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Case overview of children's thalassemia at RSAB Harapan Kita Jakarta

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ABSTRACT. Thalassemia is a hereditary blood disorder characterized by reduced alpha or beta globin chain synthesis, independent of sex or age. While thalassemia minor often presents with mild or no symptoms, thalassemia major manifests with severe anemia, pallor, fatigue, decreased appetite, and recurrent infections from birth. The aim of this research is to describe the description of cases of thalassemia children at RSAB Harapan Kita. This research is a descriptive study with a cross-sectional design regarding the description of cases of thalassemia children. Study participants were pediatric patients diagnosed with thalassemia at the hospital. Inclusion criteria encompassed individuals younger than 19 years with a documented history of comorbidities. Exclusion criteria included patients with incomplete or damaged medical records and those aged 19 years or older. Medical record data that met the inclusion criteria was 48 subjects with a minimum sample size of 41 subjects. The data used in this research was processed with SPSS ver. 25 and presented in table form. The results showed that the highest proportion of thalassemia children was in the age group 6-11 years (41.7%), male sex (56.3%), the main complaint was pallor (87.5%), type of β thalassemia (83, 3%), pre-transfusion Hb level <9 g/dL (79.2%), and without other comorbidities (64.6%).

Keywords: blood disorders; comorbidities; pre-transfusion hemoglobin level; thalassemia children, type of thalassemia

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INTRODUCTION

Thalassemia syndrome is the most common hereditary hemolytic anemia worldwide, including Indonesia. This inherited disorder is still very rarely addressed. Since 2013 until now, the Thalassemia International Federation (TIF) has issued new standard clinical practice guidelines for non-transfusion-dependent thalassemia and transfusion-dependent thalassemia (Farmakis *et al*., 2022). Based on these guidelines, several measures should be routinely performed, such as iron overload monitoring and surveillance of thalassemia-related complications to detect such complications for early clinical management (Cappellini *et al*., 2021; Ekwattanakit *et al*., 2021).

Thalassemia is a hematological disorder resulting from genetic defects in hemoglobin, the oxygen-carrying protein within erythrocytes, leading to impaired red blood cell production (Origa, 2017; Tari *et al*., 2018; Shafique *et al*., 2021). In normal humans, red blood cells can live up to 120 days, while red blood cells in thalassemia sufferers are easily damaged and have the short lifespan, namely less than 120 days, causes thalassemia sufferers to experience anemia with symptoms of pale face, weakness, dizziness and reduced appetite (de Back *et al*., 2014; Van Zwieten *et al*., 2014; Ghosh *et al*., 2023). The anemia experienced and blood transfusions performed on thalassemia sufferers aim to maintain hemoglobin levels because in thalassemia sufferers there is a decrease in production (Lal *et al*., 2018; Wanchaitanawong *et al*., 2021). Thalassemia is classified into two primary genotypes, α-thalassemia and β-thalassemia, based on molecular determinants, while clinically, the disease spectrum encompasses three primary phenotypes: thalassemia minor, intermedia, and major (Viprakasit & Ekwattanakit, 2018; Zhong *et al*., 2023). Furthermore, from a therapeutic perspective, thalassemia can be categorized as either non-transfusion dependent (NTDT) or transfusion dependent (TDT) (Cappellini *et al*., 2021). Patients with thalassemia major require frequent blood transfusions

to sustain life, which can lead to iron overload, causing organ damage and potentially fatal complications if left unmanaged (Mohamed, 2017; Taher & Saliba, 2017; Pinto & Forni, 2020).

It is estimated that every year there are around 300000 to 500000 babies born with hemoglobin disorders and about 40% of all children aged 6–59 months are affected by anaemia, including thalassaemia (WHO, 2023). Indonesia is a developing nation with an upper-middle-income status, ranking fourth globally in terms of population and tenth in terms of gross domestic product adjusted for purchasing power parity (Work Bank, 2023). Despite being categorized as an upper-middle-income nation, Indonesia exhibits disparities in healthcare access, with a disproportionate allocation of resources towards urban centers. Consequently, rural areas often grapple with substandard primary healthcare facilities, hindering the timely diagnosis and management of diseases like hemoglobinopathies. Indonesia has around 5-10% carriers of the beta thalassemia gene, 1-33% carriers of the Hb E gene, and 6-16% carriers of the alpha thalassemia gene (Kemkes, 2022a). Thalassemia cases increase every year, in 2018 with a total of 8761 cases, and 2019 with a total of around 10500 cases, and 10973 cases in 2021 (Kemkes, 2022b). Conversely, the prevalence of thalassemia in eastern Indonesia is notably lower. This disparity may be attributed to the limited accessibility of quality healthcare services in the region. Consequently, a significant proportion of thalassemia cases remain undiagnosed and underreported.

Given the escalating incidence of thalassemia in Indonesia, a comprehensive investigation of pediatric thalassemia cases at a national hospital is warranted. This study aims to describe the description of cases of thalassemia children at RSAB Harapan Kita, a specialized maternal and child healthcare facility situated in West Jakarta, prioritizes the treatment of congenital and hereditary disorders, including thalassemia. The hospital's established infrastructure for thalassemia management suggests its suitability for collecting robust data to accurately characterize the national prevalence of this condition.

MATERIALS AND METHODS

This cross-sectional descriptive study utilized secondary medical records from RSAB Harapan Kita collected between November and December 2022. The research subjects were children with thalassemia at the hospital with inclusion criteria being patients with thalassemia aged <19 years and having a history of comorbidities or other comorbidities while the exclusion criteria were patient data with damaged or incomplete medical records and patients with thalassemia aged ≥19 years old. Medical record data that met the inclusion criteria was 48 subjects with a minimum sample size of 41 subjects.

The research conducted has passed ethical clearance with No. SLKE: 1344/SLKE-IM/UKKW/FKIK/KE/IX/2022 issued by the Medical and Health Research Ethics Committee, Faculty of Medicine and Health Sciences, Universitas Kristen Krida Wacana.

Data analysis. Data were processed using the SPSS ver. 25 by collecting secondary data from medical records in sociodemographic (age and gender), type of thalassemia, main complaints, pre-transfusion Hb levels and comorbidities. The data were processed descriptively and the results of the analysis were presented in tabular form.

RESULTS AND DISCUSSION

Medical record data was collected in the form of age, gender, main complaint, type of thalassemia, pre-transfusion Hb level, and comorbidities. In Table 1, the highest proportion of children suffering from thalassemia based on age category is 6-11 years, amounting to 20 children (41.7%), followed by 12-18 years, 15 children (31.3%), and the lowest in the 0-5 years age category, amounting to 13 children (27.1%). The highest proportion of children suffering from thalassemia based on gender category were males, amounting to 27 children (56.3%) while females amounted to 21 children (43.7%). The highest proportion of children suffering from thalassemia based on the main complaint category was pallor, 42 children (87.5%), followed by appetite disorders, 5 children

(10.4%), and the lowest was an enlarged stomach, 1 child (2.1%). The highest proportion of children suffering from thalassemia based on thalassemia type category was β thalassemia with 40 children (83.3%) while α thalassemia with 8 children (16.7%). The majority of children with thalassemia had pre-transfusion hemoglobin levels <9 g/dL, amounting to 38 children (79.2%) while with pre-transfusion hemoglobin levels ≥9 g/dL there were 10 children (20.8%) with an average of 7.167 g/dL. The proportion of children suffering from thalassemia without comorbidities was 31 children (64.6%) and those with comorbidities in the form of hepatosplenomegaly were 16 children (33.3%) and heart disease was 1 person (2.1%).

Table 1. Characteristics of children with thalassemia at RSAB Harapan Kita Jakarta

Variable	n = 48	Percentage (%)
Age category (year)		
0-5	13	27.1
6-11	20	41.7
12-18	15	31.3
Total	48	100
Mean	9.69	
Median	9	
Minimum	3	
Maximum	17	
Gender		
Male	27	56.2
Female	21	43.8
Total	48	100
Main complaint		
Appetite disorder	5	10.4
Growing belly	1	2.1
Pallor	42	87.5
Total	48	100
Type of thalassemia		
Alpha	8	16.7
Beta	40	83.3
Total	48	100
Pre-transfusion Hb level		
≥9 g/dL	10	20.8
<9 g/ dL	38	79.2
Total	48	100
Mean	7.167	
Median	6.9	
Minimum	3.6	
Maximum	13.4	
Comorbidities		
Hepatosplenomegaly	16	33.3
Heart failure	1	2.1
No	31	64.6
Total	48	100

Thalassemia is an autosomal recessive blood disorder equally affecting both sexes, resulting in an equivalent probability of transmitting the disease to offspring (Laghari *et al*., 2018; Huang *et al*., 2020; Ali *et al*., 2021). In contrast to the findings of Putri *et al*. (2015), which reported a higher prevalence of thalassemia among female participants (n=9, 60%) compared to males (n=6, 40%) from a sample of 15 individuals, the present study did not observe a similar gender distribution among affected patients. However, the findings of this study align with those of Sawitri & Husna (2018),

who reported a relatively equal distribution of thalassemia among 50 participants, with 27 males (54%) and 23 females (46%).

Thalassemia can manifest as early as birth or within the first two years of life, affecting both α and β thalassemia subtypes with varying degrees of severity, ranging from minor to major (Malakar *et al*., 2016; Unissa *et al*., 2018; Wahidiyat *et al*., 2022). Thalassemia minor typically presents with no discernible clinical manifestations throughout life, while thalassemia intermedia is often diagnosed in early childhood or even adulthood with less severe symptoms compared to thalassemia major, obviating the need for regular blood transfusions. In contrast, thalassemia major manifests with pronounced clinical features as early as 3-6 months of age, necessitating lifelong blood transfusions. Our findings indicate that the middle childhood age group (6-11 years) is particularly susceptible to the impact of thalassemia compared to other age cohorts. While thalassemia is not age-specific, the heightened surveillance of school-aged children by parents and educators may facilitate earlier detection of health anomalies, including those associated with thalassemia. Nonetheless, it is crucial to acknowledge the heterogeneous presentation of thalassemia in terms of severity, genetic predisposition, and disease course. The findings of our study corroborate the results of Safitri *et al*. (2015), which identified a predominance of thalassemia cases among children aged 6-11 years at Arifin Achmad hospital, Pekanbaru, with a frequency of 25 cases (44.6%).

Our findings indicate that pallor constitutes the predominant clinical manifestation among children with thalassemia treated at RSAB Harapan Kita Jakarta, accounting for approximately seven eighths of reported symptoms. This aligns with the established understanding that thalassemia primarily presents with pallor due to the condition's impact on hemoglobin production and function (Trehan *et al*., 2015; Prathyusha *et al*., 2019; Singh *et al*., 2019). The diminished levels and impaired functionality of hemoglobin, a crucial oxygen-carrying component of red blood cells, result in reduced oxygen delivery to tissues, consequently manifesting as pallor (Allali *et al*., 2017; Helms *et al*., 2018). The underlying mechanisms contributing to hemoglobin dysfunction include iron deficiency, an essential component for oxygen binding, and structural abnormalities within the hemoglobin molecule, encompassing alterations in synthesis rate and amino acid sequence (Gallagher, 2013; Thom *et al*., 2013; Coates, 2014; Auerbach & Adamson, 2016). These results are in line with the findings of Fatmasyithah & Rahayu (2014), who reported pallor as the most main complaint in 80% of pediatric thalassemia cases within North Aceh general hospital.

Beta thalassemia exhibited a significantly higher prevalence among children compared to alpha thalassemia, constituting approximately 83.3% of cases. According to Wahidiyat *et al*. (2022), an estimated 2500 infants in Indonesia are born with β-thalassemia major annually. The elevated incidence of beta thalassemia in Indonesia is attributable to a complex interplay of genetic and environmental factors. Widyastiti *et al*. (2023) highlight the role of inherited globin gene mutations in increasing susceptibility to the disorder. Furthermore, the persistence of consanguineous marriages within Indonesian culture represents a substantial risk factor for beta thalassemia transmission (Wahidiyat *et al*., 2021; Susanah *et al*., 2022).

Pediatric patients exhibiting pre-transfusion hemoglobin levels below 9 g/dL constituted the predominant demographic within our study cohort. Individuals with β-thalassemia, particularly those with β-thalassemia major, characteristically present with pre-transfusion hemoglobin levels below this threshold, resulting in anemia secondary to hemoglobin degradation (Maempel *et al*., 2016; Sardar *et al*., 2018). Lifelong blood transfusions are necessitated to manage this chronic condition. Conversely, patients with α-thalassemia major typically exhibit fatal outcomes in the neonatal period, while those with α-thalassemia minor remain clinically asymptomatic. The mean pre-transfusion hemoglobin (Hb) level among thalassemia patients at RSAB Harapan Kita was determined to be 7.167 g/dL, classifying these individuals within the severe anemia category (grade 3) as defined by a hemoglobin range of 6.5-7.9 g/dL. These findings align with the WHO's criteria for anemia in thalassemia patients, which stipulates a pre-transfusion Hb level below 8 g/dL. The preponderance of thalassemia patients managed at RSAB Harapan Kita Jakarta, exhibited a severe disease course as

evidenced by pre-transfusion hemoglobin levels. These findings underscore the imperative for comprehensive education and preventative measures targeting parents of children with thalassemia to mitigate disease progression and associated complications. As a specialized national referral center for maternal and child health, RSAB Harapan Kita Jakarta primarily admits patients with advanced disease states requiring intensive care. Consequently, patients presenting with mild to moderate thalassemia symptoms are typically managed at lower-tier healthcare facilities (type B and C hospitals) at the provincial and district levels. This referral system influenced the sample size of the present study.

Regular blood transfusions have been instrumental in extending the lives of individuals with thalassemia (Shah *et al*., 2019; Tarım & Öz, 2022). However, the management of associated complications has emerged as a significant challenge. Comorbidities arising from chronic anemia or iron overload, a consequence of frequent transfusions, can manifest as cardiac failure, hepatosplenomegaly, endocrine dysfunction, growth retardation, and skeletal abnormalities, with subsequent impacts on physical and mental well-being (Saliba *et al*., 2020; Mattia *et al*., 2021). Hepatosplenomegaly, indicative of hemolytic anemia and exacerbated by iron accumulation, and cardiac failure, the leading cause of mortality in thalassemia, resulting from severe anemia or iron-induced cardiomyopathy, were identified as prevalent comorbidities in our study, albeit with low frequency relative to the patient population without comorbidities. Children with thalassemia devoid of comorbidities exhibit superior treatment responsiveness, improved long-term prognosis, and a reduced risk of severe complications, thereby fostering a greater likelihood of a healthy and productive life. In addition to medical interventions, comprehensive family and environmental support is essential for thalassemia patients. Emotional and social encouragement can significantly ameliorate the challenges associated with the condition and enhance overall quality of life.

CONCLUSION

Our study cohort comprised 48 children with thalassemia from RSAB Harapan Kita, predominantly aged 6-11 years (41.7%) and male (56.3%). Pallor was the primary presenting symptom in 87.5% of cases. Beta thalassemia was the predominant thalassemia type (83.3%), with a mean pre-transfusion hemoglobin level below 9 g/dL in 79.2% of patients. Notably, 64.6% of the cohort did not exhibit comorbid conditions.

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