drug-susceptible TB treatment. They involve a combination of drugs from groups A and B, with close monitoring by pediatric specialists. Shorter or longer regimens are chosen based on the patient's response, ensuring comprehensive care.

Prevention focuses on vaccination, proper treatment adherence, and preventive therapy for those exposed to TB. The COVID-19 pandemic disrupted TB vaccination programs, increasing child mortality rates. Strengthening these programs is vital to control the spread of MDR-TB.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 08, 2024

Treatment for children with MDR-TB requires expert consultation. Bedaquiline and Delaminid are used based on age and weight considerations, with child-friendly formulations preferred. Regular monitoring and dosage adjustments are crucial for effective treatment outcomes.

Despite advancements, DR-TB remains a global health issue with high mortality and morbidity. Access to appropriate treatment is limited, and many patients do not receive the necessary second-line medications. The need for rapid drug susceptibility testing and comprehensive treatment plans is critical to managing and preventing DR-TB in children. Enhanced public health strategies and global cooperation are essential to address the MDR-TB crisis effectively.

This study aims to evaluate the clinical and demographic characteristics of MDR-TB in children at a tertiary care health center in South India.

Aims

1. To determine the prevalence of Multidrug-Resistant Tuberculosis (MDR-TB) in the pediatric population.
2. To evaluate the clinical and demographic characteristics of children diagnosed with MDR-TB.

Objectives

1. To analyze the demographic profile, including age, gender, and socio-economic status of children with MDR-TB.
2. To identify and document the clinical presentations, symptoms, and comorbid conditions associated with MDR-TB in the pediatric population.

Materials and Methods

Source of Data: Data was collected from the paediatric department of GGH Kurnool and the district tuberculosis center.

Sample Size: The study included 40 MDR-TB cases from September 2022 to August 2024, based on the prevalence of MDR-TB (0.6-23%).

Inclusion Criteria:

- Age >1 month to 18 years
- Diagnosed with MDR-TB
- Provided informed consent

Exclusion Criteria:

- Age <1 month or >18 years
- Did not provide informed consent

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 08, 2024

Study Type: This was a combined prospective and retrospective cross-sectional observational study.

Patients and their parents were informed about the study and provided written consent. Ethical clearance was obtained from the institutional ethical committee. Data were recorded in a structured proforma to determine the clinical and demographic profile and associated comorbid conditions of MDR-TB. Relevant investigations were conducted, and data were computerized and analyzed using statistical methods.

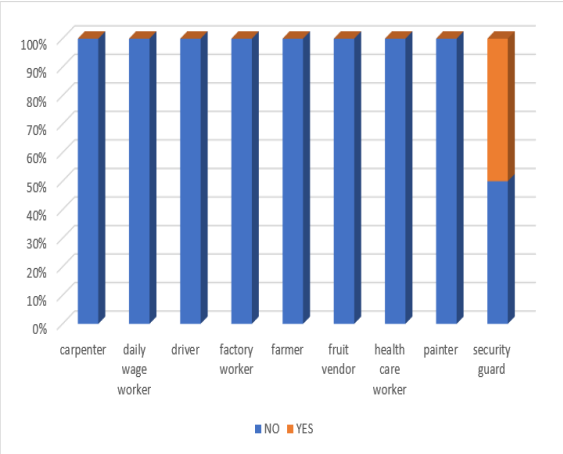
Descriptive statistics, contingency table analysis, and chi-square test were used for statistical analysis. A p-value < 0.05 was considered statistically significant. Analysis was performed using SPSS version 25.0.

Results :

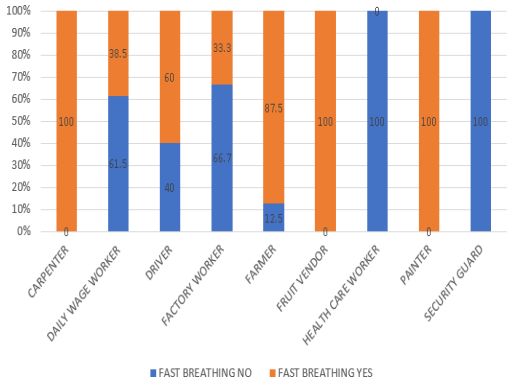
Demographic profile, including age, gender, and socio-economic status, of children with MDR-TB.				
Gender	**Female**	**male**	**Total**	
≤15 years	4(66.7%)	2(33.3%)	6(100.0%)	Chi-square=0.009, p=0.926
>15 years	22(64.7%)	12(35.3%)	34(100.0%)	
Fast breathing	No	Yes	Total	
≤15 years	5(83.3%)	1(16.7%)	6(100%)	Chi-square=4.191, p=0.041
>15 years	13(38.2%)	21(61.8%)	34(100%)	
Past TB treatment	**No**	**Yes**	**Total**	
≤15 years	3(50%)	3(50%)	6(100%)	Chi-square=5.164 p=0.023
>15 years	30(88.2%)	4(11.8%)	34(100%)	
HIV Status	**Negative**	**Positive**	**Total**	
≤15 years	5(83.3%)	1(16.7%)	6(100%)	Chi-square=5.812, p=0.016
>15 years	34(100%)	0	34(100%)	
CKD	**No**	**Yes**	**Total**	
≤15 years	4(66.7%)	2(33.3%)	6(100%)	Chi-square=11.930, p=0.001
>15 years	34(100%)	0(0%)	34(100%)	
Chest x ray	**Abnormal**	**Normal**	**Total**	
≤15 years	1(16.7%)	5(83.3%)	6(100%)	Chi-square=4.191, p=0.041
>15 years	21(61.8%)	13(38.2%)	34(100%)	
Anemia	**No**	**Yes**	**Total**	
≤15 years	1(16.7%)	5(83.3%)	6(100%)	Chi-square=0.049, p=0.825
>15 years	7(20.6%)	27(79.4%)	34(100%)	

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 08, 2024

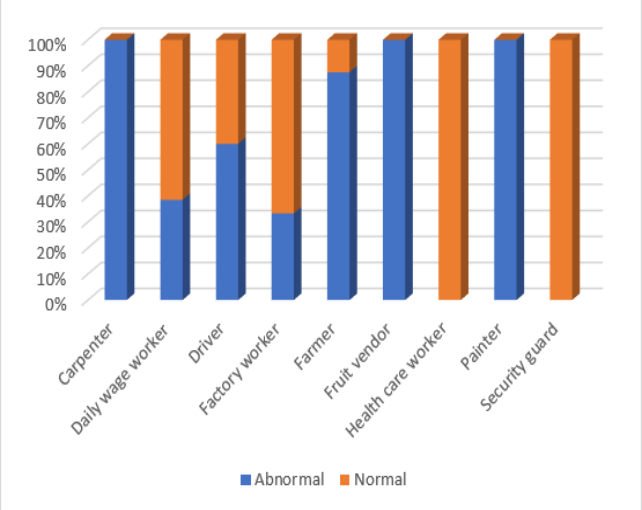
Malnutrition	**No**	**Yes**	**Total**	
≤15 years	2(33.3%)	4(66.7%)	6(100%)	Chi-square=0.475, p=0.491
>15 years	7(20.6%)	27(79.4%)	34(100%)	
BCG status	**No**	**Yes**	**Total**	
Extra pulmonary	3(60%)	17(48.6%)	20(50%)	Chi-square=0.229, p=0.633
Pulmonary	2(40%)	18(51.4%)	20(50%)	
Mantoux	**Negative**	**Positive**	**Total**	
Extra pulmonary	5(71.4%)	15(45.5%)	20(50%)	Chi-square=1.558, p=0.212
Pulmonary	2(28.6%)	18(54.5%)	20(50%)	



COMPARISON OF PARENT'S OCCUPATION WITH FAST BREATHING



COMPARISON OF PARENT'S OCCUPATION WITH SEIZURES



COMPARISON OF PARENT OCCUPATION WITH CHEST X RAY

Fast Breathing: In children ≤15 years, most did not have fast breathing (83.3%), while only 16.7% did. In children >15 years, more than half had fast breathing (61.8%), and

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 08, 2024

38.2% did not.

Past TB Treatment: For children ≤15 years, half had previously received TB treatment. In children >15 years, the majority had not received past TB treatment (88.2%).

HIV Status: All children ≤15 years with MDR-TB, except one (16.7%), were HIV negative. All children >15 years were HIV negative.

Chronic Kidney Disease (CKD): No children ≤15 years had CKD, but all children >15 years did not have CKD.

Chest X-ray Results: Most children ≤15 years had normal chest X-rays (83.3%), while only 16.7% had abnormal results. For children >15 years, 61.8% had abnormal chest X-rays, and 38.2% had normal results.

Anemia: Anemia was less common in children ≤15 years (16.7%) compared to children >15 years (79.4%).

Malnutrition: Similar to anemia, malnutrition was less common in children ≤15 years (66.7%) compared to children >15 years (79.4%).

BCG Status: The BCG vaccination status was similar in both extra pulmonary and pulmonary TB cases.

Mantoux Test: For children with extra pulmonary TB, the Mantoux test was positive in 45.5% and negative in 71.4%. For pulmonary TB, the Mantoux test was positive in 54.5% and negative in 28.6%.

Discussion:

Tuberculosis (TB) is an infectious disease primarily caused by a specific bacterium, infecting around 25% of the world's population. In 2022, an estimated 10.6 million people fell ill with TB worldwide, including 5.8 million men, 3.5 million women, and 1.3 million children. TB is curable and preventable, but multidrug-resistant TB (MDR-TB) remains a public health crisis and health security threat.[7]

In a study involving 40 MDR TB children, the prevalence of MDR TB was studied along with clinico-demographical profile and associated comorbid conditions in paediatric population. The study found that 10.92% of MDR TB cases were in the paediatric age group.

The study highlights regional disparities in the burden of drug-resistant TB among pediatric patients globally, including economic levels, less compliance for drugs, limited surveillance data, and lower detection rates in certain regions. Urgent interventions are needed, particularly in low-income and developing countries, to reduce the burden of

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 08, 2024

MDR TB.

The study found that a majority of participants were females, with a female to male ratio of 13:7. Females outnumbered males in some studies, possibly due to biological and behavioral differences in seeking healthcare. In a retrospective study carried out by Mazta et al.[8] where a ten-year data was analyzed outlining the demographic profile of childhood TB, a similar sex distribution was found, with 64.5% females and 35.5% males when including all forms of Tuberculosis. Socio-economic status distribution was similar, with around 50% belonging to the upper lower (UL), 27.5% to the lower middle (LM), and the remaining 22.5% to the lower
(L) class. This is similar to the research by Mauskar Vinayak Anupama [9]where more than 60% of patients belonged to upper lower and lower socioeconomic class as per Modified Kuppuswamy Classification.

The majority of patients with multidrug-resistant tuberculosis (MDR) TB know their BCG vaccination status, but 12.5% are not sure. BCG marks are present in only 2 patients with MDR TB, and the absence of a BCG mark is associated with disseminated disease in 46% cases. Routine BCG vaccination is recommended for children exposed continually to pulmonary TB caused by M. tuberculosis strains resistant to isoniazid and rifampicin. In the study by Shrestha et al[10]. BCG mark was seen in 86.6% patients. They found that absent BCG vaccination was significantly associated with disseminated TB.[11]

A history of contact with tuberculosis patients is also important, as most transmission occurs in households and children less than 3 years of age are at highest risk of progressing to disease following primary infection with M. tuberculosis. Active contact tracing and screening of high- risk household contacts can help diagnose diseased children earlier and lessen advanced disease. In a study by Vijayasekaran D et al[12], 85% of children having pulmonary cavitatory tuberculosis had definite history of contact with an adult with tuberculosis.

Loss of weight and nutritional status is another significant factor in MDR TB. A majority of 77.5% had loss of weight, while the remaining were normal in weight. Around 40% were undernourished, and undernutrition was associated with failure to culture-convert at 2 months and death. Children with culture proven MDR-tuberculosis tend to be young and malnourished, frequently HIV-infected, and often present with radiological features of advanced disease. The association between the grade of malnutrition and immediate outcome at discharge was statistically significant with severely malnourished

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 08, 2024

patients having the highest risk of dissemination in an article by Mauskar Vinayak Anupama and Gopan Amrit. Loss of weight was 58.3% in < 5 years, 77.8% in 5-10 years and 75% in >10 years of age in a research study by Shah Ira and Chilkar Sujeet.[13]

HIV status is also a concern, with around 2.5% of patients being HIV positive and 97.5% being negative. HIV coinfection and the presence of extrapulmonary tuberculosis predict death, and once MDR-tuberculosis is identified and treated appropriately with individualized therapy, children with the disease have a good prognosis, even in areas with a high prevalence of HIV coinfection.[14] About 10.3% were HIV co-infected in research by Shah Ira and Chilkar Sujeet. A study conducted in New York city by Gordin et al[15], they revealed that HIV and TB co-infected patients were significantly more likely to develop resistance to at least one drug (37% vs. 19%) and MDR (19% vs. 6%) than those without HIV infection.

The study analyzed ESR levels, chest X-rays, Mantoux tests, and AFB in childhood TB patients. Around 55% had ESR levels 40 and above, with raised ESR found in 90.2% of the study population. The differences in ESR levels among different studies reflect the interrelation among various factors, including differences in study populations, methodologies, disease characteristics, and contextual factors. Raised ESR was found in 90.2% of this study population in an article by Mauskar Vinayak Anupama and Gopan Amrit.

Chest radiography showed that 46% of children had severe chest radiographic changes at diagnosis, with malnutrition and severe chest radiographic changes associated with failure to culture-convert by month2, unsuccessful treatment outcome, and death. There was a high proportion with a positive smear, and nearly half had cavities, severe broncho-pneumonic changes, or miliary opacification on a chest radiograph. On chest radiology, consolidation was found in 22(53%), hilar lymphadenopathy in 16(39%), pleural effusion in 15, Miliary TB in 8, collapse in 4, cavity in 3 and pneumothorax in 2 patients in a research paper by Mauskar Vinayak Anupama and Gopan Amrit.[9]

The occurrence of positive Mantoux tests and multidrug-resistant tuberculosis (MDR-TB) in the pediatric age group seem to be interconnected. A positive Mantoux test indicates exposure to the TB bacterium but raises concern for latent TB infection, which can progress to active disease, especially in children with compromised immune systems. Around 61.8% had a positive Mantoux test in a paper by Shah Ira and

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 08, 2024

Chilkar Sujeet.[14]

Acid fast bacilli (AFB) were isolated in 14% of children in various fluid/histological specimens, and poor yield of AFB in tuberculosis in children may be due to paucibacillary nature of illness and inability of young children to give appropriate sputum samples. In the study by Panigatti et al[16], acid fast bacilli (AFB) were isolated in 13 (14 %) children in various fluid/histological specimens.

Almost 50% of TB cases were pulmonary, and 50% were extra-pulmonary. Malnourished children had more extra pulmonary tuberculosis and more disseminated TB. Controlling MDR- TB requires a holistic approach that considers both drug resistance and the various ways TB can present clinically. According to Shah Ira and Chilkar Sujeet[20] TB Lymphadenopathy was present in 16.7 %, TB Osteomyelitis in 8.3% and TB Meningitis in 8.3% in age group below 5 years.

It is important to understand the connection between different types of tuberculosis and multidrug-resistant tuberculosis in order to effectively manage patient care, use the right diagnostic methods, and create strategies to prevent the spread of drug-resistant strains. Controlling MDR-TB requires a holistic approach that considers both drug resistance and the various ways TB can present clinically.

Conclusion:

The prevalence of MDR TB in this study was 10.92%. The mean age of 40 MDR-TB cases was 16.63±2.13 years in this study. Median age was 17. The 13:7 female-to-male ratio in this study may be due to biological and behavioral variations in healthcare seeking. 50% of cases are upper-lower class and rural, largely daily wage workers from Kurnool. Common symptoms include fever (100%) and cough (100%) with quick breathing (55%), weight loss (77.5%), appetite loss (65%), vomiting, seizures, and altered sensorium (2.5%).

4) 87.5% know BCG vaccination status, 62.5% have cervical lymph nodes, 77.5% have no TB history, and 82.5% have never been treated for TB. 55% of cases had 40+ ESR, 40% had >40% lymphocyte count, 55% had abnormal chest x-ray, 82.5% had positive Mantoux test, 12.5% had positive AFB, 100% had positive CBNAAT, 50% had pulmonary and 50% extra pulmonary tuberculosis. The study found co-morbidities of anemia (80%), malnutrition (77.5%), HIV (2.5%), and CKD (5%).

REFERENCES

1. World Health Organization. Global Tuberculosis Report 2012. Geneva: WHO Press;

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 08, 2024

2012.

2. Falzon D, Gandhi N, Migliori GB, Sotgiu G, Cox HS, Holtz TH, Hollm-Delgado MG, Keshavjee S, DeRiemer K, Centis R, D'Ambrosio L. Resistance to fluoroquinolones and second-line injectable drugs: impact on multidrug-resistant TB outcomes. European Respiratory Journal. 2013 Jul 1;42(1):156-68.
3. Abubakar I, Zignol M, Falzon D, et al. Drug-resistant tuberculosis: time for visionary political leadership. Lancet Infect Dis 2013; 13: 529–539.
4. Newton SM, Brent AJ, Anderson S, Whittaker E, Kampmann B. Paediatric tuberculosis. Lancet Infect Dis. 2008 Aug;8(8):498-510.
5. Jenkins HE, Yuen CM: The burden of multidrug-resistant tuberculosis in children . Int J Tuberc Lung Dis. 2018, 22:3-6. 10.5588/ijtld.17.0357
6. Pecora F, Dal Canto G, Veronese P, Esposito S: Treatment of Multidrug-Resistant and extensively drugresistant tuberculosis in children: the role of bedaquiline and delamanid. Microorganisms. 2021, 9:1074. 10.3390/microorganisms9051074
7. Tuberculosis (who.int) last assessed on 22-03-2024.
8. Mazta, S.R., Kumar, A. and Kumar, P., 2012. Demographic profile of childhood TB cases under revised national tuberculosis control program in Himachal. *NTI bulletin*, *48*(1and4), pp.1-0.
9. Mauskar AV, Gopan A. Clinical Profile of pulmonary tuberculosis and MDR TB in children at Tertiary medical institute. Int J Contemp Pediatr 2019;6:2571-6.
10. Shrestha S, Marahatta SB, Poudyal P, Shrestha SM. Clinical Profile and Outcome of Childhood Tuberculosis at Dhulikhel Hospital. Journal of Nepal Paediatric Society. 2011 Jan 1;31(1).
11. The Role of BCG Vaccine in the Prevention and Control of Tuberculosis in the United States A Joint Statement by the Advisory Council for the Elimination of Tuberculosis and the Advisory Committee on Immunization Practices. MMWR Recomm Rep. 1996 Apr 26;45:1-8.
12. Vijayasekaran D, Selvakumar P, Balachandran A, Elizabeth J, Subramanyam L, Somu N. Pulmonary cavitatory tuberculosis in children. Indian pediatrics. 1994 Sep 1;31(9):1075-8.
13. Shah, Ira & Shetty, Naman & Goyal, Anmol & Patankar, Nikhil & Chilkar, Sujeet. (2020). Clinical profile of tuberculosis in children. Medical Journal of Dr. D.Y. Patil Vidyapeeth. 13. 10.4103/mjdrdypu.mjdrdypu_89_19.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 08, 2024

14. Shah I, Shah F. Changing prevalence and resistance patterns in children with drug-resistant tuberculosis in Mumbai. Paediatrics and international child health. 2017 Apr 3;37(2):135-8
15. Gordin FM, Nelson ET, Matts JP, Cohn DL, Ernst J, Benator DE, Besch CL, Crane LR, Sampson JH, Bragg PS, El-Sadr W. The impact of human immunodeficiency virus infection on drug-resistant tuberculosis. American journal of respiratory and critical care medicine. 1996 Nov;154(5):1478-83.
16. Panigatti P, Ratageri VH, Shivanand I, Madhu PK, Shepur TA. Profile and outcome of childhood tuberculosis treated with DOTS—an observational study. The Indian Journal of Pediatrics. 2014 Jan;81:9-14.