Craniofacial bone abnormalities and malocclusion in individuals with sickle cell anemia: a critical review of the literature

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This study aims to critically review the literature in respect to craniofacial bone abnormalities and malocclusion in sickle cell anemia individuals. The Bireme and Pubmed electronic databases were searched using the following keywords: malocclusion, maxillofacial abnormalities, and Angle Class I, Class II and lass III malocclusions combined with sickle cell anemia. The search was limited to publications in English, Spanish or Portuguese with review articles and clinical cases being excluded from this study. Ten scientific publications were identified, of which three were not included as they were review articles. There was a consistent observation of orthodontic and orthopedic variations associated with sickle cell anemia, especially maxillary protrusions. However, convenience sampling, sometimes without any control group, and the lack of estimates of association and hypotheses testing undermined the possibility of causal inferences.

It was concluded that despite the high frequency of craniofacial bone abnormalities and malocclusion among patients with sickle cell anemia, there is insufficient scientific proof that this disease causes malocclusion

Keywords: *Anemia, sickle cell; Malocclusion, angle class I; Malocclusion, angle class II; Malocclusion, angle class III; Craniofacial abnormalities; Maxillofacial abnormalities*

Introduction

Sickle Cell Anemia (SCA) is a prevalent autosomal recessive hereditary blood disease in Brazil that is not related to gender and is peculiar to Blacks, though not restricted to this ethnic group, as it also manifests in Mulattos and Whites; this is explained by miscegenation with African descendents.[1-5]

SCA is a mutation of the gene that produces beta-globin, a protein needed for normal hemoglobin (HbA), which results in the production of hemoglobin S (HbS). In cases of persistently low oxygen tension, these molecules polymerize, giving a sickle shape to red blood cells.

This phenomenon decreases the plasticity of erythrocytes reducing their ability to pass the walls of blood vessels (diapedesis) and to transport oxygen, resulting in increased blood viscosity and consequent vascular occlusion, causing ischemia and local infarction.[6-8]

These changes can have several systemic consequences such as high propensity to infections, acute painful crises, leg ulcers, hemolytic crises, splenic sequestration, priapism, strokes and even chronic impairment of multiple organs and systems, with the clinical status of SCA being prone to variations because the systemic conditions of its carrier. The most commonly described findings in the oral cavity, which are non-pathognomonic but may be characteristic of the disease, are pallor of the oral mucosa, delayed tooth eruption, straight, discolored and depapillated tongue, hypomaturation or hypomineralization of enamel and dentin, pulp stones, asymptomatic pulp necrosis, hypercementosis, an unusual level of periodontitis and craniofacial bone abnormalities. [9-11]

The most common craniofacial bone abnormalities are turricephaly, jaw protrusion and the formation of a large trabecular pattern. They can determine the existence of dental malocclusion and the developmental of abnormalities of the teeth and arches, which cause aesthetic discomfort in the mildest cases and functional disorders or disabilities, in the most severe cases.[12]

Thus, the objective of this study was to critical review the literature on the presence of craniofacial bone abnormalities and dental malocclusion in SCA individuals and any possible association between these clinical manifestations and the disease.

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The authors declare no competing financial interest

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Methods

This study involved a search of the literature in the Bireme and PubMed electronic databases using the following keywords: malocclusion, Maxillofacial Abnormalities, and Angle Class I, Class II and Class III malocclusions in association with sickle cell disease. The search was limited to publications in English, Spanish and Portuguese. Literature reviews and clinical cases were excluded from the study. Inclusion of articles was performed by a single examiner who initially read the abstracts and then read full articles selected from the abstracts. The data, including information on authorship, year of publication, study site, study design, purpose, sampling technique, sample size, ethnical background, age, method of orthodontic diagnosis and main results, were listed in a table.

Results

Ten scientific publications were found however three were excluded as they were reviews of the literature. Thus, seven studies were selected (Table 1).

Table 1 - Summary of studies on craniofacial bone changes and malocclusion in sickle cell disease and their main results

Author (year)	Country	Type of study	Objective	Sampling Technique	Sample Size	Ethnical background	Age group (years)	Method of orthodontic diagnosis	Craniofacial bone changes and/or malocclusion (%)
Brown & Sebes (1986) [14]	USA	Case-control	Evaluate gnathopathy sickle	non-probabilistic	50 with SCA and 25 without SCA matched by gender and age	Black	10-45	Radiographic evaluation	Maxillary protrusion (%U)
Okafor et al. (1986) [18]	NIG	Case-control	Evaluate the oral and dental complications of SCA	non-probabilistic	37 with SCA and 24 without SCA matched by gender and age	Black	10-40	Clinical analysis	Maxillary protrusion (with SCA = 35%; without SCA= 16.6%) Overjet (with SCA = 35%; without SCA= 16.6%) Overbite (with SCA = 35%; without SCA= 16.6%)
Taylor et al. (1995) [13]	USA	Cross-sectional	Assessment of dental features of SCA	non-probabilistic	21 with SCA	Black	8-31	Radiographic evaluation	Maxillary protrusion (with SCA = 56%) Overjet (with SCA = 30-80%) Overbite (with SCA = 56%) Stepladder' trabecular pattern (with SCA = 70%)
Oredugba & Savage (2002)[15]	NIG	Case-control	Evaluate the malocclusion and malnutrition in SCA compared with matched unaffected	non-probabilistic	170 with SCA and 122 without SCA; unpaired	Black	1-18	Clinical evaluation (Angle's classification)	Maxillary protrusion (with SCA = 21%; without SCA = 2%) Malocclusion Angle Class II (with SCA= 21%; without SCA= 4%)
da Costa et al. (2005) [19]	NIG	Cross-sectional	Evaluate changes in craniofacial SCA	non-probabilistic	104 with SCA	Black	10-45	Clinical evaluation (Angle's classification)	Malocclusion, Angle Class II (with SCA= 88.5%) Overjet (with SCA= 48.2%) Overbite (with SCA= 48.2%) Spacing in the anterior segment in both arches (with SCA= 49.0%) Labial incompetence (with SCA= 39.4%)
Souza et al. (2008) [16]	BRA	Cross-sectional	Assess and quantify the changes in craniofacial skeletal pattern	non-probabilistic	30 with SCA	Black	20-46	Steiner and Downs cephalometric analysis	Maxillary protrusion (%U) Mandibular retrusion (%U) Increased mandibular plane (%U) Convex facial profile (%U)
Onyeaso & da Costa (2009) [17]	NIG	Cross-sectional	Investigate the severity of malocclusion in SCA	non-probabilistic	176 with SCA	Black	10-35	Clinical evaluation (IOTN; Index Complexity, Outcome and Need; DAI)	Severe malocclusion (with SCA= 50%)

USA: United States of America; NIG: Nigeria; BRA: Brazil; SCA: Sickle Cell Anemia; IOTN: Index of Orthodontic Treatment Need; DAI: Dental Aesthetics Index; %U: Percentage Unknown

Discussion

The most common craniofacial bone abnormalities in SCA individuals reported in the literature were maxillary protrusion,[13-17] overjet,[13,18,19] overbite,[13,18,19] spacing of the previous segment in both arches,[19] retrusion of mandible[16] and large trabecular bone[13] (Table 1). These abnormalities may occur due to hyperplasia and expansion of the bone marrow to compensate for the short life of red blood cells as a result of disease progression.[20,21]

Craniofacial bone abnormalities are considered factors that may contribute to the development of dental malocclusion in any individual.[22] In SCA it is suggested that these factors are decisive as was highlighted by the development of severe Angle type II malocclusion.[15,17,19] Deviations of the teeth and face can produce functional chewing, swallowing, phonation and breathing disorders and even psychosocial disorders with potential effects on the self-esteem and interpersonal relationships of severely affected individuals.[23] Thus, Okafor et al.[18] recommend that SCA patients should have access to orthodontic treatment associated with phonoaudiologic support in order to alleviate or prevent these conditions.

However, considering the reported higher propensity to variations in the microcirculation of the bone tissue of the oral cavity[4] and the possibility of an increased incidence of pulp necrosis in SCA individuals without any other associated factors,[24] it is believed that there is a need to assess the impact of orthodontic mechanics on bone remodeling and the vascular supply of the dental elements of these patients before prescribing orthodontic interventions to prevent or correct dental malocclusions.

On the other hand, none of the publications in this study stated that craniofacial bone abnormalities[13-16,18,19] or dental malocclusion[13,16,17] presented by SCA individuals were caused by the disease, as, among other reasons, these were cross-sectional and case-control studies which sometimes did not have a control group, lacked estimates of association and did not perform hypothesis testing. These factors undermine the possibility of causal inferences. The best individual observational study design to allow assessments of the etiology of a disease is the cohort study because it identifies, longitudinally, what the effects of a specific situation on an individual's health are, in accordance with Hill's causality criteria.[25,26] However, all the studies selected in this review employed sampling by convenience, which is not the most appropriate enrollment technique to make inferences on a target population.[26] These studies only suggest that dental malocclusion may be associated to SCA.

Another reason for this assertion is the selection bias related to the age of the individuals investigated. This occurred in two of the selected studies, those of Oredugba & Savage[15] and of Souza et al.[16] The first evaluated 1- to 18-year-old patients, an age range of patients considered to be in the bone growth phase when malocclusion may still be unstable. The latter study investigated 20- to 46-year-old patients, that is, individuals with complete bone growth, at which time it is expected to find a higher percentage of patients with malocclusion; however this data was not given by the authors. It is believed that the results of these studies cannot be extrapolated to this population as SCA individuals have delayed bone growth due to chronic organic disorders related to the disease.[4] In other studies [13,14,17-19] there was no concern about selecting individuals in respect to the bone growth phase, although in two case-control studies[14,18] the samples were matched for age and gender.

In spite of this, it is a fact that both SCA and dental malocclusions are considered public health problems.[27,28] These results suggest a need for public health policies in relation to the implementation of community programs for early diagnosis and appropriated treatment of dental malocclusion in this population, in order to provide a better quality of life to these individuals, who already suffer due to their disease.

Another significant aspect found in this review is that there was a higher prevalence of Blacks with SCA. This can be attributed to selection bias, as the samples of all the selected studies were only composed of Afro-Brazilians. SCA is peculiar to blacks since the mutation of Hb S probably arose between 50 and 100 thousand years ago in the Paleolithic and Mesolithic periods in the central western regions of Africa, in India and in East Asia. However this disease is not restricted to this race as it also is found in Mulattos and Whites, a fact attributed to miscegenation with African descendents.[29] The introduction of SCA in Brazil was via the slave trade (the first half of the sixteenth century) and European and Asian migrations (nineteenth century).[30] According to Naoum,[31] the prevalence of this disease in the general Brazilian population is 0.04% and among blacks it is 0.22%; the highest frequency of the disease in Brazil is in Bahia.

This study is relevant as it summarizes the main findings of publications on the magnitude of injuries of an important public health issue and the possibility of effective interventions to improve the quality of life of SCA individuals. However, these results may have been influenced by some factors such as selection bias (convenience sampling, ethnical background and age), publication bias and language bias. On the latter, today most publications are in English and thus were included in this review. Publication bias may occur due to the selective publication of studies with positive results of an association; this might have influenced the results of this study.

Hence, considering the clinical relevance of SCA and the lack of publications on the subject as shown by the current study of publications, it is believed that there is a need to conduct further observational-type studies to test whether there is any association between SCA and the development of craniofacial bone abnormalities and dental

malocclusion since, as yet, no study has proven this hypothesis.

Conclusion

Despite the high frequency of craniofacial bone abnormalities and dental malocclusion among SCA patients, there is insignificant evidence that this disease is a risk factor for the occurrence of these clinical manifestations.

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