# Assessing the Difference in Time to Increase Hemoglobin Levels at 1 hour, 6 hours, and 12 hours after Blood Transfusion in Thalassemia Patients at the Regional General Hospital Dr. Zainoel Abidin Banda Aceh

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**Abstract:** *Thalassemia is a congenital blood disorder characterized by reduced production of one or more globin chains. Thalassemia patients lack healthy hemoglobin which the body needs to be properly oxygenated. Blood transfusion is the main treatment for thalassemia patients. Checking hemoglobin levels after transfusion is a common test, but until now there is no definite uniformity of time to carry out these tests, so it will be detrimental to the patient and increase the length of the patient in the hospital. Assessing the difference in time to increase in hemoglobin levels at 1 hour, 6 hours, and 12 hours after blood transfusion in thalassemia patients. This research is an observational analytic study with cross sectional design. This study was conducted by examining the hemoglobin levels of thalassemia patients after 1 hour, 6 hours, and 12 hours after transfusion in thalassemia patients aged 1-18 years with a total sample of 40 people. The statistical analysis used was paired t test. The results showed that 20 men and 20 women and Most were in the age group 10-13 (35%), with an average Hb level at admission of 7.38 g / dL (95% CI). At 1 hour post-transfusion, the patient's mean Hb level increased by 8.97 g / dL (8,59-9,35 g / dL), at 6 hours post transfusion, 8.95 g / dL (8,57-9,32 g / dL), at 12 hours post transfusion increased by 9.60 g / dL (9,17-10,03 g / dL). Significant increase in Hb levels occurred at 1 hour and 12 hours after blood transfusion.*

**Keywords:** *thalassemia; hemoglobin level; post transfusion; time of examination*

## I. Introduction

Thalassemia is a congenital blood disorder characterized by reduced production of one or more globin chains. Hemoglobin (Hb) consists of alpha and beta chains, in patients with thalassemia an error in Hb is generated. In patients with thalassemia there is a deficiency of healthy Hb which the body needs to become well oxygenated. (Elizalde, JL. 1997; Wahidiyat, PA. 2018; Hamizah, L. 2017). Thalassemia is the single most common gene disorder found. This disease was first discovered by Thomas B. Cooley in 1925 in a number of children with symptoms of anemia and an enlarged spleen after 1 year.2 The prevalence of thalassemia carrier in Indonesia is around 3% -8%. If the percentage of thalassemia reaches 5%, with a birth rate of 23 per 1,000 of the 240 million populations, it is estimated that around 3,000 babies with thalassemia are born in Indonesia each year.

Blood transfusion in thalassemia is the main treatment that has been implemented worldwide. This action is carried out regularly for life to maintain the quality of life of the person who has it. This red blood cell transfusion was given for the first time according to the Hb level. The goal of transfusion is to maintain the pre-transfusion Hb level of 9.5 g / dL to 10.5 g / dL. The transfusion interval can vary from patient to patient, usually at 4-week

intervals because the Hb reduction rate is 1 g / dL / week. (Wahidiyat, PA. 2018; Hamizah, L. 2017; Nikmah, M. 2018; Cappellini, MD. 2014)

Packed Red Cell (PRC) or red blood cells are the components of the blood most often used in transfusions, especially in thalassemia patients. The goal of PRC therapy is primarily to improve tissue oxygenation and increase the oxygen-carrying capacity of blood. Tissue oxygen demand is determined by Hb levels and haematocrit (Agarwal, 2016). In pediatric patients who require routine transfusions, transfusions are given at pre-transfusion Hb levels of 9.0-10.0 g / dL, to maintain growth and development close to growth and development in normal children.

Examination of hemoglobin levels after blood transfusion is very important because it is associated with further management. However, until now there are no definite guidelines related to the timing of this Hb examination. So sometimes it is detrimental to the patient. Even in Dr. Hospital Zainoel Abidin himself until now there are no fixed guidelines regarding the timing of Hb examination after blood transfusion. For patients with short treatment (one day care) such as thalassemia or chemotherapy, or in patients who need immediate surgery, the timing of blood sampling for checking Hb levels is crucial for further management.

A study conducted by Wiesen et al (1994) concluded that the measurement of hemoglobin levels could be taken 15 minutes after a PRC transfusion and the results showed a stable increase in Hb values. Research by Elizalde, et al1 (1997) reported that examination of Hb levels between 15 minutes and 24 hours after transfusion was very good, only about 6% of patients showed a significant difference to this measurement. Thus the experts can provide a rapid decision and follow-up management of the results of the transfusion, especially in patients with a risk of recurrent bleeding.

## II. Research Methods

The research design was analytic observational with a cross sectional study. The sample in this study was taken by consecutive sampling, which is a non-probability sampling technique, obtained 40 samples that met the inclusion criteria, namely thalassemia patients aged 1-18 years, with Hb at admission <10 g / dl, not with active bleeding and receiving transfusions. 1 bag of blood in 24 hours in the pediatric ward Dr. General Hospital. Zainoel Abidin Banda Aceh for the period of August-October 2019 and patients with transfusions of more than 1 bag in 24 hours, bleeding disorders, signs of infection or sepsis, thalassemia patients with comorbidities (impaired liver function, kidney disease, heart disease, malnutrition), died during the study and did not sign the informed consent was excluded from the study. The independent variable in this study was the time to check Hb levels (1 hour, 6 hours, 12 hours after blood transfusion), while the dependent variable was the Hb level. Analysis of the data in this study using paired t test, the data is significant if $p <0.05$. Data processing was performed with a computer program (SPSS 22.0 for windows).

Examination of Hb levels in this study was carried out using a Hemometer (Hb Test meter brand Family Dr), by taking capillary blood at the fingertips of patients who had previously been given topical local anesthesia and then cleaned using alcohol swabs, then blood was drawn using a micropipette of 7 µL and put into the Hb meter stick, wait for about 5 seconds and the result will appear on the Hb meter screen. The pyriapism is the immediate return of blood flow to the cavernous corpora which is achieved both medically and operatively (Gani, 2020).

The examination was carried out four times, namely at the time of initial admission, then after 1 hour, 6 hours, and 12 hours after the blood transfusion. This research has obtained ethical feasibility from Ethics Committee of the University School of Medicine Syiah Kuala Banda Aceh with registration number 154 / EA / FK-RSUDZA / 2019., on 12 July 2019.

## III. Discussion

The basic characteristics of thalassemia patients in dr. Zainoel Abidin Banda Aceh, who was the sample in this study, was seen from the variables of gender, age group, regional origin and the time of their routine blood transfusion. An overview of the basic characteristics of the sample of study patients is shown in Table 1.

**Table 1.** Basic Characteristics of the Study Sample

| Variable | N (%) |
|---|---|
| Gender : | |
| Man | 20 (50.0) |
| Women | 20 (50.0) |
| Age group : | |
| <5 years | 4 (10.0) |
| 5 - 9 years | 12 (30.0) |
| 10 - 14 years | 19 (47.5) |
| ≥ 15 years | 5 (12.5) |
| Origin : | |
| Pidie | 12 (30.0) |
| West Aceh | 6 (15.0) |
| North Aceh | 6 (15.0) |
| Aceh Besar | 6 (15.0) |
| Aceh Jaya | 4 (10.0) |
| Bireuen | 2 (5.0) |
| Sabang | 2 (5.0) |
| Pidie Jaya | 1 (2.5) |
| Southwest Aceh | 1 (2.5) |
| Transfusion Time: | |
| Every 2-3 weeks | 4 (10.0) |
| Every 3 weeks | 6 (15.0) |
| Every 3-4 weeks | 30 (75.0) |

Overview of the patient's Hb level thalassemia in RSUD dr. Zainoel Abidin Banda Aceh at admission, 1 hour post transfusion, 6 hours post transfusion and 12 hours post transfusion are shown in Table 2.

**Table 2.** An Overview of the Hb Levels of Thalassemia Patients

| Hb levels | Min | Maximum | Median | Mean (95% CI) |
|---|---|---|---|---|
| When Entering | 5.60 | 9,10 | 7.35 | 7.38 (7,13-7,64) |
| 1 hour post | | 11.80 | | |
| transfusion | 7.30 | | 8.75 | 8.97 (8.59-9.35) |

| | | 11.10 | | |
| --- | --- | --- | --- | --- |
| 6 hours post transfusion | 6.60 | | 9.05 | 8.95 (8,57-9.32) |
| 12 hours post transfusion | 6.90 | 12.00 | 9.50 | 9.60 (9.17-10.03) |

Table 2 presents descriptive statistics of Hb levels in the form of minimum, maximum, median, and average values and 95% confidence intervals (95% CI). Based on Table 2, it is known that the average value of Hb levels at the time of entry is 7.38 g / dL (7.13-7.64 g / dL). The median Hb level at admission showed that 50% of patients or a total of 20 people had Hb levels below 7.35 g / dL and the other 50% had Hb levels above 7.35 g / dL. At 1 hour post-transfusion, the patient's mean Hb level increased to 8.97 g / dL (8.59-9.35 g / dL) with the median value also increasing to 8.75 g / dL. Furthermore, at 6 hours post transfusion, the average Hb level decreased to 8.95 g / dL (8.57-9.32 g / dL). However, the median value at 6 hours post transfusion increased to 9.05 g / dL. The average Hb level again increased at 12 hours after transfusion to 9.60 g / dL (9.17-10.03 g / dL). At 12 hours post-transfusion, half of the patients had an Hb level greater than 9.50 g / dL.

Table 3, provides information about the calculation of the increase or decrease in Hb levels at 1, 6 and 12 hours post-transfusion. The assessment is calculated based on the Hb level at admission, so that data on changes in Hb levels can be analyzed to determine when the significant increase in Hb levels occurred after blood transfusions in patients.thalassemia.

**Table 3.** An Overview of Changes in Hemoglobin Levels in Thalassemia Patients at 1, 6 and 12 Hours Post Transfusion

| Changes in Hb Levels | Min | Maximum | Median | Mean (95% CI) |
| --- | --- | --- | --- | --- |
| 1 hour post transfusion | -0.30 | 4.10 | 1.50 | 1.59 (1.30-1.88) |
| 6 hours post transfusion | 0.00 | 3.50 | 1.60 | 1.56 (1.28-1.84) |
| 12 hours post transfusion | 0.30 | 4.40 | 2.05 | 2.22 (1.88-2.55) |

Table 3 shows that there was a change in Hb levels at 1 hour after transfusion compared to the time of admission with an average increase of 1.59 g / dL (1.30-1.88 g / dL). In addition, it is known that 50% of patients have an increase in Hb level above 1.50 g / dL which is reflected in the median value. An interesting thing happened at 6 hours post transfusion, where the mean Hb level in the patient decreased to 1.56 g / dL (1.28-1.84 g / dL) when compared with the change at 1 hour post. transfusion. The median Hb level at 6 hours post transfusion was 1.60 g / dL. Hb levels increased significantly at 12 hours post transfusion with an average increase in Hb levels of 2.22 g / dL (1.88-2.55 g / dL) from the start of admission.

Although descriptively there are differences in the increase in Hb levels at 1, 6 and 12 hours post transfusion, further analysis is needed to determine the time of significant increase in Hb levels in thalassemia patients. The statistical method that can be used to prove this is the Paired sample t test analysis or the non-parametric Wilcoxon test. Both statistical tests are used because the data in this study are paired data, namely data that comes from the same sample but is measured several times at different times.

In this study, the data normality test was performed using the Shapiro-Wilk test. The null hypothesis (Ho) in the normality test states that the data is clearh is normally distributed. Table 4 presents the results of testing the assumption for normality of data on changes in Hb levels at 1, 6 and 12 hours post-transfusion using the Shapiro-Wilk test.

**Table 4.** Testing the Assumption for Normality of Data on Changes in Hb Levels at 1, 6 and 12 Hours Post Transfusion

| Changes in Hb Levels | Statistics | *p-value* | Decision |
|---|---|---|---|
| 1 hour post transfusion | 0.958 | 0.148 | H0 is accepted |
| 6 hours post transfusion | 0.981 | 0.734 | H0 is accepted |
| 12 hours post transfusion | 0.973 | 0.445 | H0 is accepted |

Table 4 shows that the data on changes in Hb levels of thalassemia patients at 1, 6 and 12 hours post transfusion have been distributed normally as indicated by the p-value of testing> 0.05. So that the analysis of changes in Hb levels of thalassemia patients at 1, 6 and 12 hours post transfusion was carried out using the Paired sample t test method.

There are three data analyzes used to determine the time of the significant increase in Hb levels in thalassemia patients. The first analysis was to compare changes in Hb levels at 1 and 6 hours post transfusion. The second analysis was a comparison of changes in Hb levels at 1 and 12 hours post transfusion. The third analysis was a comparison of changes in Hb levels at 6 and 12 hours post transfusion. The results of the comparison analysis of Hb levels for the three times are shown in Table 5.

**Table 5.** Results of Comparative Analysis of Changes in Hemoglobin Levels in Thalassemia Patients

| Comparison | Average Value of the Difference | *t* | *p-value* | Decision |
|---|---|---|---|---|
| Data 1 - Data 2 | 0.025 | 0.163 | 0.871 | H0 is accepted |
| Data 1 - Data 3 | -0,630 | -4,170 | <0.001 | H0 is rejected |
| Data 2 - Data 3 | -0.655 | -5,474 | <0.001 | H0 is rejected |

Information:
Data 1:Changes in Hb level 1 hour post transfusion
Data 2:Changes in Hb levels 6 hours post transfusion
Data 3:Changes in Hb levels 12 hours post transfusion

Table 5 presents some important statistics in the Paired sample t test, namely the average value of the data differences, the t-test statistic and the p-value of the test. Based on Table 5, it is known that in the first analysis (comparison of data on changes in Hb levels at 1 hour and 6 hours after transfusion), the average difference in the value of changes in Hb levels is 0.025. The difference in positive values indicated that the change in Hb levels at 1 hour post transfusion was greater than the change in Hb levels at 6 hours post transfusion. Whereas in the second and third analyzes, the average difference in Hb levels was negative, indicating that the change in Hb levels at 12 hours was greater than the changes in Hb levels at 1 and 6 hours post transfusion.

The mean value of changes in Hb levels at 1 hour post transfusion did not differ much from the mean changes in Hb levels at 6 hours post transfusion. Whereas in the second analysis (comparison of changes in Hb levels at 1 hour and 12 hours after transfusion) and third (comparison of changes in Hb levels at 6 hours and 12 hours after transfusion), the null hypothesis was rejected because the p-value of the test was <0.05. This shows that the mean difference in changes in Hb levels at 1 and 12 hours post-transfusion and at 6 and 12 hours post-transfusion is not zero. In other words, there were significant differences in changes in Hb levels measured at 1 and 12 hours post transfusion and at 6 and 12 hours post transfusion. Thus, it can be concluded that the Hb level in thalassemia patients at dr. Zainoel Abidin Banda Aceh experienced a significant increase at 12 hours post transfusion. For the record, although the descriptive statistical value in Table 3 shows a decrease in Hb levels at 6 hours post transfusion, the Paired sample t test proves that the decrease in Hb levels at 6 hours post transfusion is not statistically significant.

Thalassemia is a blood disorder that is inherited due to mutations in the synthesis of beta-globin chains characterized by decreased hemoglobin, decreased erythrocyte production and anemia. The main treatment for this condition is regular red blood cell transfusion and iron chelation therapy. (Nikmah, M. 2018; KMKRI. 2018; Tari, K. 2018; Lal, A. 2018). The main indication for transfusion is if the hemoglobin level is less than 7 g / dl, while other indications are when the hemoglobin value is more than 7. g / dl accompanied by clinical features such as abnormal facial changes, impaired body development, para-spinal mass, severe bone changes and enlarged liver and spleen. (Hamizah, L. 2017; Lal, A. 2018; Wahidiyat, PA. 2018).

Hb levels of children who will receive transfusion therapy also vary widely. Generally, Hb levels below 7 g / dl have to be transfused, but sometimes there are other factors such as the appearance of hypoxic symptoms requiring transfusion even though Hb> 7 g / dl. 6,12,13 Hb levels before transfusion in patients in this study varied, ranging from 5.6 g / dl to 9.1 g / dl. The Hb level before transfusion in most patients ranges from 6 g / dl to 7 g / dl. The same result was also obtained by Ermaya, et al. 14, where the average thalassemia patient who would receive a transfusion had an Hb level> 7 g / dl. Isworo, et al15 also obtained the same results, namely the average Hb level before transfusion was 7.9 g / dl. However, different things were found by Andriastuti, et al16, in their research at Dr. Cipto Mangunkusumo in 2006-2009 concluded that the mean pre-transfusion Hb level was 6.2 g / dl. From these studies it can be seen that the Hb level before transfusion varies, but there may be other clinical conditions that cause a child to receive a transfusion.

In this study, after receiving a PRC transfusion as needed, each patient was tested for Hb levels 1 hour, 6 hours and 12 hours after the transfusion. On examination 1 hour after transfusion, the mean Hb level increased by 1.59 g / dl. Six hours later, another examination was carried out, but the average Hb level decreased (1.56 g / dl) compared to the previous examination. After 12 hours of receiving a transfusion, the Hb level increased

by an average of 2.2 g / dl, so it can be concluded that the best time to check the Hb level is 12 hours after the transfusion.

Research conducted by Elizalde, et al1 calculated the increase in Hb and hematocrit at 15 minutes, 30 minutes, 60 minutes, 120 minutes, and 24 hours post transfusion. From this study it was agreed that 15 minutes and 24 hours after transfusion were the best times for Hb and hematocrit examination. Research conducted by Karndumri, et al (2020) on 60 patients divided into three groups of examination time, namely 1 hour, 4 hours, and 24 hours concluded that the Hb level examination one hour after transfusion had an increase of 1.21 g / dl, in the group that examined four hours after transfusion there was an increase in Hb levels by 1.19 g / dl, and in the group examined 24 hours after transfusion there was an increase of 0.95 g / dl. From this study it was concluded that the increase in Hb levels did not experience a significant difference each time.

A similar study was conducted by Glatstein et al (2005) but this study assessed an increase in hematocrit after 15 minutes and 6 hours post transfusion. In this study, it was stated that the increase in hematocrit had occurred immediately after the completion of the transfusion or at 15 minutes post-transfusion and the increase was the same as 6 hours after transfusion, so that with this assessment it could be decided that after immediate transfusion, it could be ascertained whether or not additional transfusion was necessary.

Another study conducted by Hoque, et al (2015), involved 100 patients in Dhaka who examined their hemoglobin levels before transfusion, 6 hours and 24 hours post transfusion. From this study, it was found that an increase in Hb levels at 6 hours after transfusion was 0.39 mg / dl and 1.14 mg / dl an increase in Hb at 24 hours post transfusion. This study concluded that the increase in Hb level at 6 hours post transfusion was not significant, but the best increase in Hb occurred at 24 hours after transfusion. The difference in the increase in Hb levels at 6 hours and 24 hours after transfusion was very significant and statistically significant. In line with the study of Linda, et al (2018), who examined Hb levels at 6-12 hours post-transfusion and 12-24 hours post-transfusion. There was no statistically significant difference in the average increase in Hb levels at the two times of the examination.

In this study, it was found that an increase in Hb levels had occurred 1 hour after the transfusion. The difference in Hb levels at 1 hour and 6 hours post transfusion was not significant and a significant increase occurred at 12 hours post transfusion. A similar study was conducted by Audu, et al. (Audu, LI. 2015) which assessed the increase in neonatal hemoglobin levels (Elizalde, JL. 1997; Cappellini, MD. 2014. Lal, A. 2018) at 24 and 48 hours after red blood cell transfusion. This study concluded that the increase in Hb levels was the same at 1 hour and 6 hours post transfusion, a significant increase at 12 hours post transfusion. Hb levels at 12 hours, 24 hours, and 48 hours post transfusion were the same. From this study, it was found that the increase in Hb occurred in a period of 12 hours after transfusion, so it is advisable to check Hb levels at this time. Similar results obtained by Siska (2019) in her research at RSUD Dr.

Another study conducted by Wiesen et al9 assessed Hb concentration at 15 minutes, 1 hour, 2 hours, and 24 hours post transfusion. This study concluded that the increase in Hb levels had occurred at 15 minutes post transfusion. Hb measurements carried out 15 minutes post transfusion reflected a stable value. Measuring this time is very useful in reducing outpatient waiting times and reducing the need for reexamination times of 24 to 48 hours. Another study conducted by Raja et al (Raja, A. 2020) on 80 people with thalassemia who received PRC transfusions found that there was an increase in Hb levels by 3-3.26 g / dl on examination one hour after transfusion. However, this study did not check Hb levels at any other time after the transfusion.

The theory that is widely used today is that there is an increase in the Hb level of 1 g / dl per transfusion of one red blood cell unit. However, the stability of Hb levels was only reached 24 hours after the transfusion. Hb concentration at 24 hours post transfusion has increased by 110% from the value of the examination immediately after transfusion (Wiesen, AR, 1994; Shander, A. 2013) of all the studies that have been presented have different conclusions. This is due to the criteria of subjects with different backgrounds of causes of anemia. However, it can be seen that Hb levels begin to increase in the first 1 hour after transfusion and on average give the best results of increases in Hb levels 12-24 hours after transfusion.

The literature or previous studies discussing the best time to check the increase in hemoglobin concentration after blood transfusion in the last five years is very limited and there are no specific guidelines regarding this. So it is deemed necessary to carry out this research as a reference for further research and it is hoped that it can become a guideline for the institution itself.

## V. Conclusion

Examination of Hb levels in the first 1 hour after transfusion has shown a significant increase so that after direct transfusion, it can be ascertained whether or not additional transfusions are needed and is useful in reducing the waiting time for outpatients or patients who require immediate action and shortening the length of stay of patients in hospital . There was a difference in the average Hb level at 1 hour, 6 and 12 hours post transfusion. A significant increase in hemoglobin occurred at 12 hours post transfusion and this already reflected the expected Hb level. In emergency conditions that require a decision for further management, post-transfusion Hb level checks can be done 1 hour after the transfusion is complete.

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