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ORIGINAL RESEARCH

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Assessment of orthodontic treatment needs in patients with β-thalassemia major and sickle cell disease

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Abstract

Patients suffering from hemoglobinopathies may suffer from pathogic dental and orofacial features. This study aimed to assess the prevalence of malocclusion and the need for orthodontic treatment in patients with β-thalassemia major (BTM) and sickle cell disease (SCD). The study was conducted on 311 blood transfusion-dependent patients with BTM or SCD and 400 healthy individuals aged 10 to 16. The types of malocclusion were evaluated based on Angle's classification and Dewey's modification, and their oral habits were recorded using a questionnaire. The need for orthodontic treatment was assessed through the Dental Health Component of the Index of Orthodontic Treatment Need (IOTN), and the data were compared with normal participants. The Index of Orthodontic Treatment Need-Dental Health Component (IOTN-DHC) assessment showed that patients had a higher prevalence of objective need for treatment (IOTN grades 4 and 5) compared to healthy children. The prevalence of class II malocclusion was significantly higher in patients. Patients showed significantly less Angle's Class I malocclusion compared to normal participants. Oral habits were presented in 61%, 64.15% and 62.4% of normal participants, BTM and SCD patients, respectively. The higher prevalence of Angle's class II malocclusion and higher percentage of IOTN grade 4 and 5 among BTM and SCD patients reveal the importance of early orthodontic assessment and intervention in children with BMT and SDC.

Keywords

Orthodontic treatment need; Sickle cell disease; Beta thalassemia major

1. Introduction

Oral and dental management of patients with blood disorders, especially in recent years, has been one of the topics of interest to dental professionals [1]. Orthodontics is a field in dentistry that deals with diagnosing, preventing, and correcting dentofacial abnormalities. This goal is expressed in patients with altered orofacial features and severe malocclusions [2]. Many patients with blood disorders, such as coagulopathies and anemias fall in this category [3]. In life-threatening illnesses, managing the patient's main diseases proper becomes the priority of treatment. This leads to ignoring less grave conditions, such as oral and dental problems, which may eventuate in deterioration of such conditions and consequently, demanding more complex treatment strategies [3].

Hemoglobinopathies are inherited autosomal recessive diseases that influence the production and structure of the hemoglobin molecule. The most prevalent hemoglobinopathies are sickle cell disease (SCD), alpha (α)-thalassemia, and Beta (β)-thalassemia [4]. The high rate of hemoglobinopathies in Iran has been attributed to consanguineous marriages and intermediate malaria endemicity in some provinces [5]. Thalassemia is a heterogeneous group of congenital disorders characterized by defective hemoglobin synthesis that reduces red blood cells' survival and their precursors in the bone marrow [6]. Thalassemic patients, especially those suffering from Beta (β)-thalassemia, experience bone deformities due to bone marrow expansions, dentition protrusion and flaring, severe malocclusion, trabecular enlargement, and maxillary hyperplasia [6]. In its turn, sickle cell disease is the most frequent monogenic disorder (homozygosity for Glu6Val mutation) in the beta-globin gene, which produces hemoglobin S. Reports confirm that more than 300,000 infants are born with the disease each year, and it is estimated that this number will increase to more than 400,000 by 2050, both in low-income and high-income countries [7, 8]. Patients with sickle cell disease experience orofacial deformities, maxillary expansions, exaggerated protrusion of the midface, and craniofacial alterations. Craniofacial skeletal alterations and orthodontic conditions are prevalent manifestations of sickle cell disease and thalassemia patients. These are the outcome of extramedullary hematopoiesis and erythroid hyperplasia and lead to eating, speech, and emotional complications [9, 10]. The severity of hemoglobinopathy, patients' age, and treatment strategy influence these abnormalities. Patients

with these deformities and manifestations often have social appearance anxiety and functional disorders that affect their quality of life. Dealing with orthodontic conditions in these patients requires advanced treatment strategies, such as the use of several appliances, and surgical approaches [11].

Although, due to the mentioned reasons, these diseases are common globally, the long-term treatment needs of these patients have led to the negligence of their other disorders. In addition, the lack of comprehensive guidelines for managing orthodontic conditions in these patients makes it important to assess the orthodontic treatment needs [10]. The general dentists and specialists, including pediatric dentists and orthodontists should be cognizant of the patient's previous medical history and the specific measures involving the clinical management of patients with hemoglobinopathies. These health providers are responsible for following the patients closely, becoming involved in the treatment process, and referring them to other clinicians when need be. To elaborate, these patients are commonly submitted to blood transfusion, which exposes them to the risk of contamination by microorganisms; therefore, essential care should be taken to provide sufficient infection control measures during the treatment process. In addition, measures should be taken to provide a stress-free environment for the patients so that their adequate body temperature and oxygenation could be maintained throughout treatment sessions [12].

Various studies evaluated the malocclusion and the need for orthodontic treatment in different population sectors, but there is a paucity of studies on patients with blood disorders. Therefore, the primary aim of the present study was to assess the types of malocclusion and orthodontic treatment needs in children suffering from transfusion-dependent sickle cell disease and beta thalassemia patients using the Orthodontic Treatment Need-Dental Health Component (DHC) Index.

2. Materials and Method

2.1 Study population

This cross-sectional study was conducted at the orthodontics sector of dental clinics in Tehran and Isfahan provinces, Iran. The children with thalassemia or sickle cell disease were selected on a random basis from the patients regularly attending for transfusion in the thalassemic ward at Iranian Blood Transfusion Organization sites in the above-mentioned provinces. All patients aged 10 to 16 years old visiting the transfusion department during the study period were assigned to the examiners for the evaluation of the types of malocclusions and IOTN scale. One of the patients with sickle cell disease was excluded from the study due to diabetes.

Inclusion criteria for the present study included being diagnosed of sickle cell decease or beta-thalassemia who were between 10 and 16 years of age, not affected by underlying mental or other systemic conditions, with no previous history of orthodontic treatments. Individuals with dental and craniofacial anomalies and underlying systemic diseases, such as bronchial asthma, exocrine disorders, and autoimmune inflammatory disease and those who were uncooperative during the dental examination were excluded. The control group comprised four hundred sex- and age-matched children who were selected randomly from different schools in the region of the study whose data were then recorded. To get the control subjects who were representative of the real population, for each schooling level, *i.e.*, primitive, junior, and high school, both public and private systems of education were randomly selected in Isfahan and Tehran provinces and samples were proportionally allocated from each selected school. Then, sampling frames of the control population were obtained from the list of 10- to 16-year-old students from each school, and the lottery method was used to get control subjects.

2.2 Examination and data collection

A structured questionnaire was designed to collect oral habits as well as the DHC component of the IOTN scale. The questionnaire for oral habits was designed according to Alighieri *et al.* [13] study and indicated several types of these habits. The examination for evaluating the types of malocclusion was made according to the molar relationship and the criteria for orthodontic treatment needs grade were laid down by IOTN. The clinical exam was performed by two orthodontists, seven dental interns (data collectors), and an experienced supervising orthodontist. The examination followed standard protocols using a disposable mouth mirror, digital caliper, flashlight, latex gloves, and sterilized gauze. The DHC component of IOTN was determined by measuring the malocclusion on the study casts using a digital caliper component. All examiners were trained and calibrated to use the IOTN scale to assure data quality before the examination began. Examiners were evaluated on a set of twenty plaster casts previously examined, and the casts were examined one week later and evaluated using Kappa statistics. The intra-examiner agreement was employed to assess the correlation between the examiners and gold standard (intraclass correlation coefficient = 0.91 for both examiners). Case sheets were reviewed at the end of every day to ensure the accuracy of participants' data. Patients' malocclusions were classified based on Angles' classification with Dewey's modification [14–16]. IOTN-DHC is used to determine Orthodontic Treatment Need based on severity of patient's malocclusion, graded from 1–5, with 5 being the most severe.

2.3 Statistical analysis

Data analyses were performed using Statistical Package for the Social Sciences (Ver. 16.0, IBM®, Chicago, IL, USA). The frequency of types of malocclusion was assessed by determining the percentage of participants affected. The differences between sex groups were assessed using the chi-square test, and the significance level was established at $p < 0.05$. Descriptive statistics were calculated for variables and the DHC grades of the IOTN.

3. Results

The details of age and gender distribution of the participants are given in Table 1. In the present study, 311 patients (220 males and 91 females, mean age 12.67) suffering from transfusion-dependent sickle cell disease and beta-thalassemia who were

TABLE 1. Age and gender distribution of the study participants.

Sex	Beta thalassemia		Sickle cell disease		Control	
	N (%)	Mean age	N (%)	Mean age	N (%)	Mean age
Males	116 (37.29)	12.70	104 (33.44)	12.62	218 (54.5)	12.66
Females	43 (13.82)	12.52	48 (15.43)	12.58	182 (45.5)	12.49
Total	159	12.61	152	12.58	400	12.51

referred for blood transfusion were examined to assess the frequency of oral habits, types of malocclusion, and evaluate the orthodontic treatment needs using IOTN-DHC. All participants were between 10 and 16 years old.

3.1 Oral habits

Oral habits were present in 63.8% (n = 97), 62.2% (n = 99) and 61% (n = 244) of sickle cell, beta-thalassemic patients, and healthy participants, respectively (Table 2). Thumb sucking was the most frequent, followed by finger sucking and nail biting. No statistical differences were reported between patients (BTM/SCD) and normal participants for any specific oral habit, but nail-biting habit was more prevalent in female subjects ($p < 0.05$). The mean age of patients with thumb sucking habit was 11.81 years old. Regardless of being in control or patient groups, female participants (62.6%) showed a greater prevalence of oral habits than male (51.3%) subjects ($p < 0.02$). Among children with sickle cell diseases, beta thalassemia and healthy population, 28, 30 and 103 subjects had more than one habit, respectively. The two oral habits occurring most simultaneously were thumb sucking and pencil biting reported in 8, 10 and 16 subjects with sickle cell diseases, beta thalassemia and healthy population, respectively.

TABLE 2. The distribution of oral habits in the total study population.

Oral habits	SCD (n = 152)		BTM (n = 159)		Control (n = 400)	
	N	%	N	%	N	%
Any habits	97	63.8	102	64.1	244	61.0
Thumb sucking	42	27.6	49	30.8	144	36.0
Finger sucking	35	23.0	32	20.1	104	26.0
Nail biting	31	20.3	31	19.4	88	21.7
Lip biting	24	15.7	22	13.8	45	11.2
Pencil biting	11	7.2	13	8.1	21	5.2
Tongue thrusting	9	5.9	11	6.9	17	4.2
Other habits	36	23.6	31	19.4	84	21.0

Note: Some participants had more than one oral habit. SCD: sickle cell disease; BTM: β-thalassemia major.

3.2 Occurrence of Malocclusion

The analyzed data in our study reveals that Angle's Class II malocclusion occurrence was significantly higher in patients (BTM/SCD) than in the normal population ($p < 0.01$). Patients show significantly fewer Angle's Class I malocclusion compared to the normal participants ($p < 0.01$). In addition, the Class I type I subgroup was significantly fewer in SCD and BTM patients in comparison with the control subjects (Table 3). No differences in the distribution of malocclusion classes were found between genders nor between BTM and SCD patients.

3.3 IOTN dental health component assessment

The evaluation for intraexaminer reliability indicated a high agreement between the first and second readings (Kappa value = 0.91). Table 4 summarizes the prevalence rate of the IOTN-DHC grades in both patient and normal groups. Clinical examination records showed an objective need for orthodontic treatment (grades 5 and 4 of the IOTN) in 127 subjects (74 children with hemoglobinopathies and 53 children of the control group). Borderline and little need for orthodontic treatment (grades 3 and 2) were registered in 191 BTM/SCD patients and 282 control subjects. Sixty-five percent of the control population presented no need for orthodontic treatment (grade 1), while this ratio was less in both sickle cell disease and beta thalassemia patients ($p < 0.05$). IOTN-DHC scores showed orthodontic treatment need grades were significantly higher in sickle cell disease and beta thalassemia compared with the control population ($p < 0.01$). No statistically significant difference was reported between genders for any grade of IOTN-DHC.

Increased overjet was the most common types of dental problem among sickle cell and beta thalassemic patients (25% and 26.4%), followed by crowding (12.5% and 9.43%), deep overbite (9.86% and 15.78%), and spacing (5.2% and 7.5%). Increased overjet was significantly higher in patients compared to control children (25.72% *vs.* 14.75%) ($p < 0.01$). In addition, buccal crossbites, as well as tooth displacement, were significantly fewer in control children compared to the patients ($p < 0.01$). No significant differences in the malocclusion parameters distribution were found between genders or between sickle cell and beta thalassemic patients. IOTN-DHC parameters did not showed any statistically significant difference between SCD and BTM patients.

4. Discussion

The current study represents the first epidemiologic, and orthodontic investigation carried out on an Iranian population of patients with transfusion-dependent sickle cell disease and beta-thalassemia. Regarding oral habits, Laganà *et al.* [17] studied the orthodontic treatment needs of a 7-to 15-year-old

TABLE 3. Comparison of frequency of Angle's Class I (Dewey's modification), II, and III (Dewey's modification) malocclusions in SCD, BTM, and control participants.

Subjects	Normal occlusion	Angle's Class I N (%)					Angle's Class II N (%)						Angle's Class III N (%)		
		Type 1	Type 2	Type 3	Type 4	Type 5	Bimax Spacing		Div. 1	Div. 2	subDiv. 1	subDiv. 2	Type 1	Type 2	Type 3
SCD (N = 152)	4 (2.6)*	16 (10.5)*	12 (7.8)	0 (0.0)	0 (0.0)	2 (1.3)	4 (2.6)	8 (5.2)	65 (42.7)*	10 (6.5)	17 (11.1)	12 (7.8)	1 (0.6)	0 (0.0)	1 (0.6)
BTM (N = 159)	9 (5.6)*	18 (11.3)*	10 (6.2)	3 (1.8)	2 (1.2)	4 (2.6)	10 (6.2)	13 (8.1)	59 (37.1)*	11 (6.9)	14 (8.8)	4 (2.6)	0 (0.0)	2 (1.2)	0 (0.0)
Control (N = 400)	139 (34.7)	109 (27.2)	32 (8.0)	1 (0.2)	6 (1.5)	1 (0.2)	28 (7.0)	24 (6.0)	40 (10.0)	5 (1.2)	2 (0.5)	8 (2.0)	3 (0.7)	0 (0.0)	2 (0.5)

**p < 0.05: significant difference with normal control. SCD: sickle cell disease; BTM: β-thalassemia major.*

TABLE 4. Prevalence of the Dental Health Component of the IOTN in the patients and participants.

DHC category	Grades	BTM % (n)	SCD % (n)	Control % (n)
No need	1	13.2 (21)	16.4 (25)	16.2 (65)
Slight need	2	20.1 (32)	23.0 (35)	48.2 (192)
Borderline need	3	41.5 (66)	38.1 (58)	22.5 (90)
High need	4	23.8 (38)	20.3 (31)	12.7 (51)
Very high need	5	1.8 (2)	1.9 (3)	0.5 (2)

DHC: Dental health component; BTM: Beta thalassemia; SCD: Sickle cell disease.

Albanian population. They reported that more than 80% of the total sample showed oral habits, whereas approximately 60% of our study population had such habits. In a study, Gupta *et al.* [18] reported Class I, II, and III malocclusions in 44%, 55%, and 1% of the transfusion-dependent thalassemia patients, respectively, which was not in consistence with the healthy children malocclusion ratios. This result could be due to the fact that hemoglobinopathies are associated with extramedullary hematopoiesis, and bone marrow hyperplasia, leading to maxillary prominence and higher prevalence of Class II malocclusion [18, 19]. In addition, there is evidence reported in many studies about the generalized growth retardation resulting in mandibular retrusion in these patients [20–22]. However, based on the studies conducted on normal population, more than half of the healthy children presented with a class I malocclusion, which is higher than the outcomes of other epidemiologic surveys [17, 23]. In Iran, the prevalence of malocclusion in different provinces was investigated in several studies. In the study conducted on 502 students in Isfahan province, the prevalence of Class I, II, and III malocclusions were 41.8%, 27.5%, and 7.8%, respectively [24]. Arabiun *et al.* [25], in another study conducted in Shiraz province, reported that the prevalence of Class I, II, and III malocclusions were 12.78%, 9.94%, and 0.97%, respectively. One of our previous studies was also another investigation into the epidemiology of malocclusions in Iranian BMT and SCD children [9] which showed a slight discordance with this study. This difference could be justified by the family history of severe skeletal mandibular prognathism which runs through the majority of our Class III patients [9]. In another study on thalassemic patients, Treatment Priority Index scores showed definite malocclusion, handicapping malocclusion, and severely handicapping malocclusion to be significantly high in beta thalassemia subjects compared to the control population [18]. The results obtained from the current study were in line with those of Gupta *et al.*'s [18], indicating higher prevalence of Class II malocclusion among BTM and SCD patients, which can be attributed to a couple of reasons, such as the higher percentage of thumb sucking habit and/or maxillary prominence due to bone marrow hyperplasia in these patients and also possibly lower occurrence of genetic background of Class III malocclusion within our randomly selected sample. Previous studies showed that increased overjet is one of the most significant contributing factors to tooth traumatic injuries. Treating an abnormal overjet not only minimizes the risk of traumatic dental injuries, but also is beneficial from an aesthetic point of view [26, 27]. The objective need for orthodontic treatment (Grade 4, and 5) was registered in 41% of healthy children in the Laganà study [17]. Danaei *et al.* [28] studied an Iranian adolescent population through Dental Aesthetic Index, and the prevalence of participants with intense-to-disabling and disabling malocclusions was determined at 21% and 8.4%, respectively, which is significantly higher than our normal group. This discrepancy can be attributed to the differences in the ethnicity of the study populations and age groups. These findings on normal children are in line with one of our previous studies about the prevalence of malocclusion on normal Iranian children using IOTN in which an objective treatment need was recorded in 17.71% of participants [26]. The majority of orthodontic need evaluation studies have been conducted on normal population and there are few studies on thalassemic patients proper. In a British population of 12- to 15-year-old schoolchildren, about 35% of subjects were registered to have a definite orthodontic treatment need [29],

while other studies on French [30], Turkish [31], and Iraqi [32] children reported an objective treatment need (grades 4, and 5), respectively, in 21%, 16.7% and 30.1% of the populations. These findings could be explained considering the economic and social status of the studied populations. European epidemiological surveys on normal adolescents reported a lower prevalence of grade 4 and 5 IOTN-DHC, which could be attributed to preventive dental management policies [30, 33]. However, Jeelani *et al.* [33] reported grades 4 and 5 of IOTN were significantly more prevalent in thalassemic children compared to the control group; however, there were no SCD patients included in their study. In our study, this gap was bridged through which the DHC of the IOTN was used to evaluate the orthodontic treatment need, where the higher percentage of grade 4 and 5 in BTM and SCD was revealed compared to normal patients which was in line with the results obtained by Jeelani *et al.* [33]. These results can be used as source data for the prevalence of different classes of malocclusion in different age groups of BTM and SCD patients to determine the optimal timing for orthodontic treatment. These findings might suggest that preventive and early-stage orthodontic evaluation could be integrated into developing a dental-health-monitoring program in Iran aimed at increasing dental health in both patients and normal children with a more emphasis on those inflicted children who have diseases which threaten their dental health. Adopting a panoramic point of view, regular blood transfusion and monitoring of hemoglobin levels in these patients is a crucial measure to increase the life expectancy and decrease the associated complications, which otherwise might be reversed in poorly-equipped environment with the lack of proper monitoring programs.

5. Conclusions

Class II malocclusion frequency was higher in sickle cell anemic and beta thalassemic patients. Oral habits were observed in 61.88% of the study population. IOTN-DHC scores showed treatment need grades to be significantly higher in the above-mentioned patients compared to the control population ($p < 0.01$) which implies a real need for these populations to be provided with preventive orthodontic treatment. Public subsidized orthodontic treatment should be provided to BTM and SCD patients as well as healthy children registered in grades 4 and 5 of DHC.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

AUTHOR CONTRIBUTIONS

SK—designed and performed the study, collected the records, performed the measurements, and analyzed the results. SLA—analyzed the results, provided the statistical analysis of the data. MRY—performed the measurements for the different variables in SPSS and wrote the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Informed consent was obtained from patients or their caregivers, and the Medical Ethics Committee of Islamic Azad University, which complied with the Helsinki Declaration, approved this research.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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