the Journal of CONTEMPORARY DENTAL PRACTICE at www.thejcdp.com
Volume 7 Number 4 September 1, 2006

Dental Development in Subjects with Thalassemia Major

Abdalla M. Hazza'a, BDS, MDSc, DDSc;
Ghaida Al-Jamal, BDS, MS, Dip ABOMR

Abstract

Aim: The aim of this study was to evaluate the dental development of patients with β-thalassemia major and to compare it with unaffected children.

Methods and Materials: Panoramic radiographs of 44 thalassemic patients taken before the age of 16 years were examined. The subjects consisted of 29 males and 15 females ranging in age from 4.9 to 15.7 (mean = 10.8±2.9) years and 44 controls matched for age and sex. The seven left mandibular permanent teeth, second molar to central incisor, were rated on an eight stage scale using the methods described by Demirjian et al.[10] The stage of each tooth was converted to the corresponding numeric value and then all values were added to obtain a dental maturity score which corresponded to a dental age. Dental and chronologic ages were compared using a paired t-test. The relationship between the chronologic age and the amount of delay was also determined.

Results: Thirty-nine patients had a delay in the development of their dentition. The mean developmental dental delay was found to be 1.01 years ($p<0.05$). The range in delay was from 0.1 to 2.9 years. There was no significant difference between the mean chronologic and dental age of the control group ($p> 0.05$). The amount of delay in dental development increases as the patient's age increased ($p<0.05$). Males were found to have a greater delay (mean 1.16 years) than females (mean delay 0.73 years), but this difference was not statistically significant.

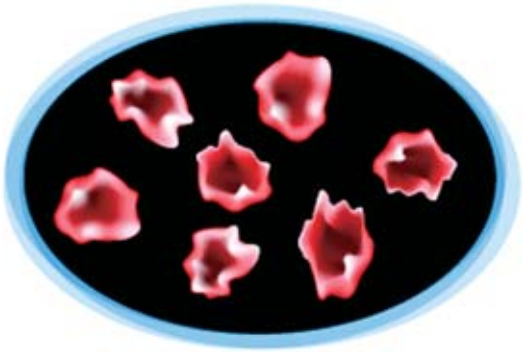
Conclusions: The delay in dental development in β-thalassemia major varied according to the patient's age. This positive correlation parallels the general growth of thalassemic children.

Keywords: Radiography, panoramic, thalassemia major, tooth development

Citation: Hazza'a AM, Al-Jamal G. Dental Development in Subjects with Thalassemia Major. J Contemp Dent Pract 2006 September;(7)4:063-070.

Introduction

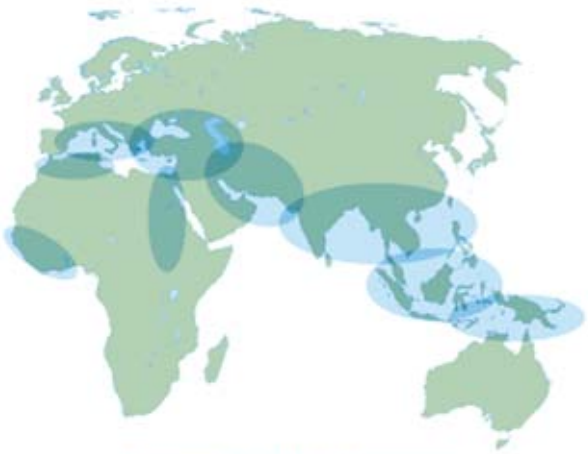
Hemoglobinopathies are the most commonly autosomal recessively inherited diseases in humans with an estimated 240 million carriers worldwide and 200 thousand homozygotes or compound hetrozygotes born each year.[1] One of these hemoglobinopathies is thalassemia. Thalassemias are a diverse group of genetic blood diseases characterized by the absence or decreased production of globulin protein chains. This results in microcytic anemia of varying degrees referred to as α and β types.[2] Based on their clinical and genetic orders thalassemias are classified mainly into major (homozygous) and minor (heterozygous) types.[3] Beta thalassemia major (Cooley's anemia) is the most severe form of congenital hemolytic anemia. It results from the abnormal synthesis of the β-chain hemoglobin usually starting to manifest as early as 4-6 months of prenatal life during the switch from HbF to HbA. Patients usually have a hematocrit of about 20%, and they usually develop all the complications of chronic anemia including growth retardation.[4,5]



Red Blood Cells of Patient With Thalassemia Major

The clinical picture of a patient with β-thalassemia does not become apparent until six months of age, whereas the α-type affects the fetus and is noted at birth. Untreated thalassemic patients have accumulations of unpaired globin chains that are not soluble in blood and precipitate within red blood cell precursors as inclusion bodies. Oxidative membrane damage occurs as a result of the accumulation of these inclusion bodies with subsequent death of the precursor cells within the bone marrow.

Additionally, there is a massive decrease in mature red blood cell production caused by hemolysis within the marrow and sequestration of these cells by the spleen leading to severe anemia. The body responds by increasing the production of red cells resulting in bone marrow expansion as well as extramedullary haemopoiesis. Patients with thalassemia major may die in early childhood from the complication of anemia if not treated. Multiple blood transfusions prolongs life to the age of 15-25 years and improves growth.[6] Growth retardation occurs invariably in thalassemia major mainly after the age of seven.[7]



Areas with a High Frequency of Thalassemia Disorders

These disorders have a markedly high frequency in the Mediterranean area, the Middle East, the Indian subcontinent, and Far East Asia where they represent a major public health problem. However, because of migration of the population, β thalassemia has spread to Continental Europe, North and South America, and Australia. Jordan has a considerable number of thalassemic patients and a large number of carriers (4-6%) of the total population.[8] In Irbid, the largest city after the capital Amman, the overall prevalence of thalassaemia is 5.93%,[8] while that of thalassaemia major is 0.1%.[9]

Although β thalassemia major is one of the most common genetic disorders causing major public health problems, the literature shows dental development in subjects with thalasaemia major has not been studied. Therefore, the aim of this study was to compare the dental maturity of a group of patients with β thalassaemia major with age and sex matched healthy controls.

Methods and Materials

The data for this study were collected from patient records in the Department of Orthodontics of the Faculty of Dentistry at the Jordan University of Science and Technology. The sample consisted of 44 panoramic radiographs of 29 male and 15 female patients with thalassemia major. The ages ranged from 4.9 to 15.7 (mean = 10.8±2.9) years. The radiographs were taken prior to dental treatment. For the purpose of comparison and to attempt to determine the validity of the findings obtained from examining the panoramic radiographs of the thalassaemic patients, a total of 44 panoramic radiographs of a control group matching in age and sex were selected randomly from the patient records of the same department. In order to assess the degree of dental development and chronologic age, the thalassaemic patients were divided into two groups. In group 1 the patient's age was ≤ 8 years old (mean age was 7.18±1.0 years). In group 2 the patient's age was > 8 years old (mean age was 12.13±2.32 years).

The panoramic radiographs were examined under ideal conditions including the use of subdued ambient room lighting, film masking, and a conventional viewing box (Exal-Type F.I.D-1, Basingstone, England) with a variable light intensity and a 2X magnifying lens (X-viewer, Malmo, Sweden). The panoramic radiographs were used to assess patient's dental ages by employing the method of Demirjian et al.[10] The radiological appearances of the seven permanent teeth on the left side of the mandible for each patient were evaluated according to developmental criteria. Each tooth was categorized into one of the eight calcification stages (A-H). Stage A is defined as the start of calcification at the most occlusal part of the tooth crypt in the form of a small inverted cone. Stage H is defined as the stage in which the apical end of the developing root is complete and the periodontal ligament space has a uniform width around the root and its apex. The intermediate stages establish a continuum. A numerical score for each tooth was then obtained using standard references for each stage, and the summed scores on all seven teeth give a dental maturity score which is converted directly into a dental age.

Before the actual research the subjects' radiographs were evaluated by two investigators who were calibrated through daily exercises on random panoramic radiographs using Demirjian's protocol, and then all radiographs were scored by the investigators independently. Of the 308 teeth scored, the level of agreement was 91.2% and never exceeded one stage.

Statistical Analysis

The data obtained were analyzed using the Statistical Package for the Social Sciences (SPSS). Means and standard deviations were calculated for each group. The difference between chronological and dental age was tested by student's paired t-test. The correlation between amount of dental development and chronological age was also determined. A statistically significant difference was considered to be present when P values were < 0.05.

Results

Of 44 thalassaemic patients, 39 demonstrated a delay in the development of their dentition. The range was from 0.1 to 2.9 years with an average of 1.01±0.83 years delay (Table 1). As shown in Table 2, the mean difference between chronologic and dental age was found to be statistically significant (p=0.00). In contrast, there was no significant difference between the mean chronologic and dental age of the control group (p=0.12).

Figure 1 shows a scattergraph of the relationship between the amount of delay and the chronologic age of the thalassaemic patients. The figure clearly shows that as the age of the thalassaemic patient increases the amount of dental development delay also increases (p<0.05). This is further confirmed by the fact that of the five cases that did not show delay in the dental development four were below the age of 8 years.

Table 1. Dental maturity of children with thalassaemia major.

Patient No.	Sex	Chronologic age	Dental age	Difference
1	Female	7.46	7.6	0.14
2	Female	4.3	4.2	-0.1
3	Female	8	7.8	-0.2
4	Female	8	7.5	-0.5
5	Female	11.46	12	0.54
6	Female	8.5	7.3	-1.2
7	Female	11.08	11.6	0.52
8	Female	11.5	10.4	-1.1
9	Female	12.3	11.8	-0.5
10	Female	14.9	12.7	-2.2
11	Female	12	9.3	-2.7
12	Female	15.75	14.6	-1.15
13	Female	13.3	12	-1.3
14	Female	8.2	7.7	-0.5
15	Female	12.5	11.8	-0.7
16	Male	8	7.1	-0.9
17	Male	6	5.4	-0.6
18	Male	7.1	7.6	0.5
19	Male	6.33	6.8	0.47
20	Male	7.36	6.6	-0.76
21	Male	7.48	6.9	-0.58
22	Male	7.9	7.6	-0.3
23	Male	8.6	8.1	-0.5
24	Male	13.75	12.1	-1.65
25	Male	9.2	7.8	-1.4
26	Male	14.17	13.1	-1.07
27	Male	8.9	7.3	-1.6
28	Male	9.15	7.8	-1.35
29	Male	13.9	11	-2.9
30	Male	14.3	12.5	-1.8
31	Male	13.5	11.6	-1.9
32	Male	10.3	9.5	-0.8
33	Male	15.2	13.5	-1.7
34	Male	11.3	10.7	-0.6
35	Male	9	8.4	-0.6
36	Male	14	12.5	-1.5
37	Male	15.78	14.4	-1.38
38	Male	10.2	9.6	-0.6
39	Male	14.17	12.3	-1.87
40	Male	14.28	12.8	-1.48
41	Male	13.42	12.1	-1.32
42	Male	14.28	12.5	-1.78
43	Male	10.2	8.9	-1.3
44	Male	11.25	8.8	-2.45

Table 2. Dental maturity scans with respect to thalassemia and controls.

	Dental Age (mean)	SD	SE	Max	Min	Chron. age (mean)	SD	SE	Max	Min
Thalassemia										
Male	9.83	2.56	0.47	14.40	5.40	11.00	3.04	0.56	15.20	6.00
Female	9.88	2.79	0.72	14.60	4.20	10.61	3.10	0.80	15.78	4.30
Total	9.85	2.60	0.39	14.60	4.20	10.86	3.00	0.45	15.78	4.30
Controls										
Male	10.03	2.28	0.42	14.40	6.60	10.00	2.44	0.45	14.15	6.50
Female	10.21	3.42	0.88	16.00	4.20	10.02	3.35	0.86	15.89	4.10
Total	10.12	2.69	0.40	16.00	4.20	10.01	2.75	0.41	15.89	4.10

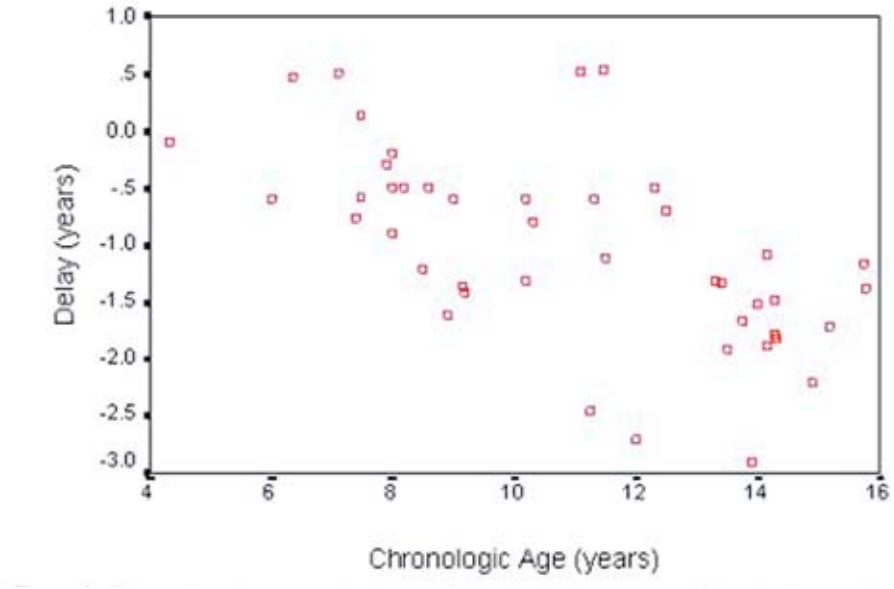


Figure 1. The relationship between the degree of delay in the development of the dentition and the chronologic age in thalassaemia major patients.

In thalassemic patients below the age of eight years there was no significant difference between the dental and chronological ages (p=0.10). The mean dental developmental delay in this group was 0.25 years. In contrast, in those above the age of eight years there was a significant difference between chronologic and dental age (p=0.00) with the mean developmental delay increased to 1.26 years. Males were found to have a greater delay (mean 1.16 years) than females (mean delay 0.73 years), however, this difference was not statistically significant.

Discussion

Determination of the dental age is important to those involved in the treatment of β thalassemia major. It is particularly useful to the orthodontist in the treatment planning for different types of malocclusion relative to maxillofacial growth. It is also of great importance to pediatric dentists concerned about the stage of development and time of eruption. Two methods were described to determine the dental age by either using tooth eruption[11] or by judging the root formation on panoramic radiographs.[10]

However, dental eruption and dental development are two separate processes. Several local factors affect tooth eruption such as, extraction of a deciduous tooth, ankylosis, and impaction or crowding of the permanent teeth.[10,12-14] In contrast, the development of the permanent teeth is not affected by the status of the primary dentition.[15-17] Therefore, tooth formation is a more reliable indicator to evaluate dental maturity than tooth eruption.[10] Furthermore, several authors concluded the use of dental development as an index of chronologic age is superior to any other developing organs or structures.[18-20] However, some criticism may arise regarding the conversion to dental age for the sample in this study since it was developed for a different population. Nevertheless, the normal control group in our study showed a close correlation between dental and chronologic ages indicating tooth development in this group similar to the normal values established by Demiriian et al.[10]

Several studies on the effect of bone marrow expansion on the craniofacial skeleton have shown enlargement of the maxilla, bossing of the skull, prominent molar eminences,[21,22] increased overjet and spacing of maxillary teeth, and other degrees of malocclusion[23-25] were the most significant findings. In some cases the lamina dura may be thinned and the roots of the teeth are shortened.[26] Delayed eruption of both deciduous and permanent teeth and high frequency of caries were also observed.[27]

In the present study an additional dental anomaly not recognized in this disorder has been demonstrated. There was a significant delay in the development of thalassemic dentition with an average of 1.01 years. Another finding of significance was the correlation between the amount of delay and the chronologic age. An increase in delay of dental development results as the thalassemic patient gets older. Growth retardation occurs invariably in β thalassemia major especially after the age of seven years.[7] The suggested causes of growth retardation and delay of bone maturation are chronic anemia,[30] endocrine dysfunction,[6] and somatomedin deficiency.[31] Furthermore, Logothetis et al.[29] have shown the patient's age and duration of clinical symptoms, severity of anemia, and the timing of both splenectomy and transfusion therapy were important in determining the development of craniofacial deformities. Considering the significant correlation between dental and skeletal development reported in the literature,[28] the amount of delay in tooth development in thalassemic patients is likely to be a direct manifestation of the general spectrum observed in this condition. This could explain the lack of significant difference between the dental and chronological ages in the thalassemic patients below the age of eight years and the presence of a significant difference in those above eight years of age.

Finally, the results obtained in this study are not conclusive due to the sample size and should be interpreted with caution. Further studies using a larger sample are necessary to confirm these findings and to elucidate precisely the reasons for this variation.

Conclusion

The present study showed the development of the thalassemic dentition is significantly delayed by approximately one year. The amount of delay progressively increases as the thalassemic patient becomes older, supporting findings of other studies that have demonstrated the same pattern in the general growth of the thalassemic patients.

References

1. World Health Organization. Community control of hereditary anemias. Bull World Health Organ. 1983; 61:63-80.
2. Duggal MS, Bedi R, Kinsey SE, Williams SA. The dental management of children with sickle cell disease and b-thalassaemia: a review. Int J Paed Dent 1996 6:227-234.
3. Weatherall JD, Clegg JB. The Thalassaemia Syndromes, 3rd ed, Oxford: Blackwell; 1981:132-174.
4. Kazazian HJ Jr. The thalassemia syndromes: molecular basis and prenatal diagnosis. Semin Hematol 1990;27:209-228.
5. Forget BG. The pathophysiology and molecular genetics of beta thalassemia. Mt Sinai J Med 1993;60:95-103.
6. Flynn DM, Fairney A, Jackson D, Clayton BE. Hormonal changes in thalassemia major. Arch Dis Child 1976;51:828-836.
7. Lapatsanis P, Divoli A, Georgaki H, Pantelakis S, Doxiades S. Bone growth in thalassemic children. Arch Dis Child 1978;53:963-965.
8. Sunna EI, Gharaibeh NS, Knapp DD, Bashir NA. Prevalence of hemoglobin S and beta-thalassemia in northern Jordan. J Obstet Gynaecol Res. 1996; 22:17-20.
9. Babiker MM, Bashir N, Sarsour N. Prevalence of thalassemia in schoolchildren in north-eastern Badia, Jordan. East Mediterr Health 1999;5:1165-1170.
10. Demirjian A, Goldstein H, Tanner JM. A new system of dental age assessment. Hum Biol 1973;45:211-227.
11. Hägg U, Taranger J. Maturation indicators and the pubertal growth spurt. Am J Orthodontics 1982;82:299-309.
12. Fanning EA. Effect of extraction of deciduous molars on the formation and eruption of their successors. Angle Orthod 1962;32:44-53.
13. McDonald RE. Dentistry for children and adolescent. St Louis: CV Mosby;1969.
14. Posen AL. The effect of premature loss of deciduous molars on premolar eruption. Angle Orthod 1965;35:249-252.
15. Fanning EA. A longitudinal study of tooth formation and root resorption. N Z Dent J 1961;57: 202-217.
16. Demirjian A, Dubuc MB, Jenicek M. Étude comparative de la croissance de l'enfant Canadian d'origine française a Montreal. Can J Publ Health 1971;62:111-119.
17. Sapoka AM, Demirjian A. Dental development of the French Canadian child. J Can Dent Assoc 1971;37:100-104.
18. Lewis AB, Garn SM. The relationship between toothformation and other maturational factors. Angle Orthod 1960;30:70-77.
19. Moorrees CFA, Flanning EA, Hunt EE. Age variation of formation stages for ten permanent teeth. J Dent Res 1963;42:1490-1502.
20. Anderson DL, Thompson GW, Popvich E. Age of attainment of mineralized stages of the permanent dentition. Forensic Sci 1976;21:191-200.
21. Kaplan RI, Werther R, Castano FA. Dental and oral findings in Cooley's anemia: a study of fifty cases. Ann NY Acad Sci 1964; 119: 664-666.
22. Cannel H. The development of oral and facial signs in β thalassaemia major. Br Dent J 1988; 164: 50-51.
23. Van Dis ML, Langlais RP. The thalassemias: Oral manifestations and complications. Oral Surg Oral Med Oral Pathol 1986; 62: 229-233.
24. Hes J, Van der Waal I, De Man K. Bimaxillary hyperplasia: the facial expression of homozygous β thalassaemia. Oral Surg Oral Med Oral Pathol 1990; 69: 185-190.
25. Elham SJ, Abu Alhaija ESJ, Hattab FN, Al-Omari MAO. Cephalometric measurements and facial deformities in subjects with β thalassaemia major. Eur J Orthod 2002; 24: 9-19.
26. Poyton HG, Davey KW. Thalassaemia: Changes visible in radiographs used in dentistry. Oral Surg Oral Med Oral Pathol 1968 25: 564-576.

27. De Mattia D, Pettini PL, Sabato V, Rubini G, Laforgia A, Schettini F. Oromaxillofacial changes in thalassemia major. Minerva Pediatr. 1996 ;48:11-20.
28. Sierra AM. Assessment of Dental and Skeletal Maturity, A New Approach. A comparison of radiographic methods of assessing skeletal and dental maturation, and an evaluation of the correlations among the various maturity indicators in the 8-12 year age. Angle Orthod 1987;57: 194-208.
29. Logothetis J, Economidou J, Constanttoulakis M, Augoustaki O, Loewenson RB, Bilek M. Cephalofacial defotmities in thalassemia major (Cooley's anemia): A correlative study among 138 cases. Am J Dis Child 1971;121:300-306.
30. Caffey J. Cooley's anemia: a review of the roentgenographic findings in the skeleton. Am J Roentg 1957;78:381-391.
31. Saenger P, Schwartz E, Markenson AL, Graziano JH, Levine LS, New MI, Hilgartner MW. Depressed serum somatomedin activity in beta-thalassemia. J Pediatr 1980;96:214-218.

About the Authors

Abdalla M. Hazza'a, BDS, MDSc, DDSc

Dr. Hazza'a is an Assistant Professor of Oral and Maxillofacial Radiology in the Department of Oral Medicine and Oral Surgery of the Faculty of Dentistry at the Jordan University of Science and Technology in Irbid, Jordan.

e-mail: hazza@just.edu.jo

Ghaida Al-Jamal, BDS, MS, Dip ABOMR

Dr. Al-Jamal is an Assistant Professor of Oral Radiology in the Department of Oral Medicine and Oral Surgery of the Faculty of Dentistry at the Jordan University of Science and Technology in Irbid, Jordan.

e-mail: ghaidaa@yahoo.com