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The Effect of Blood Transfusion Frequency on Secretor Status Titer in Saliva and Urine Specimens of Thalassemia Patients

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Abstract

Background: Thalassemia is a disease caused by a deficiency or loss of synthesis of one or more normal globin chains. In diseases that require blood transfusions, such as Transfusion Dependent Thalassemia (TDT), it is very important to examine the blood type to determine the blood to be transfused. The ABO blood type system antigen or secretor, is found in body fluids in the form of dissolved antigens, including in saliva and urine. Interference can be caused by the frequency of transfusion, which can change the secretor content in the saliva and urine of thalassemia patients, causing false negatives in the examination of secretor status. *Objectives*: This study aims to determine the effect of transfusion frequency on the titer of secretor status in saliva and urine specimens of Thalassemia patients. *Materials and Methods*: The type of study is quasi-experimental, Agglutination-Inhibition method. The research sample was 23 Thalassemia major patients. 15 patients are secretor patients, with a frequency of 1x transfusion a month were 7 people (47%), a frequency of 2x transfusion a month were 5 people (33%), and 4x transfusion a month were 3 people (20%). *Results*: The results of the study on Thalassemia patients obtained from saliva were titers between 1/8 to 1/256. From urine, the results were non-secretors. In contrast to previous studies, which stated that urinary is still detected but four times weaker than saliva. Based on the ANOVA statistical calculation, sig. 0.909 ($p>0.05$) was obtained. *Conclusions*: The conclusion is that there is no effect of transfusion frequency on the titer of secretor status in saliva or urine.

Keywords

Saliva, Thalassemia, Transfusion frequency, Urine

1. Introduction

Thalassemia is a disorder caused by a deficiency or absence in the synthesis of one or more normal globin chains. Based on the type of missing globin chain, the disease is classified into several types, with the most common being α- or ß-thalassemia. A deficiency or absence of the α chain is referred to as alpha-thalassemia, whereas a deficiency or absence of the ß chain is termed beta-thalassemia. Beta-thalassemia is further subdivided into three types—minor, intermediate, and major—depending

on the presence or absence of the beta-globin gene (Porter & Taher, 2021). In conditions requiring blood transfusion, such as Transfusion-Dependent Thalassemia (TDT), determination of blood group is of critical importance to ensure compatibility of transfused blood. In the human body, antigens of the ABO blood group system are also present in other body fluids in soluble form. These soluble antigens are encoded by the *Se* gene, located at the *Se* (FUT2) locus on chromosome 19. The expression of antigens A and B depends on the individual's A and B genotypes. Individuals with the genotype *Se*/*Se* or *Se*/*se* are classified as secretors, whereas those with the genotype *se*/*se* are classified as non-secretors, as they do not produce soluble A and B antigens (Campi, et al, 2012). This examination has been widely applied in forensic serology, and although DNA-based testing has become increasingly common, it continues to be frequently utilized (Maharani & Noviar, 2018).

The frequency of blood transfusions recommended by the Thalassemia International Federation is every 2 to 5 weeks, to maintain hemoglobin levels within the range of 95–105 g/L. Shorter transfusion intervals may be adopted with reduced blood requirements while also considering factors such as school schedules, employment, and the patient's lifestyle (Porter & Taher,2021). Saliva sample collection presents several challenges, as the method of collection may significantly influence the results. Differences in outcomes have been observed between two methods of saliva collection, namely Passive Drooling and Spitting (Azizah et al., 2023). Moreover, the urine of thalassemia patients differs from that of healthy individuals, as thalassemia patients excrete higher levels of metabolites (Capolongo et al., 2020). This may constitute an additional source of interference, aside from factors such as storage duration of saliva and urine samples. This research provides new insights into the secretor status in thalassemia patients, particularly within the forensic context. It aims to determine whether transfusion frequency affects secretor status titers in saliva and urine specimens of thalassemia patients.

2. Materials and Methods

2.1. Design of Study

Study was conducted using quasi-experimental design to determine the secretor status and titer levels of specimens in relation to the transfusion frequency of thalassemia patient receiving one, two, and four transfusion per-month.

2.2. Subject of Study

The study employed a purposive sampling technique. Saliva specimens were collected using the

passive drooling method, while urine specimens were obtained through the mid-stream collection method. Participants consisted of thalassemia patients who received blood transfusions at frequencies of once, twice, or four times per month. Ethical clearance for this study was granted under approval number 100/KEPK/EC/II/2025. A total of 24 patients participated, each providing one saliva and one urine specimen.

2.3. Method

This study utilized the agglutination-inhibition method. Antigens present in saliva and urine specimens were reacted with specific antisera, followed by incubation and neutralization, and subsequently tested against antigens expressed on the surface of red blood cells. If saliva contains the corresponding antigen, it inhibits antibody activity, thereby preventing agglutination and indicating a secretor status. Conversely, if saliva lacks the antigen, agglutination will occur, indicating non-secretor status (Maharani & Noviar, 2018).

3. Results and Discussion

3.1. Result

This study was conducted at the Health Polytechnic Bandung. The specimens used were saliva and urine of thalassemia patient with transfusion frequency between one, two and four times per-moth with total of 23 samples. The characteristic of respondents is presented in Table 1.

Table 1. Characteristic and the result by Gender, Age, Transfusion Frequency and Secretor Status

No	Gender	Total	Percentage (%)
1	Male	7	30
2	Female	16	70
No	**Age**	**Total**	**Percentage (%)**
1	8-17 Years	6	26
2	18-45 Years	17	74
No	**Transfusion Frequency**	**Total**	**Percentage (%)**
1	1	12	52
2	2	7	30
3	4	4	18
No	**Secretor Status**	**Total**	**Percentage (%)**
1	Secretor	15	65
2	Non-Secretor	8	35

Based on Table 1, the study subjects consisted of 7 males (30%) and 16 females (70%). Participants

aged 8-17 years accounted for 6 individuals (26%), while those aged 18-45 years comprised 17 individuals (74%). The distribution of transfusion frequency showed that 12 participants (52%) received transfusions once per month, 7 participants (30%) twice per month, and 4 participants (18%) four times per month. The secretor status results indicated that 15 participants (65%) were classified as secretors and 8 participants (35%) as non-secretors. Subsequent analyses included only the secretor group.

Table 2. Descriptive Test Secretor patient

No	Transfusion Frequency	Saliva Minimum Titer	Saliva Maximum Titer	Urine Minimum Titer	Urine Maximum Titer	Mean
1	Once per month	1/8	1/64	Non-Secretor	Non-Secretor	6.29
2	Twice per month	1/16	1/128	Non-Secretor	Non-Secretor	6.60
3	4 times per-month	1/8	1/256	Non-Secretor	Non-Secretor	6.67

From the descriptive analysis above, the urine data were found to be homogeneous. A total of 15 saliva and urine specimens identified as secretors were tested for normality using the Shapiro–Wilk method, as the sample size was fewer than 50. The results of the normality test were as follows:

Table 3. Test of Normality for Saliva Titer

No	Transfusion Frequency	Statistic	df	Sig.
1	1 time per-month	0.915	7	0.429
2	2 times per-month	0.961	5	0.814
3	4 times per-month	0.987	3	0.780

The significance (Sig.) values for all saliva secretor titers were not less than 0.05, H_0 was accepted, indicating that the data were derived from a normally distributed population. The subsequent analysis conducted was ANOVA. Since the normality test of saliva secretor titers indicated that the data were normally distributed, statistical testing was continued using ANOVA. This method was applied as it is a parametric test for independent variables. The results of the ANOVA test are as follows:

Table 4. ANOVA Test for Saliva titer

Groups	Sum of Squares	Df	Mean Square	F	Sig.
Between Group	0.438	2	0.219	0.096	0.909
Within Group	27.295	12	2.275		
Total	27.733	14			

Since the significance value (Sig.) for saliva was greater than 0.05, H_0 was accepted, indicating no differences across transfusion frequency variations. Based on the ANOVA statistical test, transfusion frequency did not have a significant effect on secretor status titers. The results also showed considerable variability, as patients with higher transfusion frequencies tended to exhibit more variation in titers, with changes that were not proportional.

3.2. Discussion

The results of secretor status titers in the urine of all thalassemia patients indicated a non-secretor status. Regardless of whether patients were classified as secretors or non-secretors based on saliva analysis, all urine specimens demonstrated a non-secretor profile. Urinary titers are four times weaker than those in saliva. However, in this study, urinary secretor titers in thalassemia patients consistently yielded non-secretor results, suggesting that either the urine of thalassemia patients is unable to excrete ABO antigens or the urine-producing organ not producing ABO anitgens. 100% of urine specimens exhibited agglutination beginning from the first dilution, confirming the absence of antigens (Apriliani,2024). The discrepancy between saliva and urine secretor titers was substantial, suggesting that a specific mechanism eliminated antigens that would normally be expected to be present in urine. Thalassemia patients are typically treated with iron-chelating agents such as deferasirox (DFX), deferoxamine (DFO), and deferiprone (DFP) (Saliba et al, 2015). However, this compound have effects on the status secretor titers because there is no studies have specifically examined whether their metabolites—such as ferrioxamine, deferiprone-3-O-glucuronide, or unbound drug residues—interact with urinary antigens. Nevertheless, in theory, such interactions remain possible, as the U.S. Food and Drug Administration (FDA) reported that only about 75–90% of administered doses are metabolized and excreted in urine (FDA & CDER, n.d.).

4. Conclusions

The mean titer of saliva secretor status among thalassemia patients receiving transfusions at frequencies of once, twice, and four times per-month was 6.52. In contrast, the mean titer of urinary

secretor status in these patients was consistently homogeneous non-secretors, with all specimens classified as non-secretors. Statistical analysis revealed that transfusion frequency had no significant effect on saliva secretor titers, nor did it influence urinary secretor titers in thalassemia patients. There is no effect of transfusion frequency to the status secretor titers on saliva or urine specimens in thalassemia patients. This study has its limitations to locally Thalassemia patients and for future research can explore the reason there is no titers on urine.

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