

Special Article - Blood & Its Components

SCD in Saudi Children, Teens, and Adults: A Study in Health-Related Quality of Life

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Abstract

Background: While there have been earlier studies assessing Saudi adolescents with Sickle Cell Disease (SCD), this study demonstrates that Health Related Quality of Life (HRQoL) scores were negatively associated with increasing age in the adolescent population with SCD. To date, no study has assessed HRQoL in Saudi children and adults with SCD. The aim of this study was to assess HRQoL in patients with SCD and to identify what age group was most commonly associated with poor HRQoL.

Methods: A multicenter, cross-sectional study was conducted on patients with SCD who visited the hematology outpatient clinics at King Fahad Hospital in Hofuf and King Fahad Central Hospital in Jazan, Saudi Arabia. Data were gathered using a self-administered questionnaire: patient demographics, symptoms/complications of SCD, and the RAND SF-36. Data were collected from 753 SCD patients (68 children age ≤ 14 years, 56 teenagers age 15-17 years, 290 young adults age 18-25 years, 233 intermediate-aged adults age 26-36 years, and 106 older adults age ≥ 37 years).

Results: The ages ranged from 9 to 75 years with a mean of age of 26.4 ± 10 years. As compared to children, young, intermediate-aged and older adults with SCD reported quite worse physical role functions and bodily pain. Better social function was noted in children than the intermediate-aged adults and older adults.

Conclusion: The current investigation noted age differences in HRQoL, particularly between children and adults. Future studies are warranted to focus on the reasons of age differences in HRQoL and on the very poor HRQoL of older adults.

Keywords: Sickle cell disease; Quality of life; HRQoL; Children; Teenagers; Adults

Abbreviations

ANOVA: Analysis of Variance (Fisher); HRQOL: Health Related Quality of Life; SCD: Sickle Cell Disease; SF-36: Short Form (36) Health Survey; WHOQOL-BREF: World Health Organization Quality-of-Life Scale

Introduction

Sickle Cell Disease (SCD) is considered the most common genetic disease in the eastern, western, and southern regions of Saudi Arabia [1-6]. Specifically, it is mainly spread throughout several cities: Hufuf, Qatif, and Jazan. The frequency of the SCD gene in the Hofuf region has reached 25% [4]. SCD patients tend to report fever, swelling of the hands and feet, need for blood transfusions, pulmonary hypertension, acute joint necrosis, or severe abdominal pain [7-9]. SCD complications and symptoms usually appear in childhood and last a lifetime. However, these SCD complications and symptoms could increase considerably as age increases. The average number of complications tends to increase with age in adults SCD patients [10].

SCD patients have been shown to report poorer Health Related Quality of Life (HRQoL) compared with general populations, or

patients with other chronic non-communicable diseases [10-13]. Several studies have addressed HRQoL in children or adolescents within SCD populations [12,14]. HRQoL among Saudi adolescents with SCD, aged 14-17, was assessed using the RAND Short Form (36) Health Survey (SF-36). The authors noted that poorer HRQoL has been shown to correlate with age in adolescents with SCD [14]. However, a study that utilized Pediatric Quality of Life Inventory™ (PedsQL™) Generic Scales to assess physical, social, emotional, and school functioning in children and adolescents (ages between 8-18 years), found no significant differences in PedsQL between age groups [12]. The discrepancy between the two studies could be due to the sampling populations, whereas the latest study involved children.

In adult populations, increases in age tend to reduce all SF-36 scores, which indicate poor quality of life [10]. Another study found that elderly thalassemia patients tend to report poor HRQoL [15]. Sanders et al. examined age differences in pain, coping and healthcare utilization in adults with SCD (18-62 years). They concluded that age plays an important role in healthcare utilization and coping of the SCD patients [16]. According to their study younger SCD patients (≤ 36 years old) tend to cope by ignoring pain. However, there were no differences in psychological distress or social support across the age

Table 1: Symptoms/complications of Sickle Cell Disease in relation to age groups.

Characteristics	Levels	Overall		Children		Teenagers		Young adults		Intermediate-aged adults		Older adults		P
		N=753		≤14 yrs		15-17 yrs		18-25 yrs		26-36 yrs		≥37 yrs		
		n	%	n	%	n	%	n	%	n	%	n	%	
Gender	Male	439	58.5	38	57	27	48	172	59	131	57	71	68	0.159
	Female	311	41.5	29	43	29	52	118	41	101	44	34	32	
ED visits	≥3	422	67.1	31	57	30	65	172	69	137	69	52	63	0.486
Obese	Yes	50	8.8	4	9.8	2	5	13	6.4	14	7.3	17	19	0.024*
Fever	Yes	427	58.4	27	42	35	64	163	58	146	65	56	54	0.106
Redness	Yes	237	32.5	17	27	16	30	85	30	83	37	36	35	0.065
Swelling	Yes	337	46.1	22	34	28	51	113	40	128	57	46	45	0.019*
Blood transfusion	Yes	609	82.0	45	67	44	79	242	84	196	86	82	78	0.048*
Family history of anemia	Yes	658	89.8	60	91	44	82	255	90	206	90	93	90	0.549
Family support	Yes	680	93.4	67	100	53	98	266	95	209	93	85	84	0.001*
Chronic disease other than SCD	Yes	116	15.9	8	12	6	11	37	13	38	17	27	26	0.005*
Regular exercise	Yes	254	34.3	24	36	22	39	104	36	74	32	30	29	0.171
Spleen removed	Yes	130	17.5	11	17	6	11	45	16	47	20	21	20	0.144

*. Chi-square linear-by-linear is significant at $\alpha=0.05$.

groups [16]. Edwards et al. examined the role of self-efficacy of 147 African American adults with SCD (18 years or greater). It was noted that age tends to relate negatively with physical symptoms [17]. A recent study by our group of data collected from Saudi Arabia on SF-36 in adult patients with SCD has suggested no age differences were found in SF-36 subscales [18].

All the above-mentioned literature focused on children or adults; however they lack the ability to assess and compare HRQoL across various age groups that include both children and adults. There have been a few such studies involving samples from children and adults for the reasons of assessment and comparison of the HRQoL of SCD patients in various age groups [19-21]. A study conducted at King Abdulaziz University Hospital, Saudi Arabia assessed HRQoL in patients with SCD aged between 2-48 years using the WHOQOL-BREF: World Health Organization Quality-of-Life Scale (WHOQOL-BREF) [18]. This study observed differences in WHOQOL-BREF among various age groups with children patients (2-12 years) tending to be happier than the adults patients (18 years or older) (74% versus 42%) [19]. A study conducted in Alagoas, Brazil on 40 SCD patients aged 12 to 43 years showed that the adults rather than adolescents exhibited significantly lower SF-36 scores in several domains [20].

The hypothesis tested in this study is whether any component of SF-36 subscales is significantly poorer/worse in certain age groups. To the best of our knowledge, no finding has been reported on the comparison of HRQoL across children, teenagers, and adults. The aim of the current study was to assess these differences in a large sample of people with SCD in Saudi Arabia.

Methods

A sample of 753 patients with sickle cell disease was recruited between October 1, 2014 to February 29, 2015 from the hematology outpatient clinics of two hospitals: King Fahad Hospital in Hofuf and King Fahad Central Hospital in Jazan, Saudi Arabia. The study

participants were patients with SCD of age 9 years old or greater where the patient had the ability to read and write. The current study was approved by the Ministry of Health, Kingdom of Saudi Arabia and King Abdullah International Medical Research Center, Research Protocol - RC12/127/R. The ethical approval for this study was gained by verbal consent with the IRB Log No-15-247E. Permission and assent was obtained from parents of all children and teenagers involved in the study (9 to 17 years old). Adult SCD patients who verbally consented to participate in the study were asked to complete the survey. No identifiable data gathered from participants. Sample characteristics were collected, such as age/year, gender (male/female), and engaging in regular exercise (yes/no). Clinical characteristics were also collected such as family history of anemia (yes/no), whether the spleen had been removed (yes/no), any history of blood transfusions (yes/no), the number of visits to the Emergency Department (ED) within the past six months (<3 or ≥3 visits), and the presence of chronic diseases other than SCD (yes/no). Symptoms and complications of SCD during the past six months were collected, such as swelling (yes/no), fever (yes/no), and skin redness (yes/no).

Study instrument

In the present study we utilized the Medical Outcome Study 36-Item Short Form (SF-36) [21]. The SF-36 was found to be reliable across various age groups [21]. The Arabic-translated version of RAND SF-36 Health Related Quality of Life Questionnaire [22] was used to evaluate Health Related Quality of Life in our population. The SF-36 questionnaire consists of 8 subscales that assess perceptions and feelings with regard to physical function (ten items); emotional role functions (three items); vitality (four items); physical role health (four items); emotional wellbeing (five items); bodily pain (two items); social function (two items); and general health perceptions (five items). The SF-36 subscales were scored according to RAND Health scoring. Each subscale has a single summary variable ranged from 0 = least favorable health state to 100 = most favorable health

Table 2: Characterizes differences in HRQoL of patients with SCD across the age groups (N=753).

	Children ≤14 yrs 68(9%)		Teenagers 15-17 yrs 56(7.4%)		Young adults 18-25 yrs 290(38.5%)		Intermediate-aged adults 26-36 yrs 233(30.9%)		Older adults ≥37 yrs 106(14.1%)		P
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Physical functioning	60.2	22.3	56.3	22.1	56.0	23.2	54.8	23.8	53.5	22.7	0.446
Role limitations due to physical health	54.8	35.9	51.9	36.0	35.8	34.2	36.5	37.0	34.9	39.1	0.001*
Role limitations due to emotional problems	49.5	41.1	59.3	38.1	38.1	38.5	40.2	40.2	45.1	46.1	0.004*
Vitality	55.6	14.8	51.4	16.4	47.6	18.4	48.5	19.3	46.6	20.2	0.016*
Emotional well being	64.1	15.6	62.4	16.3	61.3	17.8	57.0	20.5	58.6	21.0	0.026*
Social functioning	71.9	25.0	64.8	25.2	61.1	24.2	57.7	25.4	62.5	26.1	0.002*
Pain	61.8	28.1	50.5	27.8	49.5	27.4	47.3	27.1	45.1	29.4	0.002*
General health	52.8	11.0	50.3	11.4	48.9	14.6	46.5	17.0	47.9	15.1	0.039*

*. ANOVA test is significant at $\alpha=0.05$.

state. The reliability of the SF-36 has been assessed in a pilot study of eighty SCD patients. The reliability analysis showed acceptable internal consistency with Cronbach alpha (α) ranged from 0.6 to 0.86. The reliability analysis showed high internal consistency for vitality ($\alpha = 0.79$); physical function ($\alpha = 0.81$); bodily pain ($\alpha = 0.84$); physical role health ($\alpha = 0.84$); and emotional role functions ($\alpha = 0.86$). The other three domains had α lower than the ideal range: general health ($\alpha = 0.60$); social function ($\alpha = 0.67$); and emotional wellbeing ($\alpha = 0.67$).

Statistical analyses

Data were analyzed using IBM Statistical Package for Social Sciences (SPSS®) version 23 (Chicago, Illinois, USA). On the basis of age, SCD patients were classified into five groups: children age ≤ 14 years, teenagers age 15-17 years and adults (young adults age 18-25 years, intermediate-aged adults age 26-36 years, and 106 older adults age ≥ 37 years). Some of these cut-off points of age-groups were used in a previous study [16]. Frequency and count were used to summarize the sample characteristics (Table 1). Chi-square linear-by-linear tests were performed for associations between symptoms/complications of SCD and age spectrum (Table 1). ANOVAs (Analysis of Variance) were performed to compare quality of life subscales across various age groups (Table 2 and Figure 1). When appropriate, Tukey's multiple comparison procedure was applied for age group comparison with significant level at 0.05.

Results

Seven hundred fifty-three (N=753) SCD patients were included in the study. Age ranged from 9 to 75 years (mean age 26.4 ± 10 years). The SCD patients were distributed as the following, 68 in children group, 56 in teenagers group, and 290 in young adults group, 233 in intermediate-aged adults group, and 106 in older adults group. The majority (89.8%) of the SCD patients reported family history of anemia, 82% reported history of blood transfusions, and 93.4% reported family support. The most commonly reported symptoms were: fever (58.4%), swelling (46.1%), and skin redness (32.5%). Removal of the spleen was reported by 17.5% of the SCD patients. Symptoms and complications of sickle cell disease in relation to the age spectrum are reported in (Table 1). Swelling and blood transfusion were significantly less common in children with SCD compared with other age groups (teenagers, young adults, intermediate-aged

adults, and older adults). However, obesity and chronic diseases other than SCD were reported more frequently in the older adults with SCD than in other age groups (children, teenagers, young adults, and intermediate-aged adults). Family support was found to be less common in older adults with SCD compared with other age groups (children, teenagers, young adults, intermediate-aged adults). Gender, ED visits, fever, skin redness, and regular exercise were not significantly associated with age (Table 1).

(Table 2) characterizes the differences in HRQoL of patients with SCD across the age spectrum. According to our study, there were statistically significant age group differences on physical role function ($F=5.4, P=0.001$), emotional role functions ($F=3.4, P=0.009$), vitality ($F=2.6, P=0.038$), emotional wellbeing ($F=2.9, P=0.022$), social function ($F=4.8, P=0.001$), bodily pain ($F=3.8, P=0.004$), and General health ($F=2.5, P=0.039$), (Figure 1). No differences in physical function were noted between the various age groups. Multiple comparisons of various age groups revealed that children and teenagers with SCD had significantly higher scores on physical role functions than adults groups (young adults, intermediate-aged adults, and older adults). More specifically, Saudi children with SCD tend to experience better physical role functions as compared to young adults, intermediate-aged adults, and older adults (observed difference: 18.9, 18.3, and 19.8, respectively). Teenagers reported better emotional role functions as compared to young adults and intermediate-aged adults (observed difference: 21.1 and 19.1, respectively). More vitality was found in children than the young adults and older adults (observed difference: 8.0 and 9.0, respectively). Better social function was noted in children than the young adults and intermediate-aged adults (observed difference: 10.8 and 14.2, respectively). Saudi children with SCD tend to report less bodily pain as compared to young adults, intermediate-aged adults, and older adults (observed difference: 12.3, 14.5, and 16.7, respectively). Children tend to report better social function than young adults and intermediate-aged adults (observed difference: 10.8 and 14.2, respectively). General health scale was significantly better in children than the intermediate-aged adults (observed difference: 6.3).

Discussion

The purpose of this investigation was to assess the HRQoL in Saudi patients with SCD within various age groups across a wide spectrum of ages. In the present study we considered five age groups: children (≤ 14 years), teenagers (15-17 years), young adults (18-25

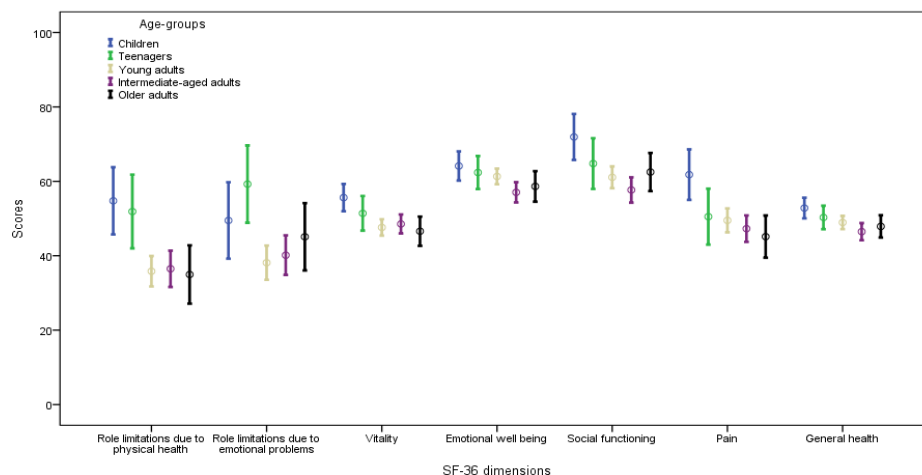


Figure 1: Differences in health-related quality of life between age-groups by the SF-36 dimensions: 95% confidence intervals.

years), and intermediate-aged adults (26-36 years), and older adults (≥ 37 years). We evaluated age differences in HRQoL for patients with SCD in a large multicenter cross-sectional study. Based on our study, adults with SCD generally tend to report poor HRQoL than children or teenagers. Research performed in Saudi Arabia has shown that the HRQoL in the adolescent population with SCD tends to get worse as the age of the adolescent increases [14]. On the other hand, two studies reported HRQoL in the adult population with SCD, and both demonstrated that age has a negative effect on HRQoL- as age increases patients tended to report a poorer quality of life [10,15]. No significant differences in HRQoL subscales were found in terms of adult age groups (Older age: Yes/No) in a study conducted by our group [18]. However, little is known about the comparison of HRQoL in children and teenagers as compared to older adults, or between more subgroups of adult patients (young adults, intermediate-aged adults, and older adults) with SCD. In addition to SCD adult data [18], the current study incorporated data from children and teenagers in the analysis for the purpose of age comparisons. Two studies involved samples from children and adults, but their patients' ages ranged between 2-48 years [19] and between 12-43 years [20]. Although no elderly patients were included in their studies, both studies revealed that old patients exhibited poorer quality of life. Our population had ages ranging from 9 to 75 years, and thus may be considered an extension of their study.

Our findings revealed that there were statistically significant differences in HRQoL subscales by age groups. According to our study, various adult aged groups tend to report poorer HRQoL than children and/or teenagers. This finding is consistent with the results of several studies, which have shown that HRQoL subscales tend to decrease with age, meaning older patients reported poorer HRQoL than the younger age group [10,11,14,15,19,20]. For instance a study reported that as the age of adolescents with SCD increases by one year, the average of several SF-36 domains tends to decrease [14]. In our study, the physical role function and bodily pain were strikingly worse in adults. It was noted that bodily pain scores decreased monotonically with age. Children tended to report less bodily pain than the young adults, intermediate-aged adults, and older adults. Saudi children with SCD tend to experience better social functioning,

general health as compared to young adults and intermediate-aged adults. It is interesting to note that the teenagers group has the highest values for emotional role functions. According to our study, children with SCD were less likely to report SCD related-complications such as swelling and blood transfusion as compared to adult patients with SCD. Our study agrees with the findings of a previous study, which concluded adult patients exhibited a higher number of SCD related-complications [10].

Several limitations of the current study were noted. Sample selection was based on purposive sampling techniques but not random sampling. The target SCD population was from outpatient clinics but not community-based, as we only surveyed SCD patients who attended outpatient clinics for medical care. Thus, the chance of being part of the study was high in SCD patients who actively attend outpatient clinics. SCD patients who did not have ability to read and write were excluded from the sample. One might hypothesize that these patients might have somewhat poorer quality of life than those who don't seek medical care, but there is no reason to believe that age effects would vary. Accordingly, our study could be generalizable only in SCD patients who attend outpatient clinics for medical care. The findings were based on self-reported data, and associations do not confirm causality. Some of the sub-samples may have been small to detect important differences between age-groups. The SF-36 is suitable for self-report to individuals who are age 14 years and older, while our population included age 9 years and older. However, several strengths of this study should be noted. The study was able to enroll SCD patients from two centers in Saudi Arabia, Hofuf and Jazan, and was able to recruit a large sample size of 753 SCD patients. The study covers a broad age range of patients with SCD. We compared HRQoL of SCD patients in various age groups (children, teenagers, young adults, intermediate-aged adults, and older adults) with ages ranging from 9 to 75 years. This is the first investigation nationally and internationally to report age-specific HRQoL in patients with SCD that encompassed such a wide range of ages.

Conclusion

Differences in HRQoL subscales appeared to depend on age in patients with SCD. Adults with SCD reported poorer physical role

functions and worse bodily pain than children with SCD. Adults with SCD reported significantly more SCD-related swelling and blood transfusion than children. It is highly recommended that hematologists routinely assess the quality of life of adult patients and SCD-related complications, since they tend to exhibit poorer quality of life. Additionally, future studies are warranted to focus on the reasons for the HRQoL differences shown between the five age groups with SCD.

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