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REVIEW

Health-Related Quality of Life of Children and Adolescents with Sickle Cell Disease in the Middle East and North Africa Region

A systematic review

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جودة الحياة المرتبطة بصحة الأطفال والمراهقين المصابين بداء الخلايا المنجلية في منطقة الشرق الأوسط وشمال افريقيا

مراجعة منهجية

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ABSTRACT: Sickle cell disease (SCD) can significantly impair the health-related quality of life (HRQOL) of children and adolescents. This review aimed to assess current evidence regarding the HRQOL of children and adolescents with SCD in the Middle East and North Africa region. A systematic search of various databases was conducted to identify relevant articles, including MEDLINE® (National Library of Medicine, Bethesda, Maryland, USA), Scopus® (Elsevier, Amsterdam, the Netherlands), Cumulative Index to Nursing and Allied Health Literature®, Masader (Oman Virtual Science Library, Muscat, Oman) and EBSCOhost (EBSCO Information Services, Ipswich, Massachusetts, USA). A total of 533 articles were identified; however, only 10 were eligible for inclusion in the final analysis. Results from these studies showed that children and adolescents with SCD had compromised HRQOL compared to their healthy peers, particularly in terms of physical, psychosocial, familial, financial and academic functioning. Therefore, interventions are necessary to improve overall HRQOL outcomes for this population.

Keywords: Sickle Cell Disease; Health-Related Quality Of Life; Infants; Children; Adolescents; Middle East; North Africa.

الملخص: يمكن لداء الخلايا المنجلية أن يضعف بشكل كبير جودة الحياة المرتبطة بصحة الأطفال والمراهقين. هدفت هذه المراجعة إلى تقييم الأدلة الحالية المتعلقة بالأطفال والمراهقين المصابين بداء الخلايا المنجلية في منطقة الشرق الأوسط وشمال إفريقيا. تم إجراء بحث منهجي لقواعد البيانات المختلفة لتحديد المقالات ذات الصلة، بما في ذلك ميدلاين (المكتبة الوطنية للطب، بيثيسدا، ميريلاند، الولايات المتحدة الأمريكية)، سكوبس (أيلسيفير، أمستردام، هولندا)، الفهرس التراكمي للتمريض والأدب الصحي المتحالف، مصادر (مكتبة عمان الافتراضية للعلوم، مسقط، عمان)، وايبيسكو (ايبيسكو لخدمات المعلومات، إبسويتش، ماساتشوستس، الولايات المتحدة الأمريكية). تم تحديد ما مجموعه 533 مقالة؛ ومع ذلك، كان فقط 10 منها مؤهلين للإدراج في التحليل النهائي. أظهرت نتائج هذه الدراسات أن الأطفال والمراهقين المصابين بداء الخلايا المنجلية قد تعرضوا لنقص في جودة الحياة المرتبطة بالصحة مقارنة بأقرانهم الأصحاء، لا سيما من حيث الأداء البدني والنفسي والاجتماعي والعائلي والمالي والأكاديمي. لذلك، فإنه من الضروري القيام بالتدخلات المناسبة لتحسين النتائج الإجمالية لجودة الحياة المرتبطة بالصحة لهذه الفئة من السكان.

الكلمات المفتاحية: داء الخلايا المنجلية؛ جودة الحياة المرتبطة بالصحة؛ الرضع؛ أطفال؛ مراهقين؛ الشرق الأوسط؛ شمال افريقيا.

Sickle cell disease (SCD) is a hereditary disorder that often results in complications including acute and chronic pain, severe anaemia, infection and stroke.[1] The disease primarily affects the development of red blood cells, resulting in the formation of haemoglobin S (Hb S), an abnormal type of haemoglobin which causes red blood cells to become sickle-shaped and inflexible. These abnormal cells clump together in the arteries, blocking blood flow to various organs and causing various complications.[1,2] The most common and severe form of SCD is sickle cell anaemia (SCA) which results when both parents inherit the Hb S variant; in contrast, sickle cell trait (SCT), which occurs when Hb S volume is <50%, is less severe.[2,3]

Overall, SCD is linked with high morbidity and mortality particularly among young children under the age of five and adolescents.[4–9] In addition, it can have adverse social and economic consequences.[10] As such, both the World Health Organization (WHO) and the

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United Nations General Assembly have confirmed that SCD represents a global public health problem.[11] Worldwide, approximately 25 million people suffer from SCD; according to the WHO, more than 300,000 infants are born with a major haemoglobin disease every year, of which SCD accounts for 200,000 cases.[4,12] Varying rates of SCD have been reported in different regions due to differences in Hb S gene prevalence (2–30%). In the USA, approximately 100,000 are affected by SCD, with one in every 365 African-American and 16,300 Hispanic-American births, while the SCT is reported in one in 13 black or African-American babies.[2] A recent survey reported that approximately 12,000–15,000 people were affected in the UK, equivalent to one in 4,600 people.[13] In the Netherlands, 800 newborns are born with SCD every year.[14]

In contrast, the global burden of SCD is more pronounced in the Middle East and North Africa (MENA) region. In Africa, approximately 10–15 million people live with SCD, with Congo and Nigeria most affected.[4,7,15–17] The high prevalence of SCD in this region is likely due to the increased frequency of consanguineous marriages particularly between first-degree relatives.[11] High rates of consanguineous marriages have been reported in Saudi Arabia (42–67%), Sudan (44–63%), Qatar (54%), the United Arab Emirates (40–54%), Jordan (29–64%), Yemen (40–45%) and Egypt (21–33%).[1,18,19] In the Middle East, the highest prevalence of SCD and SCT is in eastern Saudi Arabia (2.6% and 21%, respectively).[20] In 2015, the incidence of paediatric SCA was 2,238 in Egypt and 25,375 in Iraq.[21] Studies from Oman indicate that approximately 3,000 people live with SCD, with an estimated 118 new cases every year and SCT present in one in 370 live births.[22–25]

Young children and adolescents are more vulnerable to lifelong SCD complications such as vaso-occlusive crises (VOCs), acute splenic sequestration crises, acute chest syndrome (ACS), central nervous system infarctions, haemolytic and aplastic crises and avascular hip necrosis.[5,26,27] In children, the most common complication of SCD is painful VOCs.[28,29] These occur when the irregularly-shaped red blood cells become stuck in the small vessels, causing multiple organ infarctions including kidney, spleen, bone and brain infarctions.[30] Risk factors for VOC include exposure to cold, hypoxia, acidosis, inflammation, fatigue, physical activity and emotional stress.[31] A study of Omani children revealed that 22% of 240 children with SCD developed ACS, with 71% of cases preceded by painful VOCs.[32] In another study of Omani children with SCD, VOCs constituted the main reason for admission in 83% of 316 hospital admissions over a 12-month period.[33]

Current management of SCD focuses primarily on the maintenance of health and treatment of acute and chronic complications. Several important modalities such as hydroxyurea (HU) therapy and blood transfusions, have been found to boost patient outcomes.[34,35] In particular, HU therapy reduces the frequency of VOCs and ACS thereby reducing the need for blood transfusions and associated hospitalisation.[36] While stem cell transplantation is the intervention most likely to be curative in nature, this option is often associated with several complications.[37]

Despite recent advances in SCD treatment, the health-related quality of life (HRQOL) of children and adolescents with SCD remains poor compared to their healthy peers particularly with regards to physical, mental, social and academic domains.[38,39] Although many systematic reviews are available regarding HRQOL in children and adolescents with SCD, none focus specifically on the MENA region. As outlined earlier, the prevalence of SCD is much higher in this region; hence, understanding the impact of SCD on the HRQOL of children and adolescents in this region would be invaluable in order to inform future interventions such as premarital genetic counselling and potential lifestyle modification strategies, and to identify and prioritise patient-care decisions. Therefore, this systematic review aimed to summarise and analyse the existing empirical literature with regards to the HRQOL of children and adolescents living with SCD in the MENA region, discuss the implications of these findings on research and clinical practice and suggest strategies for improving HRQOL in this region.

Methods

This systematic review was carried out in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[40] A systematic search of various electronic databases was performed to identify articles assessing the HRQOL of children and adolescents with SCD in the MENA region published between January 2010 and March 2020 including the MEDLINE® (National Library of Medicine, Bethesda, Maryland, USA), Scopus® (Elsevier, Amsterdam, the Netherlands), Cumulative Index to Nursing and Allied Health Literature®, Masader (Oman Virtual Science Library, Muscat, Oman) and EBSCOhost (EBSCO Information Services, Ipswich, Massachusetts, USA) databases.

The search terms included the following in various combinations: "health-related quality of life", "quality of life", "sickle cell disease", "sickle cell anaemia", "Middle East", "North Africa", "infant," "children" and

"adolescents". All full-text peer-reviewed articles were included in the final analysis if they met the following criteria: (1) the articles constituted research studies assessing the HRQOL of children and adolescents with SCD aged <21 years; (2) the population of interest was relevant to the MENA region; (3) the articles were published in English between January 2010 and March 2020; and (4) the population of interest included all SCD genotypes. Articles published before 2010 and in languages other than English were excluded, as were systematic reviews, meta-analyses, editorials, case studies, pilot studies and unpublished research, as well as studies focusing on the perspectives of adults, caregivers, parents or healthcare providers.

Following the initial literature search, the authors screened the titles and abstracts of each relevant article to eliminate duplicate results. In addition, the reference lists of articles retrieved during the database search were reviewed to identify additional articles for inclusion in the analysis. Subsequently, two authors independently evaluated the full text of each article to determine its eligibility according to the inclusion criteria, with any disagreements settled by consensus. In the third step, the authors independently collected and consolidated relevant data from the articles as per Garrard's matrix method including the name and profession of the authors, year of publication of the article, purpose, design and setting of the study, period of recruitment, age group, characteristics and size of the sample, type of HRQOL instrument, type of rater (i.e. self or proxy) and relevant outcomes from the study. A total of 533 articles were initially identified during the literature search. After removing duplicates, 176 unique articles were available for further screening. Of these, 146 articles were removed because they did not meet the criteria. After screening the full text of the remaining 30 articles, 10 articles met the inclusion criteria and were included in the final analysis [Figure 1].

Two reviewers independently assessed the methodological quality of each study using an adapted version of the Newcastle-Ottawa Quality Assessment Scale, except for mixed-method studies which were assessed using the Mixed Methods Appraisal Tool.[41,42] Cross-sectional studies were scored out of 8 points, based on sample collection (four items), comparability (one item) and outcome calculation (two items). Case-control studies were scored out of 9, based on sample size (four items), comparability (one item) and outcome calculation (three items). Cohort studies were scored out of 6, based on sample selection (two items), comparability (one item) and outcome measurement (two items). Each item within the sample selection and outcome criteria received a maximum of one point, while items in the comparability criteria received a maximum of two points. In cases where there was a divergence in scoring, the reviewers discussed the item in question until a consensus was reached; if necessary, a third reviewer was consulted. Studies with final scores of <50% were considered to be of poor methodological quality.

Results

STUDY CHARACTERISTICS

A total of 10 articles were included in the systematic review [Table 1].[21,43–51] Of these, nine were observational studies, including five cross-sectional, two case-control and two cohort studies.[21,44–51] The

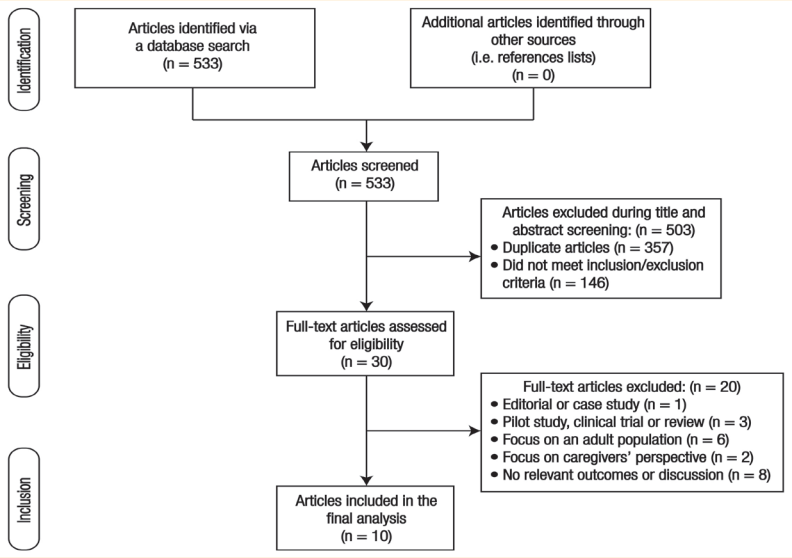

Figure 1: Diagram showing the search process used to identify articles for inclusion in the systematic review.

Table 1: Characteristics of studies assessing the health-related quality of life of children and adolescents with sickle cell disease in the Middle East and North Africa region (N = 10)[21,43–51]

Author and year of publication	Purpose	Study design	Setting	Type of participants	Sample size	Instrument	Rater	Relevant findings	Quality of study*
Boulassel *et al.*[46] (2019)	To investigate factors that affect HRQOL in children with SCA	Cross-sectional	Oman	Children with SCA aged 2–16 years and their caretakers	123	PedsQL™ V4 SCD module	Self and proxy	• Children with SCA had reduced HRQOL scores. • The lowest scores fell on the pain impact subscale, with an average of 41 ± 21% (range: 2.5–100%), suggesting that HRQOL is adversely affected by pain. • In contrast, the highest score fell on the Worry II subscale, with an average of 70 ± 28% (range: 12.5–100%).	75% (6/8)
Kambasu *et al.*[43] (2019)	To evaluate the HRQOL of adolescents with SCD	Mixed-method	Uganda	Children with SCD aged 8–17 years and their caretakers	140	PedsQL™ generic core scale and FGDs with adolescents and caretakers	Self and proxy	• HRQOL scores were low in the physical functioning, emotional functioning and academic functioning domains.	75%
Salih[51] (2019)	To examine the impact of SCA on the QOL of school-aged children in three dimensions (psychological, social and academic)	Cross-sectional	Sudan	Children with SCA aged 7–15 years	107	Structured questionnaire	Self	• SCD posed multiple social and psychological problems that need to be addressed. • Common problems included enuresis, depressive symptoms, school absenteeism and deterioration in school performance.	62.5% (5/8)
Cevher *et al.*[47] (2018)	To evaluate QOL, clinical effectiveness and satisfaction in children and young adults with SCD receiving HU therapy	Cohort	Turkey	Children aged 7–17 years and young adults aged 18–22 years with SCD who received HU therapy for ≥1 year	50 (34 children and 16 young adults)	CHQ-PF50	Self and proxy	• Both QOL and adherence to HU therapy were low, likely due to the lack of effectiveness of HU therapy, along with comorbidity, concomitant drug use and side-effects.	66.7% (4/6)
Essawy *et al.*[21] (2018)	To evaluate the QOL of children with SCA	Cross-sectional	Iraq	Children with SCA aged 6–12 years and their mothers	100	Structured questionnaire and interviews	Self and proxy	• SCA significantly affected the QOL of the children. • Two-thirds of the children had poor QOL, less than a quarter had neutral QOL and few had good QOL. • Severe pain was reported by 78% of the affected children.	75% (6/8)
Senol *et al.*[48] (2016)	To evaluate QOL, clinical effectiveness and satisfaction in patients with BTM and SCA receiving DFX chelation therapy	Cohort	Turkey	Children aged 5–18 years and adults with BTM or SCA who received DFX therapy for ≥6 months	72 (37 children and 35 adults)	CHQ-PF50	Proxy	• Patients with SCA had significantly lower HRQOL scores for general health, physical activity, role/social limitations, parental impact-time and family activities and higher scores for health transition compared to BTM patients (P <0.05).	83.3% (5/6)
Alharbi *et al.*[44] (2016)	To assess the HRQOL of children with SCA	Cross-sectional	Saudi Arabia	Children with SCD aged 6–12 years and their mothers	40	PedsQL™ generic core scale	Self and proxy	• SCD significantly affected most HRQOL domains, including physical, social, emotional and academic wellbeing domains.	87.5% (7/8)
Sehlo and Kamfar[45] (2016)	To evaluate the association of social support, disease severity and depression on HRQOL in children with SCD	Case-control	Saudi Arabia	Children with SCD aged 10–15 years and matched healthy controls aged 9–15 years	120 (60 cases and 60 controls)	PedsQL™ generic core scale	Self and proxy	• Disease severity and depression were associated with poor QOL in children with SCD.	100% (9/9)

HRQOL = health-related quality of life; SCA = sickle cell anaemia; PedsQL™ = Pediatric Quality of Life Inventory™; V4 = Version 4.0; SCD = sickle cell disease; FGDs = focus group discussions; QOL = quality of life; HU = hydroxyurea; CHQ-PF50 = Child Health Questionnaire - Parent Form 50; BTM = β-thalassemia major; DFX = deferasirox; WHOQOL-BREF = World Health Organisation Quality of Life Brief Version; SF-36 V2 = 36-item Medical Outcomes Study Short-Form Version 2.

**Methodological quality was assessed using an adapted version of the Newcastle-Ottawa Quality Assessment Scale, except for mixed-method studies, which were assessed using the Mixed Methods Appraisal Tool.[41,42] Cross-sectional, cohort and case-control studies were scored out of 8, 6 and 9, respectively, with scores of <50% considered to indicate poor methodological quality.*

Table 1 (cont'd): Characteristics of studies assessing the health-related quality of life of children and adolescents with sickle cell disease in the Middle East and North Africa region (N = 10)[21,43–51]

Author and year of publication	Purpose	Study design	Setting	Type of participants	Sample size	Instrument	Rater	Relevant findings	Quality of study*
Al Jaouni *et al.*[49] (2013)	To assess the HRQOL of patients with SCD and to measure the impact of treatment adherence on complications, disease severity, crises and outcomes	Cross-sectional	Saudi Arabia	Patients with SCD aged 2–48 years	115 (including 23 children aged 1–12 years, 33 adolescents aged 13–18 years and 25 adults aged 18–48 years)	WHOQOL-BREF	Self and proxy	• Extremely ill patients had significantly lower HRQOL scores (P = 0.002). • Pain was the main cause of hospitalisation (51.3%). • Patients with painful episodes (31.3%) and on regular narcotics had significantly lower HRQOL scores (P <0.001). • HRQOL scores decreased significantly as pain levels increased. • Patients with delayed treatment or those who did not adhere to treatment reported significantly lower HRQL scores (P = 0.001).	75% (6/8)
Amr *et al.*[50] (2011)	To evaluate HRQOL deficiencies among adolescents with SCD	Case-control	Saudi Arabia	Adolescents with SCD aged 14–18 years and age- and gender-matched healthy controls	382 (180 cases and 202 controls)	SF-36 V2	Self	• Adolescents with SCD reported poorer HRQOL scores compared to healthy adolescents, particularly in several HRQOL domains, including physical functioning, body pain and general health	88.9% (8/9)

HRQOL = health-related quality of life; SCA = sickle cell anaemia; PedsQL™ = Pediatric Quality of Life Inventory™; V4 = Version 4.0; SCD = sickle cell disease; FGDs = focus group discussions; QOL = quality of life; HU = hydroxyurea; CHQ-PF50 = Child Health Questionnaire - Parent Form 50; BTM = β-thalassemia major; DFX = deferasirox; WHO-QOL-BREF = World Health Organisation Quality of Life Brief Version; SF-36 V2 = 36-item Medical Outcomes Study Short-Form Version 2.

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final study used a mixed-method design involving both quantitative and qualitative measures.[43] Most of the authors were nurses, medicine or health sciences faculty members, psychiatrists, haematologists, pharmacists or geneticists. Four studies were conducted in Saudi Arabia, two in Turkey and one each in Iraq, Sudan, Uganda and Oman.[21,43–51]

Most of the studies focused primarily on children and adolescents aged 2–18 years.[21,43–46,48,50,51] However, two studies focused both on paediatric and young adult populations aged 18–22 years.[47,49] In most cases, self-reported measures were applied to children over the age of 8 years who were literate and capable of comprehension, with caregiver proxy reports utilised for those between 2–8 years.[21,43–47,49–51] The sample size for children and adolescents with SCD or SCA ranged from 37–180.[21,43–51]

MEASURES OF HEALTH-RELATED QUALITY OF LIFE

Various tools were used to assess the HRQOL of children and adolescents with SCD. Two studies used self-designed structured questionnaires completed during interviews.[21,51] Three studies utilised the generic core scale of the Pediatric Quality of Life Inventory™ (PedsQL™); in addition, another study applied the PedsQL™ SCD module scale, Version 4.0.[43–46] Two studies used the Child Health Questionnaire - Parent Form 50.[47,48] Finally, the WHO Quality of Life Brief Version scale and 36-item Medical Outcomes Study Short-Form was applied in one study each.[49,50] Apart from the self-designed questionnaires, all of these instruments have been previously validated for use in different populations and various languages.[43–50]

DOMAINS OF HEALTH-RELATED QUALITY OF LIFE

Four distinct HRQOL domains were identified in the studies including physical wellbeing, psychological wellbeing, family/financial wellbeing and academic functioning.[21,43–51] In certain cases, specific findings from the studies encompassed more than one of these domains because of the interconnected nature of HRQOL.

PHYSICAL WELL-BEING

Boulassel *et al.* reported that children with SCA in Oman demonstrated low HRQOL scores; in particular, the lowest scores were found on the pain impact scale thereby indicating that HRQOL in this cohort was

adversely affected by pain.[46] In Uganda, Kambasu *et al*. observed low scores in terms of physical, emotional and academic functioning among adolescents with SCD.[43] According to Cevher *et al*., both quality of life and adherence to HU therapy was low among paediatric and young adult patients in Turkey; this was attributed to the lack of effectiveness of HU therapy, in addition to comorbidity, concomitant drug use and side-effects.[47]

In Iraq, Essawy *et al*. concluded that SCA significantly affects the quality of life of children, with more than two-thirds of the cohort noted to have poor quality of life; moreover, the majority (78%) reported being in severe pain.[21] Among a cohort of SCD patients in Saudi Arabia, Al Jaouni *et al*. observed that those who were extremely ill demonstrated significantly lower HRQOL scores, with HRQOL scores decreasing significantly as pain levels increased.[49] In addition, patients with delayed or low adherence to treatment reported lower HRQL scores.[49] Finally, in another study set in Saudi Arabia, Amr *et al*. showed that adolescents with SCD had poorer HRQOL scores compared to healthy adolescents, particularly in terms of physical functioning, body pain and general health.[50]

PSYCHOLOGICAL WELL-BEING

In Sudan, Salih confirmed that SCD caused multiple social and psychological problems among school-aged children, with enuresis, depressive symptoms, school absenteeism and deterioration in academic performance being most common.[51] Additionally, Sehlo and Kamfar reported associations between poor quality of life and disease severity and depression among children with SCD in Saudi Arabia.[45]

FAMILY AND FINANCIAL WELL-BEING

In Turkey, Senol *et al*. reported significantly lower scores among a cohort of children and adolescents with SCA for various HRQOL-related subscales including general health, physical activity-related limitations, physical functioning, parental impact-time and family activities compared to patients with β-thalassaemia major.[48] In addition, the former group demonstrated significantly higher scores in terms of health transition compared to the latter.[48]

ACADEMIC FUNCTIONING

Alharbi *et al*. found that SCD significantly affected most HRQOL domains in a group of children in Saudi Arabia including physical, social, emotional and academic well-being domains.[44]

Discussion

Children with SCD undergo frequent hospitalisation due to painful crises which can affect a myriad of other facets of life including academic achievement, school attendance, social activities and sleep quality.[29,52] Moreover, SCD can affect familial relationships and the ability to engage in routine family activities; for caregivers, looking after a child with SCD can represent an emotional and financial burden.[53] Individuals with SCD also encounter stigma for a variety of reasons such as race, disability status, socioeconomic status, chronic pain and delayed growth and puberty.[54]

This systematic review examined the existing empirical literature regarding the HRQOL of children and adolescents with SCD in the MENA region. Overall, this population demonstrated poor HRQOL in all domains compared to their healthy peers including physical, psychological, familial, academic, social and financial functioning.[21,43–51] Palermo *et al*. reported similar findings in a case-control study comparing 120 healthy children to 58 children with SCD.[55] Using the Child Health Questionnaire, the researchers found that the physical, psychological and social wellbeing of children with SCD was reduced in comparison to the healthy control group.[55] After applying the PedsQL™ instrument, Dale *et al*. found that 63%, 28% and 55% of 124 children and adolescents with SCD were at risk of physical disability, poor social functioning and reduced academic performance, respectively.[39] Such findings highlight the need for urgent strategies to improve the HRQOL of children and adolescents with SCD.

Pain is a significant predictor for poor HRQOL among children and adolescents with SCD and a primary indicator of impaired physical and psychological functioning.[56] Thornburg *et al*. found that children with SCD undergoing HU therapy demonstrated better physical and cognitive function compared to those who could not take the drug due to the extent of the disorder.[57] Panepinto *et al*. revealed that poor physical HRQOL scores were correlated with clinical comorbidities, older age and lower family income.[58] Pain has also been positively associated with increased maternal and caregiver stress and impaired family functioning, thereby leading to poor HRQOL outcomes.[56] These findings are supported by those of other studies.[46,59] As such, careful pain assessment at home and prompt management is recommended in order to promote resilience among children with SCD and increase their quality of life.

Menezes *et al*. observed statistically significant gender differences in most HRQOL domains.[52]

However, contradictory findings have been reported regarding the effect of gender on pain sensation among children and adolescents with SCD. According to Andong *et al*., adolescent girls with SCD demonstrated significantly lower levels of physical activity and physical pain; in contrast, Kambasu *et al*. found that pain rates were higher in female children with SCD compared to their male counterparts.[43,60] Therefore, further studies are needed to better understand gender differences in pain perception among children and adolescents with SCD so as to tailor pain management strategies accordingly.

Various studies have reported poor cognitive and psychosocial performance in children and adolescents with SCD.[58,61,62] In a study conducted in India, Patel and Pathan reported that children with SCD demonstrated low HRQOL scores in in physical, psychosocial and cognitive areas.[61] These results are supported by other studies which revealed that children with SCD had lower self-esteem than healthy children.[58,62] With regards to family, Wonkam *et al*. found that mothers of children with SCD had a higher risk of depression compared to mothers with healthy children.[59]

Families with children affected by SCD often face financial challenges. In many developing countries, national health insurance or social welfare programmes are lacking, thus placing the financial burden of care for children with chronic diseases on the individual family. In Nigeria, Lagunju *et al*. observed that families of children with SCD often experienced severe hardship due to the child's medical expenses, adversely affecting the family's basic needs such as housing and food; moreover, loss of employment resulting from time spent caring for a child with SCD also contributed significantly to this burden.[34] Therefore, countries in the MENA region should take steps to help improve existing financial support systems for families affected by paediatric SCD, perhaps through the provision of social welfare subsidies or programmes.

Various studies have shown that children with SCD exhibit poor academic functioning compared to healthy children, with pain once again found to be a significant predictor of such outcomes.[44,52,56] Indeed, children and adolescents with SCD are often absent from school, thereby missing out on important educational experiences and daily social activities due to frequent hospitalisation secondary to pain crises, depression, social stigma and poor social support systems.[44,52] Thus, it is necessary for educators to take necessary steps to improve the academic functioning of children with SCD, for instance by establishing school- or peer-led support groups and special extracurricular classes for affected children, or by allowing special leeway with regards to high rates of absenteeism for medical reasons.

Lack of awareness of the disease has been linked with poor HRQOL outcomes among children and adolescents with SCD, especially as awareness is usually poor among both affected patients and caregivers. Shahine *et al*. found that an increase in awareness on the part of the caregiver was significantly associated with a decrease in the frequency of hospitalisation among children with SCD.[38] Another study carried out by Al-Azri *et al*. indicated that the quality of life of children with SCD in Oman remained low primarily because of a lack of awareness of the disease.[63] Therefore, health promotion and educational programmes are recommended to increase awareness of SCD and promote mandatory premarital screening to reduce the incidence of the disease in the MENA region.

Social support can have a major impact on the resilience of children with SCD such as that offered by family members, teachers, peers and friends. Several studies have concluded that greater parental support and involvement is significantly linked to decreased depressive symptoms and better quality of life in children with SCD.[45,64] Play therapy is a potential option to help children with SCD to express their emotions, improve communication with caregivers and peers and encourage socialisation. Similarly, Pandarakutty *et al*. reported that a nurse-led filial therapy and educational intervention resulted in a significant improvement in HRQOL scores among a group of children with SCD in Oman, particularly in terms of reducing emotions, improving knowledge, enhancing parental support and reinforcing family relationships.[65]

IMPLICATIONS FOR FUTURE RESEARCH

The findings of this systematic review underline an urgent need for practical measures to improve the HRQOL of children and adolescents with SCD in the MENA region. Such initiatives should focus on increasing knowledge and awareness of SCD, developing support groups to enhance the psychological wellbeing of children and adolescents with SCD and their caregivers, mitigating the economic burden of care on the families of children with SCD and strengthening existing family, social and academic support systems. Further studies are therefore necessary to help design, implement and assess the effectiveness of such strategies in this region.

LIMITATIONS

This research was subject to certain limitations. A meta-analysis could not be conducted to determine correlations between variables due to the differences

in statistical analyses across studies. In addition, articles focusing on HRQOL outcomes of children and adolescents with SCD in the MENA region which were published in other languages could not be included in the final analysis, possibly resulting in the lack of inclusion of relevant non-English language studies.

Conclusion

A systematic review of studies assessing the HRQOL of children and adolescents with SCD in the MENA region revealed that the HRQOL of this population was poor in comparison to healthy children in all domains including physical, psychological, familial, academic, social and financial functioning. As such, healthcare providers, educators and policymakers should implement strategies to improve the HRQOL of this group. The authors recommend the implementation of mandatory awareness and premarital screening programmes, thereby increasing understanding, reducing stigma and minimising the incidence of hereditary diseases such as SCD. In addition, interventions such as play therapy may help to encourage socialisation, reduce psychological stress and strengthen familial bonds. Finally, existing financial support systems should be strengthened so as to alleviate the economic burden of medical care on affected families.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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