

# Determinants of the Quality of Life of Patients with Sickle Cell Disease in Bahrain: Implications for a Patient-Centered Management Approach at the Primary Health Care

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**Background:** Sickle cell disease (SCD) is one of the most common hemoglobinopathies worldwide. Complications related to SCD can profoundly affect the quality of life of patients. This study aims to deepen the knowledge about the quality of life (QoL) of SCD patients attending the primary health care centers (PHC) in Bahrain, using the World Health Organization's Quality of Life BREF instrument (WHOQOL-BREF).

**Material and Methods:** We conducted an analytical cross-sectional study among 273 SCD patients randomly recruited from the 27 PHC in the Kingdom of Bahrain between July and August 2019. Data was collected by interviews using the WHOQOL-BREF and Pain Catastrophizing Scales (PCS). Chi-square test permitted to compare categorical data. Mann-Whitney U and Kruskal Wallis tests permitted comparisons of medians. Estimation of the importance of the factors associated with the QoL was measured by crude and adjusted odds ratios estimates. The data was analyzed using IBM SPSS software statistical package, version 25.0 (SPSS Inc., Chicago, IL, US).

**Results:** Two hundred and seventy-three (273) SCD patients completed the structural interviews, of whom 78.8% had a good QoL. The mean of overall QoL scores was (63.91, SD14.24), and total scores ranged from (28.85) to (99.04). More than half of the patients (54.6%) did not use any medication to relieve their pain, however, 24.9% and 26.4% are still relying on opioids and nonsteroidal anti-inflammatory drugs (NSAIDs), respectively. QoL of SCD patients was significantly associated with pain catastrophizing ( $P < 0.001$ ), socio-economic status ( $P < 0.001$ ), education ( $P < 0.001$ ) and pain crisis frequency ( $P = 0.021$ ). Multivariate analysis confirmed that only pain catastrophizing (AOR = 13.32,  $P < 0.001$ ) and socio-economic status (AOR = 2.82,  $P = 0.003$ ) are the predictors of the QoL of SCD patients.

**Conclusions:** Determinants of QoL are mainly socio-economic and pain catastrophizing personality traits. These findings advocate for a comprehensive approach in the management of SCD patients.

**Key words:** Quality of Life, Sickle Cell Disease, Morphine, Pain Catastrophizing, Primary Health Care, Bahrain

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## INTRODUCTION

Sickle cell disease (SCD), is an inherited autosomal recessive blood disorder that affects the structure of hemoglobin in the blood and cause the sickling of red blood cells (RBCs)<sup>1</sup>. SCD affects more than five million individuals worldwide and continues to be a major global health concern<sup>2</sup>. The disease is most common among people from Sub-Saharan Africa, the Caribbean, India, the Mediterranean basin, and the Middle East<sup>3</sup>. However, due to migration, SCD have emerged as a health problem in areas such as Europe and the United States<sup>4</sup>. The disease is caused by a single mutation in the  $\beta$ -globin gene (Hgb) that results in the amino acid substitution of glutamate to valine at the  $\beta$ -globin chain, which leads to the formation of abnormal sickle hemoglobin (Hb S)<sup>5</sup>. Unlike normal RBCs, sickled RBCs are rigid, inflexible, and can adhere to each other along vascular walls causing blockage of blood flow to body tissues, low circulation, and different complications such as pain, inflammation, and organ damages<sup>2,5</sup>. Pain is the primary characteristic of SCD. Individuals with SCD experience various types of pain including chronic pain, or recurrent episodes of acute crisis that may require hospitalization<sup>6</sup>. Vaso-occlusive crisis (VOC) is the most frequent type of crises experienced in SCD<sup>7</sup>. The frequency, intensity, location, and duration of VOC is different in each individual<sup>8</sup>. However, most patients experience crisis as debilitating, sharp, or throbbing pain that occur suddenly<sup>9,10</sup>. Different factors can trigger VOC in patients with SCD such as dehydration, extreme temperature, and higher barometric pressure<sup>2</sup>. Studies have also found that psychological characteristics such as emotional stress, anxiety, depression, catastrophizing behavior can also influence SCD pain<sup>11</sup>. QoL, is a balance state of the person's physical, spiritual, psychological, and sociocultural aspect of life<sup>1</sup>. Pain in SCD can profoundly impact the quality of life (QoL) of patients due to recurrent crisis, repeated hospital admissions, and complications related to the disease<sup>12</sup>. Patients with SCD report poor quality of life in all domains compared to the general population<sup>13</sup>. The most common psychological complications reported in SCD adults are anxiety, depression, sleep disturbances, low self-efficacy, and feeling hopelessness<sup>1,14</sup>. Complications related to SCD remain a challenge and a burden on patients, communities and healthcare systems in many countries. Different therapeutic approaches are used in the management of SCD pain. Depending on the type of pain experienced and severity, pharmacological treatment based on opioids and non-opioids analgesic therapy is prescribed. Non-pharmacological interventions including psychosocial and cognitive behavioral therapy are also used<sup>7</sup>. In the Kingdom of Bahrain, SCD is considered as one of the most common inherited blood diseases<sup>15</sup>. The prevalence of the disease in the population was previously found to be 2.1 percent<sup>16</sup>. In 2010, the prevalence of SCD in newborn babies reported to be 0.41% in the context of the national program for newborn screening of hemoglobinopathies<sup>15</sup>. This high rate of the disease may increase the burden on the healthcare system in the country<sup>17</sup>. Within the health system in Bahrain, primary health care plays an important role in providing preventive and supportive care for patients with various conditions<sup>18</sup>. Different studies have shown that uncomplicated pain crisis can be effectively managed at the primary care level without the need of tertiary care<sup>19</sup>. Information on the QoL of SCD in Bahrain is limited. The aim of this study is to deepen the knowledge about the impact of SCD on the QoL of Bahraini patients in order to provide an evidence base to improve the wellbeing of this population in the future. Indeed, Using QoL measuring tools can provide an insight of the patients' perception of their health and their expectations for the sake of the improvement of patient-doctor communication, and quality of healthcare services<sup>20</sup>. Our objectives are: i) to measure the patients QoL, using the WHOQOL-BREF tool and ii) to assess the factors that might influence the QoL of SCD patients in Bahrain. The ultimate goal is to design personalized interventions that meets the patient's needs and ensures better patient-centered care.

## MATERIAL AND METHODS

**Study Design:** We conducted an analytical cross-sectional study to evaluate the quality of life of patients with SCD in Bahrain, and to assess its determinants. The study is performed in the scope of the community-oriented research program of undergraduate students at the department of family and community medicine, college of medicine and medical sciences, Arabian Gulf University in Bahrain.

**Study Participants and Setting:** The target study population was Bahraini, male and female, adults (21 years and above), who are clinically diagnosed with SCD, and registered for follow up at the SCD clinics at the primary health care centers in the Kingdom of Bahrain. All primary healthcare centers (27 centers) provide care across all five regions of the country. A representative sample was selected using a systematic random sampling technique from the PHC register of SCD patients who have utilized the PHC services in 2019. The research team contacted participants to assess their willingness to enroll in the study. We excluded patients diagnosed with any other health condition associated with chronic pain such as arthritis, chronic pain syndrome, low back pain, and/or psychiatric chronic diseases such as epilepsy, or schizophrenia. Vulnerable patients such as patients during the episode of pain crisis, pregnant women, or patients who refuse or are unable to consent were also excluded. Eligible patients were given appointments at their nearest PHC for the structural interviews.

**Data Collection:** Data were collected during the months of July and August of the year 2019 by face-to-face structured interviews using a tested and validated questionnaire, during the pilot phase of the study.

A structured questionnaire permitted to measure the Socio-demographic characteristics, pain crisis frequency (number of pain crisis experienced during the last 12 months), prescribed relieving drugs, and pain crisis triggering factors.

QOL was measured using the World Health Organization's Quality of Life BREF Questionnaire (WHOQOL-BREF)<sup>20</sup>. It consists of 26 items: the first two items assess the responders' own perception of their overall general health and QoL, and their scores are calculated separately. Other items (from 3-26) measure the responders' wellbeing in four main domains (Physical Health, Psychological Health, Social Relationships, and Environment). All 26 items have a 1-5 Likert-type response scale. The total score for each domain is calculated by the sum of the result of items within the domain. Results on domains represent the sum of results of items. A higher sum of points represents a higher quality of life on a single domain. The domains scores and overall score are transformed into a linear scale from 0 to 100, the higher the score the better is the QoL. A score of 50 and above indicated a good quality of life<sup>21-23</sup>.

Pain catastrophizing was assessed using the Arabic validated version of the Pain Catastrophizing Scale (PCS)<sup>24</sup>. The PCS is a 13-items instrument that assess the thoughts and feelings associated with pain<sup>25</sup>. The PCS assess three dimensions of pain catastrophizing: Rumination (items 8, 9, 10 and 11), magnification (items 6, 7 and 13) and helplessness (items 1, 2, 3, 4, 5 and 12). Patients are asked to rank the degree of developing these thoughts and feelings during the period of pain based on a 5-point Likert scale (0 = not at all, 1 = to a slight degree, 2 = to a moderate degree, 3 = to a great degree, 4 = all the time). A total PCS score is computed by summing the scores of all items. PCS total score ranges from 0 to 52, the higher the score the more likely the patient is experiencing pain catastrophizing. In our study a score above the cutoff based on the first quartile of the PCS scores is indicative of clinically relevant level of pain catastrophizing, which was coherent with the cutoff score of the original study that developed this scale<sup>26</sup>.

**Statistical Analysis:** Based on power estimation, the sample size was calculated using the following formula:

$$n = \frac{Z_{1-\alpha/2}^2 P(1-p)}{E^2}$$

Z = Critical Value (1.96)

P = Population portion of good quality of life (0.25)

E = Margin of error (0.05)

n = 288

Sociodemographic and disease-related characteristics variables were displayed as mean ± SD for continuous variables, and frequency and percentages for qualitative ones. Chi-Square ( $\chi^2$ ) test was performed to test association between categorical variables, and T-test was used for continuous variables. Mann-Whitney U and Kruskal Wallis tests permitted to compare medians. Crude and adjusted odds ratios, using bivariate and multivariate analysis (logistic regression), were conducted to assess statistical associations between the different domains of quality of life and the independent variables. Statistical data analysis was performed using SPSS software statistical package, version 25.0 (SPSS Inc., Chicago, IL, US).

**Ethical Considerations:** Ethical approval of the study was obtained from the Research and Ethics Committee at the Arabian Gulf University (approval number: E002-pi-4/19) and the Ministry of Health in the Kingdom of Bahrain (approval number: AURS/325/2019). Written informed consent was sought from all patients before enrolment. All safeguards are assured for privacy and confidentiality of participants. Minors were not included for feasibility and ethical reasons.

## RESULTS

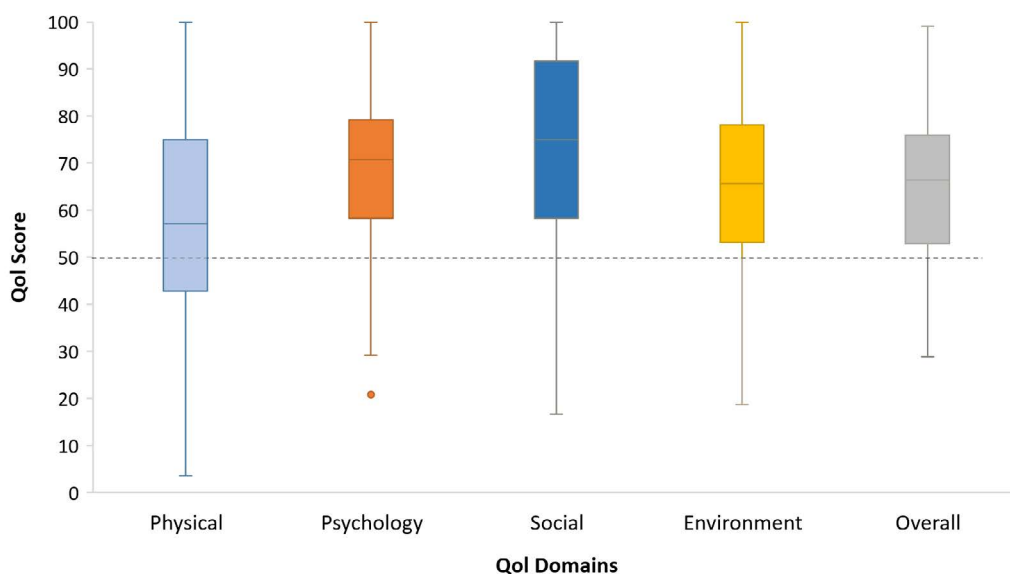
**Description of the Sample:** A total of 273 SCD patients participated in the study out of 288 needed (94.8% response rate) of whom 137 were females (50.2%) and 136 were males (49.8%). Regarding the education, 157 (57.7%) of the respondents had secondary level of education or below, while 115 (42.3%) had bachelor's degree or higher. The mean age was 37.47 years (SD = 10.46). Table.1 shows the distribution of sociodemographic variables of the study population.

**Table 1:** Description of Sociodemographic characteristics of the study sample

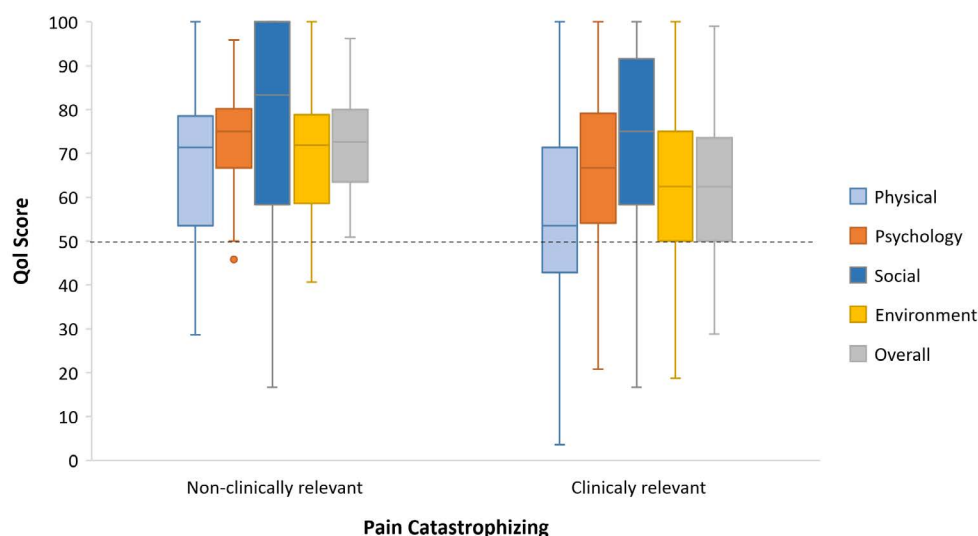
Variables	N	%
<b>Gender</b>		
Male	136	49.8
Female	137	50.2
<b>Marital Status</b>		
Single	75	27.5
Married	182	66.7
Divorced	16	5.9
<b>Educational Level</b>		
Less than secondary education	49	18.0
Secondary education	108	39.7
Bachelor's degree	109	40.1
High Studies	6	2.2
<b>Occupational Status</b>		
Employed	112	41.0
Non-Employed	161	59.0
<b>Financial Status</b>		
Low	31	11.4
Moderate	121	44.3
Good	109	39.9
Excellent	12	4.4
<b>Mean Age (S.D)</b> 37.47 (10.46)		

**The QoL of SCD Patients:** In the study sample, 215 SCD patients ranked 50 and above in the overall QoL score leading to a proportion of 78.8% with a good QoL. If we consider the different domains, this proportion was 84.2%, 83.7% 77.3% and 62.3% for psychological, social, environmental and physical domains respectively.

Figure 1 represents the distribution of different domains used to measure the QoL in SCD patients and their overall score. It shows that the median of all domains is not significantly different (Kruskal-Wallis



**Figure 1:** Distribution of SCD patients' scores among different QoL domains- - -: Cut off level for the QoL Score (above the cut off is good QoL).



**Figure 2:** Distribution of different QoL domains according to the clinical relevance of pain catastrophizing. - - -: Cut off level for the good QoL Score

H test = 94.172, df = 3, P > 0.05). In addition, the distribution of the physical domain is more scattered compared to other domains.

Different domains of QoL were compared according to the clinical relevance of pain catastrophizing by SCD patients. Analysis showed that all the medians of QoL as well as the overall QoL were significantly higher when pain catastrophizing is non clinically relevant, except for the social domain (Mann-Whitney U test, the P value: > 0.001 for the physical domain; >0.001 for the psychological domain; 0.008 for the environmental; 0.228 for the social domain) (see figure 2).

**Factors Triggering of Pain Crisis and Drugs Prescribed:** Based on patients' answers about pain crisis triggers, we noticed that changes in temperature (55.70%), physical exertion (48.40%) and psychological stress (46.50%) are the highest triggers of the episodes of pain crisis. In contrast, dehydration (33.7%), infection (22%) and the high-altitude exposure (15%) are the least factors that were identified by the patients (patients can identify more than one answer).

Analysis of the drugs prescribed for SCD patients to reduce their daily pain confirmed that more than half of the patients (54.6%) do not rely on any drugs. However, Non-steroidal anti-inflammatory drugs (26.4%) and opioids (24.9%) are the most recommended while Panadol (18.3%) was the least used drug for daily pain management, when needed.

**Determinants of the QoL of SCD Patients:** We tested the association between the sociodemographic, the economic, pain-related characteristics and pain catastrophizing trait of personality of SCD patients with overall QoL. Unsurprisingly, the analysis revealed that education and socioeconomic status are proportionally associated with overall QoL; the higher the level of each of these two factors, the better is the overall QoL of SCD patients. In addition, non-clinically relevant pain catastrophizing trait of personality of SCD patients was associated with a higher overall QoL. Moreover, high frequency of pain crisis (< 4 crises per year) was associated with lower overall QoL. On the other hand, neither the age or gender of the SCD patients nor the prescription of morphine were predictors of QoL. (See table 2)

**Table 2:** Association between the overall QoL and patients' characteristics

Factor	Overall QoL		P-value
	Low n (%)	High n (%)	
<b>Age</b>			
Less than 30 years	13 (17.1)	63 (82.9)	0.563
30 - 45 years	32 (23.4)	105 (76.6)	
Above 45 years	13 (21.7)	47 (78.3)	
<b>Gender</b>			
Male	32 (23.5)	104 (76.5)	0.358
Female	26 (19)	111 (81)	
<b>Education</b>			
Less than secondary education	18 (36.7)	31 (63.3)	0.009
Secondary education	23 (21.3)	85 (78.7)	
BSc	16 (14.7)	93 (85.3)	
High studies	0 (0.0)	6 (100)	
<b>Socio-economic status</b>			
Weak	15 (48.4)	16 (51.6)	<0.001
Moderate	18 (14.9)	103 (85.1)	
Good	25 (22.9)	84 (77.1)	
Excellent	0 (0.0)	12 (100)	
<b>Pain Frequency</b>			
4 and below	26 (16.5)	132 (83.5)	0.021
More than 4	31 (28.2)	79 (71.8)	
<b>Morphine Usage</b>			
Non-user	47 (21)	177 (79)	0.820
User	11 (22.4)	38 (77.6)	
<b>Pain Catastrophizing</b>			
Non-clinically relevant	2 (2.9)	68 (97.1)	<0.001
Clinically relevant	56 (27.9)	145 (72.1)	

Bivariate analysis by estimation of crude odds ratio confirmed that education, financial status, pain frequency and pain catastrophizing factors are significantly associated with overall QoL. Multivariate analysis of different factors permitted to refine these estimates

considering effect of other factors by a logistic regression model and the estimation of adjusted odds ratio values. As shown in table 3, the final model showed that pain catastrophizing (AOR = 13.32, P-Value > 0.001), financial status (AOR = 2.82, P-Value = 0.003), as well as pain frequency (AOR = 1.95, P-Value = 0.046) were significantly associated with overall QoL. Interestingly the pain catastrophizing personality trait has the strongest association with the QoL, on the other hand, morphine usage was not associated with this outcome among SCD patients.

**Table 3:** Association between risk factors and the QoL of sickle cell disease patients

Risk Factors	COR*	CI <sub>95%</sub>	P-Value	AOR**	CI <sub>95%</sub>	P-Value
- Education	2.12	(1.12, 4.13)	0.015	1.7	(0.85, 3.40)	0.135
- Socio-economic status	2.55	(1.38, 4.74)	0.002	2.82	(1.53, 5.56)	0.003
- Pain Frequency	1.99	(1.10, 3.60)	0.021	1.95	(1.01, 3.76)	0.046
- Morphine Usage	1.09	(0.52, 2.29)	0.820	0.75	(0.33, 1.73)	0.502
- Pain Catastrophizing	13.13	(3.11, 55.4)	< 0.001	13.32	(3.12, 57.46)	< 0.001

\* Crude Odds Ratio

\*\* Adjusted Odds Ratio

## DISCUSSION

To the best of our knowledge, this study is the first that attempted to evaluate the impact of SCD on the QoL of patients in the Kingdom of Bahrain using WHOQOL-BREF tool. We conducted an analytical cross-sectional study to examine the QoL and its determinants among a representative sample of 273 SCD patients in primary healthcare settings. Our findings showed that despite of the complications associated with SCD, most of our sample reported a moderate to good general QoL. Around 78.7% of participants ranked above the cut-off score on the (0-100) scale. The mean of QoL scores was (63.91, SD14.24), and total scores ranged from (28.85) to (99.04). A previous study in 2003, indicated that only 10% of SCD patients in Bahrain are expected to have a severe form of the disease, whereas the majority are considered to have a mild phenotype<sup>27</sup>. Like the SCD population in the neighboring eastern provenance of Saudi Arabia, previous studies confirmed that the most common haplotype in Bahraini patients is the Arab-Indian haplotype (AI)<sup>15,28</sup>. Another study conducted in the western region of Saudi Arabia found that severe complications worsened the QoL of SCD patients<sup>29</sup>. An alternative to explain the low impact of SCD on QoL of patients is the so-called “disability paradox”, where majority of patients with severe disabilities tend to self-rate as very happy with their QoL and overall health<sup>30,31</sup>.

In this study, more than half of the study participants (54.6%) did not rely on any daily medication and less than 25% relied on opioids to relief their pain. Other medications such as NSAIDs were used in 72 participants (26.4%). The prescription of opioids is not significantly associated with the overall and subdomains of QoL in our study sample. A contrasting result was reported in a study among a USA population, where the disease is more severe; this study reported a significant association between daily usage of opioid analgesics and the physical and psychological QoL<sup>32</sup>. We examined triggers for pain crises in Bahrain SCD patients. Most of our patients (50.7%) reported temperature changes as the main trigger for their pain crisis. This finding agrees with a previous study in Kuwait that identified this factor as the main trigger for SCD pain crises<sup>33</sup>. Other triggers

identified by participants in this study were physical exertion (48.40%), and psychological stress (46.50%). These findings corroborate results from a previous study of SCD patients in Bahrain<sup>34</sup>. The impact of frequent pain crisis on the QoL was reported elsewhere<sup>35</sup>. In contrast to this observation, pain crisis frequency was not significantly associated with participants QoL in our study (AOR = 1.7, P = 0.135). We did not find a significant association between gender and total QoL scores, or subdomains total scores. A similar observation was reported in a study in Saudi Arabia<sup>36</sup>. However, education level of the participants was not significantly associated with their QoL which disagree with previous findings from a study of SCD patients in Bahrain<sup>15</sup>.

Other factors were also evaluated in the study, we noticed that the QoL of SCD patients is mostly associated with psychological factors shown by pain catastrophizing trait of personality (AOR = 13.32, P < 0.001). This result is consistent with the evidence from previous studies that indicated that patients with SCD are at higher risk to catastrophize their pain in comparison to patients with other chronic diseases<sup>37,38</sup>. The negative impact of pain catastrophizing on SCD patients QoL was also observed in a cohort study by the PiSCES project<sup>39</sup>.

In our study we favored the use of the WHOQOL-BREF tool, for the first time in Bahrain, to evaluate the QoL of SCD patients. Indeed, the validity and utility of this tool have been shown to be excellent in many contexts including in SCD patients<sup>40</sup>. The correlation between different domains as well as the overall QoL showed a high correlation coefficient between all domains (Physical, Social, Psychological, and environmental), and the overall QoL. These findings demonstrated that, in our hands, the WHOQOL-BREF scale is a valid tool to evaluate the QoL for SCD patients.

## LIMITATIONS OF THE STUDY

The enrollment of our participants was through PHC register of all SCD patients. However, despite the representativeness of our sample, patients seeking care in the tertiary health care facilities, and minors were not included in this study, for whom the disease might be more severe. This could underestimate the impact of the severe form of SCD on the QoL. Some questions in our study are related to events that took place in the past 12 months. This might affect our findings by a recall bias. Unfortunately, we were not able to crosscheck some results available in the previous medical forms of the patients. A prospective study design is the most robust to address these limitations.

## PERSPECTIVES

An estimation of the validity and reliability of WHOQOL scale is needed to evaluate the relevance of this tool in the context of SCD patients in Bahrain. This work is presently in progress by our team. A prospective study on a representative sample of SCD patients in Bahrain is the best study design for a valid estimation of their QoL of SCD and its determinants. A qualitative study using in depth interviews or a focus group design might be more informative to decipher other facets of the quality of life that are not included in quantitative scales.

## CONCLUSION

**This cross-sectional study contributed to the global effort to understand the impact of SCD on patients’ quality of life. Majority of our participants had a moderate to good overall QoL. Determinants of poor QoL in the SCD population in Bahrain, are mainly related to socio-economic and psychological factors. Our findings demonstrate a good performance of the management of SCD patients at the primary health care level in Bahrain. It**

advocates for a psycho-social, behavioral approach to better improve their QoL.

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**Potential Conflict of Interest:** None.

**Competing Interest:** None.

**Sponsorship:** None.

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