



# Prevalence of Malocclusion in Patients with Thalassemia Major: A Cross-sectional Study

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## Abstract

**Background:** Iran lies in the world's thalassemia belt; accordingly, the beta-thalassemia gene is carried by 4% of the Iranian population. Due to the dearth of research and literature available on the prevalence of malocclusions in the Iranian population with beta-thalassemia major, this study was conducted to determine the prevalence and severity of facial abnormalities among patients who were referred to Bu-Ali Sina Hospital, Sari, Iran.

**Methods:** This descriptive cross-sectional study was conducted on 200 patients with thalassemia major who were referred to the care unit of Bu-Ali Sina teaching and therapeutic Hospital, Sari, Iran, in 2018. The patients were then visited by a trained dentist who had been given the necessary theoretical and practical training. Malocclusion was classified based on Angle's classification. Spacing, overcrowding, overjet, and overbite were measured, and the distances were recorded based on a checklist.

**Results:** The prevalence of malocclusions obtained was 87.5%, which included malocclusions of Class I (34%), Class II (31%), and Classes III (22%) amongst patients. There was no significant relationship between the type of malocclusion and gender ( $P = 0.77$ ). Moreover, no significant difference was observed among patients with thalassemia major and different classes of malocclusions in terms of age both in males ( $P = 0.49$ ) and females ( $P = 0.58$ ).

**Conclusions:** Malocclusions are common among adolescents and adults with thalassemia, which is not associated with age or gender. Therefore, patients should be regularly visited and followed up by a dentist to manage and control their dental problems. In addition, effective and preventive measures, as well as health education should be seriously considered in these patients.

**Keywords:** Malocclusion, Overcrowding, Spacing, Thalassemia Major

## 1. Background

Thalassemia is an inherited blood disorder involving abnormal hemoglobin formation due to the decreased synthesis of different types of polypeptide chains. The most severe form of this disorder is beta-thalassemia, which arises from mutations in the *HBB* gene on chromosome 11 (1-3). Alpha/beta imbalance, ineffective erythropoiesis, and chronic anemia in patients with thalassemia occur due to the defect in the synthesis of the beta-globin chains (4).

The prevalence of beta-thalassemia is 1.5%, and its annual incidence has been estimated at 1 per 100,000 population (2). Iran lies in the world's thalassemia belt; accordingly, the beta-thalassemia gene is carried by 4% of the Ira-

nian population. About three million thalassemia carriers and more than 25,000 patients with thalassemia major have been currently identified in Iran (5).

Thalassemia major is the most severe form of beta-thalassemia. There is great clinical variability in the systemic signs and symptoms of patients with beta-thalassemia major. Bone changes, retardation of growth, and splenomegaly are some of the consequences of this disease, which occur due to severe anemia in childhood (6). Patients with thalassemia major are at risk of osteoporosis; therefore, they can experience much discomfort associated with bones and teeth (7). The chances of enlargement of the upper jaw (chipmunk face), malocclusion, migration, and spacing of upper anterior teeth, short crowns and roots of teeth, as well as discolored teeth, are

increased in patients with thalassemia (8-10). Moreover, dental decay is higher among patients with thalassemia, compared to the normal population (10).

The access of patients with beta-thalassemia major to oral and dental care is a main concern of the dental health care providers. However, patients refer to dentists when their teeth are severely damaged and require emergency dental services. This is due to the fact that patients are involved in serious medical complications of thalassemia, which may lead to neglect issues related to the health of their teeth (9, 11). The risk of abscess and infection, as well as their spread into the tissues of the neck and face is higher during the advanced stages of dental decay. In these stages, there is no other way but to extract the teeth.

## 2. Objectives

Due to the dearth of research and literature available on the prevalence of the severity and types of malocclusions in adolescent and adult patients with beta-thalassemia major, this study was conducted to assess the prevalence of facial abnormalities and malocclusions in patients with thalassemia major referred to Bu-Ali Sina Hospital in Sari, Iran.

## 3. Methods

This descriptive cross-sectional study was conducted on patients with thalassemia major who were referred to the care unit of Bu-Ali Sina teaching and therapeutic Hospital, Sari, Iran, in 2018.

### 3.1. Study Design

In total, 200 cases were selected using simple random sampling from all patients with thalassemia major aged between 13-39 years, who were referred to the care unit of Bu-Ali Sina Hospital for routine examinations, blood infusion, and treatment. The sample size was determined considering  $\alpha = 0.05$ ,  $\beta = 0.2$ ,  $d = 0.08$ , and  $P = 84\%$  (12). The patients were visited by a trained dentist who had been given the necessary theoretical and practical training. Demographic characteristics and clinical data were gathered and recorded based on a checklist.

In this study, normal occlusion was defined as the presence of all teeth; normal shape, size, and location of teeth; proper molar-overbite relationship (maximum 3mm) and proper overjet (maximum 2mm); no space between the teeth; and lack of rotation, overcrowding, and crossbite.

On the other hand, malocclusions were classified based on Angle's classification as follow: Class I (neutral

occlusion): The mesiobuccal cusp of the upper first permanent molar is placed in the mesiobuccal groove of the first lower permanent molar; Class II (distocclusion): The first permanent molar mesiobuccal groove is placed after the mesiobuccal cusp of the upper first permanent molar; Class III (mesiocclusion): The first permanent molar mesiobuccal groove is placed before the mesiobuccal cusp of the upper first permanent molar.

In the absence of maxillary and mandibular first molars, occlusion is assessed according to the following criteria: Class I: Tip of the maxillary canine tooth is placed between the mandibular canine and the mandibular first premolar; Class II: Tip of the maxillary canine tooth is placed between the mandibular canine and the mandibular lateral incisor; Class III: Tip of the maxillary canine tooth is placed between the mandibular first and second premolar.

The distance between the most prominent labial margins of the incisal edge of the maxillary to the labial surface of the mandibular teeth was calculated for determining the overjet. Furthermore, for assessing the overbite, the vertical relationship between the upper and lower incisors was calculated as the vertical distance between the edge of the upper and lower central incisor when the posterior teeth were in contact. Following that, the distances were calculated in millimeters, and values more than 2mm were considered increased overbites.

### 3.2. Ethical Considerations

The study protocol was approved by the Ethics Committee of Sari University of Medical Sciences, Sari, Iran, IR.MAZUMS.REC.1398.492. Before the study, the research objectives and procedures were explained to each case or his/her parents separately, and if the patient showed willingness, the examination was performed. They were then assured that their information would remain confidential.

### 3.3. Statistical Analysis

The obtained quantitative and qualitative data were analyzed in SPSS software (version 25) through the chi-square and ANOVA. A p-value less than 0.05 was considered statistically significant.

## 4. Results

In total, 200 patients with thalassemia major and the mean age of  $27.04 \pm 6.1$  years (age range: 13-39 years) were included in this study. It should be mentioned that the majority ( $n = 104$ ; 52%) of the patients were male. Tooth condition was normal in 12.5% ( $n = 25$ ) of patients with thalassemia major, and the prevalence of malocclusions

was obtained at 87.5%. Furthermore, 69 (34%) patients had malocclusion of Class I, and 62 of them had malocclusion of Class II. Moreover, malocclusion of Classes III was reported in 22% ( $n = 44$ ) of patients with thalassemia major. **Table 1** tabulates the malocclusion class of patients with thalassemia major based on gender. According to the obtained results, there was no significant relationship between the type of malocclusion and gender ( $P = 0.77$ ).

Moreover, the frequency of males and females was statistically similar in patients with normal teeth. The mean age of thalassemia major patients with various malocclusion classes is shown in **Table 2**, which showed no significant difference among patients with thalassemia major and different classes of malocclusion in terms of age both in males ( $P = 0.49$ ) and females ( $P = 0.58$ ).

Spacing was reported in 13% ( $n = 26$ ) of patients with thalassemia major. However, there was no significant difference between patients with spacing and those without spacing in terms of gender ( $P = 0.206$ ). The mean ages of the patients with and without spacing were estimated at  $28.5 \pm 6.5$  and  $26.8 \pm 6.06$  years, respectively. Furthermore, the comparison of patients with and without spacing showed no relationship between spacing and age ( $P = 0.18$ ). The frequency of crowding was determined at 28.5% ( $n = 57$ ) in patients with thalassemia major, 59.6% ( $n = 34$ ) of whom were female. There was no significant difference between the patients with and without crowding in terms of gender ( $P = 0.21$ ). Moreover, the mean age of the patients with ( $26.7 \pm 5.8$  years) and without crowding ( $27.1 \pm 6.2$  years) showed no relationship between crowding and age ( $P = 0.66$ ).

In addition, 30% of patients with thalassemia major had increased overjet ( $n = 60$ ), and 20% of them had increased or decreased overbite ( $n = 40$ ). Increased and decreased overbites were reported in 15.5% ( $n = 31$ ) and 4.5% ( $n = 9$ ) of the patients, respectively. There was no significant difference between the patients with ( $26.6 \pm 6.1$ ) and without increased overjet ( $27.8 \pm 6.1$ ) in terms of age ( $P = 0.22$ ). The mean age of the patients with increased or decreased overbite was obtained at  $27.6 \pm 6.8$  years, which showed no relationship between overbite and age ( $P = 0.44$ ).

## 5. Discussion

Thalassemia can have health-related concerns for patients and their families. Knowledge about the oral manifestations of this disease helps to provide clinical, psychological, and social support in order to achieve better treatment outcomes. This descriptive study was an attempt to compare the prevalence of malocclusion degree and types of malocclusions, as well as spacing, overcrowding, overjet, and overbite among patients with beta-thalassemia

major. The sample population was relatively young (age range: 13 - 39 years) and the female/male ratio was statistically similar. No association of malocclusion was reported regarding age and gender.

In general, malocclusion in various degrees was observed in the majority of thalassemia patients in our study. Our findings were supported by the results of other studies indicating that thalassaemic patients had higher dental caries scores, compared to the healthy controls (13-15). A study conducted by Elangovan et al. showed that the prevalence of prominent extraoral abnormalities was about 57% in the beta-thalassemia major patients. Consistent with our findings, the Class I occlusion, followed by Class II occlusion, were the most common occlusions (16). However, the prevalence of occlusions with various severities was higher in our study, compared to that of the aforementioned study (87.5% versus 57%). The Class III occlusion was reported in 22% of our patients, while they found no Class III occlusion.

In another study, Sobouti et al. assessed the prevalence of different malocclusions among Iranian adolescents. According to the results, 53%, 19.4%, and 15.6% of the patients had Class I, II, and III malocclusion, respectively. Although the mean age in our study was higher than that of the mentioned study, Sobouti et al. obtained a higher Class I malocclusion within the age range of 13 to 15 years. On the other hand, similar to our study, the aforementioned study showed a higher prevalence of Class I malocclusion among young Iranian population (17). Their findings rejected the relationship between the presence of malocclusion and beta-thalassemia major in young people.

The hyperplasia of bone marrow due to rapid red cell turnover leads to changes in the bone structures of thalassaemic patients, and its incidence is more reported in the maxilla, compared to the mandible (18, 19). This can explain the low prevalence of Class III occlusion in these patients. Due to anemia, the gums and the lining of patients with thalassemia major become pale. In addition, dry mouth and painful swelling of salivary glands lead to decreased salivary protection in the patients (11). For this reason, they are more prone to dental decay (9). Negligence of the health of their teeth due to the involvement of these patients in serious medical complications of thalassemia may be the other reason for the increased risk of dental problems in this population (9, 11).

On the other hand, we found no relationship between age and dental lesions in patients with thalassemia major, which was inconsistent with the results of other studies (20, 21). The discrepancies may be due to differences in samples. The sample population was relatively young (age range: 13 - 39 years) in this study, while other studies were performed on older patients. Pedullà et al. showed that

**Table 1.** Malocclusion Classes of Patients with Thalassemia Major Based on Gender<sup>a</sup>

Malocclusion Condition	Male	Female	Total	$\chi^2$	P-Value
Normal	11 (10.6)	14 (14.6)	25 (12.5)		
Class I	34 (32.7)	35 (36.5)	69 (34.5)		
Class II div 1	33 (31.7)	29 (30.2)	62 (31)	1.77	0.77
Class II div 2	16 (15.4)	11 (11.5)	27 (13.5)		
Class III	10 (9.6)	7 (7.3)	17 (8.5)		

<sup>a</sup>Values are expressed as No. (%) unless otherwise indicated.

**Table 2.** Mean age of Thalassemia Major Patients with Various Malocclusion Classes<sup>a</sup>

Malocclusion Condition	Male	Female
Normal	24.64 ± 5.67	23.95 ± 5.02
Class I	28.42 ± 6	27.88 ± 5.55
Class II div 1	27.53 ± 6.48	26.24 ± 6.11
Class II div 2	27.03 ± 5.82	26.39 ± 5.29
Class III	23.11 ± 4.16	22.61 ± 4.12
Analysis of variance	P= 0.49	P= 0.58

<sup>a</sup>Values are expressed as mean ± SD unless otherwise indicated.

severe gingivitis and probing pocket depth scores were worse in older patients with severe beta-thalassemia major, compared to those with beta-thalassemia intermedia and the general population. Moreover, they reported a higher rate of decayed-missing-filled teeth in patients with beta-thalassemia major. It is worth mentioning that dental problems, including gingival and periodontal status, were affected by thalassemia major only in older patients. These findings indicate that age plays an important role in the oral compliance and formation of plaque deposits. They also compared two subgroups of beta-thalassemia major and intermedia in terms of dental problems and indicated no relationship between age and dental problems in patients with beta-thalassemia intermedia (4).

Some problems existed when recruiting a higher number of patients in the older age range in this study. Moreover, the recruiting process lasted almost one year; however, the evaluation of oral hygiene levels showed that types of malocclusions (spacing, overcrowding, overjet, and overbite) had no significant association with age and gender. Similar to our study, another study showed a higher rate of spacing, openbite, crowding, mouth breathing, and increased overjet in thalassemic patients, compared to healthy controls (22). In general, the Class II malocclusion is associated with prominent maxillary anterior teeth, spacing, increased overjet, and decreased over-

bite (23). The most common type of problem is crowding, which occurs in thalassemic patients due to discrepancies between tooth size and arch length (24). Similarly, a higher rate of increased overjet and decreased overbite in thalassemic patients, compared to healthy control, was confirmed in a study performed by Abu Alhaija et al. (23).

The results of the present study highlight the importance of dental care in thalassemic patients. Moreover, facial appearance of patients with  $\beta T$  is unique because of the increased formation of red blood cells caused by erythroid hyperplasia in the bone marrow. Due to the increased malocclusion in patients, orthodontic treatment is affected by these conditions. Early orthodontic diagnosis and management enable favorable prognosis and minimize the subsequent complications (25). Since infection is one of the main concerns of thalassemia patients, preventive measurements, including the implementation of oral hygiene instructions, diet counseling, and the use of topical fluoride are of critical importance. Finally, further studies with larger sample sizes and control groups are recommended to be conducted on the malocclusions of patients affected with beta-thalassemia major to check the present findings.

### 5.1. Limitations and weaknesses

The obtained results of the present study cannot be generalized to other populations due to the lower sample size and single-centered nature of the study. The incompleteness of some medical records and inaccessibility were other important limitations of this study. Therefore, it is suggested that further multicenter studies with larger sample sizes and control groups be performed on the malocclusions in patients affected with beta-thalassemia major.

### 5.2. Conclusions

The high prevalence of malocclusion is common among adolescents and adults with thalassemia, which is not associated with age or gender. Patients should be regularly visited and followed up by dentists to control and

manage their dental problems. According to the high incidence of malocclusion in older patients with thalassemia major, effective preventive measures, health education, and dental treatment are required for this group.

### Footnotes

**Authors' Contribution:** Study concept and design: P. N., and A. S.; Analysis and interpretation of data: J. C., and H. K.; Drafting of the manuscript: T. E.; Critical revision of the manuscript for important intellectual content: S. I. Statistical analysis: A. S.

**Conflict of Interests:** There was no conflict of interest.

**Ethical Approval:** The study protocol was approved by the Ethics Committee of Sari University of Medical Sciences, Sari, Iran, IR.MAZUMS.REC.1398.492.

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