

CHARACTERISTICS OF PEDIATRIC TUBERCULOSIS PATIENTS HOSPITALIZED AT DR. SOEBANDI PUBLIC HOSPITAL JEMBER

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ABSTRACT

Tuberculosis (TB) remains a major public health problem globally. TB in children is an important component in TB control. The diagnosis of TB in children until now is still challenging, underdiagnosis often occurs in primary health facilities in Indonesia. This study aims to describe the demographic and clinical features of pediatric tuberculosis patients hospitalized in a tertiary care center. This study reviewed medical records of children with TB who were hospitalized in a referral hospital in Jember, East Java, Indonesia from January 2018 through December 2019. Among 96 patients, 33,3% happened in the age group of 15-18 years, 53.1% were females, 35,4% had severely underweight nutritional status, majority (84,4%) live in rural area, 79,2% without known TB contact history and 81.1% were new cases. Pulmonary TB was the most common diagnosis (80,2%). Only 4.1% had co-infection with Human Immunodeficiency Virus (HIV) and 4.2% were reported to be resistant to anti-TB drugs. The most common symptoms were fever (84.3%), cough (65.6%), and dyspnea (65.6%). The miliary lesion was the most common lesions on chest X-ray examination results. The successful therapy reached a percentage of 61.4% of all cases. The majority of pediatric TB patients were diagnosed clinically and chest X ray. Examination of HIV status and drug-sensitivity testing is low. The rate of successful therapy was still under WHO target.

Keywords: tuberculosis, children, characteristics

1. INTRODUCTION

Tuberculosis (TB) remains a major public health problem caused by *Mycobacterium tuberculosis* (MTB). Although this disease is preventable and curable, it is still one of the top ten causes of death with 10.0 million TB cases globally. Meanwhile, Indonesia sits on the third position out of the 30 countries that categorized as high-burden countries of TB, after India and China.¹ Tuberculosis in children is an important component in TB control because it represents the recent transmission of TB in communities.^{2,3} World Health Organization (WHO) estimated that in 2018, there were 1.1 million children in the world suffering from TB and 205,000 of

them died because of it, including children with HIV.⁴

Tuberculosis in children is often considered as a less serious problem since it is not the main source of TB transmission (due to paucibacillary nature) and the diagnostic difficulties. The exact epidemiological characteristics of TB in children are still unknown, 55% of pediatric TB cases were missed (under-reporting or under-diagnosis) in 2017.³ Therefore, the Indonesian Pediatric Society created a scoring system that can help to establish the diagnosis of TB in children. The criteria used in the scoring system are contact history with TB cases, Tuberculin Skin Test

(TST), nutritional status, fever, cough, lymph nodes enlargement, swelling of the bones or joints, and chest X-ray examination result. However, not all primary health care in Indonesia has facilities to do TST or chest X-ray, so underdiagnosis often occurred.⁵ The aim of this study is to describe the demographic and clinical characteristics of pediatric tuberculosis patients hospitalized in the endemic area.

2. METHOD

This retrospective study reviewed the medical records of children with TB hospitalized in dr. Soebandi Public Hospital from January 2018 to December 2019. The sampling method used a total sampling technique. There were 14 variables discussed in this study, the demographical and clinical data.

The demographical data included age, gender, body weight and height (nutritional status), and geographic location. The clinical data included the type of patients based on previous treatment history, contact history with TB cases, supporting examination for diagnosis, clinical manifestations, type of TB based on anatomic location of the disease, chest X-ray examination results, HIV status, treatment given, drug-sensitivity test results, and outcomes of treatment. Ethical clearance for this study was obtained from the Research and Ethics Committee of the Faculty of Medicine, Jember University (no. 1.393/H25.1.11/KE/2020).

The research was approved by dr. Soebandi Public Hospital proved by the existence of a research permit. The information obtained was made anonymous and identified before analysis to ensure confidentiality.

3. RESULT

The number of pediatric TB cases hospitalized at dr. Soebandi Public Hospital Jember in 2018-2019 were 96 children, 81.1% of them were new cases, and the most cases happened in the group of a teenager aged 15-18 years (33.3%). There were more female pediatric TB patients rather than males. Female pediatric TB patients were mostly diagnosed with pulmonary TB (58.8%) compared to males (53.3%). The majority of patients came from rural areas (84.4%).

The nutritional status of pediatric TB patients was mostly severely underweight. Only 20.8% of patients reported having a contact history with positive TB cases, and most of them were from family, especially mothers. Only 4.1% of pediatric TB patients were tested positive for HIV, meanwhile, 31.4% were screened but they showed negative results (Table 1).

The majority of clinical symptoms were fever (84.3%), cough (65.6%), and dyspnea (65.6%). Other clinical manifestations that occurred were following the location of organs that were infected. The symptoms such as unconsciousness, seizures, neck stiffness (+), nausea, and vomiting were the most common symptom in pediatric TB patients which were diagnosed with TB meningitis, while abdominal pain, nausea, and vomiting, often occurred in pediatric TB patients which were diagnosed with abdominal TB, peritoneal TB or both. Pulmonary TB was the most common diagnosis (80.2%), 56.3% of them were single diagnoses of pulmonary TB and the other 23.9% were pulmonary TB cases accompanied by abnormalities of extrapulmonary TB (Table. 2).

Table 1. Characteristics of Pediatric TB Patients Based on Demographical, Nutritional Status, Contact History, HIV Status and Treatment History

Variables	Frequency (n)	Percent (%)
Age (Years)		
0-4	21	21.9
5-9	15	15.6
10-14	28	29.2
15-18	32	33.3
Gender		
Male	45	46.9
Female	51	53.1
Geographical Location		
Rural area	81	84.4
Urban area	15	15.6
Nutritional Status		
Normal	32	33.3
Underweight	26	27.1
Severely underweight	34	35.4
Overweight	3	3.1
Unknown	1	1.1
Contact History		
Yes	20	20.8
No	76	79.2
HIV Status		
Positive	4	4.1
Negative	32	33.3
Untested	60	62.6
Treatment History		
New case	78	81.1
On therapy	8	8.3
Recurrent	5	5.3
Drop out	5	5.3

Tuberculin Skin Test (TST) was performed in 26 pediatric TB patients and was positive in 21 patients, while 5 other patients showed negative results. Acid-Fast Bacillus (AFB) smear examination was conducted on 11 pediatric patients, 8 of them were positive, while the other 3 showed negative results. Chest X-ray examination

was conducted on 77 pediatric TB patients, 64.9% of all cases were single lesions and the other 16.3% were multiple lesions. The single lesions that were most frequently detected were miliary lesion (16.9%) and in the multiple lesions group, the most common lesion was infiltrate + pleural effusion which were 4.2% of all cases.

Table 2. Clinical Features of Pediatric TB Patients

Clinical Features	Frequency (n)	Percent (%)
Signs and Symptoms		
Fever	81	84.3
Cough	63	65.6
Dyspnea	63	65.6
Weight loss	55	57.3
Anemia	56	58.3
Nausea	24	25.0
Loss of consciousness	21	21.8
Vomiting	23	23.9
Abdominal pain	18	18.7
Seizure	15	15.6
Headache	8	8.3
Night sweating	6	6.2
Neck stiffness	5	5.3
Weakness of limbs	4	4.1
Back pain	3	3.1
Odynophagia	2	2.1
Chest pain	2	2.1
Cervical lymphadenopathy	2	2.1
Lump on back area	2	2.1
Lump on suprapubic area	1	2.1
Swelling of joint	1	1.1
Site of TB Diseases		
Pulmonary	54	56.3
Pulmonary +extrapulmonary	19	19.8
Extrapulmonary	23	23.9

Other examinations were conducted in accordance with the clinical depiction experienced by patients and the results were summarized in Table 3.

Table 3. Diagnostic Test Conducted on Pediatric TB Patients

Diagnostic Test	Frequency (n)	Percent (%)
TST	26	27.1
Positive	21	21.8
Negative	5	5.3
AFB stain	11	11.4
Positive	8	8.3
Negative	3	3.1
Histopathology	4	4.1
Lumbar Puncture	6	6.2
Head CT	13	13.5
Abdominal CT	3	3.1
Abdominal USG	12	12.5
<i>Thoracocentesis</i>	3	3.1
<i>MRI</i>	2	2.1
Hemoglobin Levels		
Anemia	56	58.3
Normal	13	13.5
Unknown	27	28.2
Radiological Findings		
Single lesion	50	64.9
Miliary tuberculosis	13	16.9
Infiltrate	12	15.6
Pleural effusion	12	15.6
Consolidation	7	9.0
Pneumothorax	2	2.6
Normal	2	2.6
Pericardium effusion	1	1.3
Atelectasis	1	1.3
Multiple Lesions	13	16.9
Unknown	14	18.2

The majority of pediatric TB patients who completed their treatment received a four-drugs regimen for the intensive phase and two-drugs regimen therapy for the continuation phase (77.1%) (Table 4). A four-drugs regimen consists of Isoniazid (INH), Rifampicin (RIF), Pyrazinamide (PZA), and Ethambutol (EMB), while a two-drugs regimen is INH and RIF only. However, there was a difference in the duration of treatment. A drug-sensitivity test was performed in 10 pediatric TB patients, 3

patients were proven to have Multi-Drug Resistant Tuberculosis (MDR TB) and another patient was resistant to RIF (Rifampicin-Resistant Tuberculosis/RR TB). The final results of the treatment showed that successful therapy reached a percentage of 61.4% (13.5% were cured, 47.9% were completed their treatment). Another 38.6% of the other pediatric TB patients showed unsuccessful treatment results, 23.9% of them died and 14.5% were unknown.

Table 4. Treatment Given, Drug-sensitivity Test Results and Treatment Outcomes of Pediatric TB Patients

Treatment and Outcomes	Frequency (n)	Percent (%)
Treatment		
2 (INH-RIF-PZA-EMB) / 4 (INH-RIF)	60	62.5
2 (INH-RIF-PZA-EMB) / 10 (INH-RIF)	14	14.6
2 (INH-RIF-PZA) / 4 (INH-RIF)	21	21.8
INH-RIF-PZA-EMB-SM	1	1.1
Drug-sensitivity Test Results		
Test done	10	10.4
Not resistant	6	6.2
TB MDR	3	3.1
TB RR	1	1.1
Test not done	86	89.6
Treatment Outcomes		
Successful treatment	59	61.4
Cured	13	13.5
Treatment completed	46	47.9
Unsuccessful treatment	37	38.6
Died	23	23.9
Unknown	14	14.5

4. DISCUSSION

In this study, most cases happened in the group of teenagers aged 15-18 years old and the least cases happened in the group of children aged 5-9 years old. These results were similar to a previous study conducted in Australia which showed the most cases of TB in children happened in the 15-19 age group and the least ones happened in the 5-9 age group.²

There were more female pediatric TB patients rather than males. It was consistent with a study conducted in Pakistan and Ethiopia where there were more TB cases in females (52.8% and 55.4%).^{6,7} Previous study in Brazil mentioned that female children had nearly three times greater chance of developing pulmonary TB than boys.⁸

Research on more than 82,000 children in Puerto Rico, Ontario, and Alaska was found that compared to males, females had higher rates of developing TB disease during adolescence and early adulthood. Girls and early adulthood groups tend to be confined at home to do housework; thus, it could expose them to MTB bacteria if there were smear-positive cases in the household, but in general, there was no significant difference in sex distribution of pediatric TB cases.⁹

The majority of the TB patients in this study were from rural areas (84.4%), these results were similar to the previous study in Pakistan.⁶ People in rural areas might have lower knowledge about TB and worse health-seeking behavior than people in urban areas. Besides, low-economic conditions can also be a factor that caused many cases in rural areas. The nutritional status of pediatric TB patients was mostly severely underweight. A previous study in Pakistan also shows that 90% of all participants were underweight. Malnutrition is a predefined risk factor for TB in children. Poor

nutritional status can worsen the immune system that can facilitate the occurrence of infectious diseases including TB. TB infection can also cause depression in the immune system and create an inflammatory process that can worsen the nutritional status.⁶ The finding of TB-HIV co-infected patients in this research was very low (4.1%), considering that Jember was a region that sits on the third position with the highest number of HIV cases in East Java, Indonesia. Data on TB-HIV co-infection in children is felt to be very poor currently. TB in children is much more prevalent in developing countries due to poor socio-economic conditions, malnutrition, overcrowding, and HIV co-infection.⁷

The result of this study indicated that most patients were without known contact TB history. Tracing of contact history is very important to identify the source of transmission. A previous study in Pakistan also showed that the majority of sources of TB transmission in children came from parents, with a higher proportion from mothers than fathers. This was regarded as children were closer and spent more time with mothers compared to their fathers at home.¹⁰ The majority of hospitalized pediatric TB patients were new cases (81.1%). The high number of new TB patients indicated that the transmission rate was increasing. The result of this study was in line with the previous study in Congo that showed 97.5% of the total hospitalized TB patients were new cases.¹¹ A previous study in Ethiopia also showed new cases as a majority as much as 98.2%, while 39.8% were hospitalized due to additional conditions other than TB; namely, severe malnutrition and delayed diagnosis of TB.¹² TB in children usually manifested with similar signs and symptoms to acute pneumonia. Accordingly, it caused late diagnosis and prolonged the duration of hospitalization, even could increase mortality.¹³ If TB cases in adults continue to

increase yearly, then there is a probability of increasing TB cases among children.

The indication for hospitalization of pediatric TB patients is when the patient experiences shortness of breath; has decreased consciousness and has serious complications. The most common symptoms in pediatric TB patients were fever (84.3%), followed by cough (65.6%), and dyspnea (65.6%). This study showed that dyspnea has arisen in 65.6% of pediatric TB patients. The number was quite high even though dyspnea was not included in the TB scoring system that used to diagnose TB in children in Indonesia. A previous study in India showed that dyspnea arises in 46% of the total pediatric TB patients.¹⁴ The most common etiology of dyspnea in children is asthma, acute respiratory infections (ARI), such as pneumonia, bronchiolitis, effusion or empyema, pneumothorax, as well as the presence of foreign bodies in the respiratory tract.¹⁵ The many symptoms of dyspnea in this study were caused by the diseases accompanying TB, 31 pediatric TB patients were reported to have concomitant conditions, that is pneumonia, pleural effusion, asthma, and pneumothorax.

Pulmonary TB was the most common diagnosis, 56.3% was a single diagnosis of pulmonary TB and another 23.9% were cases of pulmonary TB accompanied by extrapulmonary TB. This is consistent with studies conducted in Turkey and Australia which showed pulmonary TB was the most cases with a percentage of 51.9% and 56.1%.^{2,16} The majority of pediatric TB patients in this study were diagnosed clinically and chest X ray. Although the gold standard for TB diagnosis was to find the germ causing TB, which was the MTB germ on culture examination, it was not performed on all patients due to the challenge in obtaining the sample. A study in China supported that it was less likely to confirm bacteriologically children due to the difficulty of sample collection,

paucibacillary nature, non-specific tests, and low sensitivity of those test.³ Children under the age of 15 represented more than 25% of the infected population, but they often released a small number of bacteria (paucibacillary disease), so it was difficult to be detected.¹⁷ Data related to TST and AFB stain examination were not known in some samples because the related data could not be found in the medical records. As a retrospective study, the data source of this study only comes from patient medical records, there is some incomplete information so that the necessary data cannot be obtained.

Treatment given to pediatric TB patients in this study was in accordance with the instructions of the Ministry of Health of the Republic of Indonesia. The patients who received a four-drugs regimen for 2 months (the intensive phase) and two-drugs regimen for 4 months after (the continuation phase) had diverse diagnoses, namely pulmonary TB, peritoneal TB, TB lymphadenitis, TB pleurisy, TB pericarditis, abdominal TB, and pulmonary TB which was accompanied by several previously mentioned diagnoses. While pediatric TB patients with miliary TB, TB meningitis, spondylitis TB, and pulmonary TB which accompanied by one of the previously mentioned diagnoses were treated with a four-drugs regimen for 2 months and two-drugs regimen for 10 following months, the continuation phase is longer. Resistance cases to TB drugs found in this study were low, 3 pediatric TB patients proven to have MDR TB were categorized as drop-out patients based on a history of TB treatment. The emergence of MDR TB cases or drug resistance is thought to be due to negligence or non-compliance of TB patients in taking the drugs as prescribed so that TB bacteria are resistant to the drug.¹⁸ Successful therapy in this study reached 61.4%. These results were consistent with research conducted in Ethiopia and Congo where successful

therapies existed 49%, 69.6%, respectively.^{7,11} The percentage of treatment success in this study was still lower than the standard set by the WHO which is 85%. Therefore, several efforts need to be done to improve TB treatment outcomes in children.

In this study, the patients who died were quite a lot. If the patients who died were associated with the patient diagnosis, 47,8% of the patients who died were caused by pulmonary TB cases with extrapulmonary abnormalities, with TB meningitis being the most common diagnosis. Meningeal TB was the most common diagnosis, both in the extrapulmonary TB group and as a disease accompanying pulmonary TB. TB meningitis was the most serious TB complication in children.¹⁶ Children aged under 5 years old were included in high-risk groups and more likely to experience severe diseases, such as miliary TB or meningeal TB.¹⁹ Children with the worse condition, usually have signs of meningeal irritation, cranial nerve paralysis, neurological deficits, sensory changes, and movement disorders. The majority of patients who came to dr. Soebandi Public Hospital were already at the worse stage because most of them came with decreased of consciousness.

5. CONCLUSION

In conclusion, the majority of hospitalized TB patients were diagnosed clinically and chest X ray. Examination of HIV status and drug-sensitivity testing is still very low. Successful therapy outcomes had a greater proportion but had not yet reached the target set by WHO. It is necessary to increase collaborative efforts between health sectors starting from primary health care facilities to referral hospitals to increase TB prevention and control in the community. The pediatric TB cases reported in this study only represent a small fraction of the total TB burden. In addition, further

prospective studies are needed to identify other potential sociodemographic, behavioral factors, and clinical features that could help establish the diagnosis of TB in children.

REFERENCES

- [1]. World Health Organization. Global Tuberculosis Report 2019. Geneva: World Health Organization; 2019.
- [2]. Al Yazidi LS, Marais BJ, Wickens M, Palasanthiran P, Isaacs D, Outhred A, et al. Overview of paediatric tuberculosis cases treated in the Sydney Children's Hospitals Network, Australia. *Public Heal Res Pract.* 2019;29:1–8.
- [3]. Tao NN, Li YF, Liu YX, Liu JY, Song WM, Liu Y, et al. Epidemiological characteristics of pulmonary tuberculosis among children in Shandong, China, 2005-2017. *BMC Infect Dis.* 2019;19:1–9.
- [4]. World Health Organization. Tuberculosis [Internet]. 2020. Available from: <https://www.who.int/news-room/fact-sheets/detail/tuberculosis>
- [5]. Nurwanti MA, Chrysanti, Sudarwati S. Application of Scoring System Components in Children Diagnosed with Tuberculosis in Jatinangor Primary Health Care, Sumedang. *Althea Med J.* 2017;4:495–500.
- [6]. Laghari M, Sulaiman SAS, Khan AH, Memon N. A prospective study of socio-demographic, clinical characteristics and treatment outcomes of children with tuberculosis in Sindh, Pakistan. *BMC Infect Dis.* 2019;19:1–11.
- [7]. Tilahun G, Gebre-Selassie S. Treatment outcomes of childhood tuberculosis in Addis Ababa: A five-year retrospective analysis. *BMC Public Health* [Internet]. 2016;16(1):1–10. Available from: <http://dx.doi.org/10.1186/s12889-016-3193-8>
- [8]. Sousa GJB, Silva JC de O, Queiroz TV de, Bravo LG, Brito GCB, Pereira A de S, et al. Clinical and epidemiological features of tuberculosis in children and adolescents. *Rev Bras Enferm.*

- 2019;72:1271–8.
- [9]. Seddon JA, Chiang SS, Esmail H, Coussens AK. The wonder years: What can primary school children teach us about immunity to mycobacterium tuberculosis? *Front Immunol.* 2018;9:1-20.
- [10]. Laghari M, Sulaiman SAS, Khan AH, Talpur BA, Bhatti Z, Memon N. Contact screening and risk factors for TB among the household contact of children with active TB: A way to find source case and new TB cases. *BMC Public Health.* 2019;19:1–10.
- [11]. Aketi L, Kashongwe Z, Kinsiona C, Fueza SB, Kokolomami J, Bolie G, et al. Childhood tuberculosis in a sub-saharan tertiary facility: Epidemiology and factors associated with treatment outcome. *PLoS One.* 2016;11:1–13.
- [12]. Ramos JM, Pérez-Butragueño M, Tesfamariam A, Reyes F, Tiziano G, Endirays J, et al. Comparing tuberculosis in children aged under 5 versus 5 to 14 years old in a rural hospital in southern Ethiopia: An 18-year retrospective cross-sectional study. *BMC Public Health.* 2019;19:1–9.
- [13]. Nantongo JM, Wobudeya E, Mupere E, Joloba M, Ssengooba W, Kisembo HN, et al. High incidence of pulmonary tuberculosis in children admitted with severe pneumonia in Uganda. *BMC Pediatr.* 2013;13:1-8.
- [14]. Gupta N, Kashyap B, Dewan P, Hyanki P, Singh NP. Clinical spectrum of pediatric tuberculosis: A microbiological correlation from a tertiary care center. *J Trop Pediatr.* 2019;65:130–8.
- [15]. Risteska-Nejashmij V, Stojkowska S, Stavrikj K. Dyspnea in children as a symptom of acute respiratory tract infections and antibiotic prescribing. *Open Access Maced J Med Sci.* 2018;6:578–81.
- [16]. Bayhan Gİ, Tanır G, Metin Ö, Şimsek H, Aydın-Teke T, Öz FN, et al. Pediatric tuberculosis in Turkey: A review of 8-years period in a tertiary care hospital. *Turk J Pediatr.* 2015;57:431–8.
- [17]. Unterweger M, Götzinger F, Bogyi M, Zacharasiewicz A, Mädel C, Tiringier K, et al. Childhood tuberculosis in Vienna between 2010 and 2016. *Wien Klin Wochenschr.* 2019;131:356–61.
- [18]. Baya B, Achenbach CJ, Kone B, Toloba Y, Dabita DK, Diarra B, et al. Clinical risk factors associated with multidrug-resistant tuberculosis (MDR-TB) in Mali. *Int J Infect Dis [Internet].* 2019;81:149–55. Available from: <https://doi.org/10.1016/j.ijid.2019.02.004>
- [19]. Huynh J, Marais BJ. Multidrug-resistant tuberculosis infection and disease in children: a review of new and repurposed drugs. *SAGE journals [Internet].* 2019;6(Therapeutic Advances in Infectious Disease):1–16. Available from: journals.sagepub.com/home/tai%0D .