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IMPACT OF PAIN, ANXIETY AND DEPRESSION ON THE QUALITY OF LIFE OF INDIVIDUALS WITH SICKLE CELL DISEASE

IMPACTO DA DOR, ANSIEDADE E DEPRESSÃO NA QUALIDADE DE VIDA DE INDIVÍDUOS COM DOENÇA FALCIFORME

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Abstract: Introduction: Sickle cell disease (SCD) is the most common hemoglobinopathy in the world. Hemoglobin polymerization leads to erythrocyte rigidity and vaso-occlusion, which leads to pain and other changes in the body, seriously affecting quality of life (QoL). **Objective:** To analyze the impact of trigger points, pain intensity, Catastrophizing, Central nervous system sensitization, Anxiety and Depression on the QoL of adults with SCD. **Method:** This is a cross-sectional descriptive study. Sociodemographic data were collected and the Portuguese-Brazilian Central Awareness Inventory, the Brief Pain Inventory, the Hospital Anxiety/Depression Scale, the Portuguese Pain Catastrophizing Scale and the Short Form Health Survey 36 (SF-36) were applied. performed to define associations (Chi-square or Fisher's exact) and correlation (Pearson's correlation test). The alpha level was 5% and the beta was 80%. **Results:** 100 individuals with SCD participated. 69% were women. Age 34.14+10.12 years. Pain

intensity 4.20+2.67; 71% had chronic pain; 60% had generalized pain; 59% had central nervous system sensitization; 33% had Anxiety; and 18% had Depression. The lowest average QoL score was for the Physical Appearance domain (35.55+40.16). Anxiety, pain intensity, CS and Catastrophizing correlated with all QoL domains. Anxiety and CS had a significant negative influence on the Mental Health domain, explaining 46.6% of the outcome. Catastrophizing and CS had a significant negative influence on General Health, explaining 29.8% of the outcome; and Anxiety, Lower limb pain and Depression had a significant negative influence on the Pain domain, explaining 27% of the outcome. **Conclusion:** Anxiety, Depression, Catastrophizing and SC are significant factors that impact QoL. In a population of individuals with SCD, the main objective is pain control, which leads to chronic pain directly affecting these predictors and, inevitably, QoL.

Keywords: Sickle Cell Disease, Quality of life, Central nervous system sensitization, Catastrophizing, Depression, Anxiety.

INTRODUCTION

Sickle cell disease (DF) is the most common hemoglobinopathy in the world, with 275,000 newborns annually with this disease[1]. Hemoglobin polymerization leads to erythrocyte stiffness and vaso-occlusion, which leads to pain and other changes in practically all organs of the body[2]. The most frequent symptoms in individuals with PD are acute joint pain, intense fatigue, leg ulcers, pallor and jaundice, with comorbidities, such as infections, heart disease, renal failure, stroke and others[3]. This disease is characterized by its prevalence in underdeveloped countries, affecting the low-income population[1]. Brazil has high rates, with higher prevalence in the state of Bahia[4,5].

FD has been extensively studied, focusing on pathophysiology and treatments that reduce acute attacks that lead to hospitalization[6,7]. Medical treatments increased life expectancy, allowing individuals to be exposed longer to the comorbidities of the disease[7]. In this context, chronic pain syndrome develops in 30-40% of adults with PD[8], significantly impacting the functionality of individuals with DF[7].

The participation of central nervous system (CNS) sensitization in the perpetuation and increase of pain in individuals with SCD has been studied providing sufficient evidence of its contribution to the chronicity of pain[2,9–11]. The evaluation of CNS sensitization in individuals with PD has been recommended[12]. The use of reliable methods, such as Quantitative Sensory Testing, Conditioned Pain Modulation and CS Inventory, can help clinical professionals better understand the changes that chronic pain brings and how much it can impact the quality of life[2,9,10].

Quality of life (QoL) is conceptualized as the "patient's evaluation of how their well-being and level of functioning, compared to the perceived ideal, are affected by individual health"[13]. The Short FormHealth Survey (SF-36) is a valid and reliable instrument developed to thoroughly examine the state of health for clinical practice and research, for health policy studies and

investigations of the general population. It has eight domains that assist in the definition and approach of treatments[13,14].

In the last decade, studies on the impact of pain on QoL have increased due to the development of chronic pain. Studies analyzed financial burdens[15,16], education, work and disease management with the publication of recommendations[17,18]. Low quality of life in sickle cell individuals has been associated with various everyday problems, such as prejudice[15].

Emotional dysfunctions such as depression, first, then anxiety and catastrophization have been identified as participants in the clinical picture of patients with PD, interfering with the pain profile[19,20]. These studies have shown that the quality of life in sickle cell disease may be affected by complex factors that doctors and researchers should better understand[21,22].

This study analyzed the impact of tender points, pain intensity, catastrophization, central sensitization, depression and anxiety on quality of life in individuals with sickle cell disease.

METHODS

This descriptive cross-sectional study is part of a cross-randomized clinical trial registered in REBEC n. TN: U1111-1243-3020, already published(23), with adults diagnosed with PD. The inclusion criteria were to have a diagnosis of PD, to be of legal age and not to have had acute crises in the last ten days. The exclusion criteria were to have cognitive limitation to be able to answer the questionnaires of this research on their own.

One hundred individuals answered all the questionnaires. The study participants were recruited between October 2019 and October 2022, registered in Basic Health Units of Recôncavo Baiano, and members of the sickle cell association of the municipality of Feira de Santana-BA.

The Free and Informed Consent Term was read to all participants according to Resolution 466/2012 of the National Health Council of Brazil. This study was approved by the Ethics and Research Committee of the Northeast Adventist University Center of Education (CAAE nº 94835218.8.00000.0042). It was clarified to each individual that he was free to deny participation or abandon the interview at any time.

Contact with PD carriers occurred in two ways, through the UBS of the region, with authorization of the health departments of the municipalities and with the association of people with Sickle Cell Disease in the region. The sample was for convenience. Two properly trained researchers applied the questionnaires to all participants.

Procedures:

Individuals with PD underwent screening at the local Basic Health Unit or at home. After reading, explaining and signing the Free and Informed Consent Term, the questionnaires were

answered by the participants to the researchers. In this study, the researchers read each question to each individual. The sociodemographic questionnaire gathers information about age, sex, education, marital status, race, religion and pain levels. Several collection instruments were applied, as described below.

Brazilian Portuguese Central Awareness Inventory. Designed as an easy-to-apply screening for individuals at high risk of CS, it also helps classify chronic pain. It consists of twenty-five questions with five possible answers, from never to always. It is an ordinal scale; each answer has a value from zero to four[24].

Brief Pain Inventory for Brazilian Patients. It consists of nine items arranged in two dimensions: the intensity of pain and its impact on the patient's life. The Inventory asks to evaluate the intensity of pain and the interference of pain in general activities, mood, ability to walk, daily work, relationship with other people, sleep and pleasure of living on an 11-point scale ranging from zero (no pain) to ten (as bad as possible). It includes a body diagram to evaluate the location of pain, measures the percentage of pain relief and asks to describe which treatments are being used to control pain. A high score represents high intensity or pain interference(25).

Portuguese Pain Catastrophization Scale. It consists of thirteen items that evaluate thoughts, feelings and catastrophic behaviors when you are in pain(26). It is divided into three domains: helplessness, expansion and rumination. The items are evaluated on a 5-point Likert scale, in which intensity and frequency information is represented, with the following five response levels for each item: (0) minimum, (1) mild, (2) moderate, (3) intense, (4) very intense. The total score of the catastrophization scale varies from 0 to 52 points.

Hospital Anxiety and Depression Scale (HADS). It consists of fourteen self-reported questions divided into two subscales: one for Anxiety and the other for Depression. The subject will evaluate each item using an ordinal scale ranging from zero (non-existent symptom) to three (very severe symptom)[27].

Short Form Health Survey 36 (SF-36).It is composed of thirty-six multidimensional questions that will provide a crude scale of eight concepts: functional capacity, physical aspects, pain, general state of health, vitality, social aspects, emotional aspects and mental health. It has a final score from zero to 100, where zero corresponds to the worst general state of health and 100 to the best general state of health [28].

Statistical analysis:

The association between the presence of chronic pain (i.e., yes or no) and pain distribution (i.e., localized, regional and generalized) was analyzed by Chi-square or Fisher's Exact tests in the comparison of frequency distributions. The clinical factors related to pain, such as Anxiety, pain intensity, Catastrophication, Central sensitization, number of drugs used, Depression and body

distribution of painful points (i.e., lower limbs, trunk, abdominal region, upper limbs, head and neck, shoulders and back, sacral loin region), were analyzed using the Pearson correlation test with the quality of life domains of the SF-36 (i.e., functional capacity, physical aspects, pain, general state of health, vitality, social aspects, emotional aspects and mental health). All significant correlations were included in multiple linear regression analysis models, using the forward method to analyze the impact of the general domains of quality of life by the SF-36. In all statistical tests, the alpha significance level was 5%, and Beta was 80%.

RESULTS

Demographic characteristics

One hundred adults diagnosed with PD, identified in basic health units of six cities of the Bahian Recôncavo, participated in this study with HbSS and HbSC genotype. 69 women and 31 men were included, with an average age of 34.14 (SD 10.12) (Annex I, Table 1).

Table 1 - Demographic characteristics of participants

	Average (DP)	**Frequency (%)**
Sex		
Men		31 (31%)
Women		69 (69%)
Age, in years	34.14 (10.12)	
18 - 29		35 (35%)
30 - 39		34 (34%)
40 - 50		26 (26%)
Educational Level		
Complete and incomplete elementary school		33 (33%)
Complete and incomplete high school education		52 (52%)
Complete and incomplete higher education		15 (15%)
Marital status		
With a partner (married or in a stable relationship)		39 (39%)
Without a partner (single, divorced, widowed)		61 (61%)

Self-declared race		
Black		85 (85%)
Brown		14 (14%)
White		1 (1%)
Religion		
Catholic		48 (48%)
Evangelical		35 (35%)
No religion		15 (15%)
Outher		2 (2%)
Genotype		
HbSS		65 (65%)
HbSC		35 (35%)
With Government benefit		
With benefit		58 (58%)
Without benefit		42 (42%)
Has a signed portfolio		6 (6%)

Population size – 100. SD = standard deviation
Source: Prepared by the authors, 2025.

The subject's average financial income was lower than the country's minimum wage, established at R$ 1,212.00.

Clinical characteristics

The mean pain of the 100 individuals who participated in the study was 4.20±2.67 (SD) on the visual analog scale (VAS); 71% of them had chronic pain, established as daily pain in the same region at least in the last three months, and 59% had CS. Pain distribution: 22% had localized pain, 18% had regional pain and 60% had generalized pain. Of the sample, 18% had probable Depression, 33% had probable Anxiety and 10% had probable Depression and Anxiety (Annex II, Table 2).

Table 2 - Participants' pain characteristics

	Average (DP)	**Frequency (%)**
Pain intensity (monthly average)	4,20 (2.67)	
Pain at the time of the interview	2,31 (2.80)	
With chronic pain		71 (71%)

Pain distribution		
Localized pain		22 (22%)
Regional pain		18 (18%)
Diffuse pain		60 (60%)
Number of trigger points	14,06 (10,12)	
Trigger points in the lower limbs		90 (90%)
Trigger points in the upper limbs		80 (80%)
Trigger points in the lumbosacral region		73 (73%)
Trigger points in the thoracic region		31 (31%)
Trigger points in the abdominal and inguinal region		25 (25%)
Medications in use		
Number of medications used daily	2,82 (1,45)	
Polypharmacy (use of 4 or more medications daily)		34 (34%)
Level of improvement after use of pain medication (%)	60,50 (32,60)	
Central Sensitization		
Average	46,17 (18,48)	
With central sensitization		59 (59%)
Catastrophism		
About 40 points		41 (41%)
Average	34,78 (12,17)	

Population size – 100. SD = standard deviation
Source: Prepared by the authors, 2025.

In the interview, patients were asked about what medications they ingested daily. 89% used folic acid, 27% used hydroxyurea and 61% used dipyrone. Only three (3%) used medication for Depression and one (1%) for Anxiety.

Quality of life results (SF-36)

The lowest average quality of life scores were for the Physical Aspect domain (35.55 ± 40.16) and General Health Status domain (38.31 ± 23.51) (Annex III, Table 3).

Table 3 - Quality of life (SF-36)

Domain	Average	DP
Functional Capacity	45,79	26,30
Physical Aspects	35,55	40,16
General Health Status	38,31	23,54
Pain	44,67	24,31
Vitality	45,50	21,13
Social Aspect	56,05	30,89
Emotional Aspect	40,11	39,61
Mental Health	53,62	26,11

Source: Prepared by the authors, 2025.

Associations of pain descriptors with chronic pain and pain distribution

Associations were found between Chronic Pain with Anxiety (X^2= 25.32 p<0.001) and Depression (X^2= 12.71 p=0.002). An association was also found between pain distribution and Anxiety (X^2=13.35, p=0.010).

Correlations between clinical factors related to pain and the eight domains of Quality of Life (QoL)

Anxiety, pain intensity, Central Sensitization and Catastrophization were significantly correlated with all eight QoL domains. Among these results, it is possible to highlight that Anxiety presented a moderate negative correlation with the Mental Health domain (r = -0.670; p<0.001); CS presented a moderate negative correlation with the Mental Health domain (r = -0.584; p<0.001); CS also presented a moderate negative correlation with the Vitality domain (r = -0.530 p<0.001); and Catastrophization presented a moderate negative correlation with the General Health status domain (r = -0.525; p<0.001) (Annex IV, Table 4).

Table 4 - Correlation with Quality of Life Domains (SF-36)

Quality of Life Domains (SF-36)									
Variables		**CF**	**AF**	**Dor**	**SGS**	**V**	**AS**	**AE**	**SM**
Central Sensibilization	P	.000	.002	.000	.000	.000	.000	.001	.000
	r	-.406	-.301	-.407	-.438	-.530	-.453	-.330	-.584
Anxiety	P	.015	.005	.000	.000	.000	.000	.004	.000
	r	-.244*	-.277	-.404**	-.366**	-.415**	-.453**	-.286**	-.670**
Pain Intensivity	P	.055	.000	.000	.000	.000	.000	.000	.000
	r	-.193	-.348**	-.378**	-.386**	-.402**	-.415**	-.401**	-.446**
Catastrophizing	P	.032	.005	.001	.000	.003	.000	.003	.000
	r	-.217*	-	-	-	-.296	-	-	-

			.332**	.332**	.525**		.384**	.302**	.418**
Depression	P	.009	.175	.000	.001	.000	.000	.002	.000
	r	-.261	-.137	-.381**	-.342**	-.437**	-.470	-.313**	-.464**
Number of trigger points	P	.003	.008	.000	.022	.082	.467	0.98	.013
	r	-.298*	-.263*	-.389**	-.230*	-.175	-.074	-.166	-.249

Functional Capacity = CF; Physical Aspects = AF; General Health Status = SGS; Vitality = V; Social Aspects = AS; Emotional Aspects = AE; Mental Health = SM.
** The correlation is significant at 0.01 (2-tailed).
* The correlation is significant at 0.05 (2-tailed).
Source: Prepared by the authors, 2025.

Impact of clinical factors related to pain on Quality of Life

The analysis of the multiple linear regression model by the forward method showed that the SC and Depression scores impacted four domains of quality of life. Pain intensity had an impact on three of the eight domains. Finally, Catastrophization and the painful points of the lower limbs impact two domains each.

The element that most impacted the physical and mental components was identified. The results showed a significant negative influence of Catastrophization and CS on the General Health Status, which is a physical component ($F(2.95) = 21.592$ $p<0.001$; adjusted $R^2 = 0.298$), explaining 29.8% of the outcome; anxiety, trigger points without lower limbs and depression had a significant negative influence on the Pain domain (physical component) ($F(2.95) = 15.207$ $p<0.001$; adjusted $R^2 = 0.270$), explaining 27% of the outcome. The other covariables of the physical components impacted less than 20%.

As for the mental components, the results showed a significant negative influence of Anxiety and CS on the Mental Health domain ($F(2.95) = 43.014$ $p< 0.001$; adjusted $R^2 = 0.464$), explaining 46.4% of the outcome. CS and Depression had a significant negative influence on the Vitality domain ($F(2.95) = 23.826$ $p< 0.001$; adjusted $R^2 = 0.320$), explaining 32% of the outcome. The Social Aspects domain was impacted by Depression and pain intensity ($F2.95) = 19.941$ $p<0.001$; adjusted $R^2 = 0.28$), explaining 28% of the result. The other covariables of the mental components impacted less than 20% (Annex V, Table 5).

Table 5 - Predictor variables of Quality of life.

	Standardized Coefficients	**95% Confidence Interval**		***t***	**Sig.**	***R²***	***R² Change***
PREDICTORS	***Beta***	**Lower Bound**	**Upper Bound**				
CAPACITY FUNCIONALITY							

Constant	-	60.953	86.623	11.413	.000	-	-
Central sensitization	-.326	-.737	-.180	-3.271	.001	.153	-
Trigger points lower limbs	-.195	-2.45	-.003	-1.990	.049	.179	.034
PHYSICAL ASPECTS							
Constant	-	53.983	99.475	6.697	.000	-	-
Pain intensity	-.262	-6.994	-.849	-2.534	.013	.114	
Catastrophism	-.211	-1.363	-.018	-2.037	.044	.142	.037
BY							
Constant	-	62.781	82.575	14.580	.000	-	-
Anxiety	-.175	-1.962	.218	-1.588	.116	.177	
Trigger points lower limbs	-.258	-2.585	-.385	-2.682	.009	.227	.057
Depression	-.266	-2.886	-.373	-2.575	.012	.270	.050
GENERAL HEALTH STATUS							
Constant	-	65.764	91.091	12.295	.000	-	-
Catastrophism	-.398	-1.151	-.374	–3.897	.000	.269	-
Central sensibilization	-.229	-.544	-.033	-2.24	.027	.298	.036
VITALITY							
Constant	-	67.125	86.352	15.847	.000	-	-
Central sensibilization	-.404	-.679	-.237	-4.115	.000	.280	-
Depression	-.252	-2.422	-.310	-2.568	.012	.320	.046
SOCIAL ASPECTS							
Constant	-	78.904	103.375	14.787	.000	-	-
Depression	-.379	-4.468	-1.567	-4.130	.000	.219	-
Pain intensity	-.279	-5.328	-1.116	-3.037	.003	.281	.068
EMOCIONAL ASPECTS							
Constant	-	57.826	90.987	8.909	.000	-	-
Pain intensity	-.324	-7.589	-1.882	-3.294	.001	.147	-
Depression	-.203	-4.012	-.081	-2.067	.041	.175	.036

MENTAL HEALTH							
Constant	-	82.649	103.112	18.021	.000	-	-
Anxiety	-.501	-3.912	-1.495	-4.432	.000	.447	-
Central sensibilization	-.228	-.631	-.005	-2.020	.046	.464	.023

Source: Elaborated by the authors, 2025.

DISCUSSION

This study aimed to analyze the impact of trigger points, pain intensity, catastrophization, CS, depression and anxiety on the QoL domains. We identified that anxiety, depression, catastrophism and CS had an important impact on at least one domain as predictors of QoL. The evaluation of SC stood out because 59% of our individuals were diagnosed with it. Most individuals in this research were unaware of these diagnoses. Sixty percent of the sample reported generalized pain, an important characteristic of SC[29]. This highlights the importance that people with FD need specific evaluation and management [12].

The intensity of pain had an important impact on the domains of QoL. The greater the pain, the lower the score of the domains, specifically of the physical, social and emotional aspects. If the pain is not treated, chronic pain will settle and potentiate other contributors [8–9,29,30]. The most compromised QoL domains were physical aspects and general health status, similar to the results of the research in northern Brazil[15].

The individuals in our study had depression levels similar to those of the studies, but with higher levels of anxiety [20,31]. Few individuals use medication for depression and less for anxiety. A possible explanation for the high anxiety rate may be the fact that the adults participating in this study reside in small cities and without easy access to the state capital, where specialized care is provided, such as hospitalizations and blood transfusions. A study showed that access limitations can contribute to high levels of anxiety due to concern with medical care for subsequent crises, and associated anxiety with fear that the condition could reduce life expectancy[32].

Only twenty-seven participants in this study use hydroxyurea daily, which remains the basis of disease-modifying therapy[33] and raises the quality of life[34]. However, it is important to clarify that it is eleven times more expensive than folic acid, the main drug used for the DF in Brazil, where government health is responsible for the supply of these medicines. Dipyrone is mainly used for pain; more than 60% of subjects use it daily, confirming the high incidence of pain[19].

Only six individuals in the study work as employees; generally, individuals with PD have fewer job opportunities, perhaps due to the fear of frequent absences from their possible employers, since employers have registered unfavorable attitudes towards individuals with

PD[35] . DF impacts work[36] and educational skills[37]. Work is essential for subsistence and maintenance of mental well-being, gives meaning to life and drives human growth[38]. Individuals with DF seek government help; in this case, almost sixty percent have some financial benefit. The government benefit is low; more is needed to cover personal expenses, so many depend on family members, regardless of age. Therefore, the financial burden that DF causes in this population may be similar to that of other populations of underdeveloped countries[8], affecting their quality of life.

An association was identified between the number of pain points in the lower limbs and anxiety; the most frequent clinical causes of pain in the lower limbs are avascular necrosis in the hip and chronic infarction in the lower limbs and vaso-occlusive pain[8,39]; but psychological suffering has already been associated with multiple sensitive points, regardless of age. These findings imply that psychological interventions can be effective for chronic pain disorders in adults of all ages[40]. An association was identified between psychological suffering and sedentary lifestyle [41]. Light physical exercises can benefit these individuals[42].

Our study had some limitations, the sampling was done by convenience method, and our prediction result should be interpreted with caution because it is a cross-sectional study; a future longitudinal study will be necessary to confirm our findings.

CONCLUSION

Anxiety, depression, catastrophization and central sensitization significantly impact the quality of life in individuals with SCD, evidenced in a population of high incidence in Bahia-Brazil. It is necessary that doctors, health professionals and researchers pay attention to the relationship between clinical factors and predictors of quality of life.

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