

# Differences in HRQOL among Children with SCD Who Received Hydroxyurea and Those Who Did Not: A Quantitative Comparison Study

Yusra Al Nasiri<sup>1</sup>, Amal Al Sabahi<sup>2</sup>, Karima Al Hanai<sup>2</sup>, Mohammed Al Hanai<sup>2</sup>, Shah Mohammed Wasifuddin<sup>2</sup>, Nawal Al Mashayki<sup>2</sup>, Mudhar Al Adawi<sup>3</sup>, Kamla Al Nassri<sup>4</sup> and Salah Al Awaidy<sup>5\*</sup>

<sup>1</sup>Oman College of Health Sciences, Ministry of Health, Muscat, Oman

<sup>2</sup>Department of Pediatric Hematologist Oncologist, National Oncology Centre Royal Hospital, Ministry of Health, Muscat, Oman

<sup>3</sup>Department of Nurse Affairs, Royal Hospital, MOH, Muscat, Oman

<sup>4</sup>Intensive Care Unit, Sultan Qaboos University Hospital, Muscat, Oman

<sup>5</sup>Ex Ministry of Health, Muscat, Oman

*Received: 19 February 2025*

*Accepted: 14 May 2025*

\*Corresponding author: [salah.awaidy@gmail.com](mailto:salah.awaidy@gmail.com)

DOI 10.5001/omj.2025.72

## Abstract

**Introduction:** Hydroxyurea has been recommended for patients with sickle cell disease. It reduces the complications from the disease by increasing the production of fetal hemoglobin. Hydroxyurea is not always prescribed to children with SCD in Oman, and not much research has been done to compare the Health-Related Quality of Life (HRQOL) of children with SCD who are prescribed hydroxyurea. Thus, this study examined HRQOL differences between children with Sickle cell disease who received hydroxyurea and those who did not.

**Methods:** A cross-sectional investigation was conducted on children recruited from a hematology clinic at a tertiary hospital in Oman. We collected the data using two questionnaires: HRQOL-SCD and HRQOL-Generic. A one-way ANOVA was conducted.

**Results:** A total of 74 children (Male = 47%, Female = 53%) completed the questionnaire; 33 children were on hydroxyurea and 41 were not taking the drug. The findings elicited a significant difference in the HRQOL scores between the children who were receiving hydroxyurea and those who were not taking the drug [ $F(1.68) = 419.4$ ,  $p$ -value = .001]. The regression analysis revealed that hydroxyurea appeared a significant predictor for the improvement of HRQOL among children with SCD. The  $R^2$  of .87 showed that 87% of the variability in the child-reported HRQOL-GENERIC, was explained by parental familiarity, self-efficacy, child age, sex, and receiving hydroxyurea,  $R^2 = .87$ ,  $F(8, 69) = 52.4$ ,  $p$ -value < .001.

**Conclusions:** The results showed that hydroxyurea improved the children's HRQOL compared to those who did not receive the drug. These findings support the use of the hydroxyurea in children to improve their HRQOL and reduce vaso-occlusive episodes. We recommend enhancing parents' understanding of

the significance of hydroxyurea and devising strategies to promote children's medication adherence. It is important to modify the SCD management protocol to optimize the HRQOL among children with SCD.

**Keywords:** Sick cell disease; SCD; children; Hydroxyurea; Health Related Quality Of Life; HRQOL; Oman

## Introduction

Sickle Cell Disease (SCD) is a blood disorder known as hemoglobinopathies. This disorder causes lifelong morbidities and is associated with many complications affecting different body systems.<sup>1</sup> In SCD, red blood cells that are shaped like crescents tend to block the flow of blood to tissues, leaving them without enough oxygen.<sup>2,3</sup> The main genetic constitutions of SCD are hemoglobin SS (HgbSS), which is the most severe form; hemoglobin SC (HgbSC); and hemoglobin S beta thalassemia (HgbSβ). SCD affects millions of individuals around the globe. Globally, the meta-estimate for the birth prevalence of SCD is approximately 112 per 100,000 live births. The higher prevalence was reported in Africa with 1,125 per 100,000 live births and Europe with an estimation of 43.12 per 100,000 live births. The number of individuals living with sickle cell disease globally rose from approximately 5.46 million in 2000 to about 7.74 million in 2021, marking a 41.4% increase. While the total number of neonates diagnosed with sickle cell disease increased globally by 13.7%, reaching approximately 515,000 births annually due to population growth in regions such as the Caribbean and western and central sub-Saharan Africa.<sup>4</sup> These statistics illustrate the critical global burden of sickle cell disease on children, which highlights the need for targeted health interventions and evaluates the current management protocols.<sup>5</sup> In the United States of America, according to the SCD Association, it is estimated that 70,000 to 100,000 persons in the US have SCD, and 3 million carry the trait form of the disease.<sup>6</sup> SCD mainly affects individuals of the African American ethnic group. According to the Centers for Disease Control and Prevention (CDC), 1 in 500 African Americans and 1 in 36,000 Hispanic Americans are born with SCD each year, and 1 in 13 African Americans are born with sickle cell trait.<sup>6</sup>

SCD in Oman is a common genetic blood disorder that increases the mortality and morbidity rates in the country.<sup>7</sup> According to the *Ministry of Health Annual Health Report 2020*, a total of 309 annually diagnosed school-age children and 286 newly diagnosed preschool children. This could be due to the consanguinity marriages in the country.<sup>8</sup> In Oman, the birth prevalence of sickle cell trait is 6%, while beta-thalassemia is 2%. The prevalence of sickle cell is 0.2%; which contributes to high mortality rates in children aged five and morbidity years.<sup>9</sup> For children below the age of 5 years, there were more than 81000 deaths compared to 40 for cause-specific sickle cell disease mortality across other causes estimated by the GBD in 2021.<sup>4</sup> Given this huge burden, sickle cell disease management and investigation need to be incorporated into the currently available health surveillance systems and aim to direct the resources to screen, improving access to treatment such as hydroxyurea and prevention.<sup>4</sup>

Sickle Cell Disease leads to various complications that affect the Health Related Quality of Life (HRQOL) in children. HRQOL is a significant patient-reported consequence in children and provides a detailed concept of SCD burden on children with SCD. Moreover,<sup>10</sup> HRQOL is a significant predictor of morbidity and mortality consequences. One of these complications is a vaso-occlusive crisis, which is characterized by sharp and intense pain.<sup>11</sup> Vaso-occlusive pains occur around six times per year in children with SCD, and this pain may last up to four days.<sup>12,13</sup>

These painful episodes differ in prevalence and intensity.<sup>14</sup> Managing these painful episodes mainly starts in patients' homes, and sometimes, patients need hospital admission if the pain is persistent.<sup>14</sup> Vaso-occlusive painful episodes typically manifest as pain in the chest, back, or lower or upper limbs.<sup>13</sup> Extreme cold or hot environments, dehydration, the presence of other illnesses, and stress trigger these events.<sup>15</sup> Due to frequent vaso-occlusive pain events, children with SCD tend to have lower baseline HRQOL than healthy children.<sup>15,16</sup> SCD varies in severity (mild to severe); therefore, children with the more severe type of sickle cell usually present with worse HRQOL than those with the mild disease form.

Penicillin and blood transfusions are the usual treatments for children with SCD.<sup>15</sup> Recently, experts have recommended hydroxyurea drug therapy for patients with SCD. Hydroxyurea is the option for treating sickle cell patients that is promising in reducing the complications from the disease.<sup>17</sup> Even though this medicine doesn't cure the disease, it does help make fetal hemoglobin (Hb F), which improves circulation and lowers the number of vaso-occlusive events.

Research has found that the use of hydroxyurea is associated with improvements in HRQOL.<sup>15</sup> Hydroxyurea has been studied and found to reduce chest syndrome episodes, painful crises, and the need for frequent blood transfusions or hospital stays.<sup>10</sup> Moreover, hydroxyurea could delay spleen infarction, kidney, lung, or even brain damage. It was found that the hydroxyurea drug could help the red blood cells remain stable and more flexible. Therefore, the red blood cells flow easily, even in tiny vessels. This occurs because hydroxyurea raises the level of fetal hemoglobin (Hb F), and therefore, red blood cells do not change to a crescent shape. Thus resulting in fewer complications of the disease and better HRQOL of children with SCD.<sup>7,10,15</sup>

Research has suggested that children who were put on hydroxyurea became stable and quite asymptomatic, which decreased the burden of the disease among families and positively impacted the children's HRQOL. A cross-sectional study was conducted among children from 3 to 18 years old to assess HRQOL in children with sickle cell disease.<sup>18</sup> Children in this study rated their HRQL less than their parents but with no significant difference, except for social functioning ( $p = 0.047$ ). Recruitment of children was done at hematology clinics, and they were requested to fill out the PedsQL survey. This study presented a significant difference ( $p < .001$ ) in the total score of HRQOL of children who were taking the treatment on a daily basis (HRQOL score *median* = 75, IQR = 62.0-86.4) and those who were not taking the treatment (HRQOL score *median* = 69.0, IQR 54.1- 81.6). The study also proved that physical activities were significantly less when compared with those who did not start hydroxyurea (*median* = 71.4, *Inter range Range IQR*= 58.6,  $p < .001$ ) than in children who were on hydroxyurea (*Median*= 79.7, IQR = 62.5).<sup>17</sup> The non-users had several interferences with school attendance and lower scores in the physical domain compared to children who were adherent to hydroxyurea drug.<sup>17</sup> children who did not use hydroxyurea had frequent pain crisis and complications that interfered with regular school attendants.<sup>17</sup>

Similarly, a qualitative study on medication adherence among children was conducted and included ten children and adolescents in the interview.<sup>19</sup> The study found that children had some memory lapses, lacked self-management, and encountered barriers in their social life. This highlighted that the HRQOL is affected among children with sickle cell disease. The researchers concluded that SCD children experience several barriers to medication adherence and that urges the necessity for a comprehensive treatment plan to analyze the children's issues around medication adherence which results in better HRQOL.

A cross-sectional study in Saudi Arabia aimed to examine the impact of hydroxyurea drug among children.<sup>1</sup> The study concluded that, those who have low adherence to hydroxyurea perceive higher benefits in disease control (mean  $\pm$  SD =  $5.77 \pm 2.99$ ).<sup>1</sup> Another three studies investigated the impact of Hydroxyurea adherence on the HRQOL among children with SCD.<sup>11,16</sup> The studies investigated the predictors of HRQOL in a group of children (78) who are affected with SCD ( $M$  age =11.3,  $SD$ = 3.92 years). Children completed the PedsQL during a clinic visit. The Adherence & Self-Care Inventory tool was utilized to measure treatment adherence. Results revealed that HRQOL is correlated with hydroxyurea adherence with a score of ( $R$ = .88). The adherence to hydroxyurea drug was a significant predictor for the improvement in the HRQOL scores.<sup>11,16</sup>

In Oman, not all children are prescribed hydroxyurea, and there is a limited information about the use of hydroxyurea and HRQOL among children with SCD in Oman. Therefore, additional assessment of the impact of hydroxyurea on HRQOL is deemed important to examine the impact of the drug on HRQOL among children with SCD. In addition, no similar studies have been conducted in Oman, and to our

knowledge, this is the first study in Oman of this kind. Therefore, this study sought to investigate the differences in HRQOL between children who were on hydroxyurea treatment compared to children who were not initiated with this drug in Oman. We hypothesized that HRQOL would be higher with children who are compliant with hydroxyurea therapy regardless of disease severity compared to those who have not initiated yet or are not taking the drug regularly.

## Methods

This was a cross-sectional study among school-aged children (8–12 years) who were recruited from a hematology clinic of the Royal Hospital in Oman. The head nurse of the pediatric hematology clinic recruited the children. A simple random technique selected the participants from the list of children who attended the clinic appointment. The head nurse selected the children based on even numbers on the list. We used power analysis to estimate the required sample size for the study. To estimate the optimal sample size, Slovin's formula was used  $n = Z^2(p(1-p))/M^2$  with a confidence level of 95% and  $M=0.05$ , and considering a 10% attrition rate, 74 samples were found appropriate for the study.

**Hypothesis 1a:** The HRQOL scores of children receiving hydroxyurea drug will be higher than the children who were not using the drug.

**Hypothesis 1b:** Use of Hydroxyurea will be a significant predictor of the improvement of HRQOL in children affected with SCD.

We collected the data using two questionnaires, the HRQOL-SCD and HRQOL-Generic child versions, which measure the children's HRQOL (8-12 years). The Pediatric Quality of Life Inventory Scale (HRQOL-GENERIC) included 23 items for measuring four dimensions of HRQOL. The reliability of the tool is (0.95). HRQOL-SCD is a disease-specific tool consists of 43 items with nine scales. The reliability of the tool is 0.93. Previous studies extensively used both tools to measure HRQOL among children with SCD.<sup>20,,21,22</sup>

The data analysis was done using SPSS (version 24). Frequencies, means, and standard deviations were used to describe the participants. The HRQOL scores were reversely transformed to a (0-100) scale; the higher the scores indicated better HRQOL. The reliability of all tools were examined and showed very good reliability for both tools ( $r > 0.9$ ). One-way ANOVA was run (Normality, linearity, multicollinearity, Independence of errors) were met for the analysis. ANCOVA was also done to examine the interactions between HRQOL, gender and hydroxyurea use.  $p$ -value ( $<0.05$ ) is considered significant in this study. Missing data were excluded from the analysis. Linear regression was run to identify the predictors of HRQOL, assumptions were met for the analysis.

The Ministry of Health scientific research committee granted ethical approval under the number MOH/CSR/22/25828. Before conducting the studies, we provided the children with assent form to sign. Also, an information sheet and consent form were given to the parents of those children to read and sign before the data was collected. Parents and children were informed that their participation is voluntary and they can withdraw anytime from the study. We also explained that the data will remain confidential and the tools will not identify any names. Both parents and children were given some time to decide on their participation, and only the willing participants were included in the study. Children were asked to fill in the two tools on HRQOL (child versions).

## Results

A total of 74 children (Male = 47%, Female = 53%) completed the questionnaire; 33 children were on hydroxyurea (Male = 16, Female = 17), and 41 were not taking the drug [Table 1]. A one-way ANOVA was

conducted to investigate the differences in HRQOL of children who receive hydroxyurea in comparison to those who don't receive hydroxyurea.

**Table 1:** Children's demographics

	Children (N= 74)	Mean (%)
<b>Age</b>		10 ±1.3
Means (SD) in years		35 (47)
<b>Sex</b>		39 (53)
Male		33 (45)
Female		41 (55)
On Hydroxyurea		
Not on Hydroxyurea		

The findings elicited a significant difference in the HRQOL scores [Table 2] between the children who were receiving hydroxyurea and those who were not taking the drug (HRQOL-SCD) [ $F(1,68) = 419.4$ ,  $p > 0.001$ ]. Children on hydroxyurea reported higher HRQOL scores than children who weren't ( $M=69.35$ ,  $SD=10.14$ ;  $M=51.99$ ,  $SD=7.98$ ).

**Table 2:** Mean Differences in HRQOL scores

Use of hydroxyurea (N=33)		Mean	Std. Deviation
HRQOL-SCD	On hydroxyurea	69.35	10.14
	Not on hydroxyurea	51.55	7.98
HRQOL_Generic	On hydroxyurea	68.55	11.98
	Not on hydroxyurea	61.99	14.98
Female (n=17)	on hydroxyurea	69.04	11.1
Male (n=16)	on hydroxyurea	64.75	14.07

Similarly, the findings showed a significant difference in HRQOL scores reported on the (PedsQL-generic) [ $F(1,68)=239.8$ ,  $p = .3$ ]. Children on hydroxyurea reported higher HRQOL scores than children who were not ( $M=68.55$ ,  $SD=11.98$ ;  $M=61.99$ ,  $SD=14.98$ ).

Furthermore, the study identified the predictors of HRQOL, and hydroxyurea appeared as a significant predictor for the improvement of HRQOL in children with SCD. Compliance with the hydroxyurea drug (Beta = 2.4,  $t = 1.31$ ,  $p = .2$ , partial  $\eta^2 = .16$ ) was a significant predictor of the child-reported HRQOL-GENERIC. The  $R^2$  of .87 showed that 87% of the variability in the child-reported HRQOL-GENERIC was explained by parental familiarity, self-efficacy, child age, sex, receiving hydroxyurea,  $R^2 = .87$ ,  $F(8, 69) = 52.4$ ,  $p$ -value  $< .001$  [Table 3].

**Table 3:** Predictors of HRQOL.

		Unstandardized Coefficients		Standardized Coefficients		95% CI for B		
		B	Std. Error	Beta	t	Sig.	Lower Bound	Upper Bound
Constant								
Use of hydroxyurea (HRQOL-SCD tool)		5.187	1.474	.216	3.520	.001	2.240	8.134

### Use of hydroxyurea

(PedsQL-generic tool)

2.407

1.837

.063

1.310

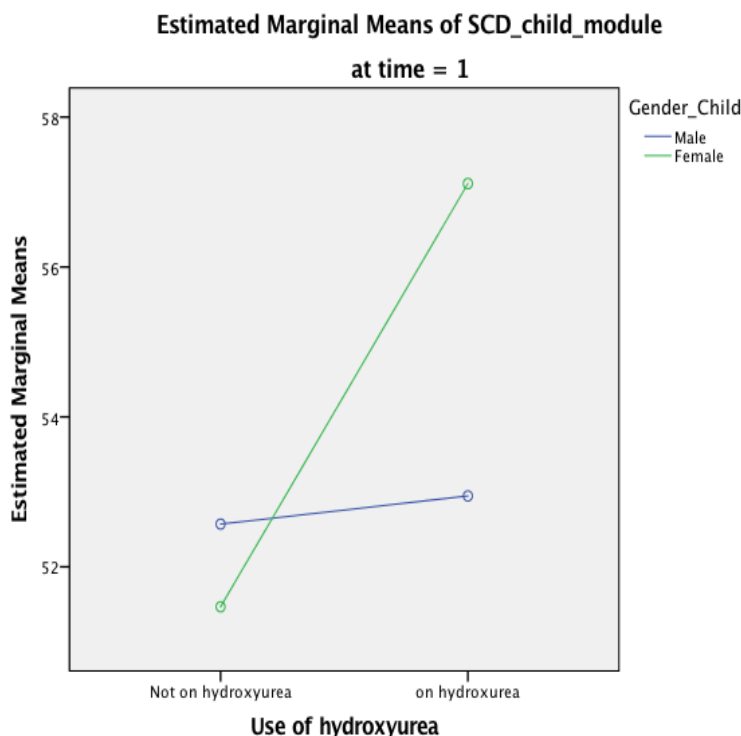
.01

-0.837

6.467

*RQOL-SCD \*\*R square: .79, F-test = 29.59 and  $p < .001$ , PedsQL-Generic \*\*R square: .87, F-test = 52.4 and  $p < .001$*

Furthermore, the use of the hydroxyurea drug appeared a significant predictor in the HRQOL-SCD disease-specific tool ( $Beta = 5.2$ ,  $t = 3.52$ ,  $p = .001$ , partial  $\eta^2 = .41$ ). The  $R^2$  of .79 indicated that 79% of the variability in the child-reported HRQOL-SCD was accounted for by parental familiarity, self-efficacy, child gender, and use of hydroxyurea,  $R^2 = .79$ ,  $F(8,69) = 29.59$ ,  $p < .001$  (Table 3). In addition, the study examined a 3-way interaction between gender, hydroxyurea, and HRQOL scores. The results showed that females on hydroxyurea reported higher HRQOL scores than male children ( $M = 69.04$ ,  $SD = 11.1$ ;  $M = 64.75$ ,  $SD = 14.07$ ); however, the difference was not significant. Figure (1) suggests a non-significant interaction between gender, hydroxyurea, and HRQOL [ $F(1,68) = 238.8$ ,  $p = .5$ ].



**Figure 1:** 3-way interactions between gender, hydroxyurea and HRQOL scores.

## Discussion

This study added to the existing body of knowledge related to HRQOL among the pediatric population with SCD. Moreover, the uniqueness of the study is that females showed higher HRQOL than their counterparts. Overall, the study emphasized what other research has found about the HRQOL of people who take their medications as prescribed, especially hydroxyurea.<sup>15,18</sup>

The results of the study indicated that children with SCD who were receiving hydroxyurea reported higher HRQOL scores than children who were not using the drug. Our findings were similar to other findings, which found that hydroxyurea users had higher QOL scores than non-users.<sup>11</sup>

The non-users had several interferences with school attendance and lower scores in the physical domain. Also, similar findings were reported in previous studies and concluded that participants with

higher hydroxyurea adherence perceived more hydroxyurea benefits and had better emotional outcomes.<sup>16</sup> The results from those studies revealed that adolescents with more negative perceptions of using hydroxyurea reported worse fatigue, pain, anxiety, and depression. Our findings showed that hydroxyurea was a significant predictor of the improvement in HRQOL. The finding is consistent with the study of other studies which identified hydroxyurea as a significant predictor for the improvement of QOL scores.<sup>22</sup> In addition, the study concluded that adherence to the hydroxyurea drug was a significant predictor for the improvement in the HRQOL scores.<sup>22</sup>

The finding has demonstrated that the use of hydroxyurea is associated with improvements in HRQOL. It was found that hydroxyurea treatment increases the amount of fetal hemoglobin (Hb F), and therefore, red blood cells are less likely to change into the sickle shape. This, in turn, leads to fewer complications of the disease and improves the Health-Related Quality of Life (HRQOL) of children with Sickle Cell Disease (SCD).<sup>23,24</sup> Furthermore, the study findings revealed that females on hydroxyurea reported higher HRQOL scores than male children, but the difference was not significant. The explanation of higher scores of HRQOL by females could be linked to higher adherence of females to drugs. However, it is unclear why the direction of the association between gender and hydroxyurea intake appeared.

The study was a cross sectional investigation and the data was collected only at one point in time. The study had a small sample size; which limits the generalization of the findings. In addition, we did not measure medication adherence of children to hydroxyurea drug and did not evaluate the health care utilization for SCD patients, number of visits, and hospitalization to be able to correlate it with the use of hydroxyurea.

It is recommended to conduct a primary randomized controlled trial study to investigate the effect of the hydroxyurea drug on HRQOL, healthcare application, visits, hospitalization, Hgb-F production, and disease complications. It is also recommended to recruit a larger sample size in future studies. Future studies should also measure medication adherence and identify barriers to adherence.

Findings elicited that the use of hydroxyurea was associated with an improvement in HRQOL; children with SCD who were compliant with hydroxyurea reported higher HRQOL scores than children who were not using the drug. Hydroxyurea treatment results in fewer complications of the disease and better HRQOL in children with SCD. Therefore, we recommend enhancing parents' understanding of the significance of hydroxyurea and devising strategies to promote children's medication adherence. It is recommended to include in the SCD management protocol that all children with SCD take hydroxyurea drugs to reduce disease complications and improve their HRQOL.

## **Author contributions**

All authors read and approved the final manuscript.

## **Funding**

No funds used to produce this manuscript

## **Availability of data and materials**

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

## Ethics approval and consent to participate

As this manuscript contains no identifiable information, the need for ethics approval was waived. Written informed consent was obtained from the patient guardian (one of the parents) and assent form was taken from the children who participated in the study.

## Competing interests

The authors have declared no competing interests.

## References

1. Madkhali MA, Abusageah F, Hakami F, Zogel B, Hakami KM, Alfaifi S, et al. Adherence to hydroxyurea and patients' perceptions of sickle cell disease and hydroxyurea: A cross-sectional study. *Medicina (Kaunas)* 2024 Jan;60(1):124.
2. Panepinto JA, Torres S, Varni JW. Health-related quality of life in children and adolescents with sickle cell disease: A systematic review. *Pediatr Blood Cancer* 2019;66(11):277-289.
3. Green NS, Smaldone A, Simon LE, Oyeku SO, Lobner K, O'Brien SH, et al. Greater barriers to hydroxyurea associated with poorer health-related quality of life in youth with sickle cell disease. *Blood* 2018;••:132.
4. Thomson AM, Kassebaum NJ, Nicholas M, Naghavi M, McHugh S; GBD 2021 Sickle Cell Disease Collaborators. Global, regional, and national prevalence and mortality burden of sickle cell disease, 2000-2021: a systematic analysis from the Global Burden of Disease Study 2021. *Lancet Haematol* 2023 Aug;10(8):e585-e599.
5. Wastnedge E, Waters D, Patel S, Morrison K, Goh MY, Adeyoye 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 Dec;8(2):021103.
6. Centers for Disease Control and Prevention. What is sickle cell disease? | CDC. 7 [cited 2022 August 18]. Available at: <https://www.cdc.gov/ncbddd/sicklecell/facts.html>.
7. Al Nasiri YA, Al Mawali AH. Health-related quality of life in children with sickle cell disease: A concept analysis. *J Contemp Med Sci* 2019;5(1):59-63 .
8. Ministry of Health. Annual health report 2020: Annual health report 2020. 7 [cited 2024 Jan 28]. Available at: [https://www.moh.gov.om/en/web/statistics/annual-reports/-/asset\\_publisher/aQdmeIpTn5pS/content/-2-22?inheritRedirect=false&redirect=https%3A%2F%2Fwww.moh.gov.om%2Fen%2Fweb%2Fstatistics%2Fannual-reports%3Fp\\_p\\_id%3D101\\_INSTANCE\\_aQdmeIpTn5pS%26p\\_p\\_lifecycle%3D0%26p\\_p\\_state%3Dnormal%26p\\_p\\_mode%3Dview%26p\\_p\\_col\\_id%3Dcolumn-2%26p\\_p\\_col\\_count%3D1](https://www.moh.gov.om/en/web/statistics/annual-reports/-/asset_publisher/aQdmeIpTn5pS/content/-2-22?inheritRedirect=false&redirect=https%3A%2F%2Fwww.moh.gov.om%2Fen%2Fweb%2Fstatistics%2Fannual-reports%3Fp_p_id%3D101_INSTANCE_aQdmeIpTn5pS%26p_p_lifecycle%3D0%26p_p_state%3Dnormal%26p_p_mode%3Dview%26p_p_col_id%3Dcolumn-2%26p_p_col_count%3D1).
9. Wali Y, Kini V, Yassin MA. Distribution of sickle cell disease and assessment of risk factors based on transcranial Doppler values in the Gulf region. *Hematology* 2020 Dec;25(1):55-62.
10. Elendu C, Amaechi DC, Alakwe-Ojimba CE, Elendu TC, Elendu RC, Ayabazu CP, et al. Understanding Sickle cell disease: Causes, symptoms, and treatment options. *Medicine (Baltimore)* 2023 Sep;102(38):e35237.
11. Tarazi RA, Patrick KE, Iampietro M, Apollonsky N. Hydroxyurea use is associated with executive functioning and nonverbal skills in young children with sickle cell disease (SCD). *Authorea* 2020 .
12. Di Maggio R, Hsieh MM, Zhao X, Calvaruso G, Rigano P, Renda D, et al. Chronic administration of hydroxyurea (HU) benefits Caucasian patients with sickle-beta thalassemia. *Int J Mol Sci* 2018 Feb;19(3):681.
13. Ballas SK. How I treat acute and persistent sickle cell pain. *Mediterr J Hematol Infect Dis* 2020 Sep;12(1):e2020064.
14. Gollamudi J, Karkoska KA, Gbotosho OT, Zou W, Hyacinth HI, Teitelbaum SL. A bone to pick-cellular and molecular mechanisms of bone pain in sickle cell disease. *Front Pain Res (Lausanne)* 2024 Jan;4:1302014.
15. Sendy JS, Alsadun MS, Alamer SS, Alazzam SM, Alqurashi MM, Almudaibigh AH. Frequency of painful crisis and other associated complications of sickle cell anemia among children. *Cureus* 2023 Nov;15(11):e48115.



16. Mwazyunga Z, Ambrose EE, Kayange N, Bakalemwa R, Kidenya B, Smart LR, et al. Health-related quality of life among children with sickle cell anaemia in Northwestern Tanzania. *Open J Blood Dis* 2022 Jun;12(2):11-28.
17. Bailey M, Bonner AD, Brown S, Thompson M. PRO91 reduction in HRQOL with increasing VOC frequency among patients with SCD. *Value Health* 2020;23:S345 .
18. Kuriri FA. Hope on the horizon: New and future therapies for sickle cell disease. *J Clin Med* 2023 Sep;12(17):5692.
19. Abadesso C, Pacheco S, Machado MC, Finley GA. Health-related quality of life assessments by children and adolescents with sickle cell disease and their parents in Portugal. *Children (Basel)* 2022 Feb;9(2):283.
20. Curtis K, Lebedev A, Aguirre E, Lobitz S. A medication adherence app for children with sickle cell disease: Qualitative study. *JMIR Mhealth Uhealth* 2019 Jun;7(6):e8130.
21. Sousa KH, Kwok OM. Putting Wilson and Cleary to the test: analysis of a HRQOL conceptual model using structural equation modeling. *Qual Life Res* 2006 May;15(4):725-737. .
22. Al Sabbah M, Mohamed M, Kamal A, et al. Is Hydroxyurea Treatment Changing the Life of Children with Sickle Cell Disease? *Dubai Med J*. 2023;6(4):301-309 .
23. Badawy SM, Thompson AA, Lai JS, Penedo FJ, Rychlik K, Liem RI. Health-related quality of life and adherence to hydroxyurea in adolescents and young adults with sickle cell disease. *Pediatr Blood Cancer* 2017 Jun;64(6).
24. Al Sayigh NA, Shafey MM, Alghamdi AA, Alyousif GF, Hamza FA, Alsalman ZH. Health-related quality of life and service barriers among adults with sickle cell disease in Saudi Arabia. *Ethiop J Health Sci* 2023 Sep;33(5):831-840.