

Research Article

Dental caries and growth impairment among children with thalassemia major in relation to some salivary constituents

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Abstract: Background: A single gene mutation causes beta-thalassemia, an autosomal recessive disorder. It is hemolytic anemia that needs constant blood transfusions for life. In children and adolescents with thalassemia major, no clear concepts are found concerning the association between beta-thalassemia and growth retardation is a common side effect. Saliva contains a variety of biochemists, which may affect the severity of dental caries. Aim: This research aimed to evaluate the link between β -thalassemia major, dental caries and growth impairment in relation to some salivary constituents. Materials and Method: As part of an investigation at the Basra/Iraqi Thalassemia Center, 40 thalassemic children aged 10 to 12 were compared to 40 healthy controls in terms of dental caries (who were the same age and gender as the study group). Anthropometric measurements were used to assess their physical development. A sample of unstimulated whole saliva was taken from each child to determine salivary calcium, phosphorus, and alkaline phosphatase enzyme concentrations. Result: For both the primary and permanent dentition, dental caries experience (dmft/DMFT) was higher among β -thalassemic children, with a statistically significant difference. A higher percentage of thalassemic youngsters were found to be underweight. Although salivary constituents like calcium, phosphorus, and alkaline phosphatase enzyme were higher in the control group than in the study group, there was no statistically significant difference between the two groups. Conclusion: Dental caries and growth impairment were associated with beta-thalassemia major.

Keywords: β -thalassemia major, body mass index, children, dental diseases, salivary constituents.

Introduction

The blood illnesses, known as thalassemias, are handed down through generations and are marked by decreased or missing production of globulin protein chains. Thalassemias are either major (β -thalassemia), with the most severe clinical manifestations, or minor (α -thalassemia), with mild and clinically asymptomatic clinical manifestations. A thalassemia intermediate variant is also possible. These types of conditions are becoming more common in Mediterranean-bound countries. The predominant symptoms and indicators of thalassemia appear in the first two years of life. The affected newborns show signs of severe anemia, jaundice, extreme pallor, decreased physical activity, poor eating, irritability, and increased drowsiness due to their illness. Recurrent fever, spontaneous fractures, bleeding and susceptibility to many infections are the most prevalent symptoms. Hepatosplenomegaly and developmental retardation are also common ⁽¹⁻³⁾. Repeated blood transfusions make thalassemic children

vulnerable to various diseases, and they become transfusion-dependent for the rest of their lives to replenish their depleted red blood cells. Some of the most common oral and face health issues they deal with include dental caries, paler gums, a burning tongue, swollen salivary glands, a dry mouth, and low IgA levels, all of which lead to inadequate salivary protection ^(4,5).

The saliva generated by the salivary glands contains a variety of defensive mechanisms, including immunological and enzymatic systems. Saliva may protect the mucosa from mechanical damage and aid healing by acting as an epidermal growth factor. Carious processes may be altered in a variety of ways by using it. In addition to reducing plaque buildup on tooth surfaces, saliva flow may speed up the clearance of carbohydrates from the teeth ^(6,7).

Dental caries may be treated using saliva's remineralizing powers. Saliva becomes supersaturated with the ions that make up the mineral content of the teeth when the pH increases over 5.5. (calcium, phosphate, and hydroxyl ions). After ingesting sugar, saliva and plaque grow unsatisfied, and the tooth dissolves below this level. Mineral crystals in the enamel are damaged; therefore, calcium and phosphate ions in saliva begin to fix them. This process is known as "remineralization." ⁽⁸⁾. Just a few clinical studies have examined the oral health of thalassemic individuals, including dental and periodontal issues ⁽⁹⁻¹¹⁾. There was a delay in both deciduous and permanent tooth eruption, as well as a high rate of caries; moreover, The degree of systemic sickness was connected to dental caries illness. In mixed dentition, there was a strong inverse connection between transfusion requirements and caries ⁽¹²⁾. The theoretical risk of oral and dental diseases in thalassemia major (TM) patients remains high.

Alkaline phosphatase (ALP) is a calcium-phosphorous-binding protein and phosphor hydrolytic enzyme ⁽¹³⁾. Catalyzing the hydrolysis of monoesters and the transfer of phosphorus may be significant in the mineralization of teeth, and ALP, which can be found in species from bacteria to humans, may improve salivary phosphate content and the balance of demineralization to reinforcing enamel ⁽¹⁴⁾. ALP's job in the bone matrix is to determine the pH at which a molecule has a net neutral charge, resulting in hydroxyapatite crystals forming ^(15,16).

For all of the above, it was decided to conduct this study to gain knowledge regarding the oral health problems of this target group, which may allow the setting for a preventive program for these medically comprised children. The null hypothesis that there is no link between β -thalassemia major, dental caries and growth impairment in relation to some salivary constituents

Subjects, Materials and Methods

Sample Selection

After receiving ethical permission (334) according to the Declaration of Helsinki Guidelines ⁽¹⁷⁾, this case-control research was conducted from May 2021 to August 2021.

It was carried out in a thalassemia centre in the Iraqi governorate of Basra. The Ministry of Health would conduct the clinical examination and laboratory biochemical analysis after receiving ethical permission. In this study, using G power 3.1.9.7 (Program written by Franz-Faul, Universitatit Kiel, Germany) with the power of the study=80%, alpha error of probability=0.05, assume the cohen's D effect size as 0.65 (medium)¹ under all these conditions the sample size was 40 subjects for each group (total subjects =80). So 40 children aged 10 to 12 years who were attending a thalassemia facility for their routine blood transfusion regime were included in a study group.

The control group (40 children) was made up of normal youngsters of the same age and gender who are in good health as the study group, chosen from the patient's relatives who accompanied them to the clinic. After explaining the research's goals and obtaining written consent from the parents, a patient information sheet was gathered for each participant before the commencement of the trial.

Selection criteria

The children in the study had been diagnosed with beta-thalassemia major before. Diabetes mellitus and other disorders that affect dental caries or saliva characteristics were left out of the study. Healthy controls were children in good health, did not have any systemic ailments, and did not use any medications. Those whose parents declined to participate and just partially completed the study's questionnaire were omitted.

Data collection

Children were told to wash their teeth and cease eating and drinking for roughly two hours before the clinical examination at the thalassemia facility after receiving their regular blood transfusions. Meanwhile, each child in the research was interviewed to get demographic information, which was entered on a unique case sheet ⁽¹⁸⁾.

Oral examination was done and dental caries experience was recorded according to the criteria of WHO by dmfs for primary teeth and DMFS for permanent teeth⁽¹⁹⁾.

Children wore light clothes and without shoes or shoes when weighed. In this posture, the child stood straight with arms alongside their body and heels, calves, hips, shoulders, and head against the wall, with the head positioned according to Frankfort's design. The BMI was calculated based on their age and gender, and all measuring protocols followed the CDC growth chart ⁽²⁰⁾.

In a controlled environment, Navazesh and Kumar suggested obtaining unstimulated salivary samples from each patient ⁽²¹⁾. Spitting was used as the collection technique in this research, and the children were instructed to swallow all of their extra salivae before sitting with their heads bent forward and grabbing the collecting tube with their right hands. The youngsters were asked to spit into a collection tube for five minutes to collect saliva that had not been encouraged. During the process, they were told not to swallow any saliva.

The clear supernatant was separated by micropipette and distributed on sterile disposable test tubes for biochemical analysis after centrifugation at 3000 rpm for 10 minutes. The calcium, phosphorus, and ALP concentration was evaluated in salivary supernatant samples using auto analyzer equipment and salivary kits with various biochemical assays. Calcium and phosphorus concentrations were measured in micromoles per liter (mmol/L), and ALP enzyme activity was measured in microunits per liter (IU/L).

The statistical analysis was performed using the Statistical Package for the Social Sciences, version 22. The mean and standard deviation were computed for both groups for each clinical measure. It compared study and healthy groups for dental caries in baby and adult dentition. To measure and compare correlations, Pearson used the correlation coefficient (r). The significance threshold was chosen at $p < 0.05$.

Results

Clinical examination indicated that both groups under the study were affected by dental caries. The mean of dmfs/DMFS, as well as its component (ds/DS, fs/FS) among the thalassemic children was higher than that found among the healthy group with a statistically significant difference ($p < 0.05$). Except for (ms/Ms, DMFT), the results were not significant, Table 1. While Table 2 revealed that BMI was lower in the study group compared to the control with a statistically significant difference.

Table 1: Dental caries experience among the study groups.

Variables	Groups				T-test	df	p-value
	β-thalassemia		Healthy				
	Mean	±SE	Mean	±SE			
ds	5.550	0.837	2.450	0.471	3.227	61.422	0.002*
ms	2.675	0.629	1.600	0.454	1.386	70.977	0.170**
fs	0.000	0.000	0.200	0.089	2.243	39.000	0.031*
dmfs	8.225	1.130	4.250	0.784	2.890	69.505	0.005*
dmft	3.950	0.431	2.200	0.391	3.007	77.266	0.004*
DS	5.525	0.591	3.175	0.232	3.705	50.734	0.001*
MS	0.436	0.220	0.725	0.330	0.729	67.608	0.469**
FS	0.225	0.141	0.650	0.137	2.166	77.924	0.033*
DMFS	6.175	0.738	3.200	0.197	3.895	44.516	0.00000*
DMFT	3.625	0.434	4.550	0.437	1.502	77.995	0.137**

*=significant at $p < 0.05$, **=not significant at $p < 0.05$, ds, ms, fs= decayed, missing, filled surfaces of primary teeth. Ds, Ms, Fs= decayed, missing, filled surfaces of permanent teeth,

Table 2: Distribution of BMI index among groups.

Variables	Groups				t-test	df	p-value
	β-thalassemia		Healthy				
	Mean	±SE	Mean	±SE			
BMI	15.833	0.385	18.763	0.583	4.193	67.535	0.000082*

*=significant at $p < 0.05$, BMI= Body mass index.

The current research revealed that 70% of thalassemic children had a low BMI (underweight category), compared to 12.5 percent of the control group. When the BMI percentiles of the two groups were compared, a statistically significant difference was found in Table 3.

Table 3: Distribution of BMI percentile among groups.

BMI Percentile	Groups				p-value	Total	
	β-thalassemia		Healthy			N.	%
	N.	%	N.	%			
Normal weight	10	25.00	21	52.50	0.0001*	31	38.75
Under weight	28	70.00	5	12.50		33	41.25
Overweight	2	5.00	9	22.50		11	13.75
Obese	0	0.00	5	12.50		5	6.25

*=significant at p<0.05, Chi square= 29.388, df=3

Results in Table 4 showed that salivary alkaline phosphatase enzyme (ALP), phosphorous (P) and calcium (Ca) were higher in the healthy group than those in the study group but with no statistically significant difference.

Table 4: Salivary Calcium, Phosphorous and Alkaline phosphatase among groups.

Variables	Groups				t-test	df	p-value
	β-thalassemia		Healthy				
	Mean	±SE	Mean	±SE			
ALP	7.354	1.045	9.026	1.181	1.061	78	0.292*
Phosphorous	18.813	0.928	19.787	0.948	0.733	78	0.466*
Calcium	5.713	0.297	5.946	0.348	0.510	78	0.612*

*=not significant at p>0.05

Findings in Table 5 illustrate an inverse correlation between dmfs / DMFS and all salivary constituents with no statistically significant difference except for ALP, which was present with a statistically significant difference for dmfs, p<0.05.

Table 5: Correlation between salivary constituents and dental caries experience.

Variables		Groups			
		β-thalassemia		Healthy	
		dmfs	dmfs	DMFs	DMFs
ALP	r	-0.318	0.044	-0.156	-0.081
	p	0.046*	0.787**	0.335**	0.620
phosphorous	r	-0.063	0.216	-0.118	0.119
	p	0.701**	0.180**	0.469**	0.464**
calcium	r	-0.201	0.247	-0.241	-0.156
	p	0.213**	0.125**	0.133**	0.336**

r = correlation, p=p value, *=significant at p<0.05, **=not significant at p>0.05

Discussion

In this research, the main objective was to evaluate the beta-thalassemic major children concerning their dental caries experience and their body mass index. Based on previous studies, no clear concepts about this association have been made yet. No available data is found in Iraq that investigated the association between beta-thalassemia and growth retardation, so this study was the first attempt to go deeper into this issue and focus solely on the relation between dental caries and the growth impairment among beta-thalassemia major children.

For the primary teeth, the mean of dental caries experienced by surfaces (dmfs) was greater among beta-thalassemia youngsters than their controls, with a statistical significance difference. This result was in agreement with that of some studies (22,23). On the contrary, it was in disagreement with others (24-26). It was stated that no difference was found between the β -thalassemia and the control groups. The thalassemic children's high caries experience may be ascribed to a lack of desire, poor oral care, and a misalignment of the teeth (27).

Meanwhile, the results also revealed an increase in the mean value of (DMFS) with a statistical significance difference among β -thalassemic children than recorded in their controls. This result follows the findings of some studies (22,27). In contrast, it was the opposite of the conclusions documented by others (25,26), Who were assured that the two groups had a consistent mean value. Several reasons can explain the variation between the studies concerning the mean of dmft /DMFT among the β -thalassemic children, such as variation in the sample size, the place where the study was conducted, the age range of the sample in addition to the variation in the criteria used for the diagnosis (11).

The blame for increasing the cases of dental caries among β -thalassemic children could be explained by the reduction in the concentration of the electrolytes in saliva that was shown to be negatively associated with dental caries in the present study (28). In addition, it could be related to the abnormalities in the endocrine system, which affect the parathyroid functions and bone mass concerning serum ferritin, alkaline phosphatase, and calcium-phosphorus levels after a period following a blood transfusion (which is needed periodically). In addition, lysis of the red blood cell will cause the body's iron level to be raised and then stay in specific tissues, resulting in harm to those tissues. Parathyroid gland damage will affect the hormone secretions essential for maintaining calcium levels in the body, including bone and teeth (29).

There may be an explanation for the high rate of dental caries among children with beta- thalassemia who do not get regular dental treatment or who avoid the dentist for fear that they would not understand their condition (30). An increased prevalence of tooth decay has led to an increase in the number of thalassaemic patients seeking treatment in an emergency due to a lack of attention to their dental care (31). The majority of children with thalassemia major (70 percent) were found to be underweight when their body mass index was calculated (growth retardation), which follows the findings of other studies (32-34). Globally, more than 40% of thalassemic patients have growth retardation. Most of the patients with β -thalassemia major had defects (such as chronic anemia, hyper-metabolism, hypoxia (especially if the children were under-treated), Deferoxamine-induced bone dysplasia and dietary inadequacies, as well as gonadotropin secretion impairments, glandular iron deposition and diabetes, are all possible causes of this growth retardation (35-37).

Saliva constituents are an essential physicochemical characteristic of dental caries. It is mainly composed of water and a low percentage of electrolytes⁽³⁸⁾. Calcium and phosphorus are the main components of teeth; their presence in saliva significantly affects teeth remineralisation. According to this theory, salivary concentrations of hydroxyapatite-related salivary ions should be connected with a patient's dental caries status because caries is a gradual and eventually permanent modification in the hydroxyapatite structure of an impacted tooth^(39,40). Only a few researchers have explored the significance of biochemical components in saliva in oral illness, yet salivary biochemical concentrations play a significant role in oral disease⁽⁹⁾.

A lower amount of ALP in thalassemic youngsters than in healthy ones was discovered by the current study, suggesting that malnutrition may be to blame for this finding. No substantial differences existed across the groups, however. The findings of Rani et al. were in accord with this⁽⁴¹⁾.

The mean value of salivary phosphorus was found to be lower in β -thalassemic children when compared to the control group, which agreed with Siamopoulou et al.⁽⁹⁾ but disagreed with Ghasempour et al.⁽⁴²⁾, who found that the concentration of phosphorus in the β -thalassemia group was higher than their control.

In the present study, lower concentrations of salivary calcium were found among β -thalassemic children. This finding coincided with that of Babu and Shah⁽²³⁾, but it was in disagreement with the results obtained by Dhote et al., who found it higher among the β -thalassemia group⁽⁴³⁾. However, the results of this study failed to show a significant correlation between the salivary elements (Ca, P, and ALP) and dental caries, and that was in agreement with the result documented by AL-Zaidi⁽⁴⁴⁾.

These differences in the salivary minerals could be due to differences in their serum levels that are caused by the disease. This is because the frequent blood transfusions in thalassemia patients can lead to iron overload, which can cause hypogonadism, diabetes, hypothyroidism, hypoparathyroidism, and other endocrine problems⁽⁴⁵⁾.

Conclusion

Thalassemia major is a genetic blood disorder that affects a child's overall health and oral health. Iraqi children with β -thalassemia major had more cavities in both their baby teeth and their permanent teeth than healthy children; dmfs /DMFS values were significantly higher among the study group. They also had growth impairment. Meanwhile, salivary constituents including (ALP, Phosphorous and Calcium) were lower in β -thalassemic children than in their controls. For all of the above, From the moment the condition is discovered, thalassemic children and their parents should be informed about preventing and managing dental caries. The disease process may be slowed down by timely dental treatment and frequent follow-up visits.

Conflict of interest

The authors have no conflicts of interest to declare.

Author contributions

AHMJ; study conception and design. SRA; data collection. AHMJ.; Methodology. AHMJ, FA and SRA; statistical analysis and interpretation of results. AHMJ; original draft manuscript preparation. AHMJ and SRAI; Writing & editing. Supervision; AHMJ. All authors reviewed the results and approved the final version of the manuscript to be published.

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Informed consent

Informed consent was obtained from all individuals (or their guardians) who participated in this study

Conflict of interest

None.

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تسوس الاسنان وضعف النمو بين الاطفال المصابين بالثلاسيميا الكبرى نوع بيتا في العراق/البصرة شيماء رشيد علي , اسيل حيدر محمد جواد , فرقان الوائلي المستخلص:

الخلفية: مرض الثلاسيميا الكبرى هو اضطراب وراثي في الدم يؤثر على صحة الطفل بصورة عامة وصحة الفم بصورة خاصة ويحتاج الى عمليات نقل دم مستمرة مدى الحياة ويعتبر تأخر النمو من الآثار الجانبية الشائعة عند الاطفال والمراهقين المصابين بالثلاسيميا الكبرى ويحتوي اللعاب على مجموعه متنوعة من المواد الكيميائية الحيوية والتي تؤثر على حدوث وشدة تسوس الاسنان الهدف: يهدف هذا البحث الى معرفة ارتباط الثلاسيميا الكبرى بتسوس الاسنان وضعف النمو. المواد وطريقة العمل: لقد تم الفحص في مركز الثلاسيميا/محافظة البصرة. حيث تمت مقارنة 40 طفل من مرضى الثلاسيميا الذين تتراوح اعمارهم بين 10 - 12 سنة مع 40 طفل سليم (الذين كانوا من نفس العمر والجنس مثل مجموعة الدراسة) تم استخدام القياسات الانثروبومترية لتقييم تطورهم البدني وتم اخذ عينه من اللعاب الكامل غير المحفز من كل طفل لتحديد تركيزات اللعاب من الكالسيوم والفسفور وانزيم الفوسفاتيز القلوي. النتيجة: لكل من الاسنان الأولية ولدانميه قيم dmfs/DMFS اعلى بين اطفال الثلاسيميا نوع B مع وجود فرق احصائي عن المجموعة السليمة وتم العثور على نسبة عالية جدا بنقص الوزن عند الاطفال المصابين بالثلاسيميا الكبرى. المكونات اللعابية مثل الكالسيوم والفسفور وانزيم الفوسفاتيز القلوي كانت اعلى في المجموعة السليمة عنها في مجموعة الدراسة بدون فرق ذو دلالة احصائية بين المجموعتين. الاستنتاج: نظرا لقيم dmfs/DMFS التي كانت اعلى بين اطفال الثلاسيميا نوع B وبشكل ملحوظ بين مجموعة الدراسة للأطفال المصابين وكذلك نظرا لضعف النمو عند الاطفال المصابين وفي الوقت نفسه المكونات اللعابية بما في ذلك الفسفور والكالسيوم وال (ALP) التي كانت اقل في B- ثلاسيميا الاطفال مقارنة بمجموعة الاطفال السليمة. لكل ما سبق، من لحظة اكتشاف الحالة يجب ابلاغ اطفال الثلاسيميا واولياء امورهم حول الوقاية من تسوس الاسنان وادارتها وقد تتبأ عملية التسوس عن طريق علاج الاسنان في الوقت المناسب وزيارات المتابعة المتكررة لعيادة طبيب الاسنان.