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COMPREHENSIVE EVALUATION OF HYDROXYUREA TREATMENT IMPACT ON QUALITY OF LIFE IN ADULT PATIENTS WITH SICKLE CELL DISEASE AND SICKLE CELL DISEASE WITH BETA-THALASSEMIA: A DUAL ASSESSMENT USING CHQ-PF50 IN CHILDREN AND SF‑36 QUESTIONNAIRES IN ADULTS

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Abstract

Background: Sickle Cell Disease (SCD) and Sickle Cell Disease with Beta Thalassemia (BT) pose significant challenges to affected individuals due to chronic anemia and vaso-occlusive events, impacting their quality of life (QoL). Hydroxyurea has emerged as a promising therapeutic intervention, showing efficacy in managing disease severity and improving clinical outcomes in both conditions. However, the comprehensive impact of Hydroxyurea treatment on the QoL of adult patients with SCD and SCD with Beta Thalassemia remains to be fully elucidated. **Objective:** This study aims to comprehensively evaluate the influence of Hydroxyurea treatment on the QoL in adult patients with SCD and SCD with BT. The investigation includes age-specific assessments, utilizing the Child Health Questionnaire Parent Form-50 (CHQ-PF50) for pediatric evaluations and the Short Form-36 Health Survey (SF-36) for adults. **Methods:** Adult patients diagnosed with SCD and SCD with Beta Thalassemia were enrolled in the study. QoL assessments were conducted using the CHQ-PF50 for pediatric patients and the SF-36 questionnaire for adults. A comprehensive analysis was performed to examine various dimensions of QoL, including physical, emotional, and social well-being. **Results:** Initial findings indicate significant improvements in QoL dimensions among adult patients following Hydroxyurea treatment. The SF-36 questionnaire revealed enhancements in physical activity, pain management, mental health, social functioning, and overall health perception. Concurrently, pediatric assessments using the CHQ-PF50 demonstrated improvements in children's physical and emotional well-being, as reported by parents or guardians. **Conclusion:** This study contributes to our understanding of the holistic impact of Hydroxyurea treatment on the QoL in adult patients with SCD and SCD with Beta Thalassemia. The integration of age-specific assessments enables a comprehensive exploration of diverse QoL dimensions, providing valuable insights for tailored patient care strategies.

Keywords: Sickle Cell Disease, Beta Thalassemia, Hydroxyurea, Quality of Life, CHQ-PF50, SF-36.

INTRODUCTION

Sickle cell anemia is caused by a replacement of a valine residue (β6 Glu→Val) for the glutamic acid residue, which causes hemoglobin (Hb) S molecules to polymerize when oxygenated. (1). Many major health issues, such as leg ulcers, acute and chronic pain, renal failure, and vaso-occlusive crises, affect people with sickle cell

disease (SCD) (2). For those with sickle cell disease (SCD), complications are linked to noticeably shorter life spans—42 years for men and 48 years for women in the USA (3). Complications from SCD can lead to higher death rates as well as a decline in health-related quality of life (QoL), which is already quite low in this group. (4–7). According to McClish and Penberthy, people with sickle cell disease (SCD) have a lower quality of life (QoL) than people in general, and their QoL levels are most comparable to those of those receiving hemodialysis (7). Health-related quality of life demotes the impact of health status on quality of life (QoL) (5). The way people with SCD manage their illness can have an impact on their quality of life. All organ systems are impacted by SCD complications. Hence, maintaining one's health while living with sickle cell disease necessitates managing a number of drugs, such as opioids, and attending frequent hematologists and other expert appointments in addition to maintaining proper sleep patterns and hydration (2).

According to Jenerette and Murdaugh (2008), self-care is described as the practice of participating in therapeutic endeavors and proactively utilizing available resources to uphold or enhance one's health and overall quality of life." This is necessary for people to successfully manage themselves with sickle cell disease (SCD)(8). Very little research has been done on SCD self-management and self-care practices. (9,10), even though the crucial part these ideas play in affecting the quality of life for those with sickle cell disease. Reliable and rigorous metrics must be used to explore these topics in order to comprehend the intricacy of the interactions between self-care activities and QoL. Measures particular to SCD have been created for self-care and quality of life. When evaluating the effects of a condition or therapy on a child, measuring health-related quality of life (HRQL) has become more crucial as patient-centered care progresses (11,12).

Crucial elements of the experiences of individuals, such as their functional and emotional states, are recorded through HRQL evaluation. HRQL assessment has to be a crucial outcome indicator in clinical trials in order to get patients' opinions on the efficacy of therapy and to give evidence on how treatment will influence the things that patients probably care about the most. Findings from studies investigating Health-Related Quality of Life (HRQL) in children with sickle cell anemia (SCA) have not been previously disclosed or published. Since children with SCA are more likely to experience acute consequences such as stroke, pain, acute chest syndrome, and priapism, HRQL outcomes are especially important for them. Additionally, a wealth of data indicates that children with SCA frequently have low HRQL (13–15) hence demonstrating the necessity of therapeutic clinical studies targeted at enhancing these children' HRQL.

The measurement of health-related quality of life (HRQoL) is an essential patient-reported outcome that helps us understand how children with SCD live (16). It gives an evaluation of the patient's experiences with a disease, its side effects, and its medical management. The disease's broad spectrum of clinical manifestations and the frequency of hospitalization for SCD complications—mostly pain—may have a detrimental effect on patients' quality of life (QoL) (17), aside from that, modern advances in medicine have enhanced the life expectancy of SCD patients, which has heightened the need to comprehend QoL and variables predicting disease adaption (18). Generally speaking, QoL is adversely correlated with the severity of SCD (19). Hematologists and patients still face difficulties in managing sickle cell disease. Over many years of treatment advancements, patient lifespan and quality of life have

increased significantly. However, there is still a lack of acceptable understanding of the clinical consequences of psychological issues and the need for comprehensive care (20).

For SCD, hydroxyurea (HU) is the only pharmacological treatment that has been authorized. In addition to potentially reducing chronic damage to organs, it played a part in the prevention and treatment of SCD-related consequences such as painful episodes, hospital stay, transfusions, and episodes of acute chest syndrome [8–10]. Additionally, HU lowers death, increases survival, and enhances HRQoL, particularly in those with elevated fetal hemoglobin (HbF) response (21–23).

A severe illness that significantly disrupts social and educational activities, beta thalassemia major is a life-limiting and sometimes fatal disorder. Monthly blood transfusions and/or therapy for problems sometimes require children to miss school due to hospital appointments or hospitalizations. They start to lose their sense of self and grow more reliant on other people (24). Health-Related Quality of Life, or HRQoL, is often understood to be a multifaceted notion that pertains to how patients perceive the effects of their illness and treatment on their overall physical, psychological, and social functioning (25) Numerous research have examined HRQoL in patients with thalassemia, however, it is challenging to conduct direct comparisons of the results due to the various questionnaire forms that have been employed in the past (26).

SCD is a major medical condition in Dadra and Nagar Haveli, particularly affecting the tribal population that had many consanguineous marriages. This is due to the fact that SCD is an autosomal recessive disorder. As a result, this case-control study was conducted to evaluate the HRQoL dimensions among patients with SCD and SCD with BT on HU in comparison with before HU administration and to search for potential factors impacting HRQoL measurements among patients on HU. The individuals with SCD included both children and adults.

MATERIALS AND METHODS

This case‑control study was carried out on patients with SCD and SCD with Beta thalassemia (BT) who have been registered at the NAMO Medical Education & Research Institute attached to Sickle Cell Anemia Project, Shri Vinoba Bhave Civil Hospital (SVBCH), Silvassa, Dadra & Nagar Haveli (DNH) over the period from October 2022 through September 2023. The study protocol was approved by the Institutional Ethics Committee of NAMO Medical Education & Research Institute & Shri Vinoba Bhave Civil Hospital, U.T of Dadra & Nagar Haveli and Daman & Diu (Ref. No. DMHS/IEC/2016/214/4321).

This study included 688 patients, in those adults with SCD were 380 (146 males and 234 females), and adults with SCD plus BT were 109 (males 52, females 57). Children with SCD were 145 (males 79 and 66 females), and children with SCD plus BT were 54 (28 males and 26 females). The short-form health survey 36 version 2 (SF-36 v2) was used to evaluate the HRQoL of people. The Child Health Questionnaire-Parent Form (CHQ-PF50) is utilized for evaluating the health of pediatric patients.

Screening of sickle cell anemia

Initially, sickle cell anemia was screened for using the sickling slide test. A pH 8.6 alkaline medium agarose gel Hb electrophoresis will be performed on those who test positive. In accordance with accepted procedures, sickle cell disease [codon 6

(GAG>GTG) mutation] will be confirmed with the Amplification Refractory Mutation System-Polymerase Chain Reaction (ARMS-PCR) (27,28). Additionally, High-Performance Liquid Chromatography (HPLC) was used to confirm sickle cell illness.

Participants must meet the following requirements in order to be considered for inclusion: they must be free from handicapping conditions, have been diagnosed with sickle cell disease (SCD), and enrolled at SVBCH; they must also be between the ages of 5 and 12 (considered child groups), and over 12 (who was regarded adult groups) for the purposes of employing different instruments. Since continuous blood transfusions are seen to be a disease-modifying treatment, patients receiving them regularly were not allowed to participate in the investigation (29–31). Children who had any ongoing physical ailments or health-related issues over the previous four weeks of data collection were also not included (32).

Hydroxyurea therapy

For patients receiving HU, the date of HU initiation, the HU dosage (mg/kg), and the daily total dose were noted. Every four weeks, patients in HU are checked on at the SVBCH outpatient hospital settings and the laboratory workup was completed there as well. The mean Hb before and after a year of HU treatment, as well as the HPLC results at the time of diagnosis, was noted.

Follow-up

Every four weeks, patients in HU are checked on at the SVBCH outpatient clinic, and the laboratory workup is carried out. The mean Hb before and after a year of HU treatment, as well as the HPLC results at the time of diagnosis, was noted. The HbF levels were reported as absolute values in g/dl. The HRQoL Data were collected by direct interview with patients and/or one of their parents who have consulted the SVBCH for routine follow‑up. Prior to their enrollment in the trial, each subject provided their informed written consent.

Methods

At the study's commencement, all eligible patients or their parents received information regarding the study's objectives, with a guarantee of confidentiality for all collected information. Upon obtaining signed, written informed consent from patients or their parents, the following data were collected: (1) Demographic and clinical characteristics of both pediatric and adult patients, utilizing the Case Report Form and Demographic Data Collection Form, and (2) the health status of pediatric patients, assessed through the Child Health Questionnaire‑Parent Form (CHQ‑PF50) (33) Assessing the quality of life in adult patients was conducted using the Short Form‑36 Life Quality Survey (SF‑36) (34).

The Questionnaire on Child Health The Health-Related Quality of Life (HRQOL) of children is evaluated using Parent Form-50 (CHQ-PF50), which is filled out by the parents- Overall health, physical capabilities, emotional and behavioral role/social limitations, physical role/social limitations, discomfort or pain in the body, behavior, and overall behavioral patterns, emotional state, self-esteem, general health state, health transition, parent impact-emotional, parent impact-time, family activities, and family cohesion are among the 50 items on this form that are divided into 15 subscales (33).

The items in this study were scored, and the scores obtained were converted to a scale with a range of 0 to 100. Better health is indicated by higher scores on this measure. Physical and mental health are the two main subjective health categories that are evaluated by the self-administered generic questionnaire known as the SF-36. Eight topics are covered by the 36 multiple-choice questions in this questionnaire: (1) physical functioning; (2) physical role limitation; (3) pain; (4) mental health; (5) emotional role limitation; (6) social functioning; (7) vitality; and (8) general health perspective. There are 36 questions in total. A separate question on SF-36 assesses health transition within the previous year. All language variations of the SF-36 are fully documented in terms of their validity and reliability (34,35). In this study, each SF-36 item's response was evaluated, and total scores were calculated using a set scoring procedure. For each of the eight health concepts, these scores were then shown on a scale from 0 to 100. Higher scores indicate that the person has a more positive opinion of their health.

Statistical analysis

The data were managed and analyzed utilizing Statistical Packages for the Social Sciences (SPSS) version 2. Descriptive statistics were employed for qualitative variables, expressed as numbers and percentages. For quantitative variables related to the health status of both pediatric and adult patients, mean ± standard deviation (SD) values were used for description.

The independent t-test facilitated the quantitative comparison between two means from distinct samples, while the Paired Sample t-test was applied to assess the means of two variables within the same sample. Univariate analysis was employed to explore the correlation between patient characteristics and SF-36 v2 scores. Statistical significance was considered at $P < 0.05$.

RESULTS

Disease‑related factors

In this investigation, HU therapy patients reported a substantial reduction in the frequency of acute painful episodes as compared to pre-HU therapy. Patients with Sickle Cell Disease (SCD) and SCD with beta-thalassemia showed substantial increases in mean hemoglobin (Hb) and hemoglobin F (Hb F) levels after receiving therapy with hydroxyurea (HU), for both adult and pediatric populations. In pediatric patients with SCD and SCD with Beta Thalassemia, the mean Hb levels showed a notable increase from baseline levels following HU therapy [(t (379) = 24.18, p=0.00001, (t (379) = 70.41, p=0.00001) respectively]. Similarly, there was a significant elevation in mean Hb F levels post-treatment compared to baseline [(t (379) = 11.07, p=0.00001, (t (379) = 36.41, p=0.00001) respectively] (Figure 1).

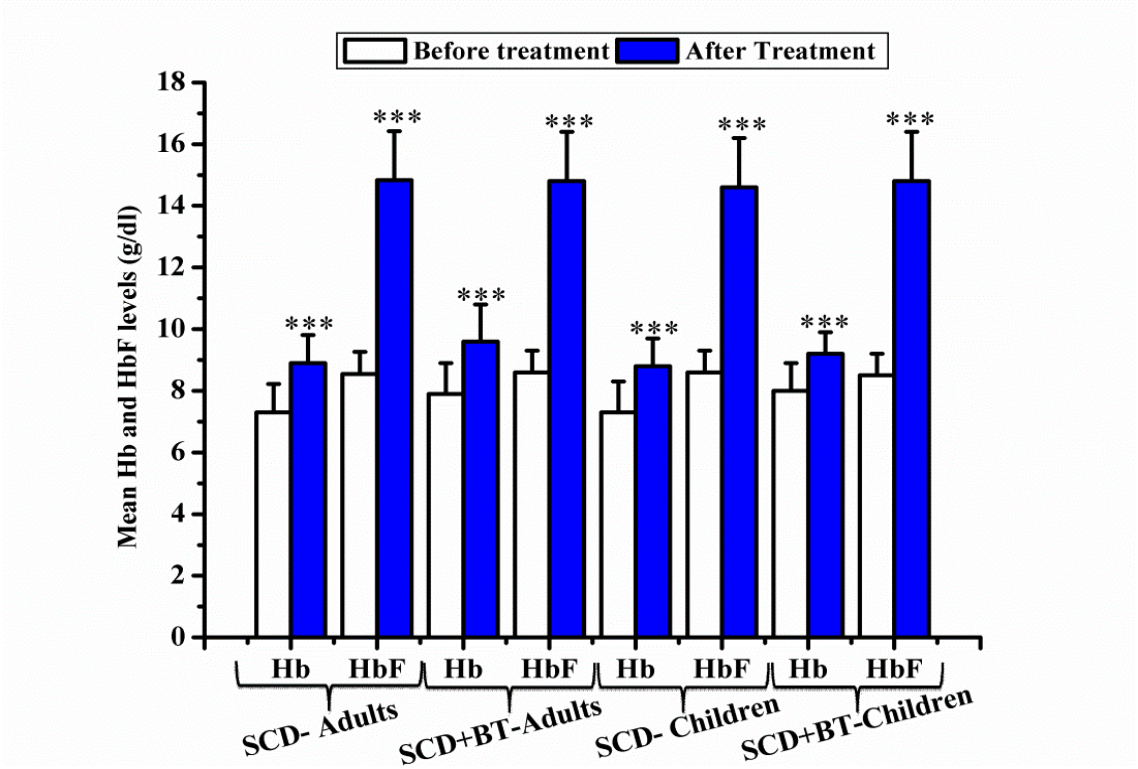

Figure 1: Hematological variables of patients with sickle cell disease, SCD with BT, in both adults and children. The statistically significant differences are shown by superscripted stars (*). ** = P <0.01, * = P <0.05, and *** = P < 0.001.

Adult patients with SCD and SCD with Beta Thalassemia also demonstrated substantial improvements in mean Hb levels after receiving HU therapy [(t (379) = 14.16, p=0.00001, (t (379) = 40.75, p=0.00001). Furthermore, the mean Hb F levels exhibited a significant increase post-treatment compared to baseline values [(t (379) = 7.82, p=0.00001, (t (379) = 26.84, p=0.00001). These findings underscore the efficacy of HU therapy in stimulating Hb and Hb F production, contributing to improvements in hematological parameters in both pediatric and adult patients with SCD and SCD with Beta Thalassemia (Figure 1).

Impact of Hydroxyurea on the quality of life of pediatric sickle cell anemia patients

CHQ-PF50 summary scores were significantly increased in the domains of General health, Physical functioning were significantly [t (144) = 4.2, p= 0.000017), t (144) = 2.5, p= 0.004906) respectively] increased after administration of hydroxyl urea. Both emotional and physical social limitations were substantially [t (144) = 2.7, p= 0.003396), t (144) = 2.6, p= 0.004005) respectively] reduced in the patents on hydroxyurea treatment. Bodily pain and discomfort severity and frequency were considerably [t (144) = 1.4, p= 0.072835, t (144) = 5.7, p= 0.00001) respectively] reduced after treatment than before. The global behavior, Emotional state, Self-esteem, and Health transition increased significantly [t (145) = 5.2, p= 0.00001, t (144) = 5, p= 0.00001), t (144) = 4.6, p= 0.00001, t (144) = 4.6, p= 0.00001) respectively] in patients on hydroxyl urea treatment than before the treatment. Parent emotional impact was significantly [t (144) = 5.1, p= 0.00001)] higher, and time spent on disease-related care on the child was significantly [t (145) = 6.4, p= 0.00001)] reduced after

treatment. Family activities and family cohesion were considerably [t (144) = 25, p= 0.00001), t (144) = 3.4, p= 0.000366) respectively] elevated in the SCD children after administration of hydroxyurea (Table 1).

Table 1: Mean health‐related quality of life scores of pediatric sickle cell anemia patients in relation to hydroxyurea therapy before and after treatment. Values are represented as mean ± SD.

Scale	Before Treatment (Mean ± SD)	After Treatment (Mean ± SD)	t-Value	p-Value
General Health	66.5 ± 5.8	69.4 ±5.7	4.2	0.000017
Physical functioning	78.3 ± 7.5	80.6±7.5	2.6	0.004906
Role/social limitations - emotional/behavioral	76.3 ± 8.5	73.5 ± 8.4	2.7	0.003396
Role/social limitations - physical	64.0 ± 8.2	61.3 ± 9.2	2.7	0.004005
Bodily pain/discomfort Severity	75.0 ± 5.8	73.8 ± 6.8	1.5	0.072835
Bodily pain/discomfort Severity Frequency	69.8 ± 7.1	65.5 ± 5.8	5.7	0.00001
Behavior	65.4 ± 6.5	62.1 ± 6.4	4.2	0.000014
Global behavior	60.4 ± 7.6	65.0 ± 7.5	5.2	0.00001
Emotional state	64.4 ± 5.7	67.8 ± 5.6	5	0.00001
Self-esteem	63.5 ± 5.6	66.5 ± 5.1	4.7	0.00001
General health state	62.6 ± 4.0	65.0 ± 6.2	3.9	0.000071
Health Transition	64.1 ± 5.0	66.7 ± 4.7	4.6	0.00001
Parent impact - emotional	52.9 ± 4.1	55.5 ± 4.2	5.2	0.00001
Parent impact - time	47.5 ±4.5	44.0 ± 4.9	6.5	0.00001
Family activities	72.4 ± 3.9	84.8 ± 4.3	25.5	0.00001
Family cohesion	67.6 ± 2.5	69.3 ± 5.5	3.4	0.000366

Impact of Hydroxyurea on the quality of life of pediatric sickle cell anemia with beta-thalassemia patients

The quality of life in children with SCD and beta-thalassemia was worse than the SCD alone; we assessed the same after the administration of hydroxyurea. The summary scores of CHQ‐PF50 were significantly increased in the aspects including General health and physical functioning significantly [t (53) = 4.6, p= 0.00001), t (53) = 2.5, p= 0.006407) respectively] increased after hydroxyl urea treatment. The emotional and physical social limitations were considerably [t(53) = 1.9, p= 0.026054), t(53) = 2.3, p= 0.010752) respectively] reduced in the patents on hydroxyurea treatment. The pain and discomfort severity and frequency were also considerably [t (53= 2.3, p= 0.010604, t (53) = 2.3, p= 0.00929) respectively] reduced after treatment. The global behavior, Emotional state, Self‐esteem, and Health transition were significantly increased [t (53) = 1.7, p= 0.042517, t (53) = 1.8, p= 0.037213), t (53) = 1.7, p= 0.038068, t (53) = 3.1, p= 0.00121) respectively] after treatment than before. Parent emotional impact was significantly [t (53) = 5.1, p= 0.00001)] higher, and time spent on disease-related care on the child was reduced after treatment but it was not statistically significant [t (53)= 1.4, p= 0.076945)]. Family activities and family cohesion were considerably [t (53) = 13.7, p= 0.00001), t (53) = 2.6, p= 0.005011) respectively] elevated in the SCD with beta-thalassemia children after the administration of hydroxyurea (Table 2).

Table 2: Mean health-related quality of life scores of pediatric sickle cell anemia with beta-thalassemia patients in relation to hydroxyurea therapy before and after treatment. Values are represented as mean ± SD.

Scale	Before Treatment (Mean ± SD)	After Treatment (Mean ± SD)	t-Value	p-Value
General Health	64.2 ± 3.0	66.8 ± 2.7	4.6	0.00001
Physical functioning	77.1 ± 4.8	79.5 ± 4.8	2.5	0.006407
Role/social limitations - emotional/ behavioral	66.5 ± 6.6	63.9 ± 7.1	2.0	0.026054
Role/social limitations - physical	71.8 ± 6.6	68.7 ± 7.0	2.3	0.010752
Bodily pain/discomfort Severity	68.3 ± 6.2	65.4 ± 6.5	2.3	0.010604
Bodily pain/discomfort Frequency	72.0 ± 6.7	68.7 ± 7.3	2.4	0.00929
Behavior	60.1 ± 5.8	56.8 ± 5.9	2.9	0.002448
Global behavior	69.2 ± 7.5	66.6 ± 8.0	1.7	0.042517
Emotional state	69.9 ± 8.6	66.9 ± 8.7	1.8	0.037213
Self-esteem	66.2 ± 6.5	68.5 ± 6.5	1.8	0.038068
General health state	64.2 ± 7.2	67.4 ± 7.1	2.3	0.011635
Health Transition	54.5 ± 6.6	58.3 ± 6.1	3.1	0.00121
Parent impact - emotional	54.0 ± 6.6	57.4 ± 6.4	2.7	0.004247
Parent impact - time	46.4 ± 9.9	43.7 ± 9.7	1.4	0.076945
Family activities	75.2 ± 13.9	77.8 ± 14.3	13.7	0.00001
Family cohesion	58.3 ± 10.2	61.2 ± 10.7	2.6	0.005011

Impact of Hydroxyurea on the quality of life of adult sickle cell anemia patients

The SF-36 summary scores regarding the quality of life in adult patients showed a significant difference between before the treatment and after the treatment with Hydroxyurea. The physical activity domain exhibited considerable elevation after the treatment before [t (379) = 6.4, p= 0.00001)], whereas limitations in the physical activities were reported earlier to the administration of hydroxyurea, it was significantly [t (379) = 9.89, p= 0.00001)] reduced after the treatment.

Even though Bodily pain episodes are common in SCD patients, it was reduced after the administration of HU, and they were statistically significant [t (379) = 9.87, p= 0.00001)]. Mental health, social functioning, vitality, and General health perception reported by the patients showed a significant elevation [t (379) = 8.4, p= 0.00001), t (379) = 8.2, p= 0.00001), t (379) = 9.3, p= 0.00001), t (379) = 6.6, p= 0.00001), t (379) = 5.8, p= 0.00001) respectively].

Emotional role limitation after the treatment was reported better than the before administration of HU it was shown statistical significance [t (379) = 9.87, p= 0.00001)]. The Health transition over the past year was observed better than in the past when they were not under the treatment [t (379) = 6.68, p= 0.00001)] (Figure 2).

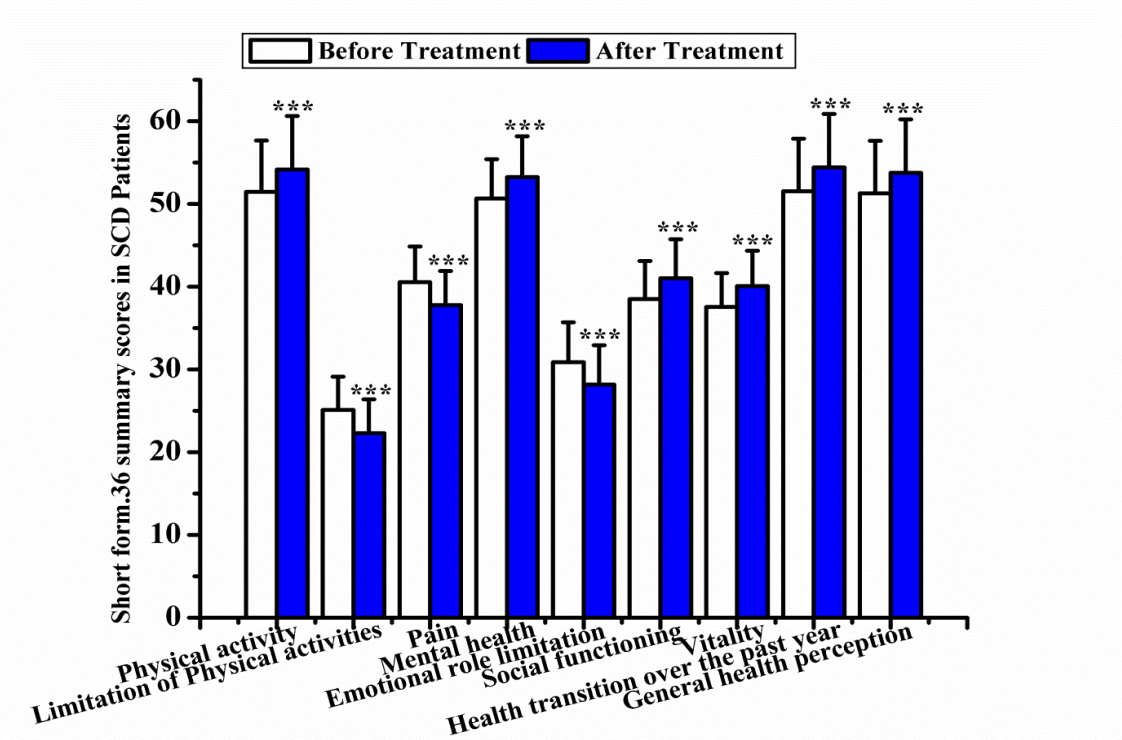

Figure 2: Mean health-related quality of life scores of Adult patients with sickle cell disease in relation to hydroxyurea therapy before and after treatment. Values are represented as mean ± SD. The statistically significant differences are shown by superscripted stars (*). ** = P <0.01, * = P <0.05, and *** = P < 0.001.

Impact of Hydroxyurea on the quality of life of adult sickle cell anemia with beta-thalassemia patients

The results of the study revealed significant improvements in SF-36 summary scores across multiple domains after Hydroxyurea treatment in adult patients diagnosed with Sickle Cell Disease (SCD) and beta-thalassemia. Participants reported increased levels of physical activity following Hydroxyurea therapy [t (108) = 2.86, p= 0.002296)]. A significant reduction in limitations related to physical activities was observed [t (108) = 7.10, p= 0.00001)].

Hydroxyurea treatment was associated with a substantial decrease in pain scores [t (108) = 7.49, p= 0.00001)]. Improved mental health outcomes were noted post-treatment [t (108) = 7.88, p= 0.00001)] (p < 0.01). Participants experienced a significant enhancement in emotional well-being [t (108) = 21.1, p= 0.00001)]. Hydroxyurea-treated individuals demonstrated improved social functioning [t (108) = 13.38, p= 0.00001)].

Increased vitality scores were observed in the study population [t (108) = 16.18, p= 0.00001)]. Participants reported positive changes in health transitions [t (108) = 15.16, p= 0.00001)]. A notable improvement in general health perception was noted [t (108) = 10.36, p= 0.00001)] (Figure 3).

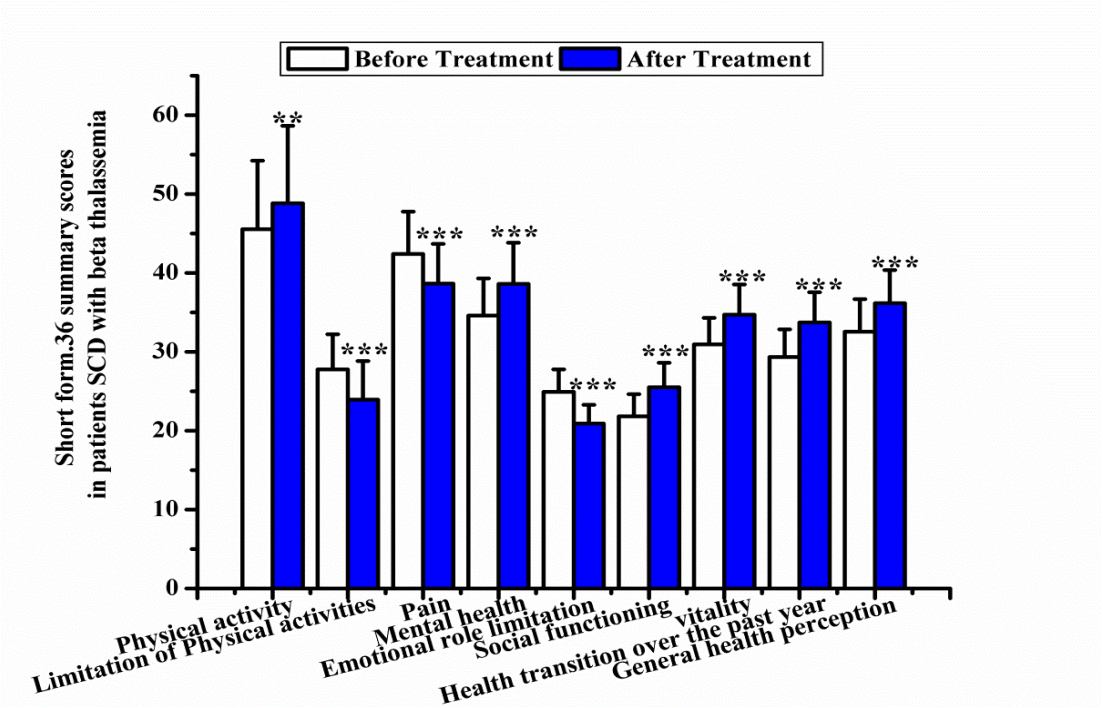

Figure 3: Mean health‑related quality of life scores of Adult patients with sickle cell disease with beta-thalassemia in relation to hydroxyurea therapy before and after treatment. Values are represented as mean ± SD. The statistically significant differences are shown by superscripted stars (*). ** = P <0.01, * = P <0.05, and *** = P < 0.001.

DISCUSSION

One of the first studies in the Dadra and Nagar Haveli (DNH) region to report the HRQoL of patients with beta-thalassemia and SCD receiving HU therapy and evaluate the impact of the treatment on all HRQoL dimensions. In this study, we measured the HRQoL of adults and children using different, suitable instruments to gather data from SCD patients. Patients with thalassemia-related SCD were shown to have superior HRQoL across all domains as compared to those who were not receiving HU treatment. Chronic disease treatment can impact a patient's biological state, psychological, social, and economic well-being, as well as their ability to live a longer, better life (36).

In addition, the present study aimed to comprehensively evaluate the impact of Hydroxyurea treatment on the quality of life (QoL) in adult patients diagnosed with SCD) and SCD with BT. This investigation incorporated the use of the Child Health Questionnaire Parent Form-50 (CHQ-PF50) for children and the Short Form-36 Health Survey (SF-36) for adults to provide a holistic perspective on the effectiveness of Hydroxyurea across different age groups.

HU has been approved by the US Food and Drug Administration and the European Medicines Agency as a commonly employed disease-modifying treatment for individuals with sickle cell disease (SCD) of all ages (37,38). The current study shows that after HU treatment is started, hospitalization rates for VOC and BT in patients with SCD significantly decline. Other studies from different nations observed similar findings (39–41).

The hematological effects of HU were demonstrated by alterations in HbF level and Hb concentration, which showed a substantial rise in HbF and Hb levels after HU therapy. This is consistent with research conducted in Yemen by Al-Nood et al., who discovered that even with low-dosage treatment, HU causes a rise in Hb F and Hb levels (42).

Moreover, Patel et al. found that following HU treatment, there was a substantial rise in HbF, total Hb, mean corpuscular volume, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration levels in India (39). The SF-36 v2 scores have been used as the basic instrumental tool for HRQoL evaluation for individuals with SCD. This instrument has been well-validated for different patient populations and occupations, and it can be administered by clinicians or by the patient at home (43).

The SF-36 questionnaire allows for a thorough evaluation of several factors influencing the quality of life in the adult population. Following Hydroxyurea therapy, our results show considerable improvements in a number of dimensions, including physical activity, pain, mental health, social functioning, and overall health perception.

The observed improvement in pain management and physical activity is consistent with other research that has demonstrated the protective effects of Hydroxyurea against vaso-occlusive crises, which in turn promotes greater functioning and physical activity (44,45). Enhancements in physiological parameters linked to Hydroxyurea treatment and the general decrease in disease burden might be responsible for the improvements in mental health and social functioning (7,46).

According to the study's results, HRQoL significantly improved for both adults and children with SCD and SCD with BT. This is consistent with research from Dale et al. in the USA, which showed that SCD patients had a poorer total HRQoL than their counterparts in good health (47). Adeyemo et al. in Nigeria (4) and Patel et al. in India (48) further said that SCD has a detrimental influence on the affected individuals' HRQoL and affects the physical, psychological, and emotional elements of their lives. It is widely known how HU treatment, a disease-modifying medication, affects patients' HRQoL who have sickle cell disease (29,48), It is consistent with our results that HRQoL was higher in all domains for SCD patients receiving HU compared to those not taking the medicine. Additionally, his research demonstrates an unfavorable correlation between the total HRQoL categories and the frequency of hospitalizations. Pereira et al. conducted a study in Brazil that showed the influence of pain crises, hospitalizations, and other SCD morbidities on the quality of life of these patients (19). A noteworthy association was seen between the hematological and HU variables, Hb level, Hb F, HU treatment dosages and duration, and every category of the SF-36 v2.

In the same way, Darbari et al. demonstrated that individuals with SCD who administered HU over a two-year period and who had a higher Hb F response than those with a lower HbF response were the only ones whose HRQoL improved (49). In comparison to the low-dose approach treatment, Estepp et al.'s study showed that HU doses larger than 20 mg/kg/day provided stronger protection against hospitalization for severe vaso-occlusive crisis or acute chest syndrome (50).

Mulaku et al. discovered in Kenya that HU treatment is linked to an increase in HbF level, which lowers the likelihood of hospital stays, excruciating crises, and sickling occurrences while also enhancing the quality of life (51). When evaluating the therapeutic advantages of HbF induction, it has been demonstrated that the favorable effects of HU on laboratory measures are dose-dependent and that "more is better."

Higher percentage HbF levels are usually obtained when using HU at the maximum tolerable dosage as opposed to lesser doses (52). The majority of research was conducted using cross-sectional methods to compare the HRQoL of SCD patients receiving HU with those who were not; however, this study monitored the patients and evaluated their HRQoL both before and after HU therapy. In conclusion, HU has helped SCD patients' quality of life, and this improvement has been more noticeable as treatment dose and duration have increased.

HRQOL involves several aspects which include domains related to emotional, physical, mental, and social functioning, and focuses on the impact health status has on quality of life. Supporting healthy emotional functioning is important not only to psychological well‑being but also to physical health as it may impact compliance with medical regimens. Reports were made about the significance of the CHQ-PF50 and SF-36 questionnaires, as well as the individual scale scores and the appropriate course of action for patients with SCD and thalassemia, both in children and adults (53). In this regard, in HU-administered pediatric SCD patients and SCD individuals who had BT, the greatest CHQ-PF50 scores were obtained for physical functioning (80.6±7.5, 77.8 ± 14.3) and family activities (84.8 ± 4.3, 79.5 ± 4.8).

Parents' or guardians' responses to the CHQ-PF50 questionnaire gave insightful information about the quality of life of the pediatric population. Our results show that therapy with Hydroxyurea has a favorable impact on a number of areas of children's well-being. Significant gains were shown in areas including overall health perceptions, emotional and social well-being, and physical functioning.

Children with beta-thalassemia and sickle cell disease (SCD) may encounter obstacles in their physical activities and endure limits that affect their quality of life in general. Our findings are consistent with other studies that have demonstrated Hydroxyurea's capacity to address these issues, resulting in improved physical function and less restrictions in daily activities (54,55).

Additionally, the beneficial effects on social and emotional well-being are in line with previous research, indicating that Hydroxyurea may help juvenile hemoglobinopathy patients achieve better psychosocial outcomes. The idea that early Hydroxyurea intervention can have significant impacts on the overall quality of life (QoL) of children with sickle cell disease (SCD) and beta-thalassemia is supported by the favorable influence on general health perceptions (2).

Our results add to the increasing amount of data that suggests Hydroxyurea is a useful treatment choice for improving the quality of life in adult patients with SCD and SCD with BT. The numerous benefits that have been noted highlight Hydroxyurea's capacity to treat both psychological and physical ailments, underscoring its all-encompassing influence on the general health of those suffering from these hemoglobinopathies.

CONCLUSION

In conclusion, the results of our comprehensive analysis using CHQ-PF50 in children and SF-36 in adults highlight the positive impact of Hydroxyurea treatment on the quality of life in patients with Sickle Cell Disease and Sickle Cell Disease with Beta Thalassemia across different age groups. These findings support the integration of Hydroxyurea into the standard care regimen for individuals with these

hemoglobinopathies, emphasizing the need for personalized and age-specific treatment strategies to optimize the overall well-being of patients.

Conflict of interest: None

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