Original Article

Depression among Patient with Sickle Cell Disease: Prevalence and Prediction

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ABSTRACT

Background: Depression is a widespread disorder with either an independent or interrelated relationship with chronic disease. **Aim:** This study aims to assess depression prevalence and its predictors among patients with sickle cell disease (SCD). **Patients and Methods:** This is a cross-sectional study conducted in Saudi Arabia where patients with SCD assessed for having depression through Patient Health Questionnaire (PHQ9). **Results:** Depression was evaluated among 88 patients with SCD with a median age of 32.6 ± 11.8. Out of 88 patients, 44 (50%) participants had some form of depression. Out of those with depression, 25 (56.8%) had mild depression and 18 (40.9%) had moderate depression. However, there was a significant relationship between depression and the number of annual emergency visits, intensive care unit admissions, and frequency of blood transfusion (P-value < 0.05). There was no significant relationship between depression with neither hemoglobin nor HbS (P-value > 0.05). However, depression score found to be inversely proportional to the HbF level. Both gender and annual emergency visits were significantly related to depression (P-value = 0.01, 0.001. respectively). **Conclusion:** Depression is quite prevalent in patients with SCD though it is still being overlooked. Several clinical and laboratory indices found to be closely linked to depression. Constellations of these factors may help early recognition of depression and disease severity modulation.

KEYWORDS: *Anemia, depression, sickle cell disease*

INTRODUCTION

Depression is a widespread disorder that affects more than 350 million people worldwide.[1] The relationship between chronic diseases and depression is described as either independent or interrelated.[2] The prevalence of depression is quite variable from one chronic disease to another. For instance, it is estimated to be as high as 80% in patients with chronic obstructive lung disease and as low as 5.8% in patients with diabetes.[3] Additionally, chronic pain appears to be a critically relevant factor for determining depression though still unrecognized in a significant proportion of patients with chronic pain.[4,5]

Sickle cell disease (SCD) is a major public health problem associated with significant pain burden and other morbidities.[6] Therefore, the cooccurrence of SCD and depression is suspected as chronic pain is documented in one-half of adults suffering from SCD.[7] Worldwide, the prevalence of depression among patients with SCD is estimated to be 39% in the adult SCD population.[8,9] Locally, two studies conducted in the southern and the eastern regions of Saudi Arabia revealed that the prevalence of depression in adults with SCD patients was 85.9 and 48.2%, respectively.[10,11]

Several studies investigated the prevalence of depression among SCD patients and many others intended to investigate its predictors.[12] Several sociodemographic factors, including low educational level, unemployment,

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and low income, were some of the identified as predictors for depression in patients with SCD.[13] Additionally, disease severity in the form of frequent vasoocclusive crisis and visits to hematology clinics and using hydroxyurea (HU) are considered as predictors.[12,14] Furthermore, outcomes from a retrospective analysis revealed that depression in patients with SCD remained a significant risk factor for increasing the length of stay during hospitalization.[15] Conversely, other studies indicate that disease severity, admissions or transfusions per year, and HU usage were poor predictors of depression among these groups of patients.[13]

There is a great discrepancy between studies regarding which factors are considered more sensitive for depression compared to the others.[12,13] Therefore, our study aims to examine depression predictors to provide a broader perspective and emphasize the role of early screening and intervention.

Methods

This is a cross-sectional study conducted in the eastern province of Saudi Arabia, where SCD is most commonly encountered compared to the other regions. The patient with SCD underwent an interview with a trained study team member. The survey includes patient demographics in the form of age, gender, level of education, and clinical data such as comorbidities, frequency of hospitalization, blood transfusion, previous surgeries, intensive care unit (ICU) hospitalization, and usage of HU. Of note, hospitalization was considered as frequent if patients had been admitted more than two times per year in the last 2 years. On the other hand, we consider blood transfusion significant if transfused more than five times in a patient's life, though literature lacks a clear definition for significant blood transfusion in patients with SCD. Depression was assessed through the Arabic version of The Patient Health Questionnaire (PHQ9) module consisting of nine items. The internal consistency reliability of the Arabic version was measured using Cronbach's alpha for the PHQ9, and the results were 0.857.[16] The PHQ9 score ranges from 0 to 27, as each of the nine items scored from 0 (stating "not at all") to 3 (stating "nearly every day"). The cut points for mild depression are 5, 10 for moderate, 15 for moderately severe, and 20 represent the thresholds for severe depression. A PHQ-9 score of 10 or greater has a sensitivity and specificity for major depression of 88%.[17]

Data was collected and analyzed using the International Business Machines Statistical Package for the Social Sciences 23. The descriptive analysis was done to show mean, median, and mode values with standard deviation for quantitative data. The categorical data was analyzed and Chi-square was used to assess any association among different variables. A sample size of 100 was calculated with an estimated marginal error of 0.05 and a confidence interval of 0.95. A *P* value less than 0.05 is considered significant.

Results

One hundred and seven SCD patients had the questionnaire administered to them and 19 were excluded due to incomplete depression questionnaire and missing laboratory investigations, with the completed form in 88 (82.2%). The participants' ages range from 14 to 70 years, with a median age of 32.6 ± 11.8 with more female respondents (M: F = 25:63; ratio of 1:2.5). Demographic and general characteristics are shown in Table 1.

Out of 88 patients, 44 (50%) participants had some form of depression. Out of those with depression, 25 (56.8%) had mild depression and 18 (40.9%) had moderate depression [Figure 1]. Of the 63 women in the study, 23 (36.5%) had depression and 21 (84%) of the 25 men had depression, with significantly more men suffered from severe form of depression.

(*P*-value = 0.0001, Figure 2). There was no significant relationship between depression with neither age nor education level, likewise, history of HU usage, previous stroke, splenectomy or cholecystectomy ($P > 0.05$). However, there is a significant positive relationship between depression and the number of annual emergency visits, ICU admissions, and frequency of blood transfusion (P-value < 0.05).

The steady-state haemoglobin and HbS value also does not have significant relationship with depression (P-value > 0.05, Table 2). However, the depression score was found to be inversely proportional

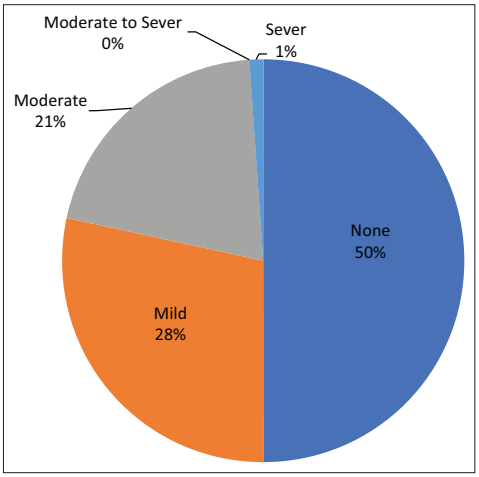

Figure 1: Depression severity among patients with sickle cell disease

Table 1: Patients' demographics and characteristics

Variable	Number (%)				
Gender	Male		Female		
	25 (28.4%)		63 (71.6%)		
Educational level	Illiterate	Primary	Intermediate	Secondary	Higher education
	5 (5.7%)	11 (12.5%)	15 (17%)	35 (39.8%)	22 (25%)
Depression classification	None	Mild	Moderate	Moderate to Severe	Severe
	44 (50%)	25 (28.4%)	18 (20.5%)	0 (0%)	1 (1.1%)
ICU admission	Yes		No		
	66 (75%)		22 (25%)		
Using hydroxyurea	Yes		No		Missing
	13 (14.8%)		47 (53.4%)		28 (31.8%)
History of stroke	Yes		No		
	1 (1.1%)		87 (98.9%)		
Blood transfusion	Yes		No		
	79 (89.8%)		9 (10.2%)		
Splenectomy	Yes		No		
	15 (17%)		73 (83%)		
Cholecystectomy	Yes		NO		
	37 (42%)		51 (58%)		

Table 2: Laboratory parameters among different depression classification

Variables	Depression classification			
	None	Mild depression	Moderate depression	Severe depression
Hemoglobin steady-state level (g/dL)	9	9	8	10
Hb A steady-state level (%)	7	8	14	0
Hb A2 steady-state level (%)	3	3	3	2
Hb S steady-state level (%)	75	77	70	88
Hb F steady-state level (%)	16	12	13	10
Creatinine steady-state level (umol/L)	43	56	65	30

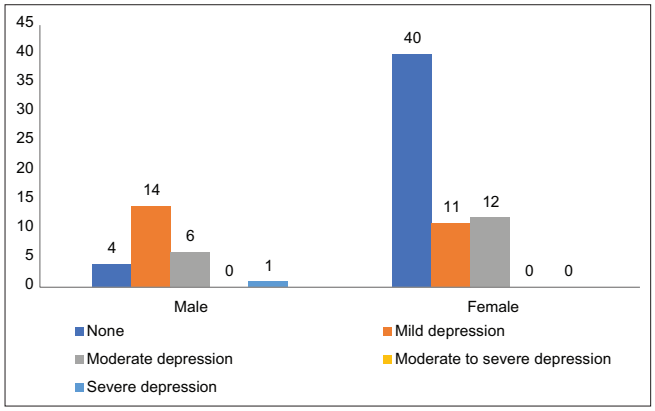

Figure 2: Prevalence of depression among different gender in patients with sickle cell disease

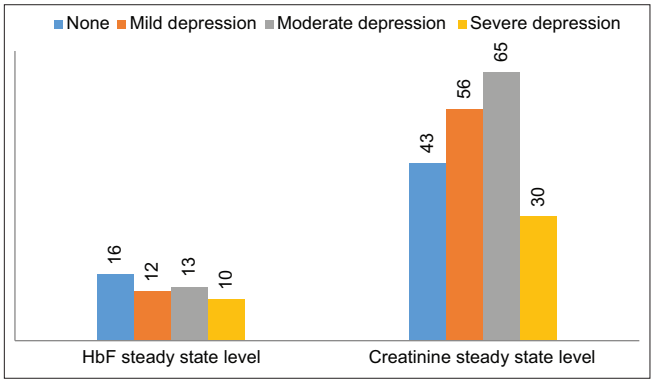

Figure 3: Correlation between hemoglobin F and creatinine levels with depression score

to the HbF level. In other words, the higher the score, the lower the HbF and vice versa. Additionally, serum creatinine level was found to be directly proportional to the depression score. The higher the creatinine, the higher the depression score (*P*-value = 0.02, Figure 3).

Ordinal regression analysis was done to predict the effect of gender, the number of annual emergency visits, ICU admission, blood transfusion, steady creatinine level, and HbF steady-state level on depression. A significant correlation was found between depression with both gender and the number of emergency visits per year (*P*-value = 0.01 and 0.001, respectively). The odd of male gender having higher depression severity is four times that of female (95% CI, 1.4–11.7). Similarly, the odd of increasing depression severity

after each Emergency department visit per year is 1.1 (95% CI, 1–1.2). On the other hand, the other factors were not found to be predictors of depression severity (*P*-value > 0.05).

Discussion

SCD is a chronic systemic disease strongly associated with reduced health-related quality of life and linked to worse physical and psychological outcomes, including depression.[18] Depression found in half of the patients with SCD in this study is around nine times as high as that in patients with other forms of chronic illness.[19] Further, our findings were more prevalent than previously reported internationally.[18]

Our study showed that depression was associated with frequent emergency room visits for vasoocclusive pain and recurrent blood transfusions, similar to previously reported findings.[13,19] Additionally, we found that male patients with SCD and those with a previous ICU admission were more likely to have depression as well. Interestingly, those with frequent ER visits, ICU admission, male individuals, and frequent blood transfusion were more likely to have moderate to severe forms of depression. On the other hand, age, education level, number of hospitalizations, or being on HU were not closely associated with depression. Likewise, previous history of stroke or surgical intervention was not associated with depression as well.

Hemolysis is the cardinal feature of SCD that contributes to phenotypic variability. Further, hemoglobin F is a major influence of disease severity and a well-known modulator of SCD pathophysiology. Its level in patients with the Arab–Indian (AI) haplotype exceeds that in any other haplotype by nearly two-fold.[20,21] Our study reveals that neither total hemoglobin nor hemoglobin S steady-state level to be associated with depression. However, the hemoglobin F level was inversely promotional to the depression score. In other words, the higher the hemoglobin F, the lower the depression score. This finding might explain why depression is more prevalent in the southern region of Saudi Arabia, where African haplotype is predominant compared to Arab Indian haplotype in the esteem region characterized by higher hemoglobin F. Contrarily, we found that the steady-state creatinine level is directly promotional to the depression score. In other words, when creatinine level rises, the depression gets higher too. Despite a close linkage between all these factors and having depression, regression analysis was only significant for males and those with frequent ER visits. In other words, these are only two factors that could predict the development of depression.

This study explored several variables and factors closely associated with the existence of depression, though there are some limitations. This is a cross-sectional study with a small sample size, which could not represent the whole SCD community. A longitudinal prospective study needed to confirm that whether depression is a modulator of the disease severity or a sequence. In conclusion, depression is quite prevalent in patients with SCD compared to other chronic diseases though it is still overlooked. Several clinical and laboratory indices were found to be closely linked to depression. Constellations of these factors may help depression prediction, early screening, and disease severity modulation.

Ethical approval

The approval was taken from the Ethical Committee in King Faisal University and King Fahad Hospital. The confidentiality maintained, in which all the information was carried through the survey representing the individuals anonymously using codes—informed verbal consent taken from the participants as well.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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