

# CRANIOFACIAL ABNORMALITIES AND MALOCCLUSION FINDINGS IN SICKLE CELL DISEASE RELATED TO ETHNIC-RACIAL POPULATIONS: A CRITICAL REVIEW OF THE LITERATURE

Igor Bottino Di Gioia Almeida<sup>1\*</sup>, Renata de Moura Cruz Quintanilha<sup>2</sup>, Marcia Pereira Alves dos Santos<sup>1</sup>

<sup>1</sup>School of Dentistry, Universidade Federal do Rio de Janeiro - UFRJ, Rio de Janeiro, RJ, Brazil.

<sup>2</sup>Department of Pathology, Postgraduate Program in Dentistry, School of Dentistry, Universidade Federal do Rio de Janeiro - UFRJ, Rio de Janeiro, RJ, Brazil.

**Palavras-chave:** Anormalidades Craniofaciais. Cefalometria. Maloclusão. Anemia Falciforme. Revisão de Literatura. Negros.

## RESUMO

**Introdução:** a doença falciforme é uma doença hematológica, hereditária, crônica, que afeta principalmente, a população negra, em escala global. Na literatura odontológica, os achados craniofaciais e oclusais relacionados à doença falciforme são discordantes, mas, em comum, desconsideram a perspectiva racial. **Objetivo:** este artigo revisou criticamente a literatura odontológica e discutiu os achados encontrados na perspectiva racial/étnica. **Fonte dos dados:** estudos primários e secundários selecionaram 146 ocorrências de quatro bases de dados da literatura científica. Dois revisores extraíram independentemente os dados dos onze estudos incluídos. **Síntese dos dados:** com base na cefalometria lateral, a maioria dos estudos concluiu que as anormalidades craniofaciais e maloclusões, como protrusão maxilar, padrão esquelético de classe II, padrão de crescimento facial vertical, perfil facial convexo, retrusão mandibular e rotação posterior da mandíbula foram os mais comuns achados para pessoas com doença falciforme. No entanto, ao considerar a perspectiva étnico-racial, não há menção na maioria dos estudos de ajustes dos padrões cefalométricos específicos para as populações racializadas, nem tampouco são consideradas características do grupo populacional e da doença falciforme em si, como sua severidade, o momento de vida em que o diagnóstico ocorreu, número e período de hemotransfusões, internações, crises vaso-occlusivas ou uso de hidroxiureia. Além disso, a ampla faixa etária em diferentes períodos de crescimento ósseo e a ausência de informação sobre tratamento ortodôntico prévio foram observadas. **Conclusão:** há omissão sobre considerações étnico-raciais para relatar anormalidades craniofaciais e maloclusões sobre doença falciforme na literatura odontológica revisada. Isto pode ser uma expressão do racismo.

**Keywords:** Craniofacial Abnormalities. Cephalometry. Malocclusion. Sickle Cell Anemia. Literature Review. Blacks.

## ABSTRACT

**Introduction:** sickle Cell Disease (SCD) is an inherited, hematological, chronic disease that mostly affects racial/ethnic groups. The dental literature discusses SCD's oral symptoms, such as malocclusion and craniofacial abnormalities, without considering the significance of a racial/ethnic perspective. **Objective:** this article critically reviewed the findings of the studies based on a racial/ethnic standpoint and SCD landmarks.

**Sources of data:** primary and secondary searches selected 146 studies from four scientific literature databases. Two reviewers independently extracted data from eleven included studies. **Synthesis of data:** most studies used lateral cephalometry and reported craniofacial abnormalities and maloclusions, such as maxillary protrusion, class II skeletal patterns, vertical facial growth patterns, convex facial profile, mandibular retrusion, and the posterior rotation of the jaw. However, there is no mention of racial or ethnic cephalometric patterns to support these findings in the studied populations. In addition, a misunderstanding occurs when overlooking the different periods of growth or ages within and between the studied groups. Furthermore, there is no mention of previous orthodontic treatment. By contrast, there is a lack of information about the medically compromised health status of people with SCD, such as the life period of SCD's diagnosis; the number and timing of blood transfusions; the medical history of hospitalizations, vaso-occlusive crises, or hydroxyurea use. **Conclusion:** racial and ethnic concerns for the diagnosis of maloclusions and craniofacial anomalies, as well as SCD landmarks, are underappreciated in the examined dental literature. Discarding them also demonstrates institutional racism.

Submitted: February 15, 2023

Modification: April 15, 2023

Accepted: April 27, 2023

### \*Correspondence to:

Igor Bottino Di Gioia Almeida

Address: Prof. Rodolpho Paulo Rocco, 325,  
Cidade Universitária da Universidade  
Federal do Rio de Janeiro, Rio de Janeiro,  
RJ, Brazil. Zip Code: 21941-617.

Telephone number: +55 (21) 99408-8739

E-mail: bottinoigor2@gmail.com

## INTRODUCTION

Sickle cell disease (SCD) is an inherited, progressive, life-threatening disease associated with a decreased quality of life and a shortened life span. This hematological genetic disease occurs by a higher presence of a recessive hemoglobin S mutation<sup>1</sup> with no gender predilection. SCD continues to be an example of healthcare inequity in Brazil and worldwide,<sup>2</sup> mainly for diasporic African groups<sup>2-4</sup> who present a high prevalence of this condition.<sup>3,4</sup>

SCD affects all organs, systems, and tissues.<sup>5</sup> The presence of acute pain crises, particularly in the long bones and joints; chronic anemia; organ failures; infections; and lung acute disorders indicate the severity of the condition.<sup>5</sup> In children, a reduction in the dimension of the upper airways can occur due to the overgrowth of the surrounding lymphoid tissues.<sup>6</sup> This may well explain a predisposition to upper airway obstruction syndrome.<sup>7</sup> Such changes can lead to mouth breathing, constitute a risk factor for malocclusion,<sup>8</sup> and even reduce the quality of life.<sup>9,10</sup> Sickle cell anemia is the most common type of SCD with the poorest prognosis,<sup>1-5</sup> including craniofacial and occlusion abnormalities.<sup>11-12</sup> The diagnose of SCD may occur during newborn screening.<sup>1</sup>

Blood transfusions, hospitalizations, and the use of medications, such as hydroxyurea, are part of the medically compromised routine of people with SCD. Hydroxyurea is one of the most widely used drugs on a global scale<sup>5,13-17</sup> and, as a myelosuppressive drug, inhibits or delays the proliferation of blood-forming cells in the bone marrow, particularly in individuals who have been taking this medication since childhood.<sup>16-18</sup> Hydroxyurea reduces the frequency of painful crises caused by the decreased life span of red blood cells and the defective vascular-endothelial qualities.<sup>1-5</sup>

Dental literature has reported many craniofacial and malocclusion alterations in people living with SCD.<sup>12,14,19-22</sup> As a protocol, to diagnose craniofacial and occlusal abnormalities, lateral cephalometric radiography is the most useful complementary exam,<sup>23</sup> as its traces illustrate the relationship between the bone bases, the facial profile (skeletal and soft tissue), and the growth pattern. For skeletal classification in orthodontic diagnosis and treatment planning, cephalometric measures for an “ideal” vertical and horizontal relationship are applied. In general, the Caucasian pattern is a reference guide, but for racial/ethnic groups, a better diagnosis is reached when applying standard measurements for this racial group<sup>24</sup> due to the relationship of normality between skeletal and dental positions that may be greatly diverse due to ethnic variations. In fact, there are dentoalveolar variations in Asian, Arabic, African, African-American, and African-Brazilian populations.<sup>25</sup>

Institutional racism is a group of practices, attitudes, and behaviors that harm people of color and is made up of unconscious bias, ignorance, carelessness, and racist stereotyping. A sign of institutional racism is not only the absence of a racial component in the studies, which is the

case for SCD, especially for populations of African origin, but researchers also neglected to take into account the inner features of each studied group. These lead to biased scientific information and unsupported clinical intervention. This article seeks to advance scientific understanding by critically analyzing dental literature on craniofacial abnormalities and malocclusion findings in SCD from a racial perspective and some features of people living with SCD.

## MATERIALS AND METHODS

Based on the study question: ‘Do the craniofacial and occlusal findings in SCD consider the features of people living with the disease for the cephalometric analysis in a racial/ethnic perspective?’ From January to February 2021, one researcher used the keywords Craniofacial Abnormality, Cephalometry, Malocclusion, and Sickle Cell Anemia to conduct database research on the Scielo, Lilacs, PubMed, and Virtual Health Library electronic sources. There were no restrictions on the period or categories of publications. The retrievals consist of full and free publications in English and Portuguese. Moreover, a manual search of each manuscript’s reference list was also conducted.

Two categories separated the studies based on title and abstract: A) Craniofacial and occlusal abnormalities measured by radiographic analysis, and B) Orthodontic treatment for people with sickle cell disease. In the sequence, group A split out into two sub-groups: A1 - craniofacial and occlusal findings measured using cephalometry; and A2: craniofacial and occlusal findings measured with non-cephalometric radiography exams. Only studies classified as group A1 were considered to answer the research question. Figure 1 shows the flowchart from identifying, selecting, including, and analyzing group A studies.

## RESULTS

Table 1 summarizes the main findings. The majority of reviewed studies used lateral cephalometry to record craniofacial abnormalities and malocclusions<sup>26-35</sup>. None of the studies that reported on craniofacial abnormalities and malocclusions among different racial/ethnic groups with SCD mentioned racial/ethnic cephalometric parameters.

The maxillary protrusion,<sup>26,29,32,35</sup> the anteroposterior relation of the class II skeletal pattern,<sup>28,29,31,33,34</sup> malocclusion,<sup>33</sup> overjet,<sup>28,34,35</sup> and mandibular retrusion<sup>29,32,35</sup> were common findings. Malocclusion was more frequent, with greater overjet and labial tilt of the maxillary central incisors. By contrast, one study<sup>30</sup> and one systematic review<sup>12</sup> did not report any craniofacial abnormalities nor malocclusion, such as maxillary protrusion or compensatory maxillary expansion, in the SCD groups. On the other hand, one study<sup>27</sup> associated the findings in the cephalometric exams with the severity of SCD.

Table 2 shows craniofacial changes in various types of radiographs, except cephalometric radiography.<sup>36-38</sup> Maxillary and mandibular bone trabeculae alterations with a coarse trabecular pattern are the most common findings in sickle cell anemia patients.<sup>36-38</sup>

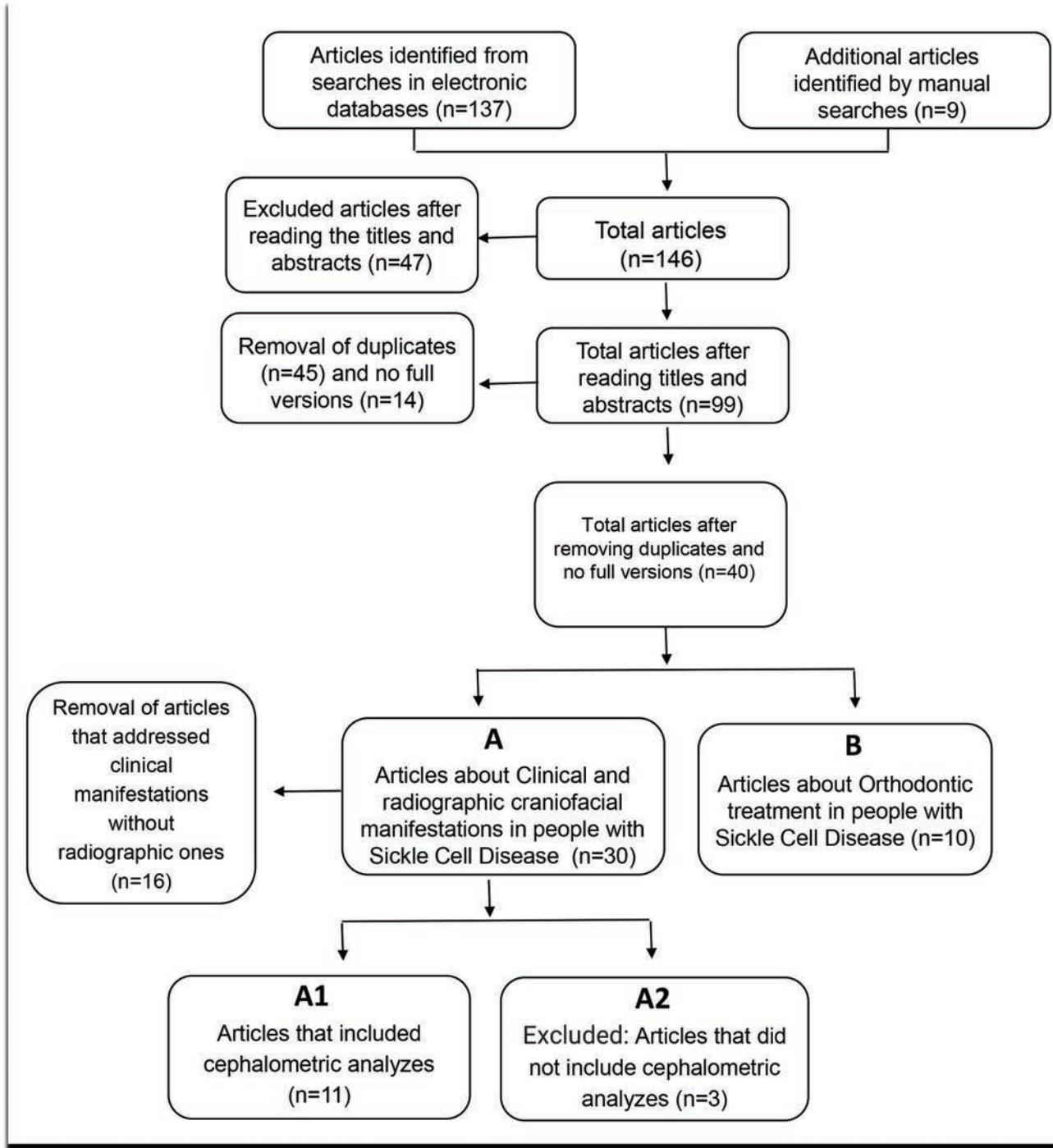


Figure 1: Flowchart of the search for the articles.

**Table 1:** Main findings of included SCD studies related to craniofacial and malocclusion changes through cephalometric radiographs.

Authors, year	Type/aim of the study	Study participants /age of participants	Age (years old)	Complementary diagnostic methods	Cephalometric findings	Craniofacial abnormalities and malocclusion
Brown & Sebes, 1986 <sup>26</sup>	Case-control study/ Analysis of sickle cell gnathopathies	75 black individuals Sickle cell group: 50 Hb SS Control group: 25 Hb AA	16-50 18-49	Lateral cephalometry	No significant differences were found for mean SNA angles between groups. (Hb SS: 82.54°; Hb AA: 81.76°)	Maxillary protrusion is due to an increase in the palate-alveolar ridge angle and not to the increased length of the hard palate.
Kavadias-Tsatsala et al., 2004 <sup>27</sup>	Cross-sectional study/Associate radiopaque lesions situated in the course of a known vessel or in the apical region of the teeth in the mandible with vaso-occlusive crises in sickle cell disease	42 Greeks with sickle cell disease	Sickle cell group: 20 - 65	Ortho and anteroposterior panoramic radiographs and lateral cephalometry	Findings related to the severity of Sickle Cell Disease and did not correlate with craniofacial abnormalities and malocclusion measured by Cephalometry.	All linear and angular measurements
Licciardello et al., 2007 <sup>28</sup>	Case-control study/ Evaluate the craniofacial morphology of Caucasians with sickle cell disease	72 Caucasian individuals: Sickle cell group: 14 Hb SS 13 Hb S $\beta$ 0 9 Hb S $\beta$ +	18.5-51.1 18.5-51.2	Lateral cephalometry	SNA angles: Hb SS/Hb S $\beta$ 0/ Hb S $\beta$ : 80.5° Hb AA: 80.4°	Vertical pattern of the face, posterior rotation of the mandible, and labial inclination of the upper incisors.

Racial perspective for oral findings in Sickle Cell Disease  
Almeida et al.

Note: Hb SS – Sickl cell anemia genotype; Hb AA – normal hemoglobin genotype ; Hb S $\beta$ 0 - Hb-S-beta 0 thalassemia; Hb S $\beta$ + Hb-S-beta + thalassemia - SNA angle - angle formed by the sella-nasion-A points; SNB angle - angle formed by the sella-nasion-B points. %U – percentage Unknown.

**Table 1:** Main findings of included SCD studies related to craniofacial and malocclusion changes through cephalometric radiographs.

Authors, year	Type/aim of the study	Study participants /age of participants	Age (years old)	Complementary diagnostic methods	Cephalometric findings	Craniofacial abnormalities and malocclusion
Costa et al., 2012 <sup>12</sup>	Review article/ Critically review craniofacial bone abnormalities and malocclusion in sickle cell disease.	Two studies <sup>26,29</sup> of seven studies including black people, from 10 to 46 years old.	10-45 <sup>26</sup> 20-46 <sup>29</sup>	Radiographic and cephalometry analysis <sup>26,29</sup>	Maxillary protusion (%U) <sup>26</sup> Maxillary protusion (%U), Mandibular retrusion (%U). Increased mandibular plane (%U) Convex facial profile (%U) <sup>29</sup>	No evidence for sickle cell disease as a risk factor for craniofacial bone abnormalities and malocclusion.
De Souza et al., 2008 <sup>29</sup>	Case-control study/ Evaluate and quantify craniofacial skeletal alterations in SCD	Sickle cell group: 30 black Hb SS patients  Control group: 30 black Hb AA patients with normal occlusion	Sickle cell group: over 18  Control group: over 18	Lateral cephalometry with Steiner and Downs tracings	Mean SNA angles: Hb SS: 85.42° Hb AA: 88.2°  Mean SNB angles: Hb SS: 78.35° Hb AA: 84.82°	Protrusion; Mandibular Retrusions; Increase in the Mandibular Plane; Convex facial profile Class II Skeletal Pattern
Maia et al., 2011 <sup>30</sup>	Cross-sectional study/Characterize the craniofacial pattern in SCD	50 Hb SS individuals without race description.	Sickle cell group: 18-43	Front and side photographs and lateral cephalometry	Mean SNA angle - Hb SS: 84.56° Mean SNB angle - Hb SS: 80.12°	No craniofacial pattern was associated;  No compensatory maxillary expansion; Maxilla length reduction (64%);  Absence of maxillary protrusion (69%)

Note: Hb SS – Sickle cell anemia genotype; Hb AA – normal hemoglobin genotype ; Hb S $\beta$ O - Hb-S-beta 0 thalassemia; Hb S $\beta$ + Hb-S-beta + thalassemia - SNA angle - angle formed by the sella-nasion-A points; SNB angle - angle formed by the sella-nasion-B points. %U – percentage Unknown.

**Table 1:** Main findings of included SCD studies related to craniofacial and malocclusion changes through cephalometric radiographs.

Authors, year	Type/aim of the study	Study participants /age of participants	Age (years old)	Complementary diagnostic methods	Cephalometric findings	Craniofacial abnormalities and malocclusion
Pithon et al., 2014 <sup>31</sup>	Case-control study/ Identify craniofacial characteristics of patients with sickle cell anemia and sickle cell trait	Sickle cell group: 15 Hb SS patients Sickle cell trait group: 15 Hb AS patients Control group: 15 Hb AA patients	mean age 20.8	Lateral cephalometry	Mean SNA angles: Hb SS: 83° Hb AS: 82.1° Hb AA: 79.7°	No compensatory maxillary expansion for the sickle cell trait and sickle cell disease groups.
Santos et al., 2018 <sup>32</sup>	Observational study/ Evaluate and describe cephalometric patterns of individuals with sickle cell disease			Mean SNB angles: Hb SS: 77.5° Hb AS: 78.3° Hb AA: 77.9°	Mean SNB angles: Class II Skeletal Pattern for sickle cell disease group	
				Mean SNA angles: 2D - sickle cell group: 82.22° 3D - sickle cell group: 83.04°	2D and 3D lateral cephalometry using Steiner and McNamara tracings 2D - sickle cell group: 80.07° 3D - sickle cell group: 79.93°	Not informed for other groups Mean SNB angles: 2D - sickle cell group: Not informed for other groups

Note: Hb SS – Sickl cell anemia genotype; Hb AA – normal hemoglobin genotype ; Hb Sβ0 - Hb-S-beta 0 thalassemia; Hb Sβ+ Hb-S-beta + thalassemia - SNA angle - angle formed by the sella-nasion-A points; SNB angle - angle formed by the sella-nasion-B points. %U – percentage Unknown.

**Table 1:** Main findings of included SCD studies related to craniofacial and malocclusion changes through cephalometric radiographs.

Authors, year	Type/aim of the study	Study participants /age of participants	Age (years old)	Complementary diagnostic methods	Cephalometric findings	Craniofacial abnormalities and malocclusion
Basyouni et al., 2018 <sup>33</sup>	Case-control study/ Determining malocclusion and craniofacial characteristics in adolescents with sickle cell disease	236 Saudi individuals.  Sickle cell group: 112 patients  Control group: 124 Hb AA patients	12-18	Digital Lateral Cephalometry	Mean SNA angles: Sickle cell group: 86.7°; Control group Hb AA: 81.5°.	Higher prevalence of malocclusion (87.5%) in sickle cell group  Greater need for orthodontic treatment in the sickle cell group
Pashine et al., 2020 <sup>34</sup>	Case-control study/ Evaluate the craniofacial and occlusal characteristics of children with sickle cell anemia	100 individuals between without race/ethnicity description  Sickle cell group: 50 Hb SS patients  Control group: 50 Hb AA patients without any systemic disease	10 - 18	Dental Models and lateral cephalometry	Mean SNA angles: Hb SS: 83.12° Hb AA: 84.1°  Mean SNB angles: Hb SS: 77.18° Hb AA: 79.52°	Delay in tooth eruption  Tendency to dental Class II (60%) and skeletal with a vertical facial growth pattern Increased overjet (62%) and overbite.
Ferreira et al., 2020 <sup>35</sup>	Case-control study/ Identify the main characteristics regarding the craniofacial shape and size in patients with sickle cell trait and sickle cell anemia	45 patients including children, teenagers, and adults. No description of race/ ethnicity.	Mean age 20.8.	Lateral Cephalometry	No quantitative measures related to SNA and SNB angles	Mandibular Retrusum  A labial tilt of the maxillary central incisors, which may suggest maxillary protrusion

Note: Hb SS – Sickle cell anemia genotype; Hb AA – normal hemoglobin genotype ; Hb S $\beta$ 0 - Hb-S-beta 0 thalassemia; Hb S $\beta$ + Hb-S-beta + thalassemia - SNA angle - angle formed by the sella-nasion-A points; SNB angle - angle formed by the sella-nasion-B points. %U - percentage Unknown.

**Table 2:** Main findings of non-included SCD studies related to craniofacial and malocclusion changes through panoramic, periapical, and interproximal radiographs.

Authors, year	Type/aim of the study	Study participants/age of participants	Diagnostic methods	Described findings
Mourshed et al., 1974 <sup>36</sup>	Case-control study/ Incidence and frequency of radiographic features in SCD	58 individuals  Sickle cell group 08 black patients with Hb SS and Hb SC without distinction between them	Panoramic, periapical, and interproximal radiography	Mandibular radiolucency and coarse bone trabeculae in 85% of patients with sickle cell disease
Arowojolu et al., 1997 <sup>37</sup>	Case-control study/ Compare alveolar bone patterns of individuals with SCD	50 random radiographs of healthy people  100 black people  Sickle cell group: 50 Hb SS patients  Control group: 50 Hb AA patients	Periapical radiography	No findings
Souza et al., 2018 <sup>38</sup>	Case-control study/ Estimate the association between sickle cell anemia and sickle cell trait with dental and mandibular changes and bone abnormalities	369 participants  (54 Caucasians, 104 blacks, and 211 of other races/ethnicities)	Periapical radiography	Changes in maxillary bone trabeculae (69.4%) and mandibular bone trabeculae (78.1%) in Hb SS individuals Partial or total loss of lamina dura more prevalent in Hb SS and Hb AS

## DISCUSSION

One way structural racism appears is when data produced from limited usage of theoretical and conceptual frameworks result in inadequately interpreted search results.<sup>39</sup> Racial prejudice prevents objective evaluation and sharing of study findings. A clear example is the non-racialized treatment of sickle cell patients.<sup>40</sup> In contrast to this trend, we searched the dental literature for craniofacial and malocclusion abnormalities linked to SCD. Based on lateral cephalometry, most studies conclude that craniofacial and occlusal anomalies, such as maxillary protrusion, the class II skeletal pattern, the vertical facial growth pattern, a convex facial profile, mandibular retrusion, and the posterior rotation of the jaw are the most common findings for people with SCD. However, there is no mention of racial or ethnic features related to specific cephalometric patterns. This is the main weakness of the reviewed studies and, consequently, of their findings.

First, it is important to mention that the bimaxillary protrusion resulting from the more labial positioning of maxillary and mandibular incisors is a common finding in African-descent populations. Previous cephalometric studies on the Brazilian black population with excellent occlusion showed the presence of protrusion of the gnathic bones as a pattern,<sup>41</sup> indicating a value for the SNA angle that was higher than that found in the SCD studies. Moreover, several studies have described dentoalveolar variations in Asian, Arabic, African, African-American, and African-Brazilian populations.<sup>24,25,42</sup> In Brazil, young African-Brazilian adults presented differences regarding dental and craniofacial characteristics when compared to European-American norms. Therefore, the cephalometric norms for some ethnic groups should be regarded carefully.<sup>24,25,42</sup> Cephalometric exams in patients with SCD must take into account the characteristics of specific groups in order to detect abnormalities. This action aids in optimizing the dental management of people with SCD, but it also increases the quality of study designs or the development of technologies, like cephalometric analysis using artificial intelligence, for example.

This viewpoint explained the variation among the examined studies. For example, for black individuals in a group with SCD, Brown *et al.*<sup>26</sup> and De Souza *et al.*<sup>29</sup> reported maxillary protrusion and mandibular retrusion related to the 85.42° and 82.54° SNA angles, respectively. On the other hand, Licciardello *et al.*<sup>28</sup> when evaluating Caucasian patients with sickle cell anemia or beta-thalassemia in comparison with control groups, found a mean SNA angle value of 80.5° for the three groups, and thus concluded that there is no tendency to maxillary protrusion. Cephalometric findings in

Sicilian patients only indicated a trend towards a more vertical face pattern. Maia *et al.*<sup>30</sup> and Pithon *et al.*<sup>31</sup> found mean values for the SNA cephalometric angle of 84.56° and 83° for people with sickle cell anemia, and 82.1° for those with a sickle cell trait. These values are within the standard deviation of the angle. There is no doubt that the adoption of cephalometry to diagnose craniofacial and malocclusion abnormalities in SCD should consider ethnic and racial plurality.

Another important point refers to the age of the cases and control groups concerning the craniofacial and occlusal features. As seen in Pashine's study,<sup>34</sup> the authors used an index not designed for mixed dentition to evaluate craniofacial and occlusal characteristics of children with sickle cell anemia. In addition, the authors described craniofacial patterns between young and adult patients as a comparable group,<sup>26,33-35,37</sup> which is a bias. Adults have complete bone growth, as opposed to younger children and teenagers, aged 10 to 18 years, who have transitory periods. In this phase, the occlusion is unstable because a series of specific alterations occur in the dental arch due to age,<sup>38</sup> along with bone growth, which are the factors that compromise the reliability of the findings.

Finally, there is no information about the medically-compromised health status of participants with SCD in the literature, such as their period of diagnosis, the frequency of pain crises, hospitalizations, blood transfusions, or their use of hydroxyurea or other medications. As known, these factors influence craniofacial and malocclusion patterns.<sup>43</sup> Furthermore, there was no mention of previous orthodontic treatment in the case or control groups in any of the reviewed papers.

Studies with sickle cell anemia patients<sup>44,45</sup> associated the compensatory growth of the bone marrow due to the intense production of blood cells, a phenomenon called hematopoiesis, with maxillary hyperplasia and changes in the dimension of the bone structure<sup>27,34-35</sup> as a response to hemolysis. Within a physiological process, there is a great demand for oxygen for the growth and development of the maxilla, leading to bone expansion. The lack of information about the use of hydroxyurea by the participants is another confounding factor, as this medication causes myelosuppression and modulates medullary bone activity on the compensatory expansion of the jaws. Silva-Pinto *et al.*<sup>17</sup> and Sant'Ana *et al.*<sup>18</sup> showed an increase in hemoglobin, fetal hemoglobin, and mean corpuscular volume, and a decrease in leukocytes and neutrophils,<sup>16-19</sup> representing a considerable improvement in the clinical and laboratory parameters of those who use hydroxyurea.<sup>18</sup> In addition, the amount of fat in the bone marrow of people with SCD is

associated with hemolysis and the regulation of bone marrow activity,<sup>46</sup> especially in children that have used hydroxyurea since childhood. Hydroxyurea is the main medication used to prevent pain crises and reduce the need for blood transfusions.<sup>47</sup> However, none of the reviewed studies indicated the level of “hematopoietically active” bone marrow as the inclusion criteria of case and control participants, nor did the use of Hydroxyurea medication in the case group.

As previously, stated, craniofacial and occlusal alterations in SCD did not occur systematically and recurrently in all people. There are exogenous and endogenous factors,<sup>48</sup> such as racial features and access to health services.<sup>48</sup> However, for Powers-Hays and McGann,<sup>40</sup> unfortunately, the social construct of race in America requires the majority of patients with SCD not only to face the consequences of a serious health condition, but also to navigate a society in which the color of their skin is often an unfair disadvantage.<sup>40</sup> Researchers should have considered this perspective.

Consisting of unconscious bias, ignorance, carelessness, and racist stereotyping, institutional racism is a collection of practices, attitudes, and behaviors that harm people of color. The absence of a racial component in the studies is a sign of institutional racism, which is the situation for SCD, particularly in populations of African descent. The presumption is that this information is irrelevant. Similar to this, several studies failed to mention whether or not a person used hydroxyurea or whether they received a diagnosis as a result of newborn screening. Despite this, the conclusions were extended more broadly to all groups, regardless of their internal characteristics. This produces skewed scientific data and unnecessary clinical action.

In fact, to have reliable knowledge about the oral health of people with SCD, high-quality studies must assume the proxy structured racism, both institutional and interprofessional, and link them to the well-defined data extraction from lifestyle complementary exams, and clinical characteristics, for oral manifestations in general, and craniofacial abnormalities and malocclusion in particular.

The study's limitations are due to the fact that this is a review study and that, despite being structured, the search and selection process might not have found all pertinent studies. Another issue is that the academic literature in the form of theses and dissertations was not included, which could have resulted in misunderstandings due to a lack of knowledge.

## CONCLUSION

In the reviewed dental literature, racial/ethnic

considerations, and SCD landmarks are underestimated. There are no racial/ethnic standpoints for craniofacial abnormalities and malocclusion diagnosis in SCD. In addition, there is no mention of important characteristics for patients with SCD. Both findings express structured racism.

## REFERENCES

1. Ware RE, de Montalembert M, Tshilolo L, Abboud MR. Sickle cell disease. *The Lancet*. 2017;390(10091):311-23. doi: 10.1016/S0140-6736(17)30193-9.
2. Safiri S, Kolahi A-A, Noori M, Nejadghaderi SA, Karamzad N, Bragazzi NL, et al. Burden of anemia and its underlying causes in 204 countries and territories, 1990–2019: results from the Global Burden of Disease Study 2019. *Journal of hematology & oncology*. 2021;14(1):1-16. doi: 10.1186/s13045-021-01202-2.
3. Piel FB, Hay SI, Gupta S, Weatherall DJ, Williams TN. Global burden of sickle cell anaemia in children under five, 2010–2050: modelling based on demographics, excess mortality, and interventions. *PLoS medicine*. 2013;10(7):e1001484. doi: 10.1371/journal.pmed.1001484.
4. Piel FB, Steinberg MH, Rees DC. Sickle cell disease. *New England Journal of Medicine*. 2017;376(16):1561-73. doi: 10.1056/NEJMra1510865.
5. National Academies of Sciences EaM. Addressing sickle cell disease: a strategic plan and blueprint for action. 2020. doi: 10.17226/25632.
6. Strauss T, Sin S, Marcus CL, Mason TBA, McDonough JM, Allen JL, et al. Upper airway lymphoid tissue size in children with sickle cell disease. *Chest*. 2012;142(1):94-100. doi: 10.1378/chest.11-2013.
7. Gulotta G, Iannella G, Vicini C, Polimeni A, Greco A, de Vincentiis M, et al. Risk factors for obstructive sleep apnea syndrome in children: state of the art. *International journal of environmental research and public health*. 2019;16(18):3235. doi: 10.3390/ijerph16183235.
8. JiménezSilva A, CarnevaliArellano R, VivancoCoke S, TobarReyes J, ArayaDíaz P, PalominoMontenegro H. Craniofacial growth predictors for class II and III malocclusions: A systematic review. *Clinical and Experimental Dental Research*. 2021;7(2):242-62. doi: 10.1002/cre2.357.
9. Fernandes MLdMF, Kawachi I, Fernandes AM, Corrêa-Faria P, Paiva SM, Pordeus IA. Oral health-related quality of life of children and teens with sickle cell disease. *Revista brasileira de hematologia e hemoterapia*. 2016;38:106-12. doi: 10.1016/j.bjhh.2016.01.004.
10. Correa MEP. Comment on: "Oral health-related quality of life in children and teens with sickle cell disease". *Revista brasileira de hematologia e hemoterapia*. 2016;38:97-8. doi: 10.1016/j.bjhh.2016.03.001.
11. Costa CP, Carvalho HL, Souza Sde F, Thomaz EB. Is sickle cell anemia a risk factor for severe dental malocclusion? *Braz Oral Res*. 2015;29. doi: 10.1590/1807-3107BOR-2015.vol29.0017.
12. Costa CP, de Carvalho HL, Thomaz EB, Sousa Sde F. Craniofacial bone abnormalities and malocclusion in individuals with sickle cell anemia: a critical review of the literature. *Rev Bras Hematol Hemoter*. 2012;34(1):60-3. doi: 10.5581/1516-8484.20120016.
13. Yawn BP, Buchanan GR, Afenyi-Annan AN, Ballas SK, Hassell KL, James AH, et al. Management of sickle cell disease: summary of the 2014 evidence-based report by expert panel members. *Jama*. 2014;312(10):1033-48. doi: 10.1001/jama.2014.10517.
14. Hsu LL, Fan-Hsu J. Evidence-based dental management in the new era of sickle cell disease: A scoping review. *The Journal of the American Dental Association*. 2020;151(9):668-77. doi: 10.1016/j.adaj.2020.05.023.

15. Bandeira FMGC, Peres JC, Carvalho EJ, Bezerra I, Araújo AS, Mello MRB, et al. Hidroxiuréia em pacientes com síndromes falciformes acompanhados no Hospital Hemope, Recife, Brasil. *Revista Brasileira de Hematologia e Hemoterapia*. 2004;26:189-94.
16. Cançado RD, Lobo C, Angulo IL, Araújo PIC, Jesus JA. Protocolo clínico e diretrizes terapêuticas para uso de hidroxiureia na doença falciforme. *Revista Brasileira de Hematologia e Hemoterapia*. 2009;31:361-6.
17. Silva-Pinto AC, Angulo IL, Brunetta DM, Neves FI, Bassi SC, Santis GC, et al. Clinical and hematological effects of hydroxyurea therapy in sickle cell patients: a single-center experience in Brazil. *Sao Paulo Med J*. 2013;131(4):238-43.
18. Sant'Ana PG, Araujo AM, Pimenta CT, Bezerra ML, Junior SP, Neto VM, et al. Clinical and laboratory profile of patients with sickle cell anemia. *Rev Bras Hematol Hemoter*. 2017;39(1):40-5. doi: 10.1590/1516-3180.2013.1314467.
19. Lopes CMI, Lira SS, da Silva Oliveira JC, Alves ELAC, de Melo Valença PA, de Menezes VA. Occlusal Disorders in Patients with Sickle Cell Disease: Critical Literature Review. *J Clin Pediatr Dent*. 2021;45(2):117-22. doi: 10.17796/1053-4625-45.2.8.
20. Helaly M, Abuaffan AH. Association between sickle cell disease and malocclusion among a sample of Sudanese children. *Indian J Dent Educ*. 2016;9(2):81-7.
21. Nancy A, Sukinah A, Maram A, Sara A, Hiba A, Manar A. Dental and Skeletal Manifestation of Sickle-Cell Anaemia and Thalassemia in Saudi Arabia; A Systematic Review. *International Journal of Pharmaceutical Research & Allied Sciences*. 2021;10(3).
22. Alves e Luna AC, Godoy F, De Menezes VA. Malocclusion and treatment need in children and adolescents with sickle cell disease. *The Angle Orthodontist*. 2014;84(3):467-72. doi: 10.2319/070913-503.1.
23. Subramanian AK, Chen Y, Almalki A, Sivamurthy G, Kafle D. Cephalometric Analysis in Orthodontics Using Artificial Intelligence—A Comprehensive Review. *BioMed Research International*. 2022;2022. doi: 10.1155/2022/1880113.
24. Naidoo LC, Miles LP. An evaluation of the mean cephalometric values for orthognathic surgery for black South African adults. Part 1: Hard tissue. *The Journal of the Dental Association of South Africa= Die Tydskrif van die Tandheelkundige Vereniging van Suid-Afrika*. 1997;52(7):495-502.
25. Oliveira TCPD, Copello FdM, Silva IMdCC, Nojima LI, Nojima MdCG. Dentofacial and skeletal pattern in African descendants from southeastern Brazil: clinical prospective study. *Dental Press Journal of Orthodontics*. 2021;26. doi: 10.1590/2177-6709.26.3.e2119288.oar.
26. Brown DL, Sebes JL. Sickle cell gnathopathy: radiologic assessment. *Oral Surg Oral Med Oral Pathol*. 1986;61(6):653-6. doi: 10.1016/0030-4220(86)90114-3.
27. Kavadia-Tsatala S, Kolokytha O, Kaklamanos EG, Antoniades K, Chasapopoulou E. Mandibular lesions of vasoocclusive origin in sickle cell hemoglobinopathy. *Odontology*. 2004;92(1):68-72. doi: 10.1007/s10266-004-0036-3.
28. Licciardello V, Bertuna G, Samperi P. Craniofacial morphology in patients with sickle cell disease: a cephalometric analysis. *Eur J Orthod*. 2007;29(3):238-42. doi: 10.1093/ejo/cjl062.
29. de Souza PHG, de Oliveira RS-MF, da Rocha JM, Gravina MA, Vitral RWF. Alterações esqueléticas crânio-faciais em portadores de anemia falciforme na cidade de Juiz de Fora. *HU Revista*. 2008;34(2).
30. Maia NG, dos Santos LA, Coletta RD, Mendes PH, Bonan PR, Maia LB, et al. Facial features of patients with sickle cell anemia. *Angle Orthod*. 2011;81(1):115-20. doi: 10.2319/012910-61.1.
31. Pithon MM, Palmeira LM, Barbosa AA, Pereira R, de Andrade AC, Coqueiro Rda S. Craniofacial features of patients with sickle cell anemia and sickle cell trait. *Angle Orthod*. 2014;84(5):825-9. doi: 10.2319/101513-764.1.
32. Dos Santos HLR, da Silva Barbosa I, de Oliveira TFL, Sarmento VA, Trindade SC. Evaluation of the maxillomandibular positioning in subjects with sickle-cell disease through 2-and 3-dimensional cephalometric analyses: A retrospective study. *Medicine*. 2018;97(25). doi: 10.1097/MD.00000000000011052.
33. Basyouni A, Almasoud NN, Al-Khalifa KS, Al-Jandan BA, Al Sulaiman OA, Nazir MA. Malocclusion and Craniofacial Characteristics in Saudi Adolescents with Sickle Cell Disease. *Saudi J Med Med Sci*. 2018;6(3):149-54. doi: 10.4103/sjmms.sjmms\_142\_17.
34. Pashine A, Shetty RM, Shetty SY, Gadekar T. Craniofacial and occlusal features of children with sickle cell disease compared to normal standards: a clinical and radiographic study of 50 paediatric patients. *Eur Arch Paediatr Dent*. 2020;21(3):303-11. doi: 10.1007/s40368-019-00484-y.
35. Ferreira WB, Nunes LA, Pithon MM, Maia LC, Casotti CA. Craniofacial geometric morphometrics in the identification of patients with sickle cell anemia and sickle cell trait. *Hematol Transfus Cell Ther*. 2020;42(4):341-7. doi: 10.1016/j.hctc.2019.10.003.
36. Mourshed F, Tuckson CR. A study of the radiographic features of the jaws in sickle-cell anemia. *Oral Surg Oral Med Oral Pathol*. 1974;37(5):812-9. doi: 10.1016/0030-4220(74)90146-7.
37. Arowojolu MO, Savage KO. Alveolar bone patterns in sickle cell anemia and non-sickle cell anemia adolescent Nigerians: a comparative study. *J Periodontol*. 1997;68(3):225-8. doi: 10.1902/jop.1997.68.3.225.
38. Souza S, de Carvalho H, Costa C, Thomaz E. Association of sickle cell haemoglobinopathies with dental and jaw bone abnormalities. *Oral Dis*. 2018;24(3):393-403. doi: 10.1111/odi.12742.
39. Jones CP. Confronting institutionalized racism. *Phylon* (1960-). 2002;7-22.
40. Power-Hays A, McGann PT. When actions speak louder than words—racism and sickle cell disease. *New England Journal of Medicine*. 2020;383(20):1902-3. doi: 10.1056/nejmmp2022125.
41. Fortes LdAP. Avaliação de medidas cefalométricas de indivíduos negros, brasileiros, portadores de oclusão excelente. 2000.
42. Bacon W, Girardin P, Turlot JC. A comparison of cephalometric norms for the African Bantu and a Caucasoid population. *The European Journal of Orthodontics*. 1983;5(3):233-40. doi: 10.1093/ejo/5.3.233.
43. Neves FS, Passos CP, Oliveira-Santos C, Cangussu MC, Campos PS, Nascimento RJ, et al. Correlation between maxillofacial radiographic features and systemic severity as sickle cell disease severity predictor. *Clin Oral Investig*. 2012;16(3):827-33. doi: 10.1007/s00784-011-0577-0.
44. Alves PV, Alves DK, de Souza MM, Torres SR. Orthodontic treatment of patients with sickle-cell anemia. *Angle Orthod*. 2006;76(2):269-73. doi: 10.1043/0003-3219(2006)076[0269:otopws]2.0.co;2.
45. Vilela LT, Barreto BCT, Bolognese AM, de Souza MMG. The Challenge of Orthodontic Treatment Against Sickle Anemia: Fear or Lack of Information? *Odontol*. 43:92-6.
46. Shapiro, L. MRI technique that measures bone marrow fat may predict SCD severity. Patients with more signs of hemolysis had less fat MRI technique that measures bone marrow fat. *Sickle Cell Disease News*. March 16, 2023. Available from: [https://sicklecellanemianews.com/news/mri-technique-that-measures-bone-marrow-fat-may-predict-scd-severity/?utm\\_source=SIC&utm\\_campaign=59ba33aff-SIC\\_ENL\\_3.0\\_UNKNOWN&utm\\_medium=email&utm\\_term=0\\_b01e3fb8e-59ba33aff-74016989](https://sicklecellanemianews.com/news/mri-technique-that-measures-bone-marrow-fat-may-predict-scd-severity/?utm_source=SIC&utm_campaign=59ba33aff-SIC_ENL_3.0_UNKNOWN&utm_medium=email&utm_term=0_b01e3fb8e-59ba33aff-74016989). Accessed on March, 19<sup>th</sup>, 2023.
47. Tonin FS, Ginete C, Ferreira J, Delgadinho M, Santos B, Fernandez-Llimos F, Brito M. Efficacy and safety of pharmacological interventions for managing sickle cell disease complications in children and adolescents: Systematic review with network meta-analysis. *Pediatr Blood Cancer*. 2023;14:e30294. doi: 10.1002/pbc.30294. Epub ahead of print.
48. Royal CDM, Babyak M, Shah N, Srivatsa S, Stewart KA, Tanabe P, et al. Sickle cell disease is a global prototype for integrative research and healthcare. *Advanced Genetics*. 2021;2(1):e10037. doi: 10.1002/ggn.2.10037.