

RESEARCH ARTICLE

Correlation of saliva characteristics and caries in beta-thalassemia major patients

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ABSTRACT

A patient with beta-thalassemia major is known to have poor oral hygiene and a high risk of caries. Some studies showed that patients with beta-thalassemia have low salivary flow rate and acidic saliva. A reduction in salivary flow rate and pH would increase caries susceptibility. The aim of this study was to determine the correlation between salivary flow rate and pH with DMFT index in patients with beta-thalassemia major. This study was a cross-sectional design. A total of 38 patients with beta-thalassemia major aged more than 12 years old at Dr. Mohammad Hoesin Palembang Hospital were included in this study. Their unstimulated saliva was collected by spitting methods, and the teeth were examined with DMFT Index. The salivary flow rate was expressed as ml/min and the pH was measured using a saliva pH indicator paper. Data were analyzed using Pearson correlation test to determine the correlation between variables. The result showed that the mean age of the patients in this study was 16.6 years old, with a higher number of female patients than males. Patients with beta-thalassemia major had low salivary flow rate (0.72 ml/5 min), acidic saliva (6.34), and high DMFT index (8.34). This correlation was statistically significant ($p < 0.01$). It can be concluded that there is a strong negative relation between DMFT index with salivary flow rate and salivary pH in patients with beta-thalassemia major.

Keywords: beta-thalassemia major; DMFT; salivary flow rate; salivary pH

INTRODUCTION

Caries is a demineralization process caused by the interactions of several factors, such as host (teeth and saliva), microorganisms, substrates (foods), and time. Caries process begins with the presence of plaques consisting of pellicles and microorganisms attached to the tooth surface. Bacteria on plaque ferment carbohydrates to become lactic acid, allowing it to be able to reduce the pH of saliva into 5.5 and dissolve hydroxyapatite.¹ Continuous demineralization forms porosity on the tooth surface. The function of saliva is important in protecting teeth against caries. The effects of saliva buffers and cleansing are capable of preventing caries by changing the condition of acidic saliva to normal conditions.²

Caries can occur with or without a systemic disease. The risk of developing caries in individuals who have systemic diseases will be higher than that

in individuals who do not have a systemic disease. This increased risk of caries can be caused by a low body defense mechanism that has an impact on the high risk of caries.³ One systemic disease that has an impact on the high risk of caries is beta-thalassemia major. Beta-thalassemia major is a hereditary blood disorder characterized by reduced or absent beta-globin chains of the hemoglobin, due to the disturbance in the synthesis of globin chains.⁴ Based on the data from Children's Health Installation at Mohammad Hoesin Palembang Hospital 2017, thalassemia had the highest number of visits and increased over years.

The oral health of pediatric patients with beta-thalassemia major was reported to be poor because their parents mostly only focus on medical procedures instead of treating their children's oral health. Al Jobouri et al stated that the DMFS score for beta-thalassemia major was high.⁵ Sushma et

al. reported that DMFS values in children belonging to the age group of 0-10 years who suffered from beta-thalassemia major reached 6.42, while the DMFS for the control group was only 0.48. The average value of DMFT in patients with beta-thalassemia major in the age group of 11-17 years was also quite high, i.e. 3.83, and the value in the control group was only 0.58.⁶

The high DMFT index in beta-thalassemia major is associated with the damage of salivary gland. Beta-thalassemia major patients need routine blood transfusions to survive. The lysis of red blood cells lead to an increase in the amount of ferritin in the body and sedimented in some tissues, such as salivary glands. The damage of salivary glands causes a decrease in salivary flow rate and drying of the mouth.⁷ The decrease in salivary flow rate affects inorganic components, such as bicarbonate and phosphates to neutralize the pH of the oral cavity. Secretory immunoglobulin A (sIgA) was also found to be low in beta-thalassemia major patients. These antibodies play an important role in controlling oral microbiota by reducing the adherence of bacteria to the oral mucosa and teeth. The reduction in sIgA influences the immune mechanisms in protecting the oral cavity from microorganisms.⁸ The aim of this study was to know the correlation of salivary pH, flow rate and DMFT index in beta-thalassemia major patients.

MATERIALS AND METHODS

This research had been approved by the Research Ethics Commission of the Central General Hospital of Mohammad Hoesin Palembang and the Faculty of Medicine of Sriwijaya University with an ethics certificate No.153/kepkrsmhfkunsri/2017. This study was an analytical observation with a cross-sectional design. It was conducted in Children's Health Installation, General Hospital of Moehammad Hoesin, Palembang. Quota sampling was used to select the samples on the basis of predetermined characteristics of beta-thalassemia major patients aged more than 12 years old. Thirty-eight patients were obtained based on the medical records at the hospital.

The operators explained to the patients about the procedure of the study. Both the patients and parents (those as the samples aged 12 to 18 years old) filled and signed an informed consent if they agreed to participate in the study. The study was conducted after the patients had blood transfusions. The saliva was taken from 9 to 11 am. The patients were instructed to brush their teeth two hours before the examination at the hospital, not allowed to eat and drink for approximately two hours before the assessment, and asked to sit in the prepared chairs.

The saliva collection technique used in this study was the spitting method. The patients were required to swallow all the remaining saliva in the oral cavity before the study began. The patients were asked to sit, bow their heads, and hold a tube with their right hands. To collect the unstimulated saliva, the patients drooled passively into the collection tube for five minutes. These patients were also asked not to swallow saliva during the procedure. The pH was assessed as soon as the saliva was collected. The assessment of the salivary pH was done using a pH indicator paper. The salivary flow rate was calculated by looking at the collected salivary volume on the tube.

To assess DMFT, all the teeth were examined using a sterile sonde and mouth mirror to evaluate decayed, missing, filled teeth. Three calibrated dentistry clinical students and two calibrated dentists performed the DMFT examination for 6 days. The results were recorded in the DMFT score section.

The data were analyzed using Pearson's correlation to compare the relationship between salivary pH, flow rate, and DMFT index in beta-thalassemia major patients. Significant statistical difference was shown with a p-value being <0.05. The strength level of the relationship was determined using Pearson's correlation.⁹

RESULTS

A study on the correlation of salivary flow rate and pH with DMFT index of patients with beta-thalassemia major was carried out in the inpatient

installation of General Hospital of Moehammad Hoesin, Palembang. The distribution of the patients is shown in Table 1.

Table 1. Distribution of beta-thalassemia major patients by sex and age

	Total	Percentage
Sex		
Male	16	42.1%
Female	22	57.9%
Age		
12-19	32	84.2%
20-27	3	7.8%
>27	3	7.8%

Table 2. Correlation of salivary flow rate, pH, and DMFT of the patients with beta-thalassemia major

	Correlation	Flow rate	pH
	Pearson correlation (r)	-0.60*	-0.62*
DMFT	Sig. (1-tailed)	0.00	0.00
	n	38	38

Pearson correlation, *= significant

Table 1 shows that the number of female patients was higher than that of males. Based on age, most patients with beta-thalassemia major were found in the age range of 12-19 years old, with a mean age of 14.4 years old. (84.2%). Meanwhile, the mean age of all the patients who participated in this study was 16.6 years old.

Patients with beta-thalassemia major had low mean flow rates (0.73 ± 0.14), low salivary pH (6.34 ± 0.34), yet high DMFT index (8.34 ± 2.65). The correlation is shown in Table 2.

Table 2 reveals that salivary flow rate had a strong correlation with DMFT in patients with beta-thalassemia major ($r = -0.60$). It also shows that salivary pH had a negative correlation with DMFT in patients with beta-thalassemia major ($r = -0.62$).

DISCUSSIONS

This study showed that most of the patients with beta-thalassemia major were female aged 12-19 years old. Bhatia *et al.* reported that female children with thalassemia showed higher frequency than male in central India.¹⁰ This condition describes that females are dominant for hereditary blood disorders. On the other hand, another study reported that males with thalassemia major showed

a higher percentage than females. However, some researchers found that beta-thalassemia major affects male and female equally.¹¹ In addition, Anshori *et al.* told that the average life expectancy of patients with beta-thalassemia major is 18 years old.¹² This explains that patients with beta-thalassemia major have short-lived expectancy. However, with improved treatment for a better quality of life, such as splenectomy and bone marrow, patients with beta-thalassemia major are able to survive until more than 30 years old.¹³

The unstimulated salivary flow rate was found to be low. The decrease in the salivary flow rate of patients with beta-thalassemia major could also be caused by routine blood transfusions performed at least once a month. The side effect of the transfusion given is an excessive load of iron in the organs (hemosiderosis), one of which is in salivary gland. This condition leads to the inflammation and blockage of the salivary gland resulting in the decrease in salivary flow rate.¹⁴ Another theory explains that an accumulation of iron deposition in salivary glands reduces the production and secretion of saliva in patients with beta-thalassemia major.¹⁵

Patients with beta-thalassemia major undergo incomplete hemoglobin formation. It leads to the decrease in oxygen in some tissues and causes inhibition of mitochondrial function to evolve the cells of the body. Mitochondria are important to as transport media and electrolytes in acinar cells. Due to its impact, salivary secretion in patients with beta-thalassemia major reduces.¹⁶ Similar to the present study, Diwan and Mohammad reported that beta-thalassemia major affects salivary flow rate.¹¹

The salivary pH found in this study was 6.34 ± 0.34 . Hans *et al.* reported that the normal pH of saliva is 6.7 to 7.4.¹⁷ Thus, it can be said that patients with beta-thalassemia major had low salivary pH. However, the results of this study are different from the results of Al Jobouri's study, showing that the salivary pH of beta-thalassemia major patients was still neutral, 7.17.⁵ In fact, the difference is due to the fact that the two studies used different saliva collection methods. Al Jobouri *et al.* collected stimulated saliva, while in this study, we collected unstimulated saliva. There were several factors

affecting the salivary pH of the patients. Decreased salivary flow rate due to routine blood transfusion predisposes the components of inorganic saliva such as bicarbonate and phosphate as saliva buffer to neutralize acid.¹⁸ The degree of saliva acidity depends on the acid and its conjugate base. The degree of saliva acidity decreases to 4-5 within 3-5 minutes after gargling or contacting with a suitable substrate, and after one hour, it returns to 7. Bicarbonate is a component with the highest function as a saliva buffer because it is easy to bind to hydrogen.¹⁹

This study also presented that DMFT index in patients with beta-thalassemia major was high. Helmi et al. summarized that the main oral manifestations of thalassemia were high caries index, malocclusion, and severe gingivitis.²⁰ Another study also reported that there was a high DMFT in patients with beta-thalassemia major.⁷ Caries experienced by patients with beta-thalassemia major is related to endocrine abnormalities. Thalassemia affects parathyroid functions and bone mineral density correlated with serum ferritin, calcium phosphorus, and alkaline phosphatase levels. Patients with thalassemia need to receive blood transfusion periodically. After some time, due to red blood cell lysis, the number of irons in the body increases and settles in some tissues, leading to the damage of the tissues. The damage of parathyroid glands influences hormone secretions to maintain calcium in the body, such as in bone and teeth.²¹ Wong et al reported that thalassemia was one factor that could cause developmental defects of the enamel.²²

Ferritin accumulation in the salivary glands induces the damage of salivary glands and causes drying mouth, consequently affecting the components of saliva which function in caries protection. One component of saliva associated with iron is lactoferrin. The function of lactoferrin in caries defense is by binding to Fe^{3+} ions needed for microorganism growth. However, due to decreased salivary flow rate, the lactoferrin component reduces, thus disrupting the ion-binding mechanism. As a consequence, many free Fe^{3+} ions stimulate the growth of microorganisms in the oral cavity and

cause tooth decay. Lactoferrin also acts as host defense protein that plays an important role in the immune system.^{23,24} The reduction of lactoferrin leads to the reduction in the immune system in saliva. Another organic component of saliva that is important for antimicrobial activity is sIgA. In fact, a decreased salivary flow leads to a decrease in sIgA in saliva, causing tooth decay.²⁵ Saliva regulates the interaction between oral tissues and normal flora. Its buffering capacity is capable of repairing teeth by supplying calcium to enamel surfaces.²³

Our finding in this study showed that there was a strong and significant negative effect between salivary flow rate and DMFT index and salivary pH and DMFT index in patients with beta-thalassemia major. Krunica et al reported that reduced salivary flow predisposed patients to oral disease such as tooth decay.²⁶ Nasiru et al. also demonstrated that lower salivary flow rate and salivary buffering capacity led to a higher DMFT index in children.²⁷ Abuaffan found that patients with beta-thalassemia major experienced more dental caries compared to normal people.²⁸

However, a lack of radiography in detecting interdental caries became one of the limitations in this study, affecting a more detailed DMFT index. Another limitation was that this study was only carried out at one referral General Hospital in Palembang, thus excluding other private hospitals. Therefore, the data obtained were limited.

CONCLUSION

From this study, it can be concluded that there is a strong negative relation between DMFT index with salivary flow rate and salivary pH in patients with beta-thalassemia major. Due to the high risk of oral disease in patients with beta-thalassemia major, education and more attention to these patients is needed to reduce dental caries and other oral diseases in order to have a longer life expectancy. The role of parents and individuals is crucial to educate and plan for dental services to detect oral disease and help prevent dental and periodontal problems. Practitioners should give these patients a follow-up care of their dental treatment regularly.

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