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ORIGINAL RESEARCH

Predictive Factors for 30-Day Readmission and Increased Healthcare Utilization in Sickle Cell Disease Patients: A Single-Center Comparative Retrospective Study

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Background: SCD poses a significant healthcare burden. Understanding the factors contributing to high healthcare utilization and readmissions is crucial for improving the quality of care provided.

Methods: This retrospective comparative observational study was conducted at King Saud University Medical City and included 160 SCD patients. A comparison was made between patients with no readmission and patients with at least one 30-day readmission. Another comparison was done between high healthcare-utilizing patients and low healthcare-utilizing patients. A regression model for 30-day readmission prediction was created.

Results: Readmission was significantly higher in patients using opioids, following up with pain clinics, and having a history of AVN (p= 0.002, p=0.028 and p=0.025 respectively). Higher healthcare utilization was associated with older age, smoking, use of opioids and GABA analogs, and psychiatric illnesses, including depression, substance use disorder, and anxiety. Predictors of 30-day readmission were hydroxyurea use (odds ratio, 2.819 [95% CI,1.082 to 7.34], p = 0.034), follow-up with pain management clinics (odds ratio, 2.248 [95% CI,1.547 to 3.266], p = 0.001), and SCD genotype (SS genotype) (odds ratio, 1.754 [95% CI,1.012 to 3.042], p = 0.045). Using the Paracetamol/Codeine combination significantly reduced the likelihood of readmission within 30 days of discharge.

Conclusion: This study identified factors associated with 30-day readmission rate and high healthcare utilization among SCD patients. Strategies to reduce readmissions may include specialized SCD clinics, educational programs for patients, improved physician awareness of mental health screening, and further research on the impact of opioid use. Limitations include retrospective nature, single-center design, reliance on self-reported data, and exclusion of critically ill patients. However, despite the limitations, this study could lay a foundation for future projects aiming to optimize care and outcomes for patients living with SCD.

Keywords: sickle cell disease, readmission, healthcare utilization, pain management

Introduction

Sickle cell disease (SCD) is an inherited genetic disorder affecting the structure of red blood cells. The prevalence of SCD varies across different regions. In countries where the prevalence of SCD traits reaches 20%, the number of affected people is approximately 2%.[1] Africa, in particular, bears a higher burden of the disease than other regions, with a prevalence reaching 40% of the population.[1] While in Saudi Arabia, according to The Saudi Premarital Screening Program, studies have indicated that 4.2% of the Saudi population are carriers, while 0.26% have the disease. The Eastern province has the highest prevalence, with 17% carriers and 1.2% affected individuals.[2]

In addition to the well-known severe medical and surgical emergencies associated with SCD, it also affects healthcare administration through high utilization rate. A retrospective study showed that Saudi patients with SCD have a high rate

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of emergency department (ED) visits, admissions, and readmissions.[3] Similarly, another study on the Saudi SCD population showed that 64.3% had three or more ED visits related to SCD over six months. It was found that male gender, being married, and having a university degree are risk factors for a higher rate of ED visits.[4] On the contrary, a systematic review showed that factors influencing the utilization of hospital services include female gender, an average age of 25–35 years, and the absence of a college degree.[5]

The determinants influencing healthcare utilization vary and exhibit uniqueness within each nation, including Saudi Arabia, depending on the specific characteristics of the healthcare system and the cultural variation.

Furthermore, genotypic variation has a role in both the severity of the disease and the extent of complications. For instance, the less common HbSC genotype in Saudi Arabia tends to exhibit milder symptoms and lower mortality rates compared to the more prevalent HbSS genotype. Similarly, the phenotype resulting from inheriting HbS with the β thalassemia gene varies based on the quantity of normal β chains present. Additionally, the concurrent presence of alpha thalassemia is associated with a relatively more benign clinical presentation.[6]

The recurrent hospital visits of SCD patients creates a significant economic burden that cannot be ignored. A US study estimated the average monthly cost per patient to be $1389, primarily driven by high utilization of hospital services, including ED visits and admissions.[7] Frequent healthcare utilization has been associated with unfavorable effects on SCD patients, including risk of infections, reduced life quality and higher rates of depression compared to those with lower utilization.[4,5,8]

Studies on SCD patients' healthcare utilization in Saudi Arabia have been limited, highlighting the need for more comprehensive research and the implementation of programs to promote better quality of care. Therefore, a thorough understanding of the key factors contributing to high utilization, particularly readmission rates, is essential. This study aimed to identify risk factors associated with 30-day readmission and increased healthcare utilization among patients with SCD.

Methodology

Study Design

This comparative retrospective observational study was conducted at King Saud University Medical City (KSUMC) in Riyadh, Saudi Arabia, which is a tertiary referral hospital, from 1 January 2016 to 31 October 2021. In total, 324 patients were identified initially via electronic medical records using the keyword "sickle cell disease". Inclusion criteria included all SCD patients aged 14 years or older who were admitted under the care of the General Internal Medicine (GIM) unit. One hundred sixty-four patients were excluded based on the exclusion criteria of (1) any patient younger than 14 years old; per hospital policy, these patients are admitted under pediatric services. (2) sickle cell trait carriers. (3) patients admitted under specialties other than GIM, and (4) patients with planned readmissions (Elective admissions).

Data Collection

Data were collected through reviewing electronic health medical records between 15 December 2021 and 15 February 2022. Direct phone calls were also made during the same period to obtain some of the demographic data lacking in the medical records and through which verbal consent was secured. We extracted patient demographic data, including age, gender, nationality, patient origin in Saudi Arabia, marital status, educational qualification, employment status, monthly income, smoking status, and average BMI. Other data included clinical characteristics such as mortality, cause of mortality, hemoglobin genotype, sickle cell disease-related medications (Hydroxyurea, Folic Acid, Penicillin, L-glutamine), home pain medications, medication compliance, blood transfusion, blood exchange including both partial blood exchange and plasma apheresis, past medical history, past surgical history, comorbidities, psychiatric disorders, complications (eg, Avascular Osteonecrosis (AVN), ACS, Priapism, Thrombosis, Infections, and Cholecystitis), number of admissions, length of admissions, ED visits, ICU admissions and outpatient clinics follow up. Limitations included missing data that could not be obtained due to the non-response of a few participants.

Statistical Analysis

Data was collected and entered into a password-protected Microsoft Excel® spreadsheet after de-identification. Data sorting before analysis was done. Data were analyzed using Statistical Package for Social Studies (SPSS 22; IBM Corp., New York, NY, USA). Continuous variables were expressed as mean ± standard deviation, and categorical variables as percentages.

Mann–Whitney test was used for continuous variables without normal distribution. Shapiro–Wilk test was used to assess the normality distribution for the variables. A p-value <0.05 was considered statistically significant.

A comparison of variables was made between the Readmission group, defined as all patients with at least one 30-day readmission (n=21), and the Non-Readmission group, which served as the comparative group, defined as all patients with only one admission during the study period (n=52). The comparison did not include those with two or more scattered admissions (i.e., > 30 days apart) during the study period (n=73).

The average utilization of healthcare facilities by the enrolled SCD patients was defined as one admission per year and four ED visits per year.[3] Based on this, two categories were established. The high utilization group whose number of admissions or ED visits per year exceeded the previously defined average, and the low utilization group had admissions or ED visits that were equal to or lower than the defined average. Meeting at least one of the criteria of high utilization (an average of >1 admission/year or >4 ED visits/year) excludes the patient from the low utilization group.

For the regression model, the intervals between patients' readmissions were calculated and divided into three outcome variables (within 30 days, 31–60 days, and 60–90 days). After that, all the predictor variables were tested for significance with all the outcome variables. The significance level of predictors was set at P-value <0.05. Accounting for at least (15) cases for each predictor, the predictors were tested for the assumptions of binary logistic regression with each outcome independently. The analyses have successfully built a good fit model with a 10.7% prediction for readmission within 30 days. However, further regression trials with other outcomes have yielded poorly fit models with low predictions (<5%).

Ethical Consideration

This study was conducted in accordance with the principles outlined in the Declaration of Helsinki. Following the approved verbal consent script for medical record-based studies, informed consent was obtained from all participants prior to their inclusion in the study through phone calls after an initial explanation of the research goals and required pieces of information. A written consent was not feasible given the inconvenience of participants attending face-to-face meetings. The investigators documented and signed each participant's call's date and time. The participants were given the option to refuse participation and freely withdraw at any time. There were no incentives or rewards given to participants. Participants' anonymity was assured by assigning each participant a code number for analysis only. The study was approved by King Saud University's College of Medicine Research Ethics Committee (IRB: E-21-6469). There was no conflict of interest.

Results

One hundred sixty patients enrolled in the study had a total of 891 admissions. 52 (32.5%) patients had no readmission during the studied period (Non-readmission group). In contrast, 21 (13.13%) were readmitted at least once within 30 days of discharge (Readmission group). Based on the average number of admissions and ED visits, the sample was divided into a high utilization group of 28 patients (17.5%) and a low utilization group of 132 patients (82.5%).

Both readmission and non-readmission groups had a similar gender distribution, mean age, marital status, employment status, and educational degree. In contrast, patients in the high utilization group were significantly older than the low utilization group (34.57 ± 8.40 vs 30.34 ± 9.05; p = 0.024; Table 1).

The regression model showed that university and diploma level of education increases the likelihood of 30-day readmission (odds ratio, 1.548 [95% CI,1.039 to 2.309], p = 0.032). On the other hand, while not statistically significant, intermediate and secondary education seems to decrease the likelihood of readmission compared to the illiterate and primary education groups (odds ratio, 0.682 [95% CI,0.297 to 1.565], p = 0.383; Figure 1).

The readmission group was originally from the country's southern region, compared to the non-readmission group (14; 73.68%, p = 0.009), and the high utilization group was either from the southern or the middle regions. Additionally,

Table 1 Readmission Group versus Non-Readmission Group and High Utilization versus Low Utilization Groups in Terms of Demographics

Characteristics	Readmission Group (n=21)	Non-readmission Group (n=52)	P value	Low Utilization (n=132)	High Utilization (n=28)	P value
Gender			0.238			0.070
Male	38.10%	48.08%		45.5%	64.3%	
Female	61.9%	51.92%		54.5%	35.7%	
Age (Mean ± SD)	32.90 ± 7.31	30.46 ± 8.93	0.270	30.34 ± 9.05	34.57 ± 8.40	0.024*
Area in Saudi			0.009*			0.463
South	73.7%	29.2%		47.9%	57.7%	
West	0.00%	2.08%		1.70%	0.00%	
East	0.00%	10.42%		6.60%	0.00%	
Middle	26.3%	58.33%		43.8%	42.3%	
Marital status			0.587			0.298
Married	52.4%	44.9%		41.7%	53.6%	
Single	47.6%	51.0%		55.1%	39.3%	
Divorced	0.00%	4.08%		2.40%	7.10%	
Widow	0.00%	0.00%		0.80%	0.00%	
Employed	55.0%	42.2%	0.340	47.9%	48.0%	0.990
Education			0.334			0.115
Low/Primary	10.0%	11.1%		10.3%	4.00%	
Intermediate/Secondary	50.0%	31.1%		37.9%	60.0%	
University/Diploma	40.0%	57.8%		51.7%	36.0%	
Smoker	20.0%	20.0%	0.382	15.4%	37.0%	0.001*
Ex-smoker	10.0%	2.22%		3.40%	14.8%	
BMI (kg/m²)			0.311			0.579
<18.5	14.3%	28.9%		18.9%	21.4%	
18.5–24.9	52.4%	50.0%		60.6%	67.9%	
25–29.9	28.6%	19.2%		15.9%	7.10%	
30–34.9	0.00%	1.92%		3.00%	0.00%	
> 35	4.76%	0.00%		1.50%	3.60%	
Diagnosis			0.456			0.613
Sickle cell disease[a]	71.4%	73.1%		78.0%	75.0%	
Sickle-thalassemia[a]	28.6%	21.2%		19.7%	25.0%	
Sickle-G6PD[b]	0.00%	5.77%		2.30%	0.00%	

Notes: *Significant p value. [a]Based on Hb electrophoresis, HbS > 90% for Sickle cell disease, HbS > 60% and HbA2 > 3.5% for Sickle-Thalassemia. [b]Based on Hb electrophoresis, HbS > 90% and G6PD deficiency.

Abbreviations: BMI, body mass index; Hb, Hemoglobin; G6PD, Glucose-6-phosphate dehydrogenase.

the high utilization group was more likely to have a smoking history (37.0% Active smokers, 14.8% Previous smokers, p = 0.001; Table 1). Consistent with the regression model, current smokers, when compared to non-smokers, showed a significantly higher likelihood of readmission (odds ratio, 2.317 [95% CI,1.502 to 3.576], p < 0.001; Figure 1).

The readmission group was more likely to use opioids as a home analgesic agent (12; 57.14% vs 10;19.6%, p = 0.002) and more likely to follow up at the pain management clinics (7; 33.33% vs 6; 11.54%, p = 0.028). Similarly, The high utilization group had significantly higher GABA analogs and opioid consumption as home analgesia when compared to the low utilization group (p-value <0.001, p = 0.012). Furthermore, higher utilization was associated with a diagnosis of substance use disorder (p = 0.067) and active follow-up in pain management clinics (p < 0.001). It is worth noting that the high-utilization group used L-glutamine, which was never prescribed to patients in the low-utilization group (p = 0.030; Table 2).

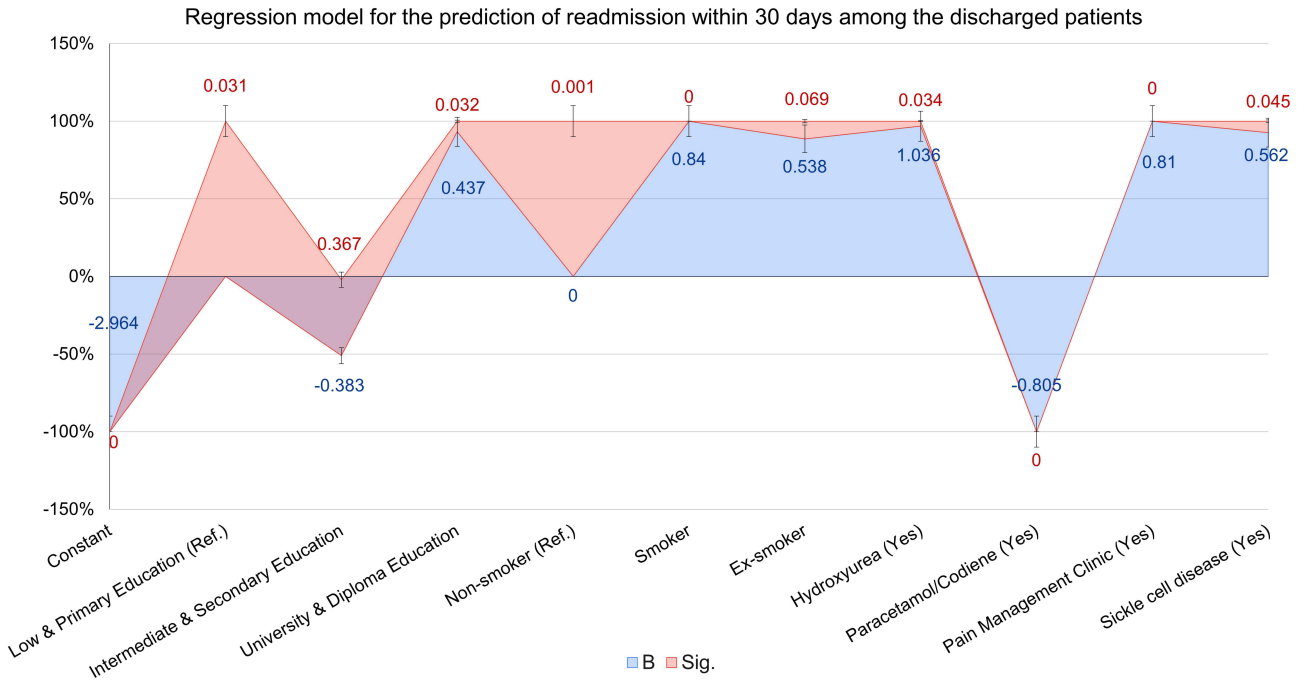

Figure 1 Regression model for the prediction of readmission within 30 days among the discharged patients.

The use of hydroxyurea (odds ratio, 2.819 [95% CI,1.082 to 7.34], p = 0.034), follow-up with pain management clinics (odds ratio, 2.248 [95% CI,1.547 to 3.266], p = 0.001), and SCD genotype (SS genotype) (odds ratio, 1.754 [95% CI,1.012 to 3.042], p = 0.045) were all significant predictors of 30-day readmission. On the other hand, using the Paracetamol/Codeine combination for pain was significantly associated with a decreased likelihood of readmission within 30 days of discharge. (odds ratio, 0.447 [95% CI, 0.3 to 0.666], p < 0.001; Figure 1).

Table 2 Readmission Group versus Non-Readmission Group and High Utilization versus Low Utilization Groups in Terms of Medical History

Characteristics	Readmission Group (n=21)	Non-readmission Group (n=52)	P value	Low Utilization (n=132)	High Utilization (n=28)	P value
Home medications						
None	0.00%	9.62%	0.173	3.80%	0.00%	0.374
Hydroxyurea	0.00%	3.85%	0.362	3.10%	3.60%	0.626
Folic acid	9.52%	11.54%	0.583	10.7%	14.3%	0.394
Hydroxyurea/Folic acid	85.7%	75.00%	0.250	82.4%	82.1%	0.970
Penicillin	–	–	–	2.30%	0.00%	0.419
L-glutamine	9.52%	0.00%	0.080	0.00%	7.10%	0.030*
Compliance to hydroxyurea	61.9%	45.1%	0.195	–	–	–
Home pain medication						
None	9.52%	13.8%	0.479	10.7%	0.00%	0.085
Paracetamol/Codiene	47.6%	29.4%	0.140	42.0%	39.3%	0.792
NSAID	14.3%	25.5%	0.438	19.8%	17.9%	0.809
Opioid	57.1%	19.6%	0.002*	32.1%	57.1%	0.012*
Paracetamol	9.52%	23.5%	0.149	20.6%	10.7%	0.172
GABA analogue	23.8%	7.84%	0.075	5.30%	28.6%	<0.001*

(*Continued*)

Table 2 (Continued).

Characteristics	Readmission Group (n=21)	Non-readmission Group (n=52)	P value	Low Utilization (n=132)	High Utilization (n=28)	P value
Comorbidities/complications						
Diabetes	0.00%	1.92%	0.712	1.50%	3.60%	0.441
Hypertension	9.52%	3.85%	0.325	5.30%	3.60%	0.703
Chronic kidney disease	4.76%	3.85%	0.645	4.50%	3.60%	0.646
Heart failure	–	–	–	3.80%	3.60%	0.718
AVN	35.0%	12.00%	0.025*	24.6%	37.5%	0.190
Surgeries						
None	42.9%	59.6%	0.193	54.5%	35.7%	0.070
Cholecystectomy	47.6%	28.9%	0.126	35.6%	60.7%	0.014*
Splenectomy	19.0%	9.62%	0.231	12.1%	17.9%	0.414
Joint replacement	0.00%	3.85%	0.505	5.30%	3.60%	0.577
Amputation	0.00%	3.85%	0.505	2.30%	0.00%	0.559
Osteotomy	0.00%	3.85%	0.505	2.30%	0.00%	0.559
Wedge lengthening	–	–	–	0.80%	0.00%	0.825
SA treated Surgically	4.76%	0.00%	0.288	1.50%	0.00%	0.680
Spine surgery	0.00%	1.92%	0.712	1.50%	0.00%	0.680
Psychiatric illness						
None	85.7%	94.2%	0.226	91.7%	75.0%	0.011*
MDD	14.3%	5.77%	0.226	6.10%	25.0%	0.002*
Anxiety	9.52%	1.92%	0.127	5.30%	21.4%	0.005*
Borderline personality	9.52%	1.92%	0.197	3.00%	21.4%	0.002*
Substance use disorder	–	–	–	2.30%	10.7%	0.067*
Hematology follow up	90.4%	78.9%	0.205	81.8%	96.4%	0.039*
Pain management follow up	33.3%	11.5%	0.028*	11.4%	53.6%	<0.001*
Blood transfusions			0.473			0.083
On demand	85.7%	88.5%		92.4%	78.6%	
Regular	–	3.85%		1.50%	3.60%	
Regular exchange	14.23%	7.69%		6.10%	17.9%	
Hospital days[a] (mean ± SD)	64.71 ± 82.56	5.81 ± 6.72	0.004*	20.03 ± 24.02	109.21 ± 102.02	<0.001*
Reason of mortality	–	–	–			0.873
PE				33.3%	0.00%	
GI bleed				33.3%	0.00%	
MOF				33.3%	0.00%	

Notes: *Significant p value. [a]Average hospital days during study period.
Abbreviations: AVN, avascular necrosis; SA, septic arthritis; MDD, major depressive disorder; PE, pulmonary embolism; GI, gastrointestinal; MOF, multiorgan failure; VOC, vaso-occlusive crisis.

The readmission group had a significantly higher average number of hospital days during the study period, with 64.7 days compared to 5.8 days in the non-readmission group (p = 0.004). Consistently, the mean length of hospital stay of the high utilization group was 109.2 days compared to 20 days in the low utilization group (p < 0.001). Regarding SCD complications, AVN was more prevalent in the readmission group compared to the non-readmission group (7; 35% vs 6; 12%, p = 0.025; Table 2).

The primary reason for admission in most patients in both groups was a diagnosis of vaso-occlusive crisis (VOC). Notably, in the high-utilization group, dehydration and menstruation were reported as more frequent triggers for the crisis when compared to the low-utilization group, where infection was the predominant trigger.

All individuals in the high-utilization group were admitted to the intensive care unit (ICU) at least once, and all had a history of ACS. Discharge against medical advice (DAMA) was significantly associated with the readmission group (15% vs 0%, p = 0.005; Table 3).

Table 3 Readmission Group versus Non-Readmission Group and High Utilization versus Low Utilization Groups in Terms of Hospital Course

Characteristics	Readmission Group (n=21)	Non-readmission Group (n=52)	P value	Low Utilization (n=132)	High Utilization (n=28)	P value
Admission diagnosis			0.268			0.973
VOC	89.5%	88.2%		92.2%	96.2%	
Pneumonia	0.00%	3.92%		1.60%	3.80%	
Priapism	0.00%	1.96%		0.80%	0.00%	
Acute Hemolytic crisis	0.00%	3.92%		1.60%	0.00%	
Aplastic Crisis	0.00%	0.00%		0.80%	0.00%	
Thrombosis	0.00%	1.96%		1.60%	0.00%	
Urinary tract infection	5.26%	0.00%		0.80%	0.00%	
Pulmonary edema[a]	5.26%	0.00%		0.80%	0.00%	
Trigger of VOC			0.163			0.024*
Non compliance	16.6%	20.5%		27.6%	26.1%	
Cold exposure	38.9%	6.82%		9.50%	0.00%	
Infection	5.56%	31.8%		28.4%	17.4%	
Menstruation	0.00%	0.00%		1.70%	8.70%	
Emotional stress	0.00%	2.27%		4.30%	0.00%	
Dehydration	16.7%	4.55%		2.60%	13.0%	
No clear trigger	16.7%	34.1%		25.0%	30.4%	
Holding HU[b]	5.56%	0.00%		0.90%	0.00%	
Physical stress	0.00%	0.00%		0.00%	4.30%	
Site of pain			0.101			0.820
Back	13.3%	27.6%		19.8%	8.30%	
Lower limbs	26.7%	20.7%		18.6%	16.7%	
Shoulders	0.00%	0.00%		1.20%	4.20%	
Generalized[c]	40.0%	48.3%		51.2%	62.5%	
Chest	0.00%	3.45%		4.70%	4.20%	
Abdomen	20.0%	0.00%		2.30%	4.20%	
Upper limbs	0.00%	0.00%		1.20%	0.00%	
Morphine regulate doses	95.0%	79.2%	0.100	81.7%	78.6%	0.698
Use of PCA	45.0%	22.9%	0.069	38.1%	42.9%	0.640
Blood transfusion	42.9%	44.2%	0.915	50.0%	35.7%	0.169
Exchange transfusion	4.76%	5.77%	0.675	3.80%	7.10%	0.430
ICU admission	0.00%	3.85%	0.505	4.5%	100%	0.250
Acute chest syndrome	0.00%	7.69%	0.249	5.30%	100%	0.253
Priapism	0.00%	1.92%	0.712	0.80%	100%	0.825
Thrombosis	0.00%	1.92%	0.712	1.50%	0.00%	0.680
Hemorrhage	–	–	–	0.80%	0.00%	0.644
Acute cholecystitis	–	–	–	0.80%	0.00%	0.825
Cholechodolithiasis	–	–	–	0.80%	0.00%	0.825

(*Continued*)

Table 3 (Continued).

Characteristics	Readmission Group (n=21)	Non-readmission Group (n=52)	P value	Low Utilization (n=132)	High Utilization (n=28)	P value
Infections			0.888			0.812
None	71.4%	70.6%		75.6%	78.6%	
Respiratory	19.1%	21.6%		18.3%	17.9%	
Blood stream	4.76%	1.96%		1.50%	0.00%	
Soft tissue	0.00%	1.96%		1.50%	0.00%	
GI	–	0.00%		0.80%	3.60%	
UTI	4.76%	1.96%		1.50%	0.00%	
FUO	–	1.96%		0.80%	0.00%	
DAMA	15.0%	0.00%	0.005*	–	–	–

Notes: *Significant p value. [a]Due to SCD related pulmonary complications and not better explained by heart failure. [b]Due to medical reasons like pregnancy. [c]More than 3 body sites.

Abbreviations: VOC, vaso-occlusive crisis; IV, intravenous; NS, normal saline; RL, ringer's lactate; D5W, dextrose 5% in water; ICU, intensive care unit; DAMA, discharge against medical advice; SCD, sickle cell disease.

Discussion

The rate of readmissions and health care utilization among patients with SCD is a critical indicator of the quality of care. In our study, demographic factors other than age and level of education did not show any significant association with increased readmission rates or higher healthcare utilization. Older age is associated with significantly higher utilization of health care services among SCD patients. This can be attributed to disease progression, complications, and age-associated comorbidities.[9]

The association between a higher level of education and higher healthcare utilization that we observed in our study was previously described in a study done on a Saudi population with SCD.[4] These results are inconsistent with findings from other international studies. For instance, two different retrospective studies on SCD patients in the US concluded that higher educational degrees were significantly associated with lower healthcare utilization, and lower educational attainment was related to higher healthcare utilization.[10,11]

Although higher education is often associated with a deeper understanding of the disease and increased compliance with treatment, the relationship between education and healthcare utilization can be influenced by various factors. Occasionally, individuals with higher levels of education tend to have greater awareness of preventive care measures, and they are more likely to take steps to maintain their well-being and, therefore, have frequent access to healthcare facilities.[12]

In the southern region of Saudi Arabia, the prevalence of SCD is among the highest in the country.[2] One of the contributing factors is the higher rates of consanguinity. Despite having an effective mandatory premarital screening program for most inherited hemoglobinopathies, some individuals still proceed with marriage and having children after being counseled about the nature of the disease, the possibility of having affected children, and potential outcomes.[2] Cultural influence and religious perspectives are major in such decisions. In societies characterized by elevated consanguinity rates, it is customary for individuals to establish interpersonal bonds with potential life partners during the early stages of their lives. Consequently, upon marriage, a substantial proportion of these individuals encounter challenges in openly declaring incompatibility. This predicament arises primarily from the associated stigmata and the apprehension of spinsterhood. Another fraction believes such circumstances are predetermined by God and considered a religious adherence to follow.[2,13]

VOC is the hallmark of SCD and is the primary cause of ED visits and hospitalizations.[14] Often, these crises are triggered by one or more factors, such as dehydration, emotional stress, and infections. However, in most cases, no apparent precipitating factor can be identified. Mensuration has been reported to be linked with VOC, particularly in women with comorbid dysmenorrhea.[14] Approaching VOC triggered by menstruation is often difficult due to its recurrent and cyclical nature and the lack of evidence-based guidelines for preventive and therapeutic measures.[15]

The high utilization of healthcare facilities among individuals with SCD was significantly associated with the risk of hospital-acquired infections, AVN, pulmonary embolism, and ACS.[16] ACS is a life-threatening SCD complication and the leading cause of ICU admissions.[17] ACS was observed in 100% of our patients in the high utilization group compared to 5.3% in the low utilization. Consistently, a systematic review concluded that infections and ACS were common complications associated with high healthcare utilization.[5] Additionally, ACS and other pulmonary complications, such as pulmonary hypertension, were identified as the most frequent causes of SCD-related deaths. Furthermore, frequent hospital admissions were reported as an independent and significant risk factor for early mortality.[18,19]

AVN is another frequently encountered complication of SCD, which exhibited a notable link with the readmission group. A retrospective cohort study done on the population in eastern Saudi Arabia found a clear relation between frequent hospitalization and the diagnosis of AVN.[20] One possible explanation is the persistent debilitating pain resulting from AVN, which is frequently difficult to distinguish from the typical VOC pain. The importance of early detection of AVN and applying evidence-based management is emphasized in the literature.[21]

Optimal pain management has been the cornerstone of VOC management in SCD. A comparative study conducted on SCD patients visiting the acute care unit demonstrated that achieving lower pain scores was associated with a lower frequency of hospitalizations.[22] The balance between providing adequate analgesia for VOC and preventing addiction has been a concern among some SCD patients. Literature suggested a potential association between substance use disorder and SCD, particularly alcohol and cocaine, as well as marijuana.[23,24]

Opioid addiction in SCD patients is a rising area of research. It was defined by Kotila et al with the term "Pseudoaddiction", which describes dependence on opioids secondary to chronic pain, such as AVN-related pain.[25] The evidence is varied, with certain studies showing potential negative effects of specific narcotics on pain perception. In contrast, others indicate no evidence of opioid use disorder in this population.[26,27]

Chronic pain management in SCD poses significant challenges. Our study observed that 57% of the readmission group and high-utilizers relied on opioids as home medication for their chronic pain. The American Society of Hematology (ASH) guidelines for managing acute and chronic SCD pain provide valuable guidance in selecting appropriate pain management agents, emphasizing minimizing opioid use for chronic pain management, and multiple alternatives were proposed based on the patient's comorbidities.[28] Among our participants, the Paracetamol/Codeine combination was found to reduce utilization in contrast to opioids only. However, shared decisions between physicians and patients in determining the most appropriate pain management is advised.

Hydroxyurea (HU) is one of the common disease-modifying agents used in SCD. The literature has shown HU's effectiveness in reducing hospitalization among SCD patients.[29] In this study, the use of hydroxyurea was found to be a predictor for 30-day readmission based on regression analysis. However, it is essential to note that these findings are limited by the unknown adherence status, which is difficult to determine due to the reliance on self-reported data.

There is a significant association between depression and the high utilization group of SCD. It is believed that depression and other psychiatric sequelae are often overlooked. A study conducted on 2145 patients from 16 countries using the International Sickle Cell World Assessment Survey (SWAY) found a 39% and 38% prevalence for depression and anxiety, respectively. Most patients reported that SCD has a negative impact on their overall quality of life.[30] Effective patient-physician communication can contribute to lower rates of readmission and healthcare utilization by improving medication compliance and enabling early screening and management of disease-related complications.[31] Furthermore, the continued improvement and implementation of specialized SCD facilities, particularly in areas with higher prevalence, can lead to better quality of life and healthcare cost reduction. For instance, a study conducted in Philadelphia implemented a multidisciplinary team approach for uncomplicated VOC, significantly reducing ED visits and admission rates as a result.[32] Similarly, a study at Johns Hopkins Hospital implemented a sickle cell infusion clinic that provided hydration and necessary narcotics for pain management during VOC, reducing overall admission rates by 15.9% and readmission rates by 7% annually.[33]

Conclusion

The high demand for healthcare facilities from SCD underscores the critical need to establish a specialized clinic dedicated to managing VOC and its related complications, including chronic pain. We recommend early screening and

educational programs within the SCD population aiming to reduce consanguinity in coordination with the recommendations of the national premarital screening.

Additionally, we encourage enhancing physicians' awareness about their role in screening SCD patients for mental illnesses and promoting the crucial role of multidisciplinary teams in preventing, screening, diagnosing, and managing mental health-related diseases.

The scope of opioid addiction within the SCD community remains underexplored, presenting a promising and vital area for research.

This study was restricted by its single-center design. Another limitation is the reliance on self-reported information, such as medication details, compliance, and history of substance use. Additionally, patients presenting to the Emergency Department with indications for immediate exchange transfusion, such as ACS or other urgent conditions, were admitted to the hematology ward and were excluded from the study. This exclusion could lead to an underrepresentation of mortality and morbidity within the enrolled population of individuals with SCD.

Disclosure

The authors declare no conflicts of interest in this work.

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