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Differences in Hemoglobin Levels in Patients with Thalassemia Major and Minor at Sultan Agung Semarang Islamic Hospital

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Abstract

Background: One of the genetic diseases that is usually detected in children is thalassemia. World Health Organization (WHO) states that thalassemia is the most common hereditary disease in the world and has been recognized as a world health problem. Indonesia is one of the countries in the world's thalassemia belt. Thalassemia major is the most severe clinical condition of thalassemia. Thalassemia minor can also be called a carrier trait and does not show clinical symptoms. Supporting examinations can be carried out with simple laboratory tests, one of which is measuring hemoglobin levels. The aim of this study was to determine the differences in hemoglobin levels in patients with thalassemia major and thalassemia minor at RSI Sultan Agung Semarang. **Method:** The type of research used was cross sectional, with a sample size of 48 people. Hemoglobin level data was obtained from the medical records of Sultan Agung Semarang Islamic hospital. The data distribution is normal, so the difference test is tested using the independent t-test. **Result:** The average hemoglobin levels in patients with thalassemia major and thalassemia minor are 5.7 mg/dL and 10.6 mg/dL. The independent t-test shows a significance value of 0.00 (<0.05). **Conclusion:** There are differences in hemoglobin levels in thalassemia major and thalassemia minor patients at Sultan Agung Semarang islamic hospital, although hemoglobin levels in both thalassemia major and minor patients are still below the reference value.

Keywords: hemoglobin, thalassemia mayor, thalassemia minor

INTRODUCTION

Thalassemia is a genetic disease characterized by blood disorders caused by impaired hemoglobin synthesis, especially in the globin chain. If globin chain synthesis decreases, it will cause anemia and microcytosis. Thalassemia is inherited in an autosomal recessive manner according to Mendel's law from the sufferer's parents. The clinical manifestations vary from asymptomatic to severe symptoms. Clinically, thalassemia is divided into three types, namely thalassemia major, thalassemia intermedia, and thalassemia minor [1].

One of the genetic diseases that is usually detected in children is thalassemia. *World Health Organization* (WHO) states that thalassemia is the most common hereditary disease in the world and has been recognized as a world health problem. Indonesia is one of the countries in the world's thalassemia belt, namely a country with a high frequency of thalassemia carriers. This is proven by epidemiological research in Indonesia which shows that the frequency of the beta thalassemia gene ranges from 3-10%. The number of thalassemia sufferers in Indonesia increased from 2012 to 2018, namely 9028 people and it is estimated that more than 2500 newborns suffer from thalassemia major. The number of thalassemia sufferers in Central Java and DIY is 920 [2,3]. Based on the results of a

survey at RSI Sultan Agung Semarang, data on thalassemia patients was obtained, namely 8.1% for toddlers aged 0-5 years, 35.1% for children aged 6-11 years, and 45.9% for early adolescents aged 12-16 years.

Thalassemia major is the most severe clinical condition of thalassemia. The condition thalassemia major occurs because the gene encoding hemoglobin on two chromosome alleles is abnormal. Patients with thalassemia major generally have low hemoglobin levels, MCV values <80 fL, MCH <27 pg, high reticulocyte counts (>14.6), high RDW counts (mean 26.8), and have nucleated blood cells. Meanwhile, thalassemia minor can also be called a trait carrier, mutant carrier, traits, or thalassemia carrier. Thalassemia carriers do not show clinical symptoms during their lifetime. This is because the gene abnormalities that occur only involve one of the two chromosomes [4,5].

The diagnosis of thalassemia major and thalassemia minor can be done in several ways, namely history taking, physical examination and supporting examinations. Supporting examinations can be carried out with simple laboratory tests, one of which is measuring hemoglobin levels. Hemoglobin is a protein rich in iron, its main function is to carry oxygen from the heart to the rest of the body. Hemoglobin in thalassemia patients experiences disorders in the globin chain. This is characterized by damage to the erythrocyte cells in the blood vessels. So the lifespan of erythrocytes is less than 100 days [6,7].

The hemoglobin levels of thalassemia patients can vary depending on the type and severity of the thalassemia they suffer from. Thalassemia major sufferers have a high level of severity. Their hemoglobin levels are usually very low, often below 7 g/dl or even lower. Thalassemia major patients require regular blood transfusions to replace damaged red blood cells and increase hemoglobin levels [8]. Meanwhile, people with thalassemia minor have one normal gene and one gene that is affected by thalassemia. The hemoglobin levels of thalassemia minor sufferers are higher than those of thalassemia major sufferers and may be within the normal range or only slightly low. Thalassemia minor patients may not require blood transfusions, and hemoglobin levels may be sufficient to support normal body needs [9].

RSI Sultan Agung Semarang is a type B hospital which is a reference for thalassemia treatment in Semarang. Data obtained from RSI Sultan Agung Semarang (2023) in the pediatric specialist and internal medicine specialist treatment rooms totaled 55 patients diagnosed with thalassemia in the age range 1-40 years consisting of 7 people aged 1-5 years (toddlers), 24 people aged 6-12 years (children), 19 people aged 12-22 years (early teenagers-late teenagers), and 5 people aged 23-40 years (adults). Data obtained from medical records in June 2024 showed that the average hemoglobin level before transfusion was below 8 g/dL, complaints of weakness and the patient looked pale, but usually if the patient's hemoglobin level was above 8 g/dL, they usually did not undergo a transfusion. Based on the description above, researchers are interested in conducting research on differences in hemoglobin levels in thalassemia major and thalassemia minor patients at RSI Sultan Agung Semarang.

METHOD

The type of research used is analytical observational. The research was carried out at RSI Sultan Agung Semarang in June 2024 with the number of samples based on the Slovin formula being 34 samples of thalassemia major and minor sufferers. The tools and materials used in this research were a digital camera, stationery, laptop and medical record archives at RSI Sultan Agung Semarang. The research began by determining the data source from the medical records installation of RSI Sultan Agung Semarang, then collecting the data that was already available in document form. Next, the data was tested for normality with the Shapiro Wilk test and tested for differences with the independent sample t-test, then presented the data in tabular form. This research has been approved by the ethics committee of RSI Sultan Agung Semarang with No.112/KEPK-RSISA/V/2024.

RESULTS AND DISCUSSION

Based on the results of research conducted on 34 samples regarding differences in hemoglobin levels in patients with thalassemia major and thalassemia minor, the following results were obtained.

Table 1. Average Hemoglobin Levels in Thalassemia Major and Thalassemia Minor Patients

Hemoglobin levels (mg/dL)	N	Minimum	Maximum	Mean ± SD
Thalassemia Mayor	17	4,1	6.8	5,7±0,8
Thalassemia Minor	17	8,1	11,8	10,6±1,0

Based on table 4, it shows that of the 34 samples studied, the hemoglobin levels of thalassemia major patients were lower than those of thalassemia minor patients. The normality of the data was tested using the Shapiro-Wilk test. If the significance value is >0.05, then the research data is normally distributed. Differences in hemoglobin levels in thalassemia major and minor patients were tested using the independent sample t-test.

Table 2. Results of the Shapiro Wilk normality test and independent sample t-test

Hemoglobin levels	N	Saphiro Wilk test	Independent sample t-test
Thalassemia Major Patients	17	0,096	0,000
Thalassemia Minor Patients	17	0,104	

From the results of the unpaired t test, it can be seen that the significance value is 0.000, which indicates that there is a significant difference between the hemoglobin levels of patients with thalassemia major and thalassemia minor. Based on the results of data collection on hemoglobin levels for 17 thalassemia major patients and 17 thalassemia minor patients, it was found that the

hemoglobin levels of thalassemia minor patients were higher than the hemoglobin levels of thalassemia major patients, namely 11.8 mg/dL. Thalassemia major and thalassemia minor are caused by genetic mutations that affect the production of globin chains which are important components of hemoglobin. Although both affect hemoglobin, the mechanisms causing abnormalities in hemoglobin levels differ between the two in terms of severity and impact [10].

Hemoglobin levels in thalassemia major sufferers are lower due to mutations in the beta globin gene (HBB) which causes the production of beta globin chains to be greatly reduced or absent altogether. This causes an imbalance in hemoglobin production, so that most of the hemoglobin produced does not function properly [11]. An imbalance in the beta globin chain causes an excess of alpha chains that cannot pair with the beta chains to form normal hemoglobin. These excess alpha chains tend to deposit inside developing red blood cells, causing aggregation and damage to these cells. Ineffective erythropoiesis is often unstable and easily damaged, causing hemolysis [12,13]. The combination of hemolysis and erythropoiesis causes chronic anemia with very low hemoglobin levels (often below 7 g/dL without transfusion). As a result, thalassemia major patients require regular blood transfusions to increase hemoglobin levels and relieve anemia symptoms [14].

This is different in patients with thalassemia minor, where the globin gene mutation only occurs in one allele of the HBB gene so that the production of globin chains is slightly reduced. The red blood cells produced tend to be smaller (microcytic) and have low hemoglobin levels (hypochromic). In contrast to thalassemia major, hemolysis and ineffective erythropoiesis are not significant. The body can usually compensate for slightly impaired hemoglobin production by increasing red blood cell production. However, these red blood cells remain imperfect and have a slightly reduced oxygen carrying capacity. So individuals with thalassemia minor have hemoglobin levels that are slightly lower than normal, but usually still within the range that does not cause serious symptoms [15].

Based on research conducted by [16] it was found that the average hemoglobin level in β-thalassemia major was mostly 7 g/dL which required routine blood transfusions and the hemoglobin level in β-thalassemia minor was more than 10 g/dL and did not require routine blood transfusions. Low hemoglobin levels are caused by hemoglobin abnormalities due to the inability of the bone marrow to form the protein needed to produce hemoglobin which causes damage to red blood cells so that sufferers experience anemia or anemia and are advised to have a transfusion. The child's hemoglobin level before the transfusion influences the accuracy of the transfusion. Based on statistical tests using the independent sample t-test different test method, a statistically significant difference was obtained with a significance value of 0.000, indicating that there was a significant difference between the hemoglobin levels of patients with thalassemia major and thalassemia minor because the significance of the independent sample t-test was <0.05.

CONCLUSION

Hemoglobin levels in thalassemia major patients were significantly different from hemoglobin levels in thalassemia minor patients at RSI Sultan Agung Semarang. The hemoglobin level of thalassemia minor patients is higher than that of thalassemia minor although it is still below the

reference value. For people, especially those who have a family history of thalassemia sufferers, they should carry out genetic counseling before marriage to prevent intermarriage carrier.

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