Original Research Article

Health Related Quality of Life of Children with Sickle Cell Anemia and Their Parents; Quantitative Study in Albaha; Saudi Arabia

ABSTRACT

Aims: To gain a better understanding of the quality of life (QoL) of children and impact of this disease on parents QoL.
Study design: Cross-sectional study.
Place and Duration of Study: The study was conducted in King Fahd Hospital, Albaha city, Albaha, Saudi Arabia, between March2020 and February 2021.
Methodology: We included 95 responses. Two different tools were used for the purpose of this study. PedsQL™ Sickle Cell Disease Module was used to measure health-related quality of life (HRQoL) in healthy children and adolescents and those with acute and chronic health conditions. Moreover, PedsQL™ Family Information Form was completed by caregivers. Median and interquartile range were used for numerical variables since they were skewed. Bivariate analyses were carried out using non-parametrical tests and Pearson correlation. The prediction of quality of life was accomplished through multivariate analysis.
Results:A total of (95) responses were analyzed. Females respondents were 52.6%. The age median was 12 (IQR=10-14). Mothers represented the most frequent informant 46.3% in this current study. Significant association was found between quality of life and certain independent factors, some of which is parental level of education ($P< .001$) and marital support ($P< .001$).
Conclusion: Sickle cell disease (SCD) is a major condition accounts for a huge burden on variable levels. This study reported that low quality of life among children affected by SCD. Higher education and current marital status of the parents were significantly associated with high quality of life in SCD patients. Number of workdays affected due to child health was significantly correlated with low quality of life.

Keywords: Sickle cell disease; Sickle cell anemia; Quality of life; Children; Saudi Arabia

1. INTRODUCTION

Sickle cell disease (SCD) and its variants are autosomal recessive disorders characterized by abnormal hemoglobin S production caused by the presence of a mutated form of hemoglobin. [1]. SCD is caused by a mutation in the β-globin hemoglobin chain, which causes the hydrophilic amino acid and glutamic acid to be replaced at the sixth position with the hydrophobic amino acid valine. Red blood cells live for 90–120 days on average, but sickle cells only live for 10–20 days [2]. SCD usually manifests itself in the first year of life. Chronic hemolysis causes a variety of symptoms, including jaundice, pigment gallstones,

splenomegaly (early in life), spontaneous splenectomy, and ulcers on the lower tibia that do not heal properly [3]. The government's most successful programs are the premarital screening program and genetic counseling program. Premarital screening is required prior to engagement and is available free of charge at all government facilities. This program appears to be a success, as it has significantly reduced the number of at-risk marriages.

Episodes of hemolytic crises can be life-threatening and can be triggered by viral or other infection or by folic acid deficiency causing reduced erythropoiesis. Acute vaso-occlusion by clusters of sickled red blood cells causes painful episodes or attacks. Vaso-occlusive crises can be triggered by infection, dehydration, or hypoxia. The vertebrae and long bones are usually affected in acute episodes [3]. The episode can last anywhere from hours to days and can result in a low-grade fever [3]. Furthermore, A known clinical picture of hemolytic anemia and vaso-occlusive crisis suggests SCD. By screening for hemoglobin S (HbS) at birth and prenatal diagnosis by chorionic villus sampling at 8-12 weeks of gestation to obtain DNA, electrophoresis confirms the diagnosis with the presence of homozygous HbS. This low-risk procedure is completely risk-free [3]. SCD is associated with high morbidity and mortality. It is characterized by acute clinical symptoms, such as painful vasculo-occlusive episodes, splenic sequestration and acute thoracic syndrome, that make the patient seek emergency services frequently, and also by chronic signs, as it affects organs and systems. Additionally, patients with SCD usually exhibit multiple organ damage because of repeated vascular occlusion, which is superimposed on a background of poor development and failure to thrive [4]. Due to their condition, many patients have frequent hospitalizations and may experience chronic pain, fatigue, hand-foot syndrome, frequent infections, delayed growth, and vision problems [4]. The aim of therapy for the SCD includes the management and prevention of acute manifestations and to prevent red blood cells clustering; last, but not least, to educate the patients and their family members regarding the disease. There is no well-developed treatment to combat the anemia. Children and their parents may suffer as a result of the disease's inability to be effectively managed, which can lead to family discord, deterioration of quality of life (QoL), increased care burden and despair, and a loss of energy [4].

Sickle cell anemia (SCA) threatens the health of many people globally. Africa has the highest prevalence of SCD, which ranges from 10% to 40%, according to the World Health Organization [5]. Furthermore, the disease affects about 2% of the population in countries where the trait prevalence is greater than 20%. Hemoglobinopathies, which affect about 2,000,000 Americans and are clinically diagnosed in 7% of the world's population, are carried by 7% of the world's population, and are clinically diagnosed in approximately 72,000 Americans [6,7]. One of the most effected group by sickle cell disease is Middle Eastern people and the first reported case of SCD in Saudi Arabia (SA) was reported in the eastern province in the 1960s [8,9]. The prevalence of SCD varies significantly across South Africa, with the Eastern province having the highest prevalence, followed by the southwestern provinces [9].According to the Saudi Premarital Screening Program, 0.26 percent of the adult population is trait carrier, and 4.2 percent of the population has SCD. In the last ten years, the Kingdom has reported 9,417 cases of sickle cell anemia, bringing the total number of cases to 145,750 [9].

The highest rates of SCD is found in Al-Ahsa region of the country (sickle cell trait 16.89% and sickle cell disease 1.20%), followed by Qunfudah and Jazan [10]. The regional distribution of SCD showed that the disease was more common in eastern region with prevalence of 145 per 10,000, followed by the southern region (Assir, Jazan, Najran and Albaha) with prevalence of 24 per 10,000 [11]. Unfortunately, despite the fact that the prevalence of SCD has been declining in all regions of Saudi Arabia, it remains higher than in other countries [9].

Premarital screening program and genetic counseling program are considered as the most successful programs that have been implemented by the government. The premarital screening program is mandatory prior to engagement and is provided free at all government facilities. This program appears to be effective, as it has reduced the number of voluntary cancellations of at-risk marriage proposals by 60%, despite the fact that the number of at-risk marriage proposals has increased by 5-fold in the last six years [12].

Quality of life (QoL) is defined by the World Health Organization (WHO) as "an individual's perception of their position in life in relation to their goals, expectations, standards, and concerns in the context of the culture and value systems in which they live" [13]. Another concept is "quality of life associated with health" which assesses the impact of health on the individual's capacity to live fully [14]. Over the last thirty years, the importance of QoL assessment has gradually become clearly prioritized, with improvements and dedication in evaluation methods focusing on subjective evaluations to measure individual perceptions of QoL of patients [15]. HRQoL (health-related quality of life) is a construct made up of biological, social and relational, psychological, and functional autonomy elements. They come together to help people assess how much better or worse their lives have become [15].

Survival and quality of life improvement for these patients is based on general and preventive measures [16]. Several changes affect the life of patients with SCD which force them to face limitations, frustrations and losses and to adapt to a new lifestyle. These changes are greatly beneficial due to the use of medications, lost working capacity and hospitalizations. Because of these events, there may be a variable impact on their health-related quality of life [17].

Despite the advances in medicine, SCD remains incurable and all we can offer is palliative care. It is therefore, a chronic disease with lifelong treatment with the quality of life (QoL) of patients being a key challenge to the patients themselves, their families and healthcare professionals [18].

Children with sickle cell anemia go through extreme health related hardships and this is a burden to their family members, especially their parents, who are their long-term care givers [19]. Also, sickle cell anemia in children create special challenges for parents. Usually, health and quality of life of these children as well as their parents are overlooked. And no study has been found to be done in Saudi Arabia regarding QoL of caretakers of these children, who are mostly young parents. And the results of this current study will gain a better understanding of the QoL of children and impact of this disease on parents QoL.

2. MATERIAL AND METHODS

A quantitative tool (PedsQL™) was used which is made up of nine dimensions, each evaluating a different domain of HRQoL: pain, pain impact, pain management and control, worrying, worrying II, emotions, treatment, communication and communication II. Subscale scores were calculated from 35 out of the 36 items (one item about self-reported health transition was not included in the scores). PedsQL™ score valued from 0 to 100, higher scores indicated better quality of life. If more than 50% of the items in the scale were missing, the scale scores should not be computed. If 50% or more items were completed: the mean of the completed items in a scale was imputed. Two questionnaires were used to assess quality of life. PedsQL™ Sickle Cell Disease Module used to measure health-related quality of life (HRQoL) in healthy children and adolescents and those with acute and chronic health conditions. In addition, PedsQL™ Family Information Form was completed by caregivers, and contained demographic information on the child and parents, including the

child's date of birth, gender, race/ethnicity, and parental education information and whether the child has a chronic health condition also information on the number of days during the past 30 days that the child needed care or missed school because of health, the number of days the parent missed work because of the child's health, and the impact of the child's health on the parent's daily work routine and ability to concentrate at work.

2.1 Data Collection Tool and Technique

Data was collected through non-probable consecutive technique using a list of all registered patients in Hematology clinic at King Fahad Hospital, Albaha, Saudi Arabia. The study investigator gained free access to PedsQL™ Sickle Cell Disease Module 16, and PedsQL™ Family Information Form 17 through contacting ePROVIDE™.

2.2Sample size

The total number of registered sickle cell disease patients in hematology clinic of King Fahad Hospital is 210. Non-probable consecutive technique was used since all those eligible to this current study based on the inclusion criteria were included (n=95).

2.3Study setting

This study was conducted in Hematology clinic at King Fahd Hospital, Albaha city, Albaha, Saudi Arabia. The hospital provides secondary health care and serve about half million populations, Albaha is a city in the south west of Saudi Arabia, and it is the smallest province in the Kingdom of Saudi Arabia.

Study variables were as follows, dependent variable: Level of QoL. Independent variables included: Emotions, attitudes and beliefs family/social relationships, morbidities/co morbidities, medical care, health insurance, employment, education, income, faith/spirituality, stress/control/predictability, activity, limitations, housing and community.

2.4Inclusion criteria

Sickle cell patient with hemoglobin SS disease because other type of SCA have no clinical symptoms therefore assumed not to have any effect on quality of life. Age group 8 – 14 years old which contained most of the cases, and those above 14 years are following in adult hematology clinic. Patients with registered files in King Fahad Hospital in Albaha, Saudi Arabia.

2.5Ethical consideration

Permission to conduct the study was obtained from the Research and Ethics Committee (Directorate of Health Affairs, Taif, Research and Studies Department) and every participant was informed about the purpose of the study and a written consent was obtained and confidentiality of the data was assured and used for the sake of the study only. Additionally,

personal questions were not included, no obligation of any kind for participation in the study. The investigator assures absence of any conflict of interest.

2.6Statistical analysis

The statistical analysis was done using the statistical package for the social sciences (SPSS, version 27.0). All numerical variables were skewed. Thus, median and interquartile range (IQR) were used for summarization. Proportion was used to summarize categorical and ordinal variables. The quality of life was measured for each case by dividing the sum of items by the number of items (43 items). The outcome variable represented the quality of life as a percentage. Bivariate analyses were carried out using non-parametrical tests (Mann-Whitney and Kruskal-Wallis) and Pearson correlation. Multivariate analysis was conducted for the prediction of quality of life. Some variables were excluded from the multivariate analyses due to violation of assumptions. The predetermined level of significance was ($P < .05$) and level of confidence (95% CI).

3. RESULTS AND DISCUSSION

3.1 Results

A total of (95) responses were analyzed. All were relatives of a child affected with sickle cell disease. Females represented 52.6%. The age range was (8-15) with a median of (12, IQR=10-14). Mothers were the most frequent informant 46.3%; followed by fathers 33.7%; then sisters and brothers 11.6% and 8.4% respectively. Fathers who were governmental employees were 48.5%; retired 21.1%; working in private section 15.8%; and 14.6% did not have a formal job. The questionnaire asked about the burden of the disease in the last (30) days. The median and IQR were as follow; number of days when the child was sick at bed and did not play (5, IQR=2-7), number of days where a person was needed to take care of the patient (5, IQR=3-9), number of days when the informant was absent from work because of the child (2, IQR=0-5), The marital status and educational level of the parents are shown in (Table 1).

Table 1. The marital status and educational level of the parents

N=95	Father (n=95)	Mother (n=95)
Marital status		
Married	77.9	77.9
Divorced	10.5	10.5
Widow	1.1	10.5
Dead	10.5	1.1
Education		
Illiterate	5.3	6.3
Primary	9.5	13.7
Secondary	13.7	18.9
High school	46.3	41.1
Diploma	9.5	7.4

University	15.8	12.6

The (43) items measuring quality of life were represented in one continuous variable. The median for quality of life was (35.5%, IQR=23.3-47.7). The minimum score for quality of life was 10.5%, while the maximum was 88.4%. Bivariate analyses showed significant differences between the groups of categorical variables. Both marital status and educational level were significantly associated with quality of life. Currently married parents were associated with a better quality of life (P < .001). Furthermore, parental level of education was significantly different; mentioned from the highest to lowest quality of life; higher education was associated with higher quality of life (P < .001).
As expected, less visits to the emergency during the last (30) days was associated with higher quality of life (P < .001). Moreover, number of hospital visits at night, days of absence from school, need of person to take care of the patient were negatively correlated with quality of life (P < .001).

The regression model was built to predict the quality of life based on the other independent variables. Due to high correlation between the independent variables, some variables were dropped from the model. Multiple regression showed significantly the increase in the QoL with mother education and the decrease with changing the work routine for parents (Table 2). The quality of life of SCA was negatively correlated with age and parental quality of life (Table 3).

Table 2. Multiple regression model

N=95	Coefficient	95% CI	*P*-value
(Constant)	50.831	36.864, 64.798	.000
What is your relationship to the child?	0.754	-0.632, 2.141	.28
Age of the child	0.105	-0.816, 1.025	.82
Gender of the child	0.610	-3.312, 4.532	.76
The occupation of the father	0.132	-1.139, 1.402	.84
The marital status of the mother	-2.334	-5.601, 0.932	.16
The education of the mother	3.190	1.341, 5.040	<.001
Does the mother work	-3.841	-8.286, 0.604	.09
In the last 30 days, how many days has your child been absent because of his health?	-1.252	-2.802, 0.298	.11
In the last 30 days, how many days has the health of the child affected your daily routine at work?	-8.855	-11.420, -6.289	< .001
In the last 30 days, how many days your child needed a person to take care of him because of his health?	-0.252	-0.870, 0.366	0.42
In the last 30 days, how many days were you absent from work because of the health of the child?	0.080	-0.736, 0.897	0.85

R= 0.875, adjusted R square= 0.732, model P < .001.

Table 3. Negative correlation between age of the child, parental factors and children quality of life

	Quality of life	
N = 95	Pearson correlation	P-value

Age of the child	-0.223	.03
In the last 30 days, how many days were you absent from work because of the health of the child?	-0.528	< .001
In the last 30 days, how many days has the health of the child affected your daily routine at work?	-0.812	< .001
In the last 30 days, how many days has the health of the child affected your concentration at work?	-0.806	< .001

3.2Discussion

Undoubtedly, sickle cell disease patients usually report low quality of life (QoL) and this, in fact, is well established in the literature [9]. Our sample showed similar results as the majority of the respondents scored a QoL of below 47.7% and some reported as low as 10.5%. Numerous factors were associated with low QoL of which two stands out: marital status and level of education. These current results agree with other studies which concluded that currently-married status and higher level of education parents are statistically associated with high quality of life among sickle cell disease patients [14]. Other studies investigating quality of life in patients with sickle cell disease stated that it is associated with the presence of other comorbidities and complications such as renal failure and recurrent acute chest syndrome [14,20,21]. Furthermore, this study showed significant association between the child QoL and a variety of factors related to patients' mothers such as level of education and marital status. Our study failed to explain the reasons behind this phenomenon, however it may imply mothers provide more favorable care and support for their children.

In our results, marital status of the parents was significantly related to the quality of life of the affected child. This is also supported by the literature, family support was associated with lower depressive symptoms in addition to increased quality of life of the patients [22]. It is important to note that low quality of life is not the only negative effect that can be experienced by the patients, depression is prevalent among SCD patients. In a study that was carried in Jazan, Saudi Arabia, the prevalence of depression among sickle cell patients was 38.2% [23].Social support can be granted by family members, teachers or even close friends. However, of all the social members, family support was significantly the most effective type of social support [22]. A study from Bahrain study the marital status of the affected adults, the results were not significantly associated with quality of life. The same study, report that of many chronic conditions, patients with SCD had significantly lower quality of life [24].

This study addressed the protective factors that may influence and help patients to have better quality of life. Family support and higher levels of education already described. In addition to that, adherence to treatment that include hydroxyurea and folic acid supplement is considered an important and unignorable protective factor that should be addressed with proper education to the affected child, the family, and care giver [25]. The relation between pain and quality of life was established in the literature [26]. However, this study did not study the pain as independent factor. Another important factor is severity of the disease that could negatively affect the quality of life, and the risk increases in the presence of depression [26].

This study has utilized the PedsQL™ Sickle Cell Disease Module 16 to measure health-related quality of life (HRQoL). The tool has a total of (43) items with answers of five points Likert scale. In the current study, the outcome variable was measured by computing the responses to all the (43) items to calculate the quality of life for each participant. The

outcome measure was a percentage representing the quality of life of the patient. However, a previous studies did not report the quality of life as a percentage. Instead, they reported the items separately [27]. On the other hand, similar reports have indicated a significant regression of disease severity and parent support on the mean score of quality of life [22].

The items of the scale in this study were obligatory to be answered, this resulted in complete dataset without any missing values, which represent one strength of the study. Furthermore, previous reports regarding sickle cell disease were done in Al-Baha region, but no previous studies have reported the quality of life of SCD patients [28,29]. The limitations of this study include; cross-sectional design that may cannot establish a good prediction or temporal relations between the variables. The limited sample size in this research impeded the generalizability of the results.

4. CONCLUSION

Sickle cell disease (SCD) is a significant issue demanding care and exhausting time, efforts and costs. This study states clearly low quality of life (QoL) among SCD patients which has been shown in the majority of the study sample. Various factors showed positive association with Patients' QoL namely, high education, marital status and family support. On the other hand, absence days and night visits to the hospital were negatively associated with patients' quality of life. Further studies are essential to explore solutions and means to improve quality of life of sickle cell disease patients which consequently is going to improve the outcome and decrease the burden related to this devastating disease.

CONSENT (WHEREEVER APPLICABLE)

All authors declare that 'written informed consent was obtained from the patient for publication of this data. A copy of the written consent is available for review by the Editorial office/Chief Editor/Editorial Board members of this journal

ETHICAL APPROVAL (WHEREEVER APPLICABLE)

All authors declare that ethical approval to conduct the study was obtained from the Research and Ethics Committee (Directorate of Health Affairs, Taif, Research and Studies Department)number (HAP-02-T-067).

REFERENCES

Strouse J. Sickle cell disease. In: Handbook of Clinical Neurology. Elsevier B.V.; 2016. Accessed 5 March 2021
Available: https://pubmed.ncbi.nlm.nih.gov/27637966/.

Fu T, Corrigan NJ, Quinn CT, Rogers ZR, Buchanan GR. Minor elective surgical procedures using general anesthesia in children with sickle cell anemia without pre-operative blood transfusion. Pediatr Blood Cancer. 2005;1:7. Accessed 5 March 2021
Available: http://doi.wiley.com/10.1002/pbc.20283.

Andreadis LEDCB. Hemolytic Anemias | Current Medical Diagnosis & Treatment 2021 | AccessMedicine | McGraw-Hill Medical. Accessed 5 March 2021
Available:https://bit.ly/3e8pTJX

Al Hajeri A, Serjeant GR, Fedorowicz Z. Inhaled nitric oxide for acute chest syndrome in people with sickle cell disease. Cochrane Database of Systematic Reviews. John Wiley and Sons Ltd; 2008.Accessed 5 March 2021
Available: https://pubmed.ncbi.nlm.nih.gov/18254121/.

Wastnedge E, Waters D, Patel S, Morrison K, Goh MY, Adeloye D, et al. The global burden of sickle cell disease in children under five years of age: A systematic review and meta-analysis. J Glob Health. 2018;8:2. Accessed 5 March 2021
Available: http://jogh.org/documents/issue201802/jogh-08-021103.pdf.

World Health Organization. Sickle-Cell Disease: A Strategy for the WHO African Region. Report of the Regional Director. 2010.Accessed 5 March 2021
Available:https://apps.who.int/iris/handle/10665/1682.

Wilson M, Forsyth P, Whiteside J. Haemoglobinopathy and sickle cell disease. Contin Educ Anaesthesia, Crit Care Pain. 2009.Accessed 5 March 2021
Available from: https://academic.oup.com/bjaed/article/10/1/24/266308.

El-Hazmi MAF, Al-Hazmi AM, Warsy AS. Sickle cell disease in Middle East Arab countries. Vol. 134, Indian Journal of Medical Research. Indian Council of Medical Research; 2011.Accessed 5 March 2021.
Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3249957/.

Jastaniah W. Epidemiology of sickle cell disease in Saudi Arabia. Vol. 31, Annals of Saudi Medicine. King Faisal Specialist Hospital and Research Centre; 2011. Accessed 5 March 2021
Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3119971/.

AlHamdan NAR, AlMazrou YY, AlSwaidi FM, Choudhry AJ. Premarital screening for thalassemia and sickle cell disease in Saudi Arabia. Genet Med. 2007:6.Accessed 5 March 2021.
Available: https://pubmed.ncbi.nlm.nih.gov/17575503/.

Al-Qurashi MM, El-Mouzan MI, Al-Herbish AS, Al-Salloum AA, Al-Omar AA. The prevalence of sickle cell disease in Saudi children and adolescents. A community-based survey. Saudi Med J. 2008;29:10. Accessed 5 March 2021.
Available: http://www.ncbi.nlm.nih.gov/pubmed/18946577.

Memish ZA, Saeedi MY. Six-year outcome of the national premarital screening and genetic counseling program for sickle cell disease and -thalassemia in Saudi Arabia. Ann Saudi Med. 2011:5Accessed 5 March 2021.
Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3119961/.

WHO. WHOQOL - Measuring Quality of Life| The World Health Organization. WHO. 2012.Accessed 5 March 2021.
Available: https://www.who.int/toolkits/whoqol.

Panepinto JA, O'Mahar KM, DeBaun MR, Loberiza FR, Scott JP. Health-related quality of life in children with sickle cell disease: Child and parent perception. Br J Haematol. 2005:8.Accessed 5 March 2021.
Available: https://pubmed.ncbi.nlm.nih.gov/16042695/.

Varni JW, Seid M, Kurtin PS. PedsQL™ 4.0: Reliability and Validity of the Pediatric Quality of Life Inventory™ Version 4.0 Generic Core Scales in Healthy and Patient Populations. Med Care. 2001:8.Accessed 5 March 2021.
Available: https://pubmed.ncbi.nlm.nih.gov/11468499/.

Behrman RE, Vaughan III VC. Nelson textbook of pediatrics.12th ed.WB Saunders company; 1983.

Pereira SA dos S, Brener S, Cardoso CS, Carneiro Proietti AB de F. Sickle cell disease: Quality of life in patients with hemoglobin SS and SC disorders. Rev Bras HematolHemoter. 2013.Accessed 5 March 2021.
Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3832312/.

Alfonso P, Ferrand S. Psicología de la Salud: TemasActuales de InvestigaciónenLatinoamérica. Vol. 42, RevistaInteramericana de Psicología/Interamerican Journal of Psychology-2008. 2008. Spanish.

Seidl EMF, Zannon CML da C. Quality of life and health: conceptual and methodological issues. 2004.Accessed 5 March 2021.
Available:https://bit.ly/3soCBt6.

Platt OS, Brambilla DJ, Rosse WF, Milner PF, Castro O, Steinberg MH, et al. Mortality In Sickle Cell Disease -- Life Expectancy and Risk Factors for Early Death. N Engl J Med. 1994:6. Accessed 5 March 2021.
Available: http://www.nejm.org/doi/abs/10.1056/NEJM199406093302303.

Miller AC, Gladwin MT. Pulmonary Complications of Sickle Cell Disease. Am J Respir Crit Care Med. 2012:6. Accessed 5 March 2021.
Available: http://www.atsjournals.org/doi/abs/10.1164/rccm.201111-2082CI.

Sehlo MG, Kamfar HZ. Depression and quality of life in children with sickle cell disease: the effect of social support. BMC Psychiatry. 2015:12. Accessed 5 March 2021.
Available: http://bmcpsychiatry.biomedcentral.com/articles/10.1186/s12888-015-0461-6.

Abushagah TM, Alsomaili M, Solan YO, Marran NM, Masmali AM, . Prevalence of Depression Among Sickle Cell Anemia Patients in Jazan, Saudi Arabia. Int J Med Dev Ctries. 2019;3:9. Accessed 5 March 2021.
Available: https://ijmdc.com/?mno=24471.

Ali E, Ch B, Alhalwachi FF, Khalil F, Ch B, Ali E. Health-Related Quality of Life in Adults with Sickle Cell Disease in the Kingdom of Bahrain (FPRP). 2017;14:3.Accessed 5 March 2021.
Available: http://scholarsmepub.com/wp-content/uploads/2017/02/SJM-213-14_last.pdf.

Al Jaouni SK, Al Muhayawi MS, Halawa TF, Al Mehayawi MS. Treatment adherence and quality of life outcomes in patients with sickle cell disease. Saudi Med J. 2013:3.Accessed 5 March 2021.
Available: http://www.ncbi.nlm.nih.gov/pubmed/23475090

Pandarakutty S, Murali K, Arulappan J, Al Sabei SD. Health-Related Quality of Life of Children and Adolescents with Sickle Cell Disease in the Middle East and North Africa Region. Sultan Qaboos Univ Med J [SQUMJ]. 2020:12. Accessed 5 March 2021.
Available from: https://journals.squ.edu.om/index.php/squmj/article/view/3936.

Alharbi E, Alamri R, AlJerayan E, Salawati H, AlMjershi S. Quality of life assessment for children with sickle cell disease (SCD) in Mecca region. Int J Med Sci Public Heal. 2016:5. Accessed 5 March 2021.
Available: http://www.scopemed.org/fulltextpdf.php?mno=211155.

Ahmed A, Abdelkarim A, Alzahrani T, Alshahrani S, Alghamdi A, Leslom A. Incidence of avascular necrosis of the head of the femur among sickle cell patients in Albaha region, Kingdom of Saudi Arabia. Int J Med Dev Ctries. 2019:12. Accessed 5 March 2021.
Available: https://www.ejmanager.com/fulltextpdf.php?mno=79926.

Alghamdi AAM, Alamri AMA, Alghamdi AHA. Perceptions about Sickle Cell Disease among Adults in Al Baha Region : A Cross-Sectional Study. Egypt J Hosp Med. 2018:1. Accessed 5 March 2021.
Available from: http://platform.almanhal.com/MNHL/Preview/?ID=2-111582.

ABBREVIATIONS

QoL: Quality of life
HRQoL: Health related quality of life
SCD: Sickle cell disease
HbS: Hemoglobin S
SCA: Sickle cell anemia
SA: Saudi Arabia
WHO: World Health Organization
IQR: Interquartile range