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ABSTRACT

This study investigated the prevalence of dental caries and periodontal condition in a population with sickle cell disease (SCD), analyzing some associations with disease severity. The Decayed, Missing and Filled Teeth index (DMFT) and Community Periodontal Index (CPI) were recorded for 99 individuals with SCD and 91 matched controls. Socio-demographic status, oral health behaviors, and history of clinical severity of SCD were assessed. Statistical comparisons were performed between the group with SCD and the control group, as well as multivariate logistic regression analyses with DMFT index and CPI as the dependent variables. The mean number of decayed teeth was significantly higher in individuals with HbSS. Older age, female gender, and daily smoking were identified as risk factors for higher DMFT, while older age and absence of daily use of dental floss were risk factors for the development of periodontal disease. In conclusion, risk factors known to cause caries and periodontal disease had more influence on oral health than the direct impact of SCD.

KEY WORDS: dental caries, periodontal disease, sickle cell disease, sickle cell anemia

Sickle cell disease does not predispose to caries or periodontal disease

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Introduction

Sickle cell disease (SCD) is one of the most widespread genetic disorders worldwide.[1] In SCD, polymerization of an abnormal hemoglobin (HbS) leads to morphologic alterations of erythrocytes.[1] Sickle cell anemia (SCA), the most common and severe form of the disease, is characterized by homozygosis for HbS (HbSS genotype).[1] SC disease (HbSC genotype) is a milder clinical presentation of SCD in which abnormal HbC induces erythrocyte dehydration, facilitating HbS polymerization.[2]

SCD mainly affects Africans and their descendants. In Brazil, more than two million people are estimated to carry the HbS gene, and more than 8,000 are affected by SCA.[3] In the United States, an estimated 100,000 people have SCD.[4]

Sickle erythrocytes show less flexibility and higher adherence to endothelium, causing vaso-occlusion of microcirculation that can result in tissue ischemia and infarction.[1] Premature destruction of altered red blood cells may lead to chronic anemia.[1] Systemic manifestations of SCD and its severity vary among individuals. Actually, two clinical subphenotypes have been reported; a vasculopathy subphenotype related to hemolysis which can lead to pulmonary hypertension, priapism, leg ulceration, and stroke, whereas a viscosity-vaso-occlusive subphenotype involves vaso-occlusive pain crisis, acute chest syndrome, and osteonecrosis.[5]

Less common than the two subphenotypes referenced above, the oral manifestations reported in subjects with SCD include pallor of the mucosa, gingival enlargement and excessive bleeding,[6] mandibular osteomyelitis,[7,8] inferior alveolar nerve paresthesia,[8-10] asymptomatic pulpal necrosis,[9-12] and enamel hypomineralization and/or hypomaturation.[13-15]

Only a few studies[15-22] have reported on the prevalence of dental caries[15-18] and periodontal disease[19-22] in patients with SCD and even these present controversial results.

The aim of this study was to investigate the prevalence of dental caries and periodontal disease in a Brazilian adult population with SCD, analyzing possible

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Table 1. Statistical comparison of mean age and gender among the study groups.

	HbSS	HbSC	Controls	*p*-value
	n = 51 (%)	n = 48 (%)	n = 91 (%)	
Gender				
Male	23 (45)	15 (31)	30 (33)	0.26
Female	28 (55)	33 (69)	61 (67)	
Mean age (SD)	31.51 (±10.16)	34.19 (±13.02)	34.05 (±11.89)	0.10

SD = standard deviation.

associations with the history of the disease and its systemic severity.

Material and methods

The study was carried out at The School of Dentistry of Federal University of Bahia, Brazil, and was approved by the Research Ethics Committee of Climério de Oliveira Maternity Hospital. All volunteers signed informed consent forms.

Subjects included 190 Brazilians of African descent who were subdivided into two groups: a group with SCD, consisting of 99 subjects with SCD (51 HbSS and 48 HbSC), and a control group comprising 91 subjects without SCD (HbAA). The group with SCD and the control group were matched according to gender, age, and socioeconomic status. The power of the sample was calculated after the study at a confidence level of 95% (significance level 95%; OR-1.5; 1-β = 75%).

Subjects were screened by the Laboratory of Genetics of Professor Edgar Santos University Hospital, the Foundation of Hematology and Hemotherapy of Bahia, or the Laboratory of Specialized Analysis in Hematology of the School of Pharmacy of Federal University of Bahia. Their hemoglobin was evaluated by electrophoresis examination. Exclusion criteria included presence of other systemic diseases and/or prolonged use of medication that could affect bone or dental enamel, such as prolonged use of antibiotics and amelogenesis imperfecta.

The history of clinical systemic severity was assessed for subjects with SCD through direct questioning about their frequency of vaso-occlusive crisis, history of stroke, clinical jaundice, femur head necrosis, and leg ulcerations. All subjects were questioned about their oral health behaviors such as: daily smoking, annual access to dental care, daily toothbrushing, and use of dental floss. Demographic characteristics studied included age (<34 and ≥34 for dental caries analysis; <32 and ≥32 for periodontal disease analysis), gender, monthly family income (<$855 or ≥$855), and highest level of schooling (≤10 years of study or >10 years of study). All dichotomized variables were made using the median distribution. These data were collected by the same interviewer without knowledge of the subjects' oral condition.

All dental examinations were carried out by the same examiner, who was blinded to the severity of the subjects' systemic problems and oral health behaviors. The dental examinations were done according to World Health Organization (WHO) recommendations.[23]

Caries prevalence was evaluated using the Decayed, Missing and Filled Teeth index (DMFT), using a standard dental chair, artificial lighting, and mouth mirror, without a radiographic examination. For all teeth (except third molars), all surfaces were examined and the worst condition was recorded. Based on the subjects' self-reported information, teeth lost for any reason other than caries were excluded from the missing teeth record.

Periodontal condition was evaluated using the Community Periodontal Index (CPI), with a WHO probe. Ten index teeth (17, 16, 11, 26, 27, 37, 36, 31, 46, 47), were probed at six sites (mesio-buccal, mid-buccal, disto-buccal, and the corresponding lingual sites) and the highest score was recorded for each sextant. If no index teeth were present in a qualifying sextant, the adjacent remaining teeth were examined. Sextants with less than two teeth were excluded. The highest resulting score was recorded as the CPI score for each subject. Five scores were used to record the CPI: 0 = healthy, 1 = gingival bleeding, 2 = calculus, 3 = shallow periodontal pocket of 3.5–5.5 mm, and 4 = deep periodontal pocket of more than 5.5 mm.

Intra-examiner reliability was calculated by Kappa analysis and was measured as 0.82 and 0.64 for the DMFT index and CPI, respectively. Statistical analysis of data included comparisons between both study groups with chi-square or Fisher's Exact test (p-value <0.05).

Bivariate and multivariate logistic regression analyses, using the backward methods, were applied considering DMFT index and CPI as the dependent variables, whereas history of clinical systemic severity, socio-demographic status and oral health behaviors were considered as independent variables. Chi-square or Fisher's exact test were applied, and independent variables that had a p-value less than 0.25 were included in the final model of logistic regression. The statistical inferences were performed by final result of OR and 95% confidence interval calculated by Poisson.

Results

The mean age of subjects was 32.66 (±11.62), ranging from 16 to 68 years. There were no significant statistical differences related to gender or age between the two groups (Table 1).

The mean DMFT was 11.8 (±6.16) for subjects with HbSS, 11.22 (±6.57) for those with HbSC, and 11.3 (±6.93) for the control group, with no significant statistical differences between the groups (p = 0.63). Mean values for decayed, missing and filled teeth for both groups

Table 2. Mean values for decayed, missing, and filled teeth for all the study groups.

	HbSS mean (SD)	HbSC mean (SD)	Controls mean (SD)	*p*-values
Decayed	4.23 (±4.19)	3.27 (±2.98)	2.91 (±3.07)	0.07
Missing	4.52 (±5.74)	4.47 (±4.72)	4.79 (±5.76)	0.93
Filled	3.13 (±3.59)	3.47 (±3.22)	3.68 (±3.93)	0.64

SD = standard deviation.

Table 3. Scores and mean CPI for all the study groups.

Group	Score					Mean
	0	1	2	3	4	
	n (%)	n (%)	n (%)	n (%)	n (%)	
HbSS (n = 51)	4 (7.8)	18 (35.3)	23 (45.1)	5 (9.8)	1 (2.0)	1.63
HbSC (n = 48)	–	17 (35.4)	18 (37.5)	11 (22.9)	2 (4.2)	1.96
Controls (n = 91)	3 (3.3)	34 (37.4)	32 (35.2)	19 (20.8)	3 (3.3)	1.83

are presented in Table 2. The only significant statistical difference observed was for mean decayed teeth, which was significantly higher in subjects with HbSS than in the control group ($p < 0.01$).

Table 3 presents scores and mean CPI for both groups. There was no statistically significant difference for mean CPI between the two groups. Because there was no association between SCD and oral condition, the impact of other variables on oral condition was analyzed by logistic regression. In these further analyses, the sample population was dichotomized (0 to 11, and 11+) with the mean value of DMFT as while periodontal condition was divided as CPI scores 0, 1, and 2 and CPI scores 3 and 4.

When evaluating the sample population, the adjusted analysis identified older age, female gender, and daily smoking as significant risk factors for persons with higher DMFT values (Table 4). Also, older age and absence of daily use of dental floss were found to be significant risk factors for the presence of deeper periodontal pockets (Table 5). When only subjects with HbSS and HbSC were evaluated, there was no statistical association between a history of clinical systemic severity of the disease and the DMFT index or CPI (Table 6).

Discussion

Our results suggest that in this population of subjects with SCD, the sickle condition (HbSS or HbSC) or the disease's clinical severity were not the main risk factors for the development of caries and periodontal disease.

In an earlier study[15] the reduced ingestion of sweets has been suggested as a possible explanation of the lower occurrence of caries in 37 subjects with HbSS (35.13%) aged between 14 and 33

Table 4. Significant risk variables considering DMFT as dependent variable.

Risk variables	DMFT <11 (n = 97) n (%)	DMFT ≥11 (n = 93) n (%)	*p*-value for bivariate analyses	Crude OR (95% CI)	Adjusted OR (95% CI)
Gender					
Male	41 (42.3)	27 (29.0)	0.06	1.79 (0.94–3.42)	1.86 (1.01–3.46)
Female	56 (57.7)	66 (71.0)			
Age					
<34 years	72 (74.2)	29 (31.2)	<0.01	6.36 (3.23–12.61)	6.03 (3.12–11.64)
≥34 years	25 (25.8)	64 (68.8)			
Daily smoking	19 (19.6)	31 (33.3)	0.03	2.05 (1.01–4.20)	2.28 (1.15–4.50)

Table 5. Significant risk variables considering CPI as dependent variable.

Risk variables	CPI 0+1+2 (n = 149) n (%)	CPI 3+4 (n = 41) n (%)	*p*-value for bivariate analyses	Crude OR (95% CI)	Adjusted OR (95% CI)
Age					
<32 years	81 (54.4)	16 (39.0)	0.08	1.86 (0.87–4.00)	2.05 (1.01–4.26)
≥32 years	68 (45.6)	25 (61.0)			
Daily use of dental floss	42 (28.2)	2 (4.9)	0.02	0.13 (0.02–0.59)	0.13 (0.03–0.59)

Table 6. Analyses between history of clinical systemic severity of patients with SCD and DMFT index and CPI.

History of disease clinical severity	DMFT			CPI		
	<11 (n = 50) n (%)	≥11 (n = 49) n (%)	*p*-value	0+1+2 (n = 80) n (%)	3+4 (n = 19) n (%)	*p*-value
Frequency of vaso-occlusive crisis						
Never	8 (16)	7 (14.3)	0.46	11 (13.7)	4 (21.1)	0.67
≤twice a month	14 (28)	11 (22.4)		20 (25)	5 (26.3)	
once or twice a year	19 (38)	21 (42.9)		35 (43.8)	5 (26.3)	
≥3 years in steady state	9 (18)	10 (20.4)		14 (17.5)	5 (26.3)	
Stroke	3 (6)	4 (8.2)	0.67	5 (6.25)	2 (10.5)	0.58
Leg ulceration	14 (28)	19 (38.8)	0.25	27 (34)	6 (31.6)	0.69
Clinical jaundice	30 (60)	28 (57.1)	0.77	51 (64)	7 (36.8)	0.09
Femur head necrosis	6 (12)	10 (20.4)	0.78	13 (16.3)	3 (15.8)	0.71

years, when compared to 24 matched controls (54%). However, there was no methodological description in this study to support the author's conclusion.[15] The long-term use of penicillin by children with SCD may delay the acquisition of *Streptococcus mutans,* which can result in a significant reduction in dental caries.[17] This advantage is limited to the period during active drug use, suggesting that there is no influence on caries subsequent to stopping the use of antibiotics.[17]

In a retrospective study[18] which did not control for confounding factors, comparison between 35 subjects with HbSS and 140 controls found that the DMFS index was 29% higher in subjects with SCD aged 18 and older, whereas there was little difference observed between groups consisting of children and adolescents. In addition, in the sample population, the mean total of missing surfaces was 41% higher for subjects with SCD.[18] Later, this same research group[16] used a standardized oral examination to compare DMFS index between 102 subjects with sickle cell (82 HbSS, 15 HbSC, 5 HbS beta-thalassemic) and 103 matched controls, aged 18–70 years. Statistical analysis adjusted for frequency of vaso-occlusive crisis, age, gender, risk factors for caries, and socioeconomic status showed that for low-income African Americans, those with SCD had significantly more decayed and fewer filled surfaces.[16] Because the control subjects were recruited among patients receiving treatment in a College of Dentistry and subjects with SCD were selected from hematological clinics at the University Hospitals, these results may not reflect the true impact of disease on caries experience. In addition, analyzing this same sample population, psychological factors were found to be associated with increased untreated caries, regardless of presence or absence of SCD.[24]

The presence of enamel hypomineralization in subjects with HbSS[14] could indicate that the hypocalcification of enamel matrix, due to metabolic and hormonal disturbances, would increase the risk of dental caries in these individuals.

In our study, the mean number of decayed teeth showed a high level of caries activity in the group with HbSS. Because this group of subjects tends to present the worst clinical phenotype, and because 69.5% of the studied population reported a monthly family income lower than $1,710 (data not shown), this result could reflect that these subjects have a lower priority in seeking dental care. Poverty can be considered a co-factor in the relationship between SCD and oral health.

Another relevant point is that the majority of individuals with SCD complained about the reluctance of dentists to treat them because of fear of trans- and postoperative complications (data not shown). This issue has been previously reported[16,22] and indicates a need for research to assess the level of knowledge and clinical guidelines for dentists in treating patients with SCD.

Dental caries is a multifactorial disease and controlling confounding factors can be a difficult challenge to overcome. In our study, the logistic regression identified older age, female gender, and daily smoking proved to be significant risk factors for higher DMFT scores, excluding the isolated effect of SCD on increased caries prevalence. Flow rate and salivary composition, hormonal fluctuation, dietary habits, genetic variations, and social role in the family, have been identified as risk factors associated with a higher prevalence of caries in females.[25] Smoking has been suggested as a risk indicator for caries development.[26–28] The main justification for this relationship seems to be an association with unhealthy behaviors,[27,29,30] and though there are other hypotheses, such as impairment of the immune system, decreased salivary function, and alteration of bacterial profile, these hypotheses need future investigation.[31] In addition, advancing age may be a factor in the caries prevalence in the our population.

SCD was also not the major risk factor for the worst periodontal condition in our study population. A more reliable evaluation of periodontal status

would include a record of full mouth plaque scores, a bleeding index as well as mobility scores, probing pocket depths, gingival recession, clinical attachment level, and furcation involvement. However, a CPI using index teeth was meant to minimize the time required for subjects to complete the research protocol, particularly by those with SCD. Despite methodological limitations, our study agrees with previous studies[19,20] that showed a lack of association between SCA and periodontal disease, when evaluating clinical attachment loss[19] and alveolar bone loss[20] in a group of 100 Nigerian adolescents where 50 had HbSS and 50 HbAA. No association between SCD and increased levels of gingivitis and periodontitis when measured by plaque and gingival indexes, probing depths, attachment level, and alveolar bone level when it was measured in a group of 78 adult patients, of which 45 had HbSS, 19 HbSC, and 14 HbS thalassemic.[21] In contrast, a greater loss of alveolar bone level was observed in children with HbSS (mean age 7.3 years).[22] This result could also be due to constant alveolar alterations due to bone growth and dental eruption, which is common in childhood.[22]

In our study, multivariate analysis showed that higher risk for periodontal pockets was significantly associated with older age and the absence of daily use of dental floss, which are recognized[32,33] as risk factors for periodontal disease.

Also in our study, the characteristics of the sample population, such as age and disease severity, showed no association between dental condition and SCD. The data of long-term outcomes show that patients with severe disease (resulting in almost 100 hospitalization days per year) have a high mortality rate and live to around 42 years of age.[34] In Brazil, morbidity among the young is even worse, with a mean age at death between 26 and 31 years.[35] Since the individuals in our study were between 16 and 68 years of age, they did not represent all the subgroups of persons with SCD, and probably excluded mainly the most severe patients. Longitudinal studies which have larger and more diverse samples, involving individuals with a lower mean age as well as hospitalized patients, should complement our data and would provide a better understanding of the relationship between the severity of SCD and oral health.

Regardless of the impact of SCD on the dental tissues, the oral health of these individuals is essential to prevent dental infections that could precipitate a vaso-occlusive crisis[36] or act as a bacterial source for development of osteomyelitis of the mandible which has lost its blood supply.[37]

Conclusion

Our data suggests that risk factors known to affect the occurrence of dental caries and periodontal disease were more important than SCD on the dental condition of subjects and controls. Recognition that subjects with SCD have a potential risk for development of dental diseases is essential to guide public policies for prevention, improving the patient's quality of life and reducing treatment costs. Because of the wide variation in clinical complications in this population, further studies are needed.

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