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ORIGINAL RESEARCH REPORT

Improved Quality of Life of Patients With Sickle Cell Disease after Allogeneic Stem Cell Transplant: Another Indication for Transplant

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Abstract

Background: **Sickle cell disease (SCD) is frequently inherited worldwide. The severity of SCD ranges from mild to severe, and the disease involves multiple complications, including pulmonary hypertension, stroke, recurrent vaso-occlusive crises, end-organ damage, and an increased mortality risk. Allogeneic hematopoietic cell transplantation (HCT) is a potentially curative option for patients with SCD.**

Objectives of the study: **The objective was to assess the quality of life of adolescent and adult patients with SCD receiving HCT pre-and post-transplant.**

Methods: **An analytical cross-sectional study was conducted. Patients with SCD with at least one year of follow-up after HCT were interviewed to assess their quality of life pre-and post-transplant. This study was conducted at the Transplant Center of King Abdulaziz Medical City, Riyadh. The participants were identified through non-probability consecutive sampling. The FACT-G questionnaire was used to assess the quality of life domains.**

Results: **Thirty-one patients were included. The median age of the respondents was 32 ± 6.3 years, and 16 were male (51.6%). The most frequent indication for stem cell transplantation (58%) was a vaso-occlusive crisis. The mean FACT-G scores pre- and post-transplantation were 55.2 ± 18.17 and 91 ± 14.58, respectively. The mean number of annual ER visits was significantly reduced from 27.3 pre-transplant to 6.6 post-transplant (P-value = 0.006). Of the respondents, 51.6% experienced no severe complications post-transplantation, and most (93.5%) reported improved quality of life.**

Conclusion: **HCT significantly improved the quality of life of adult patients with SCD, with improvements in most FACT-G score domains. Although it was not measured by the FACT-G, the frequency of ER visits and hospital admissions were reduced significantly post-transplant, reflecting an improvement in the quality of life and a reduction in the cost of therapy for patients with SCD.**

Keywords: Quality of life, Sickle cell disease, Stem cell transplantation, Complications, Indications, Alemtuzumab, Allogeneic transplantation

1. Introduction

Sickle cell disease (SCD) is an inherited red blood cell disorder [1] with an autosomal recessive mode of inheritance and is associated with high morbidity and complication rates [2]. SCD results from a point mutation (substitution of valine for glutamic acid at position 6) in the β-globin chain gene and produces abnormal hemoglobin, hemoglobin S [3].

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SCD is a multi-system disease with various symptoms and complications [3]. Disease severity ranges from mild to severe, with multiple complications and end-organ damage [4]. Associated comorbidities and mortality in young adults are primarily due to unavoidable complications, such as recurrent vaso-occlusive crises, stroke, chronic pulmonary hypertension, and avascular necrosis [4]. Patients with severe SCD experience significant morbidity, organ failure, serious complications, and severe pain, resulting in poor quality of life (QoL), including physical and psychological effects and early mortality [4]. The prevalence of SCD in Saudi Arabia varies remarkably by region; the highest incidence is in the eastern area, followed by the southwestern areas [2]. There are approximately 61,000 patients with SCD in Saudi Arabia [2,5]. The reported prevalence of the sickle cell trait ranges from 2% to 27%, and up to 2.6% of the population will have SCD [2].

Allogeneic hematopoietic cell transplantation (HCT) remains the only curative treatment for SCD [5–8]. Post-transplant patients can have a significantly enhanced QoL, with fewer hospital and emergency room visits and improvements in other aspects of their daily activities [9]. Studies regarding patient QoL provide clinicians with a better understanding of the lived experience of patients with SCD [10]. Our study aimed to assess the QoL in adolescent and adult patients with SCD receiving non-myeloablative HCT.

2. Objectives of the study

2.1. Aim of the study

This study aimed to assess the QoL of adolescent and adult patients with SCD undergoing HCT at our center.

3. Materials and Methods

This study was an analytical cross-sectional study using a survey and interview technique to assess the QoL of patients with SCD before and after allogeneic HCT. The study was conducted at King Abdulaziz Medical City, Riyadh, Saudi Arabia. All adolescent and adult patients with SCD aged 14 years and above who received allogeneic HCT and completed at least one year of follow-up post-transplantation were included. The patients who experienced transplant or graft failure were excluded. The conditioning regimen comprised alemtuzumab, 1 mg per kg, administered in gradually increasing doses from days 7 to 3 before transplantation. Total-body irradiation (TBI) was administered two days before transplantation at a dose of 300 cGy [6]. A sirolimus loading dose of 12 mg was administered one day before transplantation, then a daily dose of 4 mg from day 0 up to one year was used and adjusted to maintain levels between 10 and 15 mg in the first 3 months and 5 and 10 mg from 3 to 12 months. After 12 months, sirolimus was stopped if lymphoid chimerism exceeded 50%. Stem cells were collected from a full match-related donor through peripheral blood stem cell apheresis and infused on day zero. The data were gathered by interviewing eligible patients with SCD using a QoL survey to compare the pre-transplant period with the present. The patients were interviewed by the study team using the questionnaire.

The sample size was 45, calculated through the Raosoft calculator with a population size of 50 patients, response distribution of 50%, 5% margin of error, and 95% confidence level. However, all eligible patients were included due to the limited number of patients.

3.1. Data collection methods, instrument used, and measurements

The Functional Assessment of Cancer Therapy-General (FACT-G) questionnaire [11] was used. This 27-item questionnaire measured four health-related QoL (HRQoL) domains in cancer patients: physical, social, emotional, and functional well-being [11]. The questions were phrased such that a higher number indicated a better health state, and some items were reverse-scored [11]. Permission to use the questionnaire was obtained from the author of the FACT-G score. The FACT-G questionnaire was initially written in English but has been translated into numerous languages [12]. Each patient was interviewed in Arabic by the study team.

3.2. Data management and analysis plan

The data were entered and coded using a Microsoft Excel sheet on a password-protected computer. The data were statistically analyzed using the IBM SPSS software (version 23), with a 5% significance level. The categorical data are presented as frequency and percentage, and the continuous data as the mean and standard deviation. The paired-samples *t*-test and Wilcoxon's signed ranks test (for normally and non-normally distributed data, respectively) were used to compare the pre-and post-measurements of the continuous variables, and McNemar's chi-square test was used to compare the

pre-and post-measurements of the categorical variables.

3.3. Ethical considerations

Ethical approval was obtained from the Institutional Review Board to access the medical records. All the information was accessed only by the principal investigator and co-investigators of the study. A consent letter was distributed to the patients to obtain informed consent and as a confidentiality guarantee. The data were stored in an Excel sheet that was saved and encrypted to ensure data privacy.

4. Results

4.1. Demographic and clinical data of the participants

A total of 50 patients were screened, and 31 responded to the questions (62% response rate). Patients who had undergone HCT and completed at least one year of follow-up were eligible. The median follow-up post-HCT was 1061 days (680–1880). All the participants had successful graft function at the time of the study.

The mean age of the respondents was 32 ± 6.3 (20–44) years. Regarding sex, 51.6% were male. Over one-third of the respondents had a university-level education (38.7%). Most respondents (54.8%) were not married.

The mean number of days absent pre-HCT from school or work per month was 10.1 (0–20). Most (n = 27, 87.1%) patients had no psychological issues; four (12.9%) experienced psychological problems. Over half of the respondents (67.7%) had comorbidities. A summary of the demographic and clinical characteristics of the study sample is shown in Table 1.

The indication for stem cell transplantation is presented in Fig. 1. The most frequent indication for stem cell transplantation was a vaso-occlusive crisis (58%), followed by avascular necrosis (29%), acute chest syndrome (29%), and cerebrovascular accidents (19.4%).

4.2. FACT-G score pre-and post-transplantation

There was a significant improvement in the QoL score post-transplantation, as measured by the FACT-G score. The mean FACT-G scores pre- and post-transplantation were 55.2 ± 18.17 and 91.4 ± 14.58, respectively (Table 2).

Table 1. Sociodemographic and clinical data of the study participants (n = 31).

Variable	Category	Frequency	%
Age (Years)	Median ± SD (Range)	32 ± 6.3 (20–44)	
Sex	Female	15	48.4
	Male	16	51.6
Educational Level	Intermediate school	1	3.2
	High school	10	32.3
	Diploma	8	25.8
	University	12	38.7
Education to age	Delayed	17	54.8
	Stopped	4	12.9
	To age	10	32.3
Marital status	Married	12	38.7
	Not married	17	54.8
	Divorced	2	6.5
Psychological disorders	Yes	4	12.9
	No	27	87.1
Other Comorbidities	Yes	21	67.7
	No	10	32.3
Median follow-up	1061 (680–1880) days		

4.3. Changes in other quality measures

There was an improvement in other quality measures post-HCT (Table 3), including an improvement in physical well-being, as reflected by changes in weight and BMI pre-and post-transplant and a significant reduction in the number of days absent from school or work, hospital admissions, ER visits, and the number of blood transfusions post-transplant. The majority (n = 19, 61.3%) were regular narcotics users pre-transplantation, and this number reduced post-transplantation (n = 6, 19.4%; P-value = 0.002) (Table 3).

Over half of the respondents (n = 16, 51.6%) had no complications post-transplantation. Fifteen (48.4%) experienced some complications. Most (n = 20, 64.5%) experienced no persistent pain symptoms post-transplantation. Eleven (35.5%) experienced persistent pain symptoms. Most (93.5%) reported that their QoL improved post-transplant, and only 6.5% reported no improvement (Fig. 2).

5. Discussion

The QoL of a patient is a critical determinant of health status related to chronic diseases, such as SCD. Patients with SCD experience significant morbidities associated with poor QoL [13–16]. HCT is a potentially curative therapeutic option that can significantly change and improve QoL [17–19].

This study aimed to assess the QoL of adult patients with SCD undergoing minimal residual

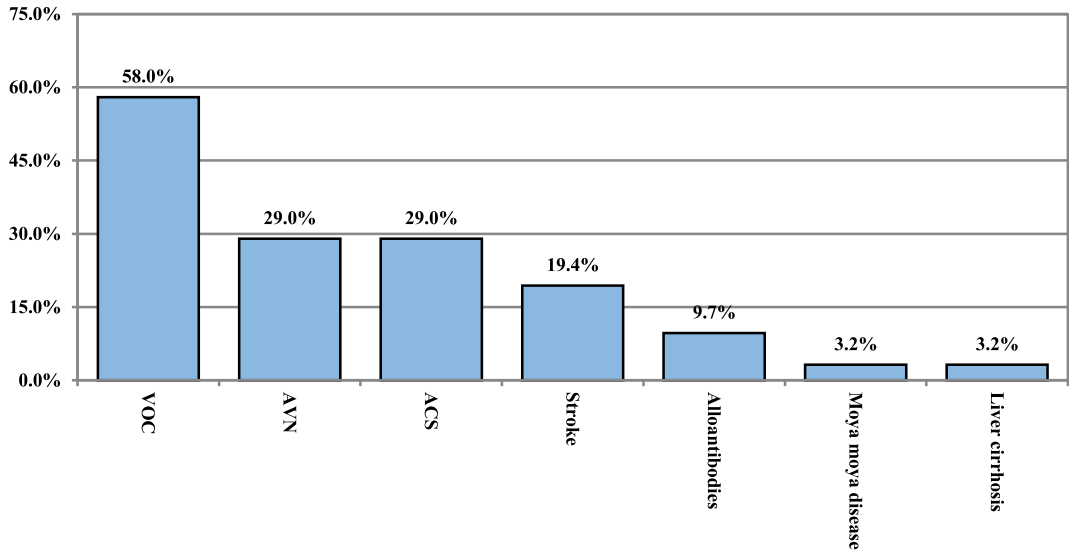

Fig. 1. Indication for transplantation.

disease HCT using a non-myeloablative regimen (alemtuzumab + TBI), with an overall survival rate of 97% and a disease-free survival rate of 87% [6,20]. The FACT-G score was used because this 27-item questionnaire measures most HRQoL domains. The FACT-G score was developed, validated, and tested primarily in patients with cancer [21]. Although SCD is considered a benign hematologic disease, many patients with SCD experience disabling chronic complications and pain. The FACT-G score is easy for patients to understand, and the completion time is 5–10 minutes. An Arabic-validated version was available from the publisher [12].

Our findings indicate a significant improvement in post-transplant QoL, as measured by the FACT-G total score and its three major domains: physical, functional, and emotional. There was some improvement in social and family well-being; however, this improvement was not statistically significant. Another group that used the FACT-G score to assess the QoL in patients undergoing autologous stem cell transplantation did not find the same improvements post-transplant, potentially because patients with malignant indications for transplant may need chemotherapy post-transplant to prevent or treat disease relapse, which may affect their QoL [15].

Other studies evaluating changes in the QoL of patients with SCD post-stem cell transplant reported a similar outcome using different assessment models. Saraf et al. described an improved QoL using the SF36 quality score for a similar population of patients with SCD and using the same non-myeloablative protocol (alemtuzumab and TBI) [22]. This cohort of 9 patients reported significant improvements at one-year post-transplant compared to pre-transplant scores in the three HRQoL domains: bodily pain, general health perceptions, and vitality [22]. Trends of improvement were noticed from pre-transplant to one-year post-transplant in other HRQoL domains, which were not statistically significant in this small sample [22]. The significant improvement in vitality and pain domain scores may be attributed to improved disease control and resolution of the illness process [22].

Bhatia et al. reported that after adjusting for demographic and medical characteristics, mixed-effects models revealed similar results for the physical, social, and emotional HRQoL domains [23]. The patients in Bhatia's study showed considerable improvement in most HRQoL parameters one year after allogeneic HCT, and the treatment

Table 2. FACT-G score pre- and post-transplantation.

Variables	Mean Pre-transplantation	SD	Mean Post-transplantation	SD	P-value
Physical Well-being	6.4	5.090	24	5.257	<0.0001
Social/Family Well-being	23	5.829	23	5.535	0.953
Emotional Well-being	11.03	6.606	19.4	4.147	<0.0001
Functional Well-being	14.8	6.773	24.632	4.116	<0.0001
Total Fact-G Score	55.1	18.172	91.4	14.581	<0.0001

Table 3. Quality measures comparison.

Variable	Transplantation		P-value
	Pre	Post	
	Mean (SD)		
Height (cm)	158.9 (8.51)	160.2 (9.41)	0.089
Weight (kg)	58.5 (15.30)	64.2 (19.22)	<0.0001
BMI (kg/m2)	23.1 (5.66)	24.9 (7.30)	0.001
The average number of days absent from school or work/month	10.0 (6.24)	0 (0)	<0.0001
Annual hospital admission number	13.9 (13.85)	2.5 (5.73)	<0.0001
Annual ER visits	27.3 (33.49)	6.6 (15.41)	0.006
Annual average blood transfusion	12.4 (14.22)	3.2 (8.74)	0.006
	Number (%)		
Regular use of narcotics	19 (61.3)	6 (19.4)	0.002
PRN use of narcotics	29 (93.5)	8 (25.8)	<0.0001

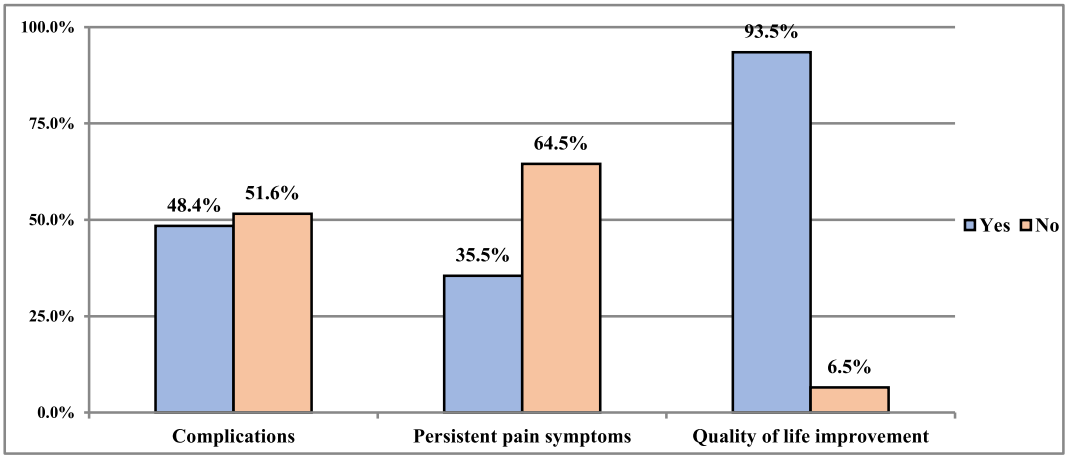

Fig. 2. Complications, symptoms, and quality of life post-transplantation.

alleviated the clinical signs of SCD [23], consistent with the results of this study.

Another important finding in our study is the significant reduction in healthcare utilization post-transplantation, including blood transfusions, ER visits, and hospital admissions (Table 3). Few studies have been conducted on healthcare utilization after allogeneic HCT among adults with SCD. A longitudinal analysis of adult patients with SCD revealed a significant reduction in the median length of hospital stay from 22 days per year pre-HCT to one day per year in the second year post-HCT [24]. The median rates of ER visits were significantly lower in the second year post-HCT (one visit per year) compared to those in the pre-HCT period (four visits per year) [25].

Our study has limitations due to being a single-center study, potentially limiting its generalizability. Only patients with successful grafts were enrolled. Patients experiencing graft failure could have worse or no improvement in their QoL, which is considered a disadvantage of HCT in patients with SCD. The pre-transplant assessment was also conducted retrospectively, which can introduce recall bias. Prospective studies with close patient monitoring are necessary to achieve the desired results. The study demonstrated that allogeneic HCT could cure patients with severe SCD and poor QoL.

6. Conclusion

HCT significantly improved the QoL of adult patients with SCD, with improvements in most domains of the FACT-G score. Other outcomes not measured by the FACT-G, such as hospitalizations and ER visits, also improved. These outcomes contributed to the reduction in the cost of therapy for patients with SCD post-transplant.

Conflict of Interest

None declared.

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