

Dental Implants in Patients with Sickle Cell Disease: A Review of Literature

Kakkar M^{1*} and Gangwani P²

¹Dental Resident, Department of General Dentistry, Eastman Institute for Oral Health, University of Rochester, USA

²Department of Oral and Maxillofacial Surgery, University of Rochester School of Medicine and Dentistry/ Eastman Institute for Oral Health, USA

*Corresponding author:

Mayank Kakkar,
Dental Resident, Department of General Dentistry,
Eastman Institute for Oral Health, University of Rochester,
625 Elmwood Ave, Rochester, NY, 14620, USA,
E-mail: mayankuever@gmail.com

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1. Abstract

1.1. Study Objective: The study aims to review the current literature on sickle cell disease and dental implant as a treatment modality for the replacement of the missing dentition.

1.2. Material and Methods: A comprehensive systematic literature review was conducted using the PubMed, Medline, Embase, Cochrane Central Register of Controlled Trials, Web of Science, Google Scholar, the US National Institutes of Health Trials Registry, WHO Library, with no language filter. The search strategies were developed to cover publications January 2010 through October 2020. Five studies met the inclusion criteria.

1.3. Results: Of the five studies included, one study investigated the changes in the bone pattern using radiographic parameters, such as 1) trabecular bone pattern (step-ladder or spider web); 2) integrity of the lamina dura (loss of sharpness and continuity, partial or complete absence, and increased thickness), in patients with SCD. Another study performed a retrospective analysis of SCD patients who had undergone oral surgery procedures in an outpatient setting. Two studies included literature reviews related to oral surgery and the management of patients with sickle cell disease. Only a single case report on dental implant placement was identified and incorporated into the systematic review.

1.4. Conclusion: Abnormal trabecular pattern secondary to medullary hyperplasia may have a negative impact on mechanical properties of the bone, thereby affecting bone-to-implant contact and osseointegration. Additionally, vaso-occlusive events in the

jaws jeopardize the blood supply, increasing susceptibility to infections and osteomyelitis. Based on the pathophysiology of the disease, it is prudent to conclude that dental implants may not be recommended in patients with SCD. However, due to a dearth of information in the literature on dental implants in SCD, we cannot conclude that it is an absolute contraindication.

2. Introduction

Sickle cell disease (SCD) is an autosomal recessive genetic disorder of the red blood cells (RBCs), characterized by abnormal hemoglobin, affecting approximately 100,000 people in the United States and > 13 million people worldwide [1]. It results due to an occurrence of a point mutation in the hemoglobin beta chain, in which glutamic acid is substituted by valine. Consequently, normal hemoglobin is replaced by an altered hemoglobin S (Hb S) molecule. Under low oxygen tension, this altered hemoglobin molecule polymerizes, causing RBCs to undergo a process called sickling (crescent shape RBCs). This renders RBCs more stiff and adherent to the endothelial cells and responsible for the vaso-occlusive crises, which in turn leads to ischemic events.

SCD affects multiple organs and leads to complications such as painful crises, stroke, splenic sequestration, acute chest syndrome, infections, and bone necrosis. Survival rates of patients with SCD in the United States have improved dramatically. Their average life span is noted to be of 48 and 42 years of age for females and males, respectively [2]. This significant improvement has been attributed to the early childhood intervention programs that include

widespread screenings, administering a pneumococcal vaccine, antibiotic prophylaxis, and the use of hydroxyurea, the medication that has shown to decrease mortality and morbidity in patients with SCD [2, 3].

Owing to the increased life expectancy of the patients with SCD, it is natural that more of such patients will be seen by oral and maxillofacial surgeons and other dental specialists. As such, these patients may present with non-restorable dentition requiring extractions and dental implants. Therefore, it is paramount that as a specialty, we are prepared to manage such patients.

SCD increases the risk for jaws changes and osteomyelitis. As a result, placement of dental implants in such patients has been a topic of concern. Thus far, no study is available to support the placement of dental implants in patients with SCD. On the contrary, there is also a lack of evidence in the literature to confirm that it is a down-right contraindication. Given there are no clinical studies pertaining to dental implants in patients with SCD, a literature review was undertaken to find articles that had discussed dental implants as a modality to replace missing teeth in patients with SCD. The aim of this study was to compile the data and present it in a concise fashion.

3. Material and Methods

3.1. Search Strategy

To address the objective of the study; a literature review was designed and implemented. A comprehensive literature review was conducted using the PubMed, Embase, Web of Science, Google Scholar, with no language filter. The search strategies were developed to cover publications from January 2010 through October 2020. Details of the search strategy are provided in table 1. In

addition, dental organization websites were searched to identify relevant articles. The references of all the included articles were searched for additional relevant studies.

Two authors MK and PG conducted database searches independently. All disagreements were resolved verbally, with strict adherence to the predetermined inclusion criteria.

3.2. Inclusion and Exclusion Criteria

The following inclusion criteria were applied: 1) publications in the English language, 2) full length manuscripts, 3) studies that discussed dental implants in patients with SCD.

The following exclusion criteria were applied: 1) studies involving patients with sickle cell trait, 2) studies reporting dental management of the SCD patient without discussing dental implants as a possible treatment option, 3) in vitro studies, 4) animal studies, 5) letters, editorials, abstracts.

3.3. Selection of the Studies

The manuscripts selected included retrospective cross-sectional study, retrospective cohort study, case report, and literature review. Two authors MK and PG conducted database searches independently. All disagreements were resolved verbally, with strict adherence to the predetermined inclusion criteria.

3.4. Data Extraction

Data extraction was also performed by authors MK and PG independently, utilizing a previously planned and prepared data extraction template. Information on the following variables was included: authors, title, year of publication, study design, results, conclusion pertaining to dental implant placement. Please refer to table 2.

Table 1: Database Search Strategies

Database	Key Words	Results	Articles Included
PubMed	("surgery, oral"[MeSH Terms] OR "oral surgical procedures"[MeSH Terms] OR "oral health"[MeSH Terms] OR (Dental[MeSH Terms]) AND (("sickle"[All Fields] OR "sickled"[All Fields] OR "sickles"[All Fields] OR "sickling"[All Fields]) AND ("cells"[MeSH Terms] OR "cells"[All Fields] OR "cell"[All Fields]))	86	3
Google Scholar	"sickle cell" (dental implant" OR "dental implants")	526	1
Web of science	(dental implant*) AND ("sickle cell")	23	0
Embase	Population – Sickle cell, Intervention – tooth implant, Comparison – none, Outcome - none	3	0
Additional from references			1

Table 2: Summary of Included Articles

Author Name	Year	Title	Study Design	Results	Conclusion
Soares-Silva et al ⁸	2020	Dental implant in a young patient with sickle cell disease: a case report	Case report	Satisfactory 18 months follow up after placement of an immediate implant to replace left central incisor	Consider implants with caution and adequate knowledge
Kawar et al ⁷	2018	Oral health management considerations for patients with sickle cell disease	Literature review	Reduction of bone mechanical properties, susceptibility for infections, decreased blood supply due to vaso-occlusive events, bony infarcts, delayed bone healing may impair the osseointegration process and long term success of implant therapy	Recommended less invasive alternative to dental implants
Prevost et al ⁶	2018	Management of patients with sickle cell disease in oral surgery. Literature review and update	Literature review	Placement of dental implant is an etiological factor contributing to osteomyelitis	Advised against implant placement in SCD
Carvalho et al ⁴	2017	Are dental and jaw changes more prevalent in a Brazilian population with sickle cell anemia?	Retrospective cross sectional	Individuals with SCD had a higher prevalence of trabecular bone changes, both in the maxilla and the mandible	Dental implants contraindicated
Stanley et al ⁵	2013	Sickle cell disease and perioperative considerations: review and retrospective report	Retrospective report	Depending on the patient's history, a blood transfusion may be preferred	No comment specific to dental implants

4. Results

The literature search revealed 641 articles. These articles were further screened, inclusion and exclusion criteria were applied, and four articles were included in our study sample. The references of all four articles were searched and one article was identified to be relevant for our review, resulting in five articles which met the inclusion criteria.

Of the five studies included, one study investigated the changes in the bone pattern using radiographic parameters, such as 1) trabecular bone pattern (step-ladder or spider web); 2) integrity of the lamina dura (loss of sharpness and continuity, partial or complete absence, and increased thickness), in patients with SCD [4]. Another study performed a retrospective analysis of SCD patients who had undergone oral surgery procedures in an outpatient setting [5]. Two studies included literature reviews related to oral surgery and the management of patients with sickle cell disease [6, 7]. Only a single case report on dental implant placement was identified and incorporated into the systematic review [8].

The cross-sectional retrospective study on jaw changes, specifically bone pattern and integrity of lamina dura, recruited a total of 246 study participants. They were divided into two groups: SCD and control, with 123 patients per group. Intra oral periapical radiographs were taken to identify jaw changes as per the set radiographic parameters. The study results demonstrated that patients with SCD had a higher prevalence of changes in the trabecular bone, such as a step-ladder appearance ($P < .001$) or spider web-like pattern ($P < .001$), as compared to the control group. As well as changes in the lamina dura were more common in patients with SCD than in the controls ($P = .021$) [4].

The retrospective analysis of 21 patients who had teeth extraction revealed, managing patients with SCD in an outpatient setting may

be a safe alternative to inpatient or no treatment at all [5]. The literature review of two articles on oral surgery and SCD resulted in the following comments specific to dental implants: 1) osseointegration process and long term success of dental implants are impaired secondary to reduction of bone mechanical properties; 2) dental implant placement can be a factor contributing to osteomyelitis of jaws [6, 7].

The only case report included in this systematic review revealed successful osseointegration of the dental implant ten months after its placement on a 15-year-old male patient, with a history of SCD. The dental implant was placed in an immediate fashion to replace an upper left central incisor [8].

5. Discussion

The purpose of this literature review was to discuss dental implants as a modality to replace missing teeth in patients with SCD, compile the available information and present it in a concise fashion.

In a case report by Soares-Silva et al., [8] the authors treated a 15-year-old male patient with an immediate dental implant to replace an upper left central incisor after the patient had sustained dental trauma, during a football match. Initially, the patient was taken for specialized care, where the pulp therapy was initiated but was not completed. Over the years, the condition worsened, compromising the patient's esthetics and self-esteem. The tooth was deemed non-restorable, as such extraction followed by immediate dental implant was planned. Ten months after surgery, the radiographic examination showed satisfactory osseointegration of the implant [8].

A review of literature conducted by Kawar et al. [7] on oral health management considerations for a patient with SCD, found no evidence in the literature to conclude that placement of a dental implant is an absolute contraindication in the patient with SCD.

However, they also documented that no literature is available to support the use of dental implants in patients with SCD. The authors concluded that based on the pathophysiology of the SCD, which leads to an abnormal trabecular pattern, compromised mechanical properties of bone, delayed bone healing, susceptibility for infections, decreased blood supply due to vaso-occlusive crises – placement of dental implants may not be prudent. They recommend that it is in the best interest of the patient to provide a non-invasive and conservative procedure (partial denture), an alternative that involves less surgical trauma [7].

A literature review performed by Prevost et al [6]. discussed the management of patients with sickle cell disease in oral surgery. The authors suggest that dental implants can increase the risk of osteomyelitis in patients with SCD. Mandible accounts for 3 to 5% of osteomyelitis cases in patients with severe SCD. Additionally, the presence of dental implants in regions where the bone medulla is infected affects prognosis for the recovery negatively. Thus, the authors advise against the placement of dental implants in the sickle cell disease patients [6].

A retrospective cross-sectional study conducted by Carvalho et al., [4] aimed to describe and differentiate dental and jaw changes (trabecular bone pattern and integrity of lamina dura) in patients with SCD and their controls. The authors recruited a total of 246 study participants. They were divided into two groups: SCD and control, with 123 patients per group. Intraoral periapical radiographs were taken to identify jaw changes as per the set radiographic parameters. The study results indicated that patients with SCD had a higher prevalence of trabecular bone changes, such as the presence of step-ladder appearance or spider weblike pattern in the maxilla and the mandible. These radiographic changes occur secondary to erythroid hyperplasia and expansion of the medullary bone as a consequence of vaso-occlusion. The study concluded that patients with SCD who have a distinctive pattern of trabecular bone and increased marrow spaces are at increased risk of developing complications after dental implant placement. Furthermore, decreased bone density can influence the formation of mature lamellar bone at the implant bone interface affecting the osseointegration process and the prognosis of the dental implant procedure [4].

A retrospective analysis by Stanley & Christian [5] on patients with SCD and outpatient procedures concluded that managing patients with SCD in an outpatient setting may be a safe alternative to inpatient or no treatment at all. It is crucial for the rendering provider to be mindful of the pathophysiology of the disease and triggering factors that could lead to crisis. One such inciting cause is decreased oxygen tension, which can lead to the sickling of erythrocytes. Therefore, it is imperative to provide perioperative supplemental oxygen and perform pulse oximeter monitoring. Although procedures involving teeth extraction and implant placement rarely cause significant blood loss, management of patients with SCD requires a pre-operative consultation with the patient's

primary care physician or hematologist. Based on the patient's disease control, anemic state, and previous history, blood transfusions may be recommended to maintain hemoglobin levels around 10 g/dL and to improve the patient's oxygen saturation potential [5].

Hemolytic anemia is reduced and/or lack of blood supply that can lead to organ damage in patients with SCD. In such patients, bones are susceptible to avascular necrosis and osteomyelitis [9]. Ischemia secondary to sickling results in infarction and necrosis of bone, which in turn provides a conducive environment for bacterial growth. Long bones are more commonly affected than bones in the maxillofacial region [9]. The mandible is at increased risk due to relatively poor vascular supply. A scoping review published by Hsu et al., [10] addressing oral health in patients with SCD and their systemic health interactions, concluded that the poor access to care, delayed recognition, inadequate systemic treatment, caries, and infection of devitalized bone are triggering factors for osteomyelitis of the jaw [10].

The present review has several major limitations. First, clinical studies involving the placement of dental implants in patients with SCD were not included, as there are none available in the literature, with the exception of just one recently published case report. Therefore, the level of evidence presented in this review is poor. Our study sample comprised of one case report that describes an individual case of implant placement in a patient with SCD and four manuscripts that just commented on dental implants in patients with SCD. Although there is a lack of data on this front, the general consensus in the literature based on our review is that patients with SCD are at higher risk of developing dental implant related complications.

6. Conclusion

The results of this review, although stand on low evidence level studies allude that the abnormal trabecular pattern secondary to medullary hyperplasia may have a negative impact on mechanical properties of the bone, thereby affecting bone-to-implant contact and osseointegration. Additionally, vaso-occlusive events in the jaws jeopardize the blood supply, increasing susceptibility to infections and osteomyelitis. Based on the pathophysiology of the disease, it is prudent to conclude that dental implants may not be recommended in patients with SCD. However, due to a dearth of information in the literature on dental implants in SCD, we cannot conclude that it is an absolute contraindication. Further studies are required to provide evidence regarding implant therapy in patients with SCD.

7. Implications for Future Research

This review has identified the need for clinical studies to assess the success of dental implants in patients with SCD. One of the most important question to answer through conducting clinical studies is: if the patients with SCD are well managed systemically and have no trabecular bone changes – can they be a candidate for dental implant?

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