Ciência & Saúde Coletiva
cienciaesaudecoletiva.com.br
ISSN 1413-8123. v.29, n.3
DOI: 10.1590/1413-81232024293.06752023

Dental caries in the permanent dentition and health-related quality of life among children and adolescents with sickle cell disease

Cáries dentárias na dentição permanente e qualidade de vida relacionada à saúde entre crianças e adolescentes com doença falciforme

Vera Lúcia Duarte da Costa Mendes (https://orcid.org/0000-0002-3322-4073) [1]
Patrícia A. Risso (https://orcid.org/0000-0002-9961-6678) [2]
Marcia Pereira Alves dos Santos (https://orcid.org/0000-0003-0349-8521) [2]

Abstract *The aim was to associate living, health and oral health conditions with the quality of life (QL) of children and adolescents (CA) with sickle cell disease (SCD). Of the 120 eligible users of a public hematological service, 106 CA with SCD from 6 to 18 years of age, and their caregivers, answered semi-structured questions about socio-demographic, health and oral health conditions. For QL, we used the validated instrument PedsQLSCD™. The oral clinical examination occurred according to the guidelines of WHO and SB Brazil 2010. The majority of CA were non-white people (88%), mean age of 10.4 (±2.9) years, family income of up to two monthly minimum wages, for 03 to 05 members, with diagnosis of sickle cell anemia by neonatal screening, hospitalizations were due allergic crises, polypharmacy and dental caries (51%) were present. "About the Impact of My Pain" was the best-fit model for the QLSCD (adjusted R^2=56%; AIC=28.67; p=0.04). Dental caries in permanent dentition worsened the QLSCD (OR=0.53; IC95%=0.35-0.78; p<0.05) and was associated with the type of school, car ownership, number of family members, of complications and of the medications. To overcome this scenario, programmatic actions are required, and implementation of public policies specifically directed towards these groups.*

Key words *Anemia sickle cell, Oral health, Quality of Life*

Resumo *Objetivou-se associar condições de vida, de saúde e de saúde bucal à qualidade de vida (QLV) de crianças e adolescentes (CA) com Doença Falciforme (DF). Dos 120 usuários elegíveis de um serviço público hematológico, 106 CA entre 6 e 18 anos de idade, e seus cuidadores, responderam questões semiestruturadas sobre condições sociodemográficas, de saúde e saúde bucal. Para a QLV, o instrumento validado PedsQL DF® foi aplicado. Na sequência, realizou-se o exame clínico bucal nas CA segundo diretrizes da OMS e do SB Brasil 2010. A maioria das CA era negra (88%), idade média de 10,4 (±2.9) anos, renda familiar de até dois salários mínimos, para 03 a 05 membros, diagnosticadas na triagem neonatal com anemia falciforme, internadas por crises álgicas, em uso de polifarmácia e com cárie dental (51%). O domínio "Sobre o Impacto da Minha Dor" foi preditivo da QLVDF (R^2 ajustado =56%; AIC=28.67; p=0,04). Nele, a cárie dental na dentição permanente piorou a QLVDF das CA (OR=0.53; IC95%=0.35-0.78; p<0,05), associando-se ao tipo de escola, posse de carro e do número de membros na família, de complicações da DF e de medicamentos. Os achados ratificam a dor como marca da DF e mostram a importância da saúde bucal na QLDF das CA. A implementação de políticas públicas específicas pode superar esse cenário.*

Palavras-chave *Anemia falciforme, Saúde Bucal, Qualidade de Vida*

[1] Instituto Estadual de Hematologia Arthur Siqueira Cavalcanti. R. Frei Caneca 8, Centro. 20211-030 Rio de Janeiro RJ Brasil. veradentista@hotmail.com
[2] Faculdade de Odontologia, Universidade Federal do Rio de Janeiro. Rio de Janeiro RJ Brasil.

Introduction

Sickle cell disease (SCD) is the most common recessive autosomal hereditary hemoglobinopathy disease in Africans and African Diaspora[1-3]. SCD occurred because of a brief genetic change at position six on chromosome 11 in the beta chain of hemoglobin. At this point, valine replaced glutamic acid, creating an HB S protein that was not functional. Individuals who have a single defective globin gene are often known sickle cell trait. In the case of a match between two sickle cell traits, there is a 25% probability that each offspring will inherit defective genes from both parents, resulting in sickle cell anemia (SS), the most common and severe form of the disease. Other types of SCD are SC disease, Sbeta thalassemia disease, and other sickle-cell disorders[4].

The global prevalence of SCD had a significant rise of 41.4% (38.3-44.9) between 2000 and 2021, with the number of individuals affected increasing from 5.46 million (4.62-6.45) to 7.74 million (6.51-9.2)[4]. In the year 2021, a rate of 97.8 was observed (with a confidence interval of 82.2-116) per 100,000 individuals across all age groups. The region encompassing North Africa and the Middle East exhibited the highest rate of 98 (with a range of 81.4 to 114) per 100,000 inhabitants. In the context of Brazil, there was a prevalence rate of 8.8 (7.8-9.7) per 100,000 individuals. The prevalence rate for the states of Rio de Janeiro and Piauí was 12.5 (11-13.9) per 100,000 population, which was lower in comparison with the states of Brasília (26.2; 22.8-28.9), Tocantins (17; 14.5-19), and São Paulo (13.2; 11.6-14.7), respectively. Nevertheless, the overall mortality burden of SCD was roughly eleven fold greater[4]. It is important to note that the lack of accurate diagnostic tools, data-gathering methods, and connections for monitoring SCD makes it difficult to establish an accurate view of the condition with regard to prevalence, death rate, and incidence around the world. This means that this public health problem is still not being fully portrayed[4].

SCD can cause a sudden acute event[2,5-7] due vaso-oclusive crises leading to cerebrovascular disease, renal impairment, cardiopulmonary disease, or act as chronic disease[2,5-7]. Consequently, this results in progressive incapacity due arthropathy, retinopathy, renal disease, urogenital disease, or skin ulceration. Moreover, SCD jeopardizes oral health by compromising the craniofacial system[8,9]. In addition to these pathological changes, SCD has complex and detrimental effects on the cognitive, psychological and social functioning of the people who have to live with this disease. All these conditions affect their quality of life[10].

The conceptual theoretical model for SCD pain emphasizes institutional and interpersonal racism[11,12] as social determinants of health[11] overcome the biological model of management and disease outcomes[12]. In the proposed framework, comorbid conditions increase likelihood of pain or worsening prognosis[12].

Oral disorders such as dental caries with endodontic involvement and advanced periodontal disease may increase hospital admissions and the risk of mortality in adults with SCD[13]. The dental literature has shown that there is an increase in the number of decayed, missing, and filled teeth in children with SCD as consequence of poor engagement with dental services and the underestimation of the importance of dental health. Thus, patients with SCD did not suffer from worse dental caries according to the meta-analysis that evaluate dental caries in SCD people in a comparison with non-SCD individuals[14]. Otherwise, even after adjustment for dental caries, low-income African Americans with SCD received less restorative treatment than low-income African Americans with no SCD[15]. In Brazil, the Black population has received simpler and less expensive dental care[16].

Inequitable access to dental care by racialized groups or receiving lower-quality care from health care providers have been demonstrated by many studies[17-19]. Barriers to Equity limit the claim of oral health for everyone[19-21]. They have emphasized the need for policymakers to make efforts to implement public policies to change this cenarium[20,21].

To the best of our knowledge, no study has yet been conditions living, health and oral health with the quality of life of children and adolescents with SCD, by using a validated pediatric quality of life inventory SCD module tool[22] in a framework model.

Methods

Study design

The Local Ethics Committee approved this cross-sectional study (number 368/2015) and it was conducted in compliance with the recommendations of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) criteria[23].

The variables of interest in the semi-structured questionnaire and the validated pediatric quality of life inventory sickle cell disease (PedsQL™ - SCD) module tool[22] with its domains for health-related quality of life of children and adolescents with SCD are shown in Figure 1.

Individuals who completed the registration process and currently maintain an active registration status in the reference service specializing in the field of hematology and blood therapy in Rio de Janeiro, Brazil, were eligible for the study.

The dental team was composed of two dentists and two dental researchers, and the calibration exercise consisted of three steps. The first step involved the presentation and discussion of the semi-structured questionnaire, considering the variables of interest for: A) living conditions; B) health status; and C) oral health status (Figure 1). In the same sequence, the same procedure occurred for the PedsQL™ SCD module[22] for training the dental team in the application of the module.

The last step occurred seven days later. A dentist and a dental researcher simultaneously examined five children, aged 6-18 years. If disagreements occurred, they were resolved by reaching consensus. In the following week, another five children had dental exams. In total, 10 children participated in this phase of the study. All data collected were blinded, and they were not included in the data analyses. The mean Kappa coefficients for both interexaminer and intraexaminer agreements were >0.80. An experienced dental researcher (MPAS) conducted these preliminary steps of the study.

Data collection, period of the study, and participants

For this study, participants between 6 and 18 years of age were selected from a list of patients registered at a hematology referral center in Rio de Janeiro, who had accessed the dentistry service during the period of the study. Thus, a total of 1.412 children and adolescents with SCD were selected. For the sample size calculation, we assumed a prevalence of oral diseases (50%±10%), confidence limits of 10%, a design effect of one, and a level of significance of 95%. The sample size was 90 children and adolescents with SCD.

From January to September 2016, 120 children and adolescents with sickle cell disease aged

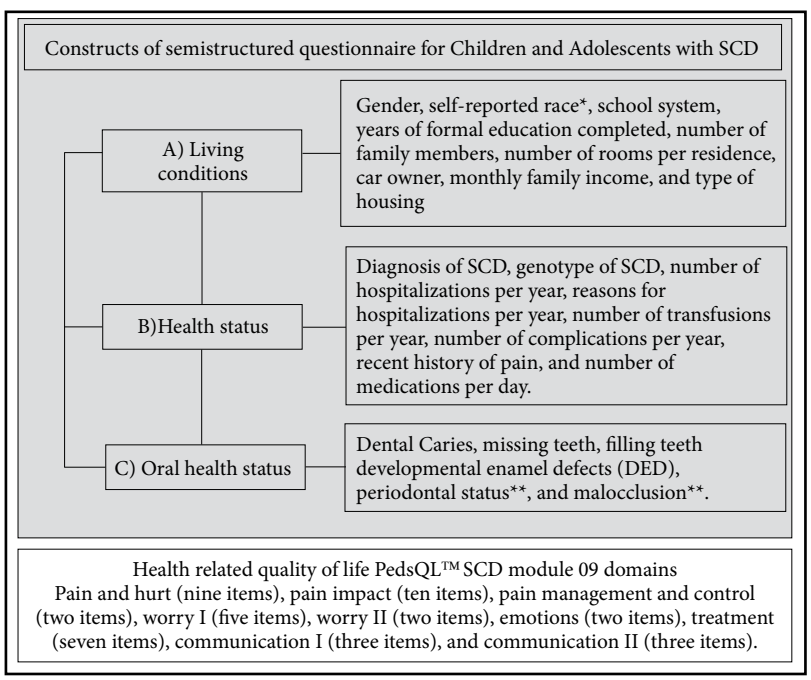

Figure 1. Variables for association with health-related quality of life of children and adolescents with SCD.

*Source: Instituto Brasileiro de Geografia e Estatística (IBGE). **Only for permanent dentition.

6 to 18 years met the eligibility criteria after the diagnosis was confirmed by hemoglobin electrophoresis and regular medical consults.

All participants provided their consent verbally and in writing. Participants under the age of 16 were also required to sign consent forms. Their parents or family members also signed the terms of consent. Fourteen people dropped out due to physical limitations, impaired cognitive ability, neurological impairment, or other systemic complications such as respiratory, cardiac, or infectious diseases. Two patients dropped out due to absences from dental consultations. As a result, 106 people took part in the study. A blinded code was assigned to all data.

In accordance with World Health Organization guidelines[24], a calibrated (weight kappa >0.80) dental workforce that consisted of two dentists (operators), one dental assistant (assistant-writer), and two researchers collected data using a plane buccal mirror, a 0.5-mm ball-point probe, and artificial illumination from a dental reflector. Before the dental exam, the patient's oral cavity was dried with a triple syringe. Subsequently, operators applied the scores for the dental caries index (DMFT/dmft), developmental enamel defects (DED) index[25] community periodontal index (CPI), and the orthodontic index for the purpose of obtaining the oral health status. Periodontal status and malocclusion were only assessed for permanent dentition. Teeth missing for any reason other than dental caries were not included.

These conditions were associated with the quality of life measured by the PedsQL™ SCD module[22] of each domain.

Quality of life evaluation

We obtained the authorization by user agreement (#5565) from the Mapi Research Trust organization in Lyon, France, to apply the PedsQL™ SCD-Module tool[22]. We used the Portuguese version 3.0 of the Pediatric Quality of Life Inventory - Sickle Cell Disease Module. The tool registered parental, child, and adolescent perceptions of quality of life according to the age of respondents.

The PedsQL SCD™ is a multidimensional validating instrument with nine domains: pain and hurt (nine items), pain impact (ten items), pain management and control (two items), worry I (five items), worry II (two items), emotions (two items), treatment (seven items), communication I (three items), and communication II (three items) with varied numbers of items per domain. According to choices of these responses, there are raw scores varying from 0 to 4 related to inverse 100-0 scale scores, respectively, with higher scores indicating better health-related quality of life and lower SCD symptoms and problems. Thus, the sum of the scores for each domain of health related quality of life were obtained by the caregivers and by the children and adolescents with SCD.

Statistical analyses

Descriptive and analytical data: Descriptive analyses and Kruskal-Wallis test were used to compare the frequencies and the differences between groups (p-value<0.05). In addition, each domain of the PedsQL™-SCD was correlated between children and adolescents to their caregivers using Spearman's coefficient (p-value<0.05).

Logical model - predictive frameworks: To analyze the association between living conditions, health and oral health with the health-related quality of life of children and adolescents with Sickle cell disease, an adjustment of the model of multiple logistic regression was applied in each of the nine domains of PedsQL™-SCD, With the aim of obtaining an equation that would explain the probability (in the group surveyed) of having a high impact (lower scores) on their health according to each domain evaluated. For this analysis, all PedsQL™-SCD domains scores were dicotomized as follows: 0, if the domain score was above 50 and less than or equal to 100, and 1, if the score was between 0 and 50. The explanatory variables adopted took into account sociodemographic, health and oral health data of children and adolescents (Figure 1). In addition to the procedures implemented, the same adjustment of the logistical model occurred for children and adolescents in permanent dentistry. The choice of the best model was based on the stepwise method which removed variables that had little or no relation to the outcome and retained those that were statistically significant (p<0.15), using the Minitab statistical tool.

The adjustment of each model was evaluated using AIC (Akaike Information Criteria) where the lowest values indicated the best fit. Finally, the goodness-fit test Hosmer-Lemeshow test determined whether a set of values observed matched those expected under the applicable model, assuming a 95% confidence level. Moreover, it evaluates how well a set of observed data fits a particular probability distribution. The main outcomes are the domains of the quality of

life associated with living conditions, health and oral health status.

An unbiased blinded statistician analyzed data using the Statistical Package for the Social Sciences (SPSS) program (version 21.0; SPSS Inc., Chicago, IL, USA).

Results

Table 1 shows the living conditions, health, and oral health situation of the children and adolescents with SCD in this study. There was no missing data. The majority of children and adolescents self-declare their race as being Black people (Black + Pardo self-reported race), with the same distribution between females and males. The mean age was 10.4 (±2.9) years. The majority of children and adolescents study in public schools, and had done from two to seven years of study. The majority of them live in their own home and received a monthly family income of up to two minimum wages for three and five family members in a one room, with no car ownership.

In terms of health conditions, the majority of children and adolescents have the sickle cell anemia obtained by the neonatal screening at earlier stages of life. In addition, the number of hospitalizations per year varied between once and three times due allergic crises or pneumonia, or their associations or anemia. Only 39 children and adolescents did not have blood transfusions in the year. All participants had some acute or chronic type of complication from SCD and took from one to six medications per day. Allergic crises, fever, splenic sequestration, anemia, treatment of gallstones, and pneumonia are the most common self-referred complications. Moreover, they report a recent history of pain of mild, moderate, or intense levels. Folic acid is the most frequently used drug (97.1%), followed by dipyrone (42.4%), hydroxyurea (19.8%), ibuprofen (16.98%), codeine (14.1%), and diclofenac (7.5%).

With regard to oral health conditions, the majority of children and adolescent have dental caries, DED, and malocclusion, at the expense of

Table 1. Living conditions, health status and oral health status of participants in the study.

Dimensions	Variables	Categories	Frequency	
			Absolute (N=106)	Relative (100%)
Living conditions	Gender	Female	53	50
		Male	53	50
	Self-reported race	Black	48	45
		Pardo	45	43
		Indigenous	1	1
		White	12	11
	School system	Free-Public sector	85	80
		Private sector	21	20
	Years of formal education completed	0≤2	24	23
		2<7	57	54
		7≤11	25	23
	Number of family members	2	06	6
		3-5	85	80
		6-9	15	14
	Number of rooms per residence	<1	42	39
		>1<2	57	54
		>2	07	7
	Car owner	Yes	24	23
		No	82	77
	Monthly Family income (reference - US$ 256.97)	<2	98	92
		2≤4	06	6
		4≤10	01	1
		Not informed	01	1
	Type of housing	Own home	86	81
		Does not own home	20	19

it continues

Table 1. Living conditions, health status and oral health status of participants in the study.

Dimensions	Variables	Categories	Frequency	
			Absolute (N=106)	Relative (100%)
Health status	Diagnosis of SCD	Early (neonatal screening)	94	89
		Late (out of neonatal screening)	12	11
	Genotype of SCD	Hb SS	89	84
		Hb SC	15	14
		Hb S/Beta thalassemia	02	2
	Number of hospitalizations per year*	0	37	34
		1-3	56	53
		4-9	06	6
		≥10	07	7
	Reasons for hospitalizations per year*	Not applicable	37	--
		Pain crisis	42	61
		Pneumonia	11	16
		Pain crisis+Pneumonia	07	10
		Anemia	03	4
		Others	06	9
	Number of transfusions per year*	None	39	36
		1-3	40	38
		4-6	04	4
		7-9	05	5
		≥10	18	17
	Number of acute or chronic complications per year*	1-3	36	34
		4-5	55	52
		6-8	15	14
	Recent history of pain**	Mild	76	72
		Moderate	18	17
		Intense	12	11
	Number of medications per day	1-2	45	43
		3-4	46	43
		5-6	15	14
Oral health status	Dental Caries	0	52	49
		1≤10	54	51
	Missing	0	91	86
		1≤2	15	14
	Filling	0	81	76
		1≤5	25	24
	DED	0	34	32
		1≤24	72	68
	Periodontal Status (CPI)***	0	31	80
		1	08	20
	Malocclusion***	0	10	26
		1	29	74

SCD: Sickle cell disease. *Per year - the latest 12 months in relation to the date of the questionnaire application. **Recent history of pain - the latest seven days from the date of the questionnaire application. ***Only in the Permanent dentition.

Source: Authors.

a minority with lost teeth, restored teeth, and the presence of periodontal disease. Sixty-seven participants had mixed dentition, and thirty-nine children and adolescents had permanent dentition. Seventy-one (67%) children and adolescents were between 6 and 11 years old; 11 (10.4%) were

12 years old; and 24 (22.6%) were between 13 and 18 years of age. There was a higher frequency of dental caries assessed by DMFT, and DED, respectively, in all groups (Table 2). However, there was no significant difference between the age groups for the dental caries (DMFT/dmft) index (p-value>0.05). In the permanent dentition, gingivitis and dental calculus affected 8 (20%) of 39 participants, while malocclusion affected 29 (74%) of 39 participants.

Table 3 shows the global score of PedsQL™ SCD-Module. There were correlations throughout all domains of quality of life between children, teens, and their caregivers, despite the fact that participants scored lower than their caregivers. "About my pain management and control" and "About the impact of my pain", respectively, were the domains that had the highest impact on the quality of life for all respondents.

Table 4 shows the five predictive models such as "About my pain management and control", "About my concerns II", "About my emotions", "About communication II", and "About the impact of my pain" for the quality of life of children and adolescents with SCD, which varied in terms of prediction, effect size, and magnitude of effect size (small, medium, or large)[26,27]. Similarly, the magnitude of the effect size ranged from weak to medium to strong. For "About Communication II", the magnitude was small (18%).

For "About my concerns II" and "About my emotions", the magnitude was medium (between approximately 27% and 36%, respectively). Finally, for "About my pain management and control"

Table 2. Median of DMFT/dmtf and developmental enamel defects (DED) index according to age group.

Index	Participants (n=106)					
	Group of ages in years					
	6-11 (n=71)		12 (n=11)		13-18 (n=24)	
	Median	SD	Median	SD	Median	SD
Healthy teeth	18.23	4.39	19.64	7.61	22.17	3.14
DMFT	2.92	2.97	1.18	2.31	2.21	2.85
Missing	0.23	0.56	0	0	0.17	0.38
Filled	0.55	1.13	0.18	0.60	0.29	0.75
Decayed	2.14	2.65	1.0	2.32	1.75	2.28
DED*	2.44	3.24	6.09	8.11	3.83	3.00

*Kruskal-Wallis Test: p-value =0.03.

Source: Authors.

Table 3. PedsQL™ SCD scores of the domains applied.

Domains	Participants				Spearman´s correlation	p-value*
	Children/Adolescents (N=106)		Guardians/Caregivers (N=106)			
	Mean	SD	Mean	SD		
About my pain	69.86	18.67	66.69	18.90	0.59	<0.01
About the impact of my pain	36.37	29.78	49.22	25.43	0.48	
About my pain management and control	35.02	37.54	47.17	33.42	0.45	
About my concerns I	61.46	36.68	61.60	33.60	0.41	
About my concerns II	73.94	39.38	73.35	38.54	0.45	
About my emotions	58.25	37.44	55.54	34.72	0.41	
About my treatment	74.92	21.93	77.67	20.36	0.33	
About communication I	73.98	31.41	75.79	22.84	0.24	0.01
About communication II	57.63	38.87	68.32	32.05	0.33	<0.01
Global score	60.15	36.11	63.93	31.37	0.49	

*Statistically significant.

Source: Authors.

Table 4. Five models for the quality of life using PedsQL SCD module for children and adolescents with sickle cell disease.

Domains	Constructs	Predictor	Estimated parameters									Goodness-of-Fit Test
			β	SE	OR	OR - Lower	OR - Upper	P value (β)	Deviance R-Sq	Deviance R-Sq (adj)	AIC	P value (Hosmer-Lemeshow test)
About my pain management and control	Living conditions	Number of family members	0.57	0.37	1.76	1.20	2.59	a	51%	43%	74.00	0.80
		Type of housing	2.43	0.83	11.31	4.80	26.66	b				
		Number of rooms per residence	-1.27	0.44	0.28	0.18	0.44					
	Health Status	Number of transfusions per year	-0.90	0.32	0.41	0.29	0.56					
		Recent history of pain	0.30	0.18	1.35	1.12	1.63	a				
		Number of medications per day	2.24	0.60	9.41	5.08	17.44	b				
	Oral health status	Number of teeth with DED	0.28	0.14	1.32	1.15	1.52					
		Missing teeth	2.26	0.95	9.58	3.57	25.76					
About my concerns II	Living conditions	Gender	-1.61	0.61	0.20	0.11	0.38		36%	30%	98.88	0.25
		Years of formal education	0.29	0.13	1.33	1.16	1.53					
		School system	-2.71	1.03	0.07	0.02	0.19					
	Health Status	Number of hospitalizations per year	-0.81	0.36	0.45	0.31	0.65					
		Number of acute or chronic complications per year	0.89	0.26	2.44	1.87	3.18					
	Oral health status	Number of teeth with DED	0.19	0.08	1.21	1.11	1.31					
		Missing teeth	1.82	0.57	6.14	3.39	11.13					
About my emotions	Living conditions	School system	-0.64	0.31	0.53	0.38	0.73		27%	22%	122.28	0.81
		Number of rooms per residence	-0.83	0.26	0.44	0.33	0.57					
	Health Status	Number of acute chronic or complications per year	0.59	0.21	1.75	1.41	2.16	a				
		Recent history of pain	0.21	0.10	1.23	1.11	1.36	b				
		Number of medications per day	0.34	0.22	1.41	1.12	1.77	a				
	Oral health status	Number of teeth with DED	0.10	0.07	1.11	1.04	1.19					
		Missing teeth	1.57	0.69	4.81	2.35	9.85	b				

it continues

Table 4. Five models for the quality of life using PedsQL SCD module for children and adolescents with sickle cell disease.

Domains	Constructs	Predictor	Estimated parameters									Goodness-of-Fit Test
			β	SE	OR	OR - Lower	OR - Upper	P value (β)	Deviance R-Sq	Deviance R-Sq (adj)	AIC	P value (Hosmer-Lemeshow test)
About communication II	Living conditions	Self-reported race	1.51	0.78	4.53	2.01	10.21		18%	14%	133.48	0.32
		School system	-1.56	0.61	0.21	0.11	0.40					
		Number of rooms per residence	-0.43	0.20	0.65	0.53	0.81					
	Health status	Number of acute or chronic complications per year	0.41	0.19	1.50	1.24	1.82					
		Number of medications per day	0.28	0.19	1.32	1.08	1.61	a				
	Oral health status	Number of teeth with DED	0.16	0.06	1.18	1.10	1.26	b				
About the impact of my pain	Living conditions	School system	-8.88	4.37	0.00	0.00	0.01	b	69%	56%	28.67	0.04
		Number of family members	3.86	2.10	47.47	5.38	418.43	a				
		Car owner	4.47	3.18	87.36	3.24	2358.68					
	Health Status	Number of acute or chronic complications per year	1.83	0.99	6.26	2.26	17.37					
		Number of medications per day	3.24	1.85	25.53	3.75	173.71					
	Oral health status	Dental caries (permanent dentition)	-0.64	0.38	0.53	0.35	0.78					

β: beta coefficient; SE: standard error. a p-value <0.15; b p-value<0.05.

Source: Authors.

and "About the impact of my pain", the magnitude was strong (51% and 69%, respectively).

The appropriateness of each model was obtained using the goodness-of-fit test a 95% confidence level (Table 4). The fit-model for the quality of life of children and adolescents affected by SCD was "About the impact of my pain" (R^2adj=56%; AIC=28.76; p<0.05) whose predictors are number of family members (OR=47.47; IC95%=5.38-418.43; p<0.15), car owner (OR=87.36; IC95%=3.24-2858.68; p<0.05), number of complications (OR=6.26; IC95%=2.26-17.37; p<0.05), the number of medications per day (OR=6.26; IC95%=2.26-17.37; p<0.05), and dental caries (permanent dentition) (OR=0.53; IC95%=0.35-0.78; p<0.05) showing stronger associations with children's and adolescents´ quality of life (69%) (Table 4).

Discussion

Our results established the presence of dental caries in permanent dentition as a predictor of pain and quality of life for children and adolescents with SCD, and pointed out that oral health status should be included in the framework of the future studies about SCD. In addition, our findings also demonstrated a worsening of the quality of life by an association between living conditions, such as the number of family members, and health status, measured by the number of medications used per day. We corroborated a previous study in that families that include children with SCD typically experience a high burden of social determinants of health that affect their quality of life[10,28,29]. That is one of reason for recognizing the multidimensionality of the social determinants of health on overall health outcomes to a larger extent than the care provided by the health team[10,28,29].

A worsened health-related quality of life has been associated with the disease severity, complications, comorbidities, hospitalizations, and pain episodes for health dimensions[5-7,10]. According to the best scientific-evidence-based recommendations[5-10], hydroxyurea, a safe and efficacious medication is capable of reducing the manifestations and complications of SCD in both adults and children, and increasing the quality of life of people with SCD[10,30]. Hydroxyurea reduces pain crisis, being a strong ally for the management of all age people with SCD[30]. This applies particularly to those patients, as seen in the present study, who have a sickle cell anemia (homozygous genotype - Hb SS). However, as observed in the present study, the minority (19.8%) of children and adolescents reported the use of this medication although they had been treated in a hematological reference center. These results sound unexpectedly because the most common barrier to the utilization of hydroxyurea among medical doctors, except haematologists who usually had prescribed hydroxyurea, was the lack of expertise in its use in the treatment of SCD[31]. Then, it appears that this led to them using more pain drugs per day due to the appearance of more complications and comorbidities[2,7,29]. Consequently, these patients could be at risk of more frequent sub-clinical and clinical vaso-occlusive events and hemolysis which could result in frequent painful crises, hospital admissions, early complications including irreversible organ damages, poor quality of life[31]. It configures a barrier to health access, we suppose.

The presence of dental caries in permanent dentition influenced the pain and impacted the quality of life of children and adolescents with SCD. All ages of children and adolescents with SCD in the present study showed worsen oral health status in comparison to caries rate for children and adolescents according to the latest national epidemiological survey in 2010[32]. It claims our attention once SCD diagnosis occurred at the earlier stages of life during neonatal screening giving many opportunities to promote oral health and to avoid the presence of oral diseases such as dental caries, periodontal disease and malocclusion, as seen in this study. This phenomenon also emphasizes the shortage of economic and social resources available to this population[33].

The SCD population is often linked to barriers to access associated with Black race or ethnicity at primary and specialty care levels[34] with insufficient provision of health services and limited accessibility to health professionals, including dentists [34,35]. This could be an expression of structured racism[33].

Thus, the findings allowed the conclusion that the domain "About the impact of my Pain" was the best model for the quality of life of children and adolescents with SCD. Despite the magnitude of the lower and upper confidence limits in the fit-model, caution is required in interpreting our encouraging findings. A short and nonrandom sample sizes explained the presence of heterogeneity in the data, which highlights an additional concern regarding the possibility of an overestimated effect size in the study[26,27]. In contrast, it is worth emphasizing that pain management has previously been referred to as a factor worsening quality of life[10], as suggested by our findings. These results also illustrate the importance of appropriateness of the instruments used for detailed data collection for evaluating interaction of lifestyle, behaviour and systemic diseases with dental caries and periodontal diseases as previously pointed out[36].

In this context, it is recommended that public policies incorporate oral health for children and adolescents with SCD into their scope of implementation. Finally, our limitations in extrapolating the results refer to the small sample size, the lack of a control group, randomization and final models. In addition, the scenario of the survey was a hematological reference center, with users already receiving health care, restricted to an age group, and a social profile mostly marked by the same living conditions. Additionally, any number of variables utilized will not represent

an exhaustive list of the factors and pathways by which structural racism operates. In the same way, any SCD variables are highly variable condition, and it is extremely difficult to predict its clinical course accurately. Thus, further in-depth research is needed, considering different populations, generations, scenarios, study designs, and statistical analyses to endorse our results. This requires interdisciplinary training and integrating theoretical frameworks to address the link between race and health outcomes, in order to connect health outcomes to racist practices and policies that prevent health equity.

Conclusions

Dental caries in permanent dentition worsened the health related quality of life of children and adolescents with SCD (OR=0.53; IC95%=0.35–0.78; $p<0.05$), and so did the type of school, car ownership, number of family members, of complications of SCD and of the medications. Taking our findings into considering, such associations could demarcate the expressions of structural racism on health, the overcoming of which requires programmatic actions and the implementation of public policies specifically directed to these groups.

Collaborations

All authors participated equally in all stages of preparation of the manuscript.

Acknowledgements

The authors would like to thank Mapi Research Trust for allowing us to use the PedsQL™ SCD module - questionnaire. We also thank Professors Gustavo Cruz and Tadeu Berenger for technical support with Statistical Operations.

References

1. Ware RE, Montalembert M, Tshilolo L, Abboud M. Sickle Cell Disease. *Lancet* 2017; 390(10091):311-323.
2. Rees DC, Brousse VA, Brewin JN. Determinants of severity in sickle cell disease. *Blood Rev* 2022; 56:100983.
3. GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* 2020; 396(10258):1204-1222.
4. GBD 2021 Sickle Cell Disease Collaborators. Global, regional, and national prevalence and mortality burden of sickle cell disease, 2000-2021: a systematic analysis from the Global Burden of Disease Study 2021. *Lancet Haematol* 2023; 10(8):e585-e599.
5. Martinez RM, Osei-Anto HA, McCormick M, editors. *Addressing Sickle Cell Disease: A Strategic Plan and Blueprint for Action*. Washington, D.C.: National Academies Press; 2020.
6. U.S. Department of Health and Human Services. National Institute of Health (NIH). National Heart, Lung, and Blood Institute (NHLBI). *Evidence-Based Management of Sickle Cell Disease: Expert Panel Report, 2014* [Internet]. [cited 2023 jan 25]. Available from: https://www.nhlbi.nih.gov/health-topics/evidence-based-management-sickle-cell-disease
7. Yawn BP, Buchanan GR, Afenyi-Annan AN, Ballas SK, Hassell KL, James AH, Jordan L, Lanzkron SM, Lottenberg R, Savage WJ, Tanabe PJ, Ware RE, Murad MH, Goldsmith JC, Ortiz E, Fulwood R, Horton A, John-Sowah J. Management of Sickle Cell Disease: summary of the 2014 evidence-based report by expert panel members. *JAMA* 2014; 312(10):1033-1048.
8. Hsu LL, Fan-Hsu J. Evidence-based dental management in the new era of Sickle Cell Disease: A scoping review. *J Am Dent Assoc* 2020; 151(9):668-677.
9. P, Ballas SK, Abas ABL, Karanth L. Treatment of dental complications in Sickle Cell Disease. *Cochrane Database Syst Rev* 2019 (12):CD011633.

10. Ojelabi AO, Yitka Graham Y, Ling J. Health-related Quality of Life Predictors in Children and Adolescents with Sickle Cell Disease: A Systematic Review. *IJTDH* 2017; 22(2):1-14.
11. Berghs M, Ola BA, Cronin de Chavez A, Ebenso B. Time to apply social determinants of health lens to addressing sickle cell disorders in Sub-Saharan Africa. *BMJ Global Health* 2020: 5(7):e002601.
12. CDM, Babyak M, Shah N, Srivatsa S, Stewart KA, Tanabe P, Wonkam A, Asnani M. Sickle Cell Disease is a global prototype for integrative research and healthcare. *Adv Genet (Hoboken)* 2021; 2(1):e10037.
13. Laurence B, Haywood Jr. C, Lanzkron S. Dental infections increase the likelihood of hospital admissions among adult patients with Sickle Cell Disease. *Community Dent Health* 2013; 30(3):168-172.
14. H, Xu X, Liu Q, Li X, Jiang W, Hu B. Association between sickle cell disease and dental caries: a systematic review and meta-analysis. *Hematology* 2020; 25(1):309-319.
15. Laurence B, George D, Woods D, Shosanya A, Katz RV, Lanzkron S, Diener-West M, Power N. The association between Sickle Cell Disease and dental caries in African Americans. *Spec Care Dentist* 2006; 26(4):95-100.
16. Chisini LA, Noronha TG, Ramos EC, Dos Santos-Junior RB, Sampaio KH, Faria-E-Silva AL, Corrêa MB. Does the skin color of patients influence the treatment decision-making of dentists? A randomized questionnaire-based study. *Clin Oral Investig* 2019; 23(3):1023-1030.
17. Jamieson LM. Racism and oral health inequities; an introduction. *Community Dent Health* 2021; 38(2):131.
18. Jamieson L, Peres MA, Guarnizo-Herreño CC, Bastos JL. Racism and oral health inequities; An overview. *EClinicalMedicine* 2021; 34:100827.
19. Como DH, Stein Duker LI, Polido JC, Cermak SA. The Persistence of Oral Health Disparities for African American Children: A Scoping Review. *Int J Environ Res Public Health* 2019; 16(5):710.
20. Peres MA, Macpherson LMD, Weyant RJ, Daly B, Venturelli R, Mathur MR, Listl S, Celeste RK, Guarnizo-Herreño CC, Kearns C, Benzian H, Allison P, Watt RG. Oral diseases: the global public health challenge. *Lancet* 2019; 394(10194):249-260.
21. D'Souza RN, Collins FS, Murthy, VH. Oral Health for All-Realizing the Promise of Science. *N Engl J Med* 2022; 386(9):809-811.
22. Panepinto JA, Torres S, Bendo CB, McCavit TL, Dinu B, Sherman-Bien S, Bemrich-Stolz C, Varni JW. PedsQL™ sickle cell disease module: feasibility, reliability, and validity. *Pediatr Blood Cancer* 2013; 60(8):1338-1344.
23. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol* 2008; 61(4):344-349.
24. World Health Organization (WHO). *Oral health surveys: basic methods*. 5ª ed. Geneva: WHO; 2013.
25. Federation Dental International. A review of the developmental defects of enamel index (DDE Index). Commission on Oral Health, Research & Epidemiology. Report of an FDI Working Group. *Int Dent J* 1992; 42(6): 411-426.
26. Ferguson CJ. An effect size primer: A guide for clinicians and researchers. In: Kazdin AE, editor. *Methodological issues and strategies in clinical research*. Washington, D.C.: American Psychological Association; 2016. p. 301-310.
27. Flório FM, Zanin L, Santos Júnior LMD, Meneghim MDC, Ambrosano GMB. Tamanho do efeito em estudos observacionais na área de Saúde Bucal Coletiva: importância, cálculo e interpretação. *Cien Saude Colet* 2023; 28(2):599-608.
28. Power-Hays, Li S, Mensah A, Sobota A. Universal screening for social determinants of health in pediatric sickle cell disease: A quality-improvement initiative. *Pediatr Blood Cancer* 2020; 67(1):e28006.
29. Hsu LL, Green NS, Donnell Ivy E, Neunert CE, Smaldone A, Johnson S, Castillo S, Castillo A, Thompson T, Hampton K, Strouse JJ, Stewart R, Hughes T, Banks S, Smith-Whitley K, King A, Brown M, Ohene-Frempong K, Smith WR, Martin M. Community Health Workers as Support for Sickle Cell Care: A White Paper. *Am J Prev Med* 2016; 51(1 Supl. 1):S87-S98.
30. Ballas SK. The Evolving Pharmacotherapeutic Landscape for the Treatment of Sickle Cell Disease. *Mediterr J Hematol Infect Dis* 2020; 12(1):e2020010.
31. Ofakunrin AO, Okpe ES, Afolaranmi TO, Olaosebikan RR, Kanhu PU, Adekola K, Dami N, Sagay AS. Level of utilization and provider-related barriers to the use of hydroxyurea in the treatment of sickle cell disease patients in Jos, North-Central Nigeria. *Afr Health Sci* 2021; 21(2):765-774.
32. Brasil. Ministério da Saúde (MS). Secretaria de Atenção à Saúde. Secretaria de Vigilância em Saúde. *SB Brasil 2010: Pesquisa Nacional de Saúde Bucal: resultados principais*. Brasília: MS; 2012.
33. Power-Hays A, McGann PT. When Actions Speak Louder Than Words Racism and Sickle Cell Disease. *N Engl J Med* 2020; 383(20):1902-1903.
34. Luna A, Gomes M, Granville-Garcia A, Menezes V. Perception of Treatment Needs and Use of Dental Services for Children and Adolescents with Sickle Cell Disease. *Oral Health Prev Dent* 2018; 16(1):51-57.
35. Costa CP, Aires BT, Thomaz EB, Souza SF. Dental care provided to Sickle Cell Anemia patients stratified by age: A population-based study in Northeastern Brazil. *Eur J Dent* 2016; 10(3):356-360.
36. Chapple IL, Bouchard P, Cagetti MG, Campus G, Carra MC, Cocco F, Nibali L, Hujoel P, Laine ML, Lingstrom P, Manton DJ, Montero E, Pitts N, Rangé H, Schlueter N, Teughels W, Twetman S, Van Loveren C, Van der Weijden F, Vieira AR, Schulte AG. Interaction of lifestyle, behaviour or systemic diseases with dental caries and periodontal diseases: consensus report of group 2 of the joint EFP/ORCA workshop on the boundaries between caries and periodontal diseases. *J Clin Periodontol* 2017; 44(Supl. 18):S39-S51.

Article submitted 14/08/2023
Approved 08/02/2024
Final version submitted 10/02/2024

Chief editors: Romeu Gomes, Antônio Augusto Moura da Silva