Sickle Cell Disease: quality of life in patients with hemoglobin SS and SC disorders

Sônia Aparecida dos Santos Pereira[1]
Stela Brener[1]
Clareci Silva Cardoso[2]
Anna Bárbara de Freitas Carneiro Proietti[1]

[1]Fundação Centro de Hematologia e Hemoterapia do Estado de Minas Gerais – HEMOMINAS, Belo Horizonte, MG, Brazil
[2]Universidade Federal de São João Del Rei – UFSJ, Divinópolis, MG, Brazil

Objective: Sickle cell disease comprises chronic, genetically determined disorders, presenting significant morbidity and high prevalence in Brazil. The goal of this study was to evaluate the quality of life of sickle cell disease patients (hemoglobin SS and SC) and their sociodemographic and clinical characteristics.

Methods: Data was collected from clinical records and semi-structured interviews consisting of clinical questionnaires and the World Health Organization Quality of Life-brief questionnaire.

Results: Interviews were conducted with 400 patients, aged between 18 and 72, treated in the Fundação HEMOMINAS in Belo Horizonte. The participants predominantly had sickle cell disease hemoglobin SS variant (65.5%), were female (61.8%), single (55.3), with up to 8 years of schooling (49.6%), and self-defined as mulattos (50%). Pain crises, hospitalizations, blood transfusions, and other morbidities of sickle cell disease had a significant impact on the quality of life of these patients.

Conclusion: Within this group, the social profile was that of low income and unemployed with sickle cell disease considered to be a significant impediment to finding a job. Evaluating quality of life as a determining factor of health is essential for the creation of specific policies and measures, appropriate for the specific characteristics and social context of sickle cell disease.

Keywords: Quality of life; Socioeconomic factors; Sickle cell trait; Questionnaires

Introduction

Sickle Cell Disease (SCD) is a group of disorders, comprising sickle cell anemia (Hemoglobin - Hb SS) and compound heterozygous disorders (Hb SC, Hb SD, Hb SG, etc.). It originated in Africa and was brought to the Americas primarily by the forced migration of native Africans for slave labor. It is now found throughout all of Europe and Asia. Due to the miscegenation of the Brazilian population, SCD has randomly spread throughout the country, although its presence is more evident where the Afro-Brazilian population is higher[1].

According to data from the Ministry of Health, around 3500 children are born with SCD each year, and the estimated number of cases of the disease is between 25,000 and 30,000. Among the general population, 4% present with the sickle trait, corresponding to a total of 7,200,000 individuals, with approximately 200,000 births per year[1-3]. Data from the National Neonatal Screening Program shows that, in the state of Minas Gerais, the occurrence of the disease among live newborns is 1:1,400, and 1:23 for the sickle trait[4].

The clinical variation has very specific presentations; SCD can vary according to the type of Hb, with Hb SS and Hb SC being the most common variants. Although SCD in the Hb SC form presents a more benign clinical evolution than Hb SS, both may present similar complications[5]. While some patients present with very severe clinical conditions, and are subject to many complications and frequent hospitalizations, others tend to show benign development, and some cases are almost asymptomatic. Both genetic and acquired factors contribute to this clinical variation. Among the acquired factors, the most important is the patient's socioeconomic conditions[1].

People in a vulnerable socioeconomic situation are more exposed to the determining social factors of the disease, which can lead to an aggravation of the patient's general health[1]. The severity of the disease is, in general, inversely proportional to the quality of life (QOL)[6]. According to the World Health Organization (WHO), the QOL is defined as "the individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns"[7]. Presented in this definition are the multiple dimensions incorporated in the individual's perception of the different aspects of life[8].

Although SCD has been largely studied in terms of population frequency and clinical variations[9,10], research that addresses aspects related to QOL of patients are relatively scarce in both the Brazilian and international literature. Therefore, as SCD is an important Public Health problem in Brazil and QOL, a relevant outcome measure for health, an investigation into the QOL of patients suffering from this disease was proposed. Simultaneously, the applicability of

the World Health Organization Quality of Life - brief (WHOQOL-BREF) questionnaire was evaluated in this population. The WHOQOL-BREF questionnaire was developed by the World Health Organization (WHO) as an attempt to develop a quality of life assessment that would be applicable cross-culturally.

Methods

A cross-sectional study was carried out in the Fundação HEMOMINAS, from August 2006 to October 2007. The participants were patients with Hb SS and Hb SC, registered in the clinic of the Blood Center in Belo Horizonte. The patients considered eligible to participate in this study were over 18-year-old adults without cognitive impairment, who signed an informed consent form and freely agreed to be interviewed.

Data collection was performed through a random selection of the sample, with an average of five individuals selected per day. Clinical and sociodemographic questionnaires were used for the interviews. The assessment of the QOL employed the WHOQOL-BREF questionnaire consisting of 26 questions - two initial questions referring to QOL and health satisfaction, and the rest classified according to physical, psychological, social relations, and environmental domains. Clinically relevant data for this study were taken directly from the patients' health records.

These instruments were tested in a pilot group consisting of 12 patients in order to standardize the vocabulary being used. Specific syntax was used in the Statistical Package for Social Sciences (SPSS) software to calculate the scores.

The method employed was the comparison of two means, taking into consideration the standard deviation. The parameters used were: 5% significance level, 90% power, and a minimal difference of five points detected in comparing the groups. With a pilot sample of 80 patients, the average QOL score was calculated for all domains of the WHOQOL-BREF scale. The physical aspect was taken as a reference for comparison of QOL scores between the Hb SS and Hb SC patient groups. The average QOL score was 59.3 with a standard deviation of 11.6. All individuals scheduled for treatment that matched the eligibility criteria and agreed to participate were interviewed giving a grand total of 400 patients even though the calculation of the sample size showed that a sample of 226 patients would have 90% power to detect a difference of 5 points in the QOL score.

Frequency distribution tables were used for the descriptive analysis of the categorical or nominal variables and central tendency measures and dispersion were utilized for the continuous variables. Significance of differences between sociodemographic and clinical characteristics of Hb SS and Hb SC patients were estimated using the Chi-square test (χ^2) when appropriate and the Mann-Whitney Test was utilized for the QOL.

The correlation of the WHOQOL-BREF questions and the average score of the QOL domain to which they relate were analyzed using the Spearman correlation coefficient. The Cronbach's alpha coefficient was used to evaluate the internal consistency of the WHOQOL-BREF for measuring QOL in SCD. EpiData 3.1 was used for data input, and Statistical Package for the Social Sciences (SPSS) version 17.0 and Epinfo version 6.4 were used for statistical analysis.

The Research Ethics Committee of the Fundação HEMOMINAS approved this study (# 139).

Results

From an initial sample of 412 patients with a diagnosis of SCD, 12 (2.9%) declined to participate. Hb SS was present in 65.5% of the patients, 61.8% were female, and 55.3% were single with ages ranging from 18 to 72 and a median age of 29.

Half the patients (50%) described themselves as mulatto and 38.5% as black. Almost 50% had up to 8 years of education and only 32% were employed. A total of 59.6% of patients said that SCD hindered their ability to find work (Table 1). The average *per capita* income was 0.93% of the minimum wage. Most patients (67.7%) lived outside Belo Horizonte and travelled an average of 250 km (from 28 to 1294) for treatment.

Significant statistical differences were found in regards to age group, marital status, family and individual income, employment status, patient as head of household, SCD as barrier for work and leisure opportunities.

The comparison between patient groups (Hb SS and SC) in respect to the clinical, sociodemographic and economic characteristics are presented in Tables 1 & 2.

Demographic profile

The most frequent age group of individuals with Hb SS was 18 to 24 years old with the commonest age group being 40 to 49 years old for those with Hb SC. One third of Hb SS patients were married, while half of the Hb SC patients were married or living as such.

Socioeconomic profile

Lower household incomes (2.08 minimum wages) and individual incomes (0.82 minimum wages) were found for participants in the Hb SS group, with only one quarter of the group being employed at the time of the study. For them, SCD was a major impediment to find work, although 78% of the individuals declared that they were the head of the household. In the Hb SC group, 28% reported not having any type of leisure time in the previous year.

Living with the disease

The median age at which SCD was diagnosed was 14 years old for Hb SS and 22 years for Hb SC. Around half of the patients with Hb SC reported having pain crisis treatment in their homes, 9.4% received blood transfusions in the previous year and 47% reported having at least one other case of SCD in their family. For the Hb SS group these values were 35.0%, 37.4% and 63%, respectively. The Hb SS group used the multi-professional treatment services provided by the Blood Center in Belo Horizonte more frequently than the Hb SC patients. When asked, 34.3% of the patients could not specify their type of Hb.

All of the clinical variables presented statistically significant differences between the groups (p-value ≤ 0.05) except for the number of pain crises in the previous month.

Table 1 - Socioeconomic, demographic and clinical characteristics of the 400 individuals with Sickle Cell Disease

	Total (n = 400)		Hb SS (n = 262)		Hb SC (n = 138)		p-value
	n	%	n	%	n	%	
Age							<0.001
18 to 24 years	121	30.3	90	34.3	31	22.5	
25 to 29 years	81	20.3	60	23.0	21	15.2	
30 to 39 years	98	24.5	69	26.3	29	21.0	
40 to 49 years	68	17.0	33	12.6	35	25.4	
50 to 59 years	23	5.8	7	2.7	16	11.6	
Above 60 years	9	2.3	3	1.1	6	4.3	
Skin color							0.075
Mulatto	200	50.0	122	46.6	78	57.6	
Black	154	38.5	111	42.4	43	31.9	
White	35	8.8	21	8.8	14	10.4	
Not informed	11	2.8	8	2.0	3	2.2	
Marital status							<0.001
Single	221	55.3	168	64.1	53	38.4	
Married or in stable relationship	149	37.3	81	30.9	68	49.3	
Divorced, separated	24	6.0	10	3.8	14	10.1	
Widow	6	1.5	3	1.1	3	2.2	
Schooling (years)							0.597
Never studied	2	0.5	1	0.4	1	0.7	
1 to 4 years	77	19.3	47	17.9	30	21.7	
5 to 8 years	121	30.3	76	29.0	45	32.6	
9 to 11 years	181	45.3	124	47.3	57	41.3	
Above 11 years	19	4.8	14	5.3	5	3.6	
Income in the last month (in minimum wage)							<0.001
Familial	2.31		2.08		2.55		
Individual	0.93		0.82		1.04		
Employment situation							0.019
Working	128	32.0	72	27.5	56	40.6	
Not working	166	41.5	122	46.6	44	31.9	
On medical leave	68	17.0	45	17.2	23	16.7	
Retired	38	9.5	23	8.8	15	10.9	
SCD as obstacle to work (n=267)	159	59.6	121	64.7	38	47.5	0.031
Patient as head of household	291	72.8	203	77.8	88	63.8	0.003
Leisure time previous year							0.034
None	97	24.3	58	22.1	39	28.3	
Little	128	32.0	89	34.0	39	28.3	
Average	89	22.3	54	20.6	35	25.4	
Significant	86	21.5	61	23.3	25	18.1	
Clinical characteristics							
Age of diagnosis (median)	36		14		22		0.004
Transfusions in the previous year (n=389)							<0.001
Yes	111		98	37.5	13	9.5	
No	287		163	62.5	124	90.5	
Number of pain crisis in the previous year	16.0		8.0		8.0		0.255
Behavior adopted for pain crisis (n=299)							0.018
Sought medical attention	54	18.1	36	18.3	18	17.3	
Treated at home	121	40.5	69	35.0	52	51.0	
Sought medical attention but was treated at home	124	41.5	92	46.7	32	31.4	
Presence of SCD in the family							0.002
Yes	210	52.6	123	47.1	87	63.0	
No	189	47.4	138	52.9	51	37.0	
Number of visits to health services in the previous year	7.7		9.3		6.0		<0.001

Table 2 - Frequency of *Ig* and *TCR* rearrangements in 44 children with precursor B-lineage acute lymphoblastic leukemia from Minas Gerais, Brazil

	Statistics	Physical domain	Psychological domain	Social relations domain	Environmental domain	General
Hb SS	Median	60.7	66.7	75.0	53.1	62.5
	Standard deviation	17.9	14.5	17.7	15.6	19.6
	Minimum	7.1	12.5	8.3	12.5	0.0
	Maximum	100.0	95.8	100.0	93.8	100.0
Hb SC	Median	60.7	66.7	66.7	53.1	62.5
	Standard deviation	18.7	16.5	19.1	15.2	18.2
	Minimal	10.7	33.3	0.0	18.8	0.0
	Maximum	100.0	100.0	100.0	87.5	100.0
p-value		0.269	0.583	0.768	0.638	0.390

Quality of Life

The 'environmental' domain presented low scores for both groups. In both Hb SS and Hb SC, the 'social relations', followed by the 'psychological' domain, presented higher scores. The 'social relations' domain is slightly better for Hb SS patients although the difference in the mean scores of the two groups was not statistically significant.

When each question of the WHOQOL-BREF instrument was analyzed in isolation, differences were found between groups on two points. The first, in the physical domain (How much do you need any form of medical treatment to live your daily life?) showed that Hb SC patients feel that they need medical assistance more frequently than Hb SS patients. The second in the psychological domain (Are you capable of accepting your physical appearance?) showed that Hb SS patients said they were more willing to accept their physical appearance than the Hb SC group (p-value > 0.05).

The applicability of the WHOQOL-BREF to measure quality of life in sickle cell disease

The correlation between the WHOQOL-BREF questions and the mean score of each of its domains varied from 0.492 to 0.759, thus presenting a highly significant correlation between the scores of each of the six domains (p-value < 0.001)

The internal consistency of the WHOQOL-BREF as measured by Cronbach's alpha coefficient was satisfactory on considering all items of the score (0.88), as well as separately, by 'physical' (0.78), 'psychological' (0.64), 'social relations' (0.54), and 'environmental domains' (0.71), and 'general QOL' (0.51) (Table 3).

Table 3 - Cronbach's alpha coefficient of the World Health Organization Quality of Life-brief questionnaire used to study the quality of life in sickle cell disease patients

	Cronbach's alpha coefficient
Physical domain	0.78
Psychological domain	0.64
Social Relation domain	0.55
Environmental domain	0.71
General QOL	0.51
All Items	0.88

Influence of the clinical conditions on quality of life

In the comparison of the QOL scores, the most relevant results regarding the clinical complications were (Table 4).

Pain crises in the previous month

A statistically significant difference was observed in participants with Hb SS disease for the 'physical' domain and 'general QOL' (p-value < 0.001). For participants in the Hb SC group, there were differences for the 'physical', 'social relations' and 'environmental' domains and 'general QOL' (p-values < 0.05). In both groups, participants that did not report any pain crises presented the highest QOL scores.

Blood transfusions in the previous year

A significant statistic difference (p-value < 0.05) was observed for Hb SS individuals for the 'psychological' domain and 'general QOL'. This difference did not occur for any domains of patients in the Hb SC group.

Other disease occurrences during the previous year

Among Hb SS patients, there was a significant difference for all domains. For individuals with Hb SC, significant differences occurred in the 'physical' domain and 'general QOL'. All participants that reported having any other disease, regardless the Hb type, had lower QOL scores.

Hospitalization in the previous year

Hb SS patients presented statistically significant differences for the 'physical', 'psychological', and 'environmental' domains and 'general QOL'. Individuals with Hb SC presented a significant difference for the 'physical' domain. Patients that did not report hospitalization in the previous year presented higher scores for QOL (p-value < 0.05).

Table 4 - Comparison of quality of life scores of the World Health Organization Quality of Life-brief questionnaire between patients with Hb SS and Hb SC

Complications	Hemoglobin		PD	PsyD	SRD	ED	gQOL
Pain crisis in the previous month	Hb SS	Yes (n = 114)	53.6	66.7	66.7	53.1	62.5
		No (n = 148)	64.3	70.8	75.0	53.1	75.0
		p-value	<0.001	0.208	0.390	0.090	<0.001
	Hb SC	Yes (n = 114)	53.6	62.5	66.7	46.9	62.5
		No (n = 148)	71.4	68.8	75.0	54.7	75.0
		p-value	<0.001	0.103	0.035	0.048	0.002
Transfusion in the previous year	Hb SS	Yes (n = 98)	57.1	66.7	75.0	53.1	62.5
		No (n = 163)	60.7	70.8	75.0	53.1	62.5
		p-value	0.125	0.007	0.748	0.765	0.015
	Hb SC	Yes (n = 13)	57.1	66.7	58.3	53.1	75.0
		No (n = 124)	60.7	66.7	66.7	53.1	62.5
		p-value	0.536	0.606	0.792	0.997	0.317
Other illnesses in the previous year	Hb SS	Yes (n = 63)	53.6	65.8	66.7	46.9	56.3
		No (n = 200)	60.7	70.8	75.0	56.3	62.5
		p-value	<0.001	0.001	0.058	0.001	<0.001
	Hb SC	Yes (n = 38)	53.6	64.6	66.7	48.4	62.5
		No (n = 100)	60.7	66.7	66.7	53.1	75.0
		p-value	0.016	0.905	0.935	0.694	0.023
Hospitalizations in the previous year	Hb SS	Yes (n = 126)	57.1	66.7	66.7	50.0	62.5
		No (n = 136)	62.5	70.8	75.0	56.3	62.5
		p-value	0.002	0.048	0.340	0.027	<0.001
	Hb SC	Yes (n = 55)	53.6	62.5	66.7	56.3	62.5
		No (n = 83)	64.3	66.7	66.7	53.1	62.5
		p-value	0.037	0.101	0.819	0.848	0.386

PD: Physical domain; PsyD: Psychological domain; SRD: Social relations domain; ED: Environment domain; gQOL: General quality of life

Discussion

SCD is chronic, non-contagious, degenerative, and self-incapacitating. It affects the patient and their family as a whole in an intense and permanent way as it is not a transitory event. In the current study, the specific clinical domains of this disease affected the QOL of individuals with SCD. Complications such as pain crises, blood transfusions, occurrence of other diseases and hospitalizations were the main factors that, when compounded with external domains such as unemployment, low income, and lack of access to health services, negatively influenced the lives of this population.

Due to the lack of QOL data for the general population in Brazil, it was not possible to make comparisons with the studied patients. A study from the United States shows that people with SCD experience a lower QOL than the general population[11].

No statistically significant difference in the QOL was found between the groups with Hb SS and those with Hb SC. There are similarities in the scores for the 'physical', 'psychological', 'social relations', and 'environmental' domains with the scores of patients with kidney failure undergoing hemodialysis[8]. These findings are consistent with a study from the United States where the QOL for SCD patients presented similarities to patients undergoing hemodialysis[11]. In a QOL study of Brazilian patients with colorectal cancer, patients with and without ostomy did not present statistically significant differences[12].

In this investigation, the 'social relations' and 'psychological' domains were the ones that most influenced the QOL of the studied groups in a positive way. Consistent with these findings, Brazilian studies using the WHOQOL-BREF to evaluate 60 patients with SCD and Schizophrenia identified higher average scores for the same domains[8].

The impact of the clinical condition on the professional lives of SCD patients was very evident in this study as it can be responsible for the generally low income and socially vulnerable condition. The expressive unemployment rate, in addition to complications due to the disease, is an obstacle for many subjects in the Hb SS group, who had more difficulties in finding employment.

A precarious financial situation and the strong interference of the disease on professional life leads to inactivity and low incomes, compromising the QOL of the individuals with SCD[13]. A study in the UK with a different social situation, portrayed the professional difficulties and fear for job security due to the limitations imposed by SCD. On the other hand, a Cuban study showed that the implementation of vocational guidance programs for work in respect to professions compatible with the disease may change this reality[15].

School absenteeism is one of the psychosocial characteristics subject to much interference by the clinical complications of SCD[14]. Less than half of the patients in this study reached the minimum eight years of schooling mandated by the Brazilian Constitution[16].

The other half completed between nine and 11 years of schooling, above the national average in 2008 of 7.1 years[17]. However, this fact is not enough to contribute to the commitment and permanence of the participants on the job market.

The reality of SCD patients is rife with social inequality in Brazil: the greater prevalence of the disease among Afro-Brazilians, in a country whose marked racial exclusion is, in part, represented by fewer professional opportunities, collaborates to the professional difficulties of these patients.

Low individual and household income was a reality among the studied groups; these factors, in addition to their specific occupations, the racial factor, and complications in SCD characterized this population as 'low socioeconomic level'. This reality shows that the implementation of policies that favor better life conditions for people with SCD is an absolute necessity.

The decentralization of medical services to treat SCD is a pressing matter. Traveling for treatment away from their place of residence, often in precarious conditions, frequently places the lives of these patients at risk, as well as overburdening the healthcare system in the State capital. Research on the circumstances surrounding the death of children with SCD in Minas Gerais State, points to the difficulty in providing transportation to the health treatment center as a contributing factor to premature deaths[18].

The clinical aspects of the disease influence the QOL of individuals with SCD. The pain crises, the blood transfusions, occurrence of other diseases and hospitalizations, in addition to the social aspects such as unemployment, low income, and difficulties to access the health service, negatively impacted the QOL of this population. Blood transfusions were more frequent in the Hb SS group, which is a reflection of the severity of the disease. The result of this is a lower QOL.

The chronic nature of SCD has been insufficiently recognized, especially in relation to its influence of pain crises and the severity of the disease on the sociocultural and psychological factors[10,19]. The frequency of the pain crises reported in this study, is comparable to other Brazilian studies with six or more crises per year[20]. Mostly individuals in the Hb SS group sought medical assistance with participants of the Hb SC group mostly being treated at home. One study reported that often, the patients who most frequently sought hospital treatment developed passive or aggressive interactions with their caretakers over time[19]. On the other hand, those who regularly treated their pain at home developed a strong sense of self-reliance, assertiveness and resistance towards hospital services. Therefore, healthcare models should reflect the diversity of the SCD population, prioritizing greater patient participation[10,21].

Although a greater percentage of participants with Hb SC reported home treatment, they claimed a more intense need for medical treatment, compared to Hb SS, the more serious variation of the disease. Studies reveal conflicting situations; on one hand they show the reluctance to seek out medical and/or hospital attention due to the lack of comprehension of medical professionals when treating these patients, and on the other, a sensation of great comfort upon becoming acquainted with their caregivers. Others, however, reported experiencing a greater control of their situation at home and amongst relatives[14].

Conclusions

The WHOQOL-BREF questionnaire has adequate validity and reliability, and includes domains that are important to measure QOL in SCD. It gave a highly significant correlation for all questions in each domain, as well as good internal consistency, proving to be a very reliable instrument in the assessment of the QOL in patients with SCD.

The inclusion of Quality of Life indicators in the clinical follow-up can help redefine specific public policies and define priorities in medical treatment provided to these patients, as well as in the evaluation and following up of results. It can also increase the possible areas of research within the subject, helping to foster a larger number of much needed Brazilian and International studies.

Acknowledgements

References

1. Brasil. Ministério da Saúde. Agência Nacional de Vigilância Sanitária - Manual de diagnóstico e tratamento de doenças falciformes. Brasilia: ANVISA; 2001. 142p.

2. Brasil. Ministério da Saúde. Manual de Educação em Saúde: auto-cuidado na Doença Falciforme. Brasília: Departamento de Atenção a Saúde, 2008. 78p.

3. Cançado RD, Jesus JA. A doença falciforme no Brasil. Rev Bras Hematol Hemoter. 2007; 29(3):204-6.

4. Brasil. Ministério da Saúde. Portal da Saúde. Doença falciforme no SUS. [Internet] [cited 2012 Jul 12] Available from: http://portal.saude.gov.br/portal/saude/Gestor/visualizar_texto.cfm?idtxt=27777

5. Zago MA, Falcão RP, Paquini R. Hematologia: fundamentos e práticas. São Paulo: Atheneu, 2004; p. 295-7.

6. Naoun PC, Alvarez FF, Domingos CR, Ferrari F, Moreira HW, Sampaio ZA, et al. Hemoglobinas anormais no Brasil: prevalência e distribuição geográfica. Rev Bras Patol.Clín. 1987; 23(3):68-79.

7. The Whoqol Group. The World Health Organization quality of life assessment (WHOQOL). Position paper from the World Health Organization. Social Science and Medicine. 1995; 10:1403-9.

8. Fleck MP, Lima FB, Polancsk CA, Trentini CM, Bandeira, D, Patrick, DL, et al. A avaliação da qualidade de vida: guia para profissionais da saúde. Porto Alegre: Artmed, 2008.

9. Araújo JT. Geographical distribution and accident of hemoglobins in Brazil. In: Inter- American Symposium on Hemoglobins: Genetic, functional and physical studies on Hemoglobins. Caracas; 1971.

10. Alvim RC. Perfil e impacto da dor em crianças e adolescentes com doença falciforme: Estudo clínico experimental do efeito do piracetam na prevenção das crises de dor [thesis]. Belo Horizonte: Faculdade de Medicina da Universidade Federal de Minas Gerais; 2002.

11. Donna KM, Penberthy LT, Bovbjerg, VE, Roberts JD, Aisiku IP, Levenson JL, et al. Health related quality of life in sickle cell patients: the PISCES project. Health Qual Life Outcomes. 2005;3:50.

12. Michelone Ade P, Santos VL. Qualidade de vida de adultos com câncer colorretal com e sem ostomia. Rev Latinoam. Enfermagem. 2004;12(6):875-83.

13. de Paiva e Silva RB, Ramalho AS, Cassorla RM. A anemia falciforme como problema de saúde pública no Brasil. Rev Saude Publica. 1993;27(1):54-8.

14. Thomas VJ, Taylor LM. The psychosocial experience of people with sickle cell disease and its impact on quality of life: qualitative findings from focus groups Br J Health Psychol. 2002;7(Part 3):345-63.

15. Svarch E, Espinosa E, Hernandez P, Martinez G, Ballester J. Resultados de los estudios realizados in Cuba sobre la hemoglobinopatia S. Sangre (Barc). 1991;36(1):37-42.

16. Brasil. Constituição 1988. Constituição da República Federativa do Brasil. Brasília, DF, Senado, 1998. [cited 2012 Dec 12] Available from: http://www.firb.br/ABNT3.pdf

17. IBGE. Instituto Brasileiro de Geografia e Estatística. [cited 2012 Dec 12] Available from: http://www.ibge.gov.br/home/presidencia/noticias/ noticia_visualiza.php?id_noticia=1455&id

18. Fernandes AP, Viana MB. Caracterização e circunstâncias da ocorrência de óbitos em crianças com doença falciforme triadas pelo Programa Estadual de Triagem Neonatal de Minas Gerais, no período de março de 1998 a fevereiro de 2005. [thesis]. Belo Horizonte: Faculdade de Medicina da Universidade Federal de Minas Gerais. 2007.

19. Maxwell K, Streetly A, Bevan D. Experience of hospital care and treatment seeking for pain from sickle cell disease: qualitative study. BMJ. 1999;318(7198):1585-90.

20. Lobo C, Marra VN, Silva RM. Painful episodes in sickle cell disease. Rev Bras Hematol Hemoter. 2007;29(3):248-8.

21. Pereira SA, Cardoso CS, Brener S, Proietti AB. Doença falciforme e qualidade de vida: um estudo da percepção subjetiva dos pacientes da Fundação Hemominas, Minas Gerais, Brasil. Rev Bras Hematol Hemoter. 2008;30(5):411-6.

xxx