

Evaluation and Comparison of Salivary Alkaline Phosphatase Levels with Periodontitis and Assessment of Radiographic Features in Patients with Beta-Thalassemia Major

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Abstract

Aim: To compare Salivary Alkaline Phosphatase levels with periodontal health and assess radiographic features using panoramic radiographs of children suffering from beta-thalassemia major.

Materials And Method: Thirty patients with Thalassemia major and thirty healthy patients of age range between 6-18 years were included. Salivary Alkaline phosphatase levels was determined by collection of saliva samples. Plaque index, Gingival index and Periodontal index and Radiographic examinations was carried. Student’s t-test

and Chi-square test was used to compare the means and differences in frequencies between thalassemic group and the control group.

Results: In all tested periodontal parameters, higher frequency of periodontal inflammation was noted in the thalassemic patients as compared with the controls. Strong positive correlation was found between Salivary Alkaline Phosphatase levels and Periodontal inflammation. Radiographic features like thin mandibular cortex, altered bony trabeculae, obliteration of maxillary sinus, absence of inferior alveolar canal, thin lamina dura, taurodontism

and short spiky roots were observed in thalassemic patients.

Conclusion: Thalassemia major may particularly be diagnosed through orofacial abnormalities and for early diagnosis of Periodontitis, saliva could be used as a screening tool for detection of Alkaline phosphatase levels.

Keywords: Thalassemia, Periodontitis, Salivary Alkaline Phosphatase, Radiographic Features

Introduction

The blood diseases present various polymorphic clinical expressions, one of which is relatively constant involvement of oral structures. Amongst various blood disorders hereditary hemolytic anemias are of considerable complexity which encompass a variety of clinical manifestations ranging from benign conditions to complex disorders posing as a public health problem. The inherited disorders of hemoglobin represent the most common monogenic diseases and around 7% of humans are carrying one of the mutations responsible for these disorders.^[1] A minimum estimate suggests that 3,00,000 children are born each year with either sickle cell anemia or one of its variants or a form of thalassemia.^[2] The World Health Organization reports that approximately 60,000 infants with thalassemia major (TM) are born each year.^[3] Thalassemia's are group of congenital anemias that have in common deficient synthesis of one or more of the globin subunits of the normal human hemoglobins. There may be homozygous or heterozygous factors. This has a bearing on the severity of the disease. Person having heterozygous gene (Thalassemia minor) usually has little or no manifestation of the disease whereas, a person having a homozygous gene (thalassemia major) is severely affected.^[4] Typical bone changes result in characteristic thalassemic face: prominent maxillary bones, flat nose bridge, frontal bossing, thinning of long

bones and joint deformities.^[5-7] It is likely that there is an association between Thalassemia major and periodontal health status.^[8-10] However, very few studies have been published on this issue. There have been several attempts over years to establish methods for diagnosis and prognosis of oral diseases by compositional analysis of saliva. Salivary diagnosis is anticipated to be particularly useful in cases where repeated samples of body fluids are needed but where drawing blood is impractical, unethical or both. Defensive responses to periodontal disease are the production of different enzymes, which may be produced or released through stromal, epithelial and inflammatory cells. A variety of important enzymes is released after cell injury and cell death. These are the enzymes that are normally located inside the cells, e.g. alkaline phosphatase, peroxidase, lactate dehydrogenase, creatine kinases, aspartate and alanine aminotransferase. This study aims to correlate Periodontal status with levels of Salivary Alkaline Phosphatase in Beta thalassemia major patients and determine various radiographic features with help of Orthopantomographs.

Materials And Method

The present in vivo study was conducted in the Department of Pediatrics, Rabindranath Tagore Medical college, Udaipur, Rajasthan, India and Department of Pediatric and Preventive Dentistry, Darshan Dental college and Hospital, Udaipur, Rajasthan, India. Ethical clearance was obtained from the Ethical committee to perform clinical and Radiological examination on patients. The study group consisted of thirty patients previously diagnosed with Beta Thalassemia major and control group consisted of thirty healthy patients. The patients and their parents were briefed in their local language regarding the study and prior written consent from patient/parent was taken. Biochemical investigation was carried by collecting the unstimulated whole mixed saliva was from each

subject and sent to Laboratory for estimation of salivary ALP levels. Dental clinical examination was carried in natural light using, mouth mirror, sickle explorer and William's periodontal probe (GDC Dental, POW6). After cleaning and isolation with cotton roll, teeth were divided into Six sextant for recording the following indices:

- Plaque Index (Pl.I) by Silness and Loe (1967)^[11]
- Gingival Index (G.I) by Loe and Silness (1963)^[12]
- Periodontal Index (P.I) by Russell (1956)^[13]

Plaque Index and Gingival Index were modified according to the criteria given by **Wei SH and Lang K (1981)**¹³ for primary and mixed dentition. All the patients were subjected to Digital Panoramic radiographs using the Orthopantomograph machine. The radiographs of the control group were compared with that of the study group to evaluate the following dento-alveolar features: Inferior alveolar canal, Pattern of trabecular bone, Thickness of cortical bone, Maxillary sinus, Short spiky roots, Taurodontism and Lamina dura.

The thickness of the inferior mandibular cortex in the molar region was defined as the distance between the inferior and superior borders of the cortex. Three measurements using the same electronic digital sliding caliper were therefore made on both left and right sides along the long axis of the first molar, which passed perpendicular to the tangent, to the lower border of the mandible. The thickness of the lower border of the mandible was considered to be normal when it measured 6 mm or more and thin when measuring 4 mm or less.

In order for the study to be more objective, a tooth was classified as taurodontic when the distance between the baseline connecting the mesial and distal points of the cemento-enamel junction and the highest point of the floor of the pulp chamber reached or exceeded 3.5 mm.

Data was analyzed using Statistical Package for Social Sciences (SPSS) version 21, IBM Inc. Independent t test,

Mann Whitney U test was used to compare the indices and Salivary ALP levels of the two groups and Pearson's correlation test was done to find the correlation between Periodontal status and Levels of Salivary ALP.

Results

Sex distribution of both thalassemic and control group was equally matched and distributed. The age range of the maximum group of participants was between 9-11 years. Table 1 shows the mean of all tested Periodontal parameters. Plaque index scores of the study group (2.047 ± 0.8403) was found to be significantly more as compared to the control group (1.520 ± 0.6020). More number of patients in Group I (Control group) had either good (26.7%) or fair (46.7%) Plaque index category whereas, in Group II (study group) greater number of patients had poor (60.0%) Plaque index category. Mean of Gingival index score in Group II was found to be higher (2.083 ± 0.6137) as compared to the control group (1.530 ± 0.6859). Greater number (48.3%) of participants in Group II (study group) had moderate gingivitis. Mean of Periodontal index score in Group II was found to be higher (2.033 ± 0.1187) as compared to the control group (1.453 ± 0.6174). Significant differences were seen in mean Periodontal scores among the two groups as $p > 0.05$. Periodontal condition of the patients in Group II (study group) were in the beginning stage (23.3%) of periodontitis and 56.7% of the patients had established periodontal lesion. Salivary ALP levels were found to be significantly more in study group (78.76 ± 28.86) as compared to the control group (55.41 ± 21.15). Significant differences were seen in mean Salivary ALP levels when compared using Mann Whitney U test among the two groups as $p < 0.05$ (Table 2). Strong Positive correlation was seen between Salivary ALP levels and Periodontal index with statistically significant p value in Group II (study group).

Salivary ALP activity was found to be positively correlated with Periodontal index.

On Radiographic examination (Table 3), **the thickness of the inferior mandibular cortex**, as measured in the area of permanent first molar using the digital caliper, was found to be between 1 mm and 4 mm (mean 2.89 ± 0.28). In the majority of patients (60%), the thickness of the inferior border was between 1 mm and 2.5 mm, whereas in the remainder it measured between 3 mm and 4 mm. In contrast, the data of the control group revealed that the thickness of the inferior border was found to be between 3 mm and 6 mm (mean 5.9 ± 0.34). The difference in mean values between the two groups was statistically significant ($P= 0.002$).

Altered Trabecular pattern and large bone marrow spaces were mainly seen in the posterior mandibular region of 17 (56.66%) patients with thalassemia major compared with four (0.89%) of the control group. A highly significant difference ($P= 0.001$) was found between the two groups

In thalassemic patients, **reduced or obliteration of maxillary sinus** was observed in 23 (76.66%) of the assessed panoramic radiographs, while ten (20%) radiographs showed complete absence of such anatomical feature on the radiograph. A highly significant difference ($P= 0.001$) was found between both groups. In the control group, small maxillary sinus was seen in one (0.3%) panoramic radiographs, but complete absence of the sinuses was not seen in this group.

Both borders of the inferior alveolar canal were decisively demonstrated in only fifteen (50%) cases of thalassemia compared with 46 (92%) control group subjects. Complete absence of both superior and inferior borders of the canal was seen in 3 (0.89%) patients. This comparison indicated significant difference ($P= 0.001$) between the two groups.

Taurodontism was noticed in 3 (10%) patients with thalassemia major. A significant difference was detected between the two groups ($P= 0.002$). Taurodonts were more common in the maxilla than in the mandible, and the maxillary first molar was the most common tooth involved, followed by the mandibular first molar.

Thin lamina dura was identified in 23 (46%) thalassemic patients, whereas only three (6.0%) radiographs of the control group showed this radiographic feature. A statistically significant difference ($P= 0.000$) was found between the thalassemic and the control groups.

Spiky roots were seen in 4 (13.33%) radiographs of those with fully developed roots in Group II, whereas only one (0.3%) radiographs of the control group showed this variation in Group I. A statistically significant difference ($p=0.000$) was found to be present between thalassemic and control group.

Discussion

Oral health problems are not life-threatening in Thalassemia major; and as a result, its oral manifestations are not well addressed in the literature. However, the oral health is very closely linked to general health and wellbeing. The recorded Periodontal values of the thalassemia patients were compared with those of the controls. Results of our study showed higher mean values in thalassemic group with respect to Plaque index (2.047 ± 0.8403), Gingival index (2.083 ± 0.6137) and Periodontal index (2.033 ± 0.1187) whereas, lower values were found in healthy counterparts. Previous studies are in accordance with the findings of this study.^[14-21] This may be due to local factors such as malocclusion and drying of the gingiva through the patient's inability to close his mouth over the protruding teeth. The chronic anorexia in some cases may predispose to gingival disorders.^[8, 19] Systemic factors including lowered resistance to infection,

nutritional deficiencies, and chronic anemia may contribute to the complexity of etiology.

Alkaline Phosphatase(ALP) is a calcium- and phosphate-binding protein and a phosphor-hydrolytic enzyme. It is membrane-bound glycoprotein produced by many cells such as polymorphonuclear leukocytes (PMNLs), osteoblasts, macrophages, and fibroblasts within the area of the periodontium and gingival crevice. ALP is an intracellular enzyme present in most of tissues and organs, particularly in bones. The presence of ALP in the saliva is usually indicative of inflammation and destruction of the periodontal tissues. Results confirm that statistically significant positive correlation was found between clinical parameters and ALP levels, which represent periodontal destruction and inflammation.

In present study, **altered bony trabeculae** was found in 56.66% of the thalassaemic subjects. Large bone marrow spaces which were easily and quickly recognized, are one of the most important radiographic features of thalassaemia (Figure 1). This enlargement may be explained by the fact that, when the ineffective erythropoiesis damages the red blood cell membrane leading to severe anemia, the body responds by increasing the production of red blood cells, consequently causing expansion of the bone marrow up to 15–30 times the normal amount.^[22]

Obliteration or reduction in size of maxillary sinuses (Figure 2) were significantly observed in 56.66% of thalassaemic patients. No radiographic sign of the sinus was evident on the radiographs of four subjects. This finding may be attributed to the bone marrow expansion causing hyperplasia of alveolar processes of the maxilla at the expense of the sinus's normal volume.^[22]

Thin mandibular cortex (Figure 3) was exhibited in 40% thalassaemic patients as compared with 30 healthy subjects; therefore, this finding suggests that the thickness of the

inferior border is a valid radiographic criterion of thalassaemia.

The inferior alveolar canal is usually seen on radiographs as two parallel lines of radiopacity: one roofs the canal and the other forms its floor. The radiopaque border of the inferior alveolar canal was not discernible (Figure 4) in 50% of the radiographs of thalassaemic patients in comparison with subjects in the control group. According to **JE Brown and J Porter (1995)**^[22] there is a link between the degree of expansion and thinning of cortical structures of the mandible and the mean hemoglobin of the patient. As the mean hemoglobin decreases, the degree of remodeling increases; thus, such a finding may explain the absence of the two radiopaque lines of the inferior alveolar canal as well as the thinning of the lower border of the mandible. In relation to the significant association between this sign and thalassaemia, caution should be taken prior to any surgical intervention in the area of mandibular molars to avoid injury to the inferior alveolar nerve.

Taurodontism (Figure 7) is usually diagnosed through a radiographic examination. The results of the present study have shown an overall prevalence of taurodontism of 14% for the thalassaemic group. Our findings suggest that taurodontism may be a feature to be considered in thalassaemia major.

Thin or Faint Lamina Dura (Figure 6) was observed in 16.66% of the thalassaemic subjects. This may be explained due to osteopenic or osteoporotic changes that occur in Thalassaemia Major.

Conclusion

1. Thalassaemia Major patient population demonstrated increased levels of Gingival and Periodontal inflammation compared to healthy counterparts.

2. Levels of Salivary Alkaline phosphatase were raised in Thalassemia Major patients and found to be in correlation with periodontal disease status.
3. Radiographic analysis revealed that most of the thalassemia major patients exhibited thinned mandibular cortex, altered trabecular pattern, enlarged marrow spaces, small or obliterated maxillary sinus, faint lamina dura and taurodontism.

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Legend Figures and Tables



Figure 1: Panoramic Radiograph showing altered trabecular pattern and enlarged marrow spaces in the alveolar bone.

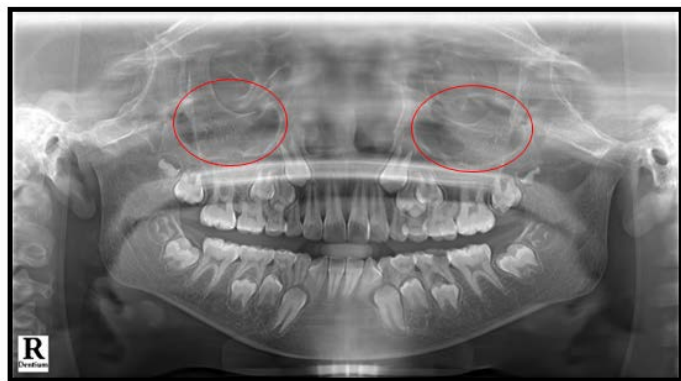


Figure 2: showing obliteration and reduction in size of maxillary sinus.



Figure 3: showing Thinned mandibular cortex



Figure 4: showing absence of inferior alveolar canal



Figure 5: showing short spiky roots of mandibular and maxillary molars



Figure 7: Showing Taurodontism of Mandibular molars



Figure 6: showing thin Lamina dura in multiple teeth

Table 1: Periodontal conditions of patients with beta thalassemia major as measured by Plaque index (Pl.I), Gingival index (G.I) and Periodontal index (P.I)

Groups	Plaque index (mean ± SD)	Gingival index (mean ± SD)	Periodontal index (mean ± SD)
Thalassemic Group	2.047± 0.8403	2.083± 0.6137	2.033± 0.6504
Control Group	1.520± 0.6020	1.530± 0.6859	1.453± 0.6174

Table 2: Group wise comparison of mean Salivary ALP levels

		Mean	Std. Deviation
Salivary ALP levels	Control group	55.4100	21.15166
	Thalassemic group	78.7653	28.86559
p value	< 0.001		

Table 3: Frequency of occurrence of Radiographic features in patients with beta-thalassemia major compared with control group.

Variables	Thalassemic group	Control group
Thin mandibular cortex	12 (40%)	4 (1.2%)
Altered bony trabeculae	17 (56.66%)	3 (0.89%)
Obliteration of maxillary sinus	23 (76.66%)	1 (0.3%)
Absence of inferior alveolar canal	15 (50%)	3 (0.89%)
Thin lamina dura	5 (16.66%)	1 (0.3%)
Taurodontism	3 (10%)	2 (0.6%)
Short spiky roots	4 (13.33%)	1 (0.3%)

Graph 1: Radiographic features of patients with β -thalassemia major using panoramic radiograph

