Saudi Journal of Medicine (SJM)
Scholars Middle East Publishers
Dubai, United Arab Emirates
Website: http://scholarsmepub.com/

ISSN 2518-3389 (Print)
ISSN 2518-3397 (Online)

Depression, Anxiety and Stress among Bahraini Adults with Sickle Cell Anemia

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Article History
Received: 08.10.2018
Accepted: 17.10.2018
Published: 30.10.2018

DOI:
10.21276/sjm.2018.3.10.5

Abstract: Sickle cell disease is a chronic, inherited disorder. Complications from SCD place patients at risk for poor psychosocial adaptation, including symptoms of depression anxiety and stress. To measure the prevalence of depression, anxiety and stress in adults with sickle cell anemia in the Kingdom of Bahrain, and to study the factors related to the development of depression, anxiety and stress in these patients, we did a cross-sectional study that involved administering Depression Anxiety Stress Scales (DASS-21). A total number of 343 patients above 18 years, with sickle cell disease were recruited by convenient sampling from Salmaniya medical complex, health centers and sickle cell disease society. Participants also completed a survey of demographic data with specific inquiries about common sickle cell anemia risk factors and complications. From 343 participants (199 males &144 females) 53.9% were depressed, 70.8% had anxiety and 51.6% were stressed. A significant association was seen for depression and female gender(p-value 0.041), lower educational level (p-value 0.005), unemployment (p-value 0.01), number of emergency visits (p-value 0.008), hospital admissions (p-value 0.005) and medications like anti-depressants (p-value <0.001). Similarly, anxiety was significantly associated with female gender (p-value 0.031), unemployment (p-value 0.017), hospital admissions (p-value 0.047) and medications (like MST, codalgin and anxiolytics). Stress, however, was not found to be associated with any of the socio-demographic factors but was significantly associated with number of emergency visits (p-value 0.001), hospital admissions (p-value 0.008) and medications (like MST, codalgin and anxiolytics). We found the prevalence of depression to be (53.9%), anxiety (70.8%) and stress (51.6 %) among the studied population. Screening of sickle cell anemia patients for depression, anxiety and stress symptoms is recommended at regular intervals.
Keywords: Depression, anxiety, stress, Bahrain, sickle cell anemia.

INTRODUCTION

Background

Sickle cell anemia is a chronic hemoglobinopathy that is inherited in an autosomal recessive pattern. Most common form of sickle cell disease is homozygous HbS disease (HbSS). Hemoglobin S (HbS), results from the substitution of a valine for glutamic acid as the sixth amino acid of the beta globin chain, which produces a hemoglobin tetramer (alpha2/beta S2) that is poorly soluble when deoxygenated [1]. Other variants include sickle cell hemoglobin C disease and sickle cell Beta thalassemia [2].

Sickle cell disease predominates among people from African, Asian, Arabic and Mediterranean countries [1]. In the united states, it was estimated that more than 70,000 individuals are affected, approximately about 1 in 500 African American [3].

In Saudi Arabia premarital screening program estimate the prevalence of sickle cell gene in the adult population at 4.2% for sickle-cell trait and 0.26% for sickle-cell disease [4]. In the kingdom of Bahrain, the newborn screening study conducted in Bahrain during 1984-1985 revealed 2.1% incidence rate of sickle cell disease. Similar study done in 2005 showed 0.9% of newborns were suffering from sickle cell disease [5].

In Bahrain, The Ministry of Health in February 2014 estimated that around 5,000 people currently suffer from sickle cell disease, but according to the Sickle Cell Society the number was 18,000 a few years ago [6].

Patients with SCD commonly report low self-esteem and feelings of hopelessness as a result of frequent pain, hospitalizations and loss of schooling (in children) and employment (in adults) [7]. One of the first studies examining depression and sickle cell disease in 1981 showed that depression occurred more frequently than expected in sickle cell disease patients. These individuals were treated with anti- depressants and both depression and pain were responsive to

antidepressant treatment [8]. Previous studies also show depression and age were significantly associated with emergency treatment and hospital admissions [9].

In 2008 PiSCES project (Pain in Sickle Cell Epidemiology Study) showed that 27.6% of sickle cell disease patients from a sample of 232 patients were depressed and 6.5% had any anxiety disorder. Both depressed and anxious subjects had poorer functioning in all eight SF-36 subscale. The anxious subjects had more pain crisis and used opioids more often [10].

A more recent study done in the United States in 2014 at NIH Clinical Center evaluated sleep disturbance, depression and effect of pain in 328 adult sickle cell disease patients using Pittsburgh Sleep Quality Index and Beck Depression Inventory Scale 2. Results showed 71.2% had sleep disturbance and 20.6% had a score indicating depression with both being more common in those with frequent pain episodes [11].

Regionally, a study was done in Saudi Arabia in 2009 at King Fahad General Hospital on depression and anxiety in sickle cell disease adolescents. It was done on 110 adolescents with sickle cell disease and 202 adolescents without sickle cell disease as a control group . The study revealed that 29% with sickle cell disease and 32% without sickle cell disease were screened positive for one or more psychiatric disorder. Adolescents with sickle cell disease showed higher prevalence of adjustment and anxiety disorders compared to their peers [12].

In Bahrain, in 2010 at Salmaniya Medical Complex , the association of sickle cell anemia and Vaso-occlusive crisis with depression, anxiety and stress was investigated among Bahraini adolescent patients and controls. This was a cross-sectional study that involved providing Depression Anxiety Stress Scales (DASS-21) to SCA patients with (n=138) and without (n=105) VOC. Significantly higher proportion of VOC patients was found among the severe-extremely severe anxiety (P<0.002) and stress (P=0.001) groups. Adjusting for age, sex, income, number of affected individuals per family, and HbS levels, mild-moderate (P=0.042; odds ratio=2.00; 95% confidence interval=1.03-3.91) and severe-extremely severe (P=0.004; odds ratio=4.43; 95% confidence interval=1.59-12.34) anxiety were independently associated with VOC. Both depression and stress were not associated with VOC after adjusting for these covariates. These results suggest a positive contribution of VOC to the increased rates of anxiety disorders among SCA patients, thereby recommending counseling SCA patients with repeated VOC for these psychological comorbidities, in particular anxiety [13].

Sickle cell disease is one of the commonest reasons for hospital admissions in Bahrain and it considered one of the most significant causes of morbidity and mortality. A very recent study was done in 2017 on the Health-Related Quality of Life in Adults with Sickle Cell Disease in Bahrain. Adults with SCD in Bahrain showed significant impairment in all domains of HRQOL when compared to the general population [14]. However depression, anxiety and stress were not studied specifically in adults of Bahrain.

Aim

- To improve psychological wellbeing of sickle cell anemia patients.

OBJECTIVES

- To measure the prevalence of depression, anxiety and stress in adults with sickle cell anemia in the kingdom of Bahrain.

METHODS

Study design: Cross sectional study .

Sample size and sampling

This research included sickle cell anemia Bahraini patients aged 18 years and above.

The sample were recruited by convenience method during the time interval from 5th to 16th of June 2016 using:

- Manual distribution of the questionnaire
- Filling an online questionnaire.

A Self- Administered questionnaire was manually distributed among the attendants of Outpatient Clinics in SMC and the following health centers:

Bilad Alqadeem health center, Naim health center, Jidhafs health center, Shaikh Jaber Alsubah health center, Yousif engineer health center, Ahmed Ali Kanoo, Albudaiya health center, Alkuwait health center, Sitra health center, Hamad Town health center and Mohamed jassim Kanoo health center due to the availability of SCD clinic.

Verbal consent was taken from all participants and educational leaflets about the alarming symptoms of depression, anxiety and stress were distributed.

Health Centers

Patients attending the SCD clinic, which is functional once weekly at the health centers mentioned above, were approached while waiting for their appointment. But most of these clinics were cancelled during the data collection period and the number of attendants was small with majority of patients being in the pediatric age group. So, the majority of the sample was recruited from the treatment room of those health centers. The total number recruited was 88 participants.

SMC

Patients were approached in the waiting area of SMC Hematology morning clinic and SMC-SCD evening clinic. The total number of those attendees who agreed to participate was around 99.

Society

Survey monkey was used to generate an online questionnaire, which was distributed using WhatsApp messages to the general population and through SCD-society through their mobile data base. Total number of respondents was 242.

Exclusion criteria

Adults who could not read or write, Non-Bahrainis, pregnant women and aged below 18 years old were excluded from the study sample.

Questionnaires

For participant recruited from salmanyia medical complex and health centers, a verbal consent was taken. For those participated in survey monkey, an introduction about the study, aims and objectives and confidentiality of results was clearly stated. the selected participants filled a self- administered questionnaire (Arabic version of DASS 21), Subjects completed a survey of demographic data with specific inquiries about common sickle cell anemia demographical and clinical factors and complications. It included questions about: gender, age, educational level, employment, marital status, habits (smoking and alcohol), other chronic diseases, other hemoglobinopathies, use of medications (e.g. antidepressants), frequency of need of analgesia, number of admissions in hospital and Intensive care unit , and the presence of sickle cell anemia complications.

The DASS 21 is a 21 item self- report questionnaire designed to measure the severity of a range of symptoms common to both Depression and Anxiety but it's not a categorical measure of clinical diagnosis. The essential function of the DASS is to assess the severity of the core symptoms of Depression, Anxiety and Stress [15].

It's validity and reliability is well established. The reliability coefficient of depression, anxiety and stress scales range from 0.81 to 0.97, and the three subscales showed discriminative ability to differentiate between psychiatric patient and non-psychiatric patients [16].

In completing the DASS, the individual is required to indicate the presence of a symptom over the previous week. Each item is scored from 0 (did not apply to me at all over the last week) to 3 (applied to me very much or most of the time over the past week) [17].

For scoring the scale to which each item belongs is indicated by the letters D (Depression), A (Anxiety) and S (Stress). For each scale (D, A & S) sum the scores for identified items. Because the DASS 21 is a short form version of the DASS (the Long Form has 42 items), the final score of each item groups (Depression, Anxiety and Stress) needs to be multiplied by two (x2).

Once multiplied by 2, each score can now be transferred to the DASS profile sheet, enabling comparisons to be made between the three scales and also giving percentile rankings and severity labels [17].

DASS Severity Ratings

Severity	Depression	Anxiety	Stress
Normal	0-9	0-7	0-14
Mild	10-13	8-9	15-18
Moderate	14-20	10-14	19-25
Severe	21-27	15-19	26-33
Extremely Severe	28+	20+	34+

Statistical analysis:

SPSS 23 was used for data entry and analysis.

- Frequencies and percentages were computed for categorical variables.
- Overall scores were computed for depression, anxiety and stress scales.
- Cross tabulations were computed for depression anxiety and stress in relation to source of data, demographical data, clinical characteristics of sickle cell disease patients and the usage of medications.

- Chi- Square test was used to evaluate the association between categories, P- Value less than 0.05 was statistically considered significant.
- For the sake of analysis and study of association, we combined all participants found to have depression, anxiety and stress, ranging from mild to extremely severe, according to the DASS 21 scale.

Ethical consideration

Consent was taken and confidentiality was maintained. Educational leaflets about depression ,anxiety and stress were distributed to all participants after completion of the questionnaire. Approval from research committee was taken before commencing the research.

RESULTS

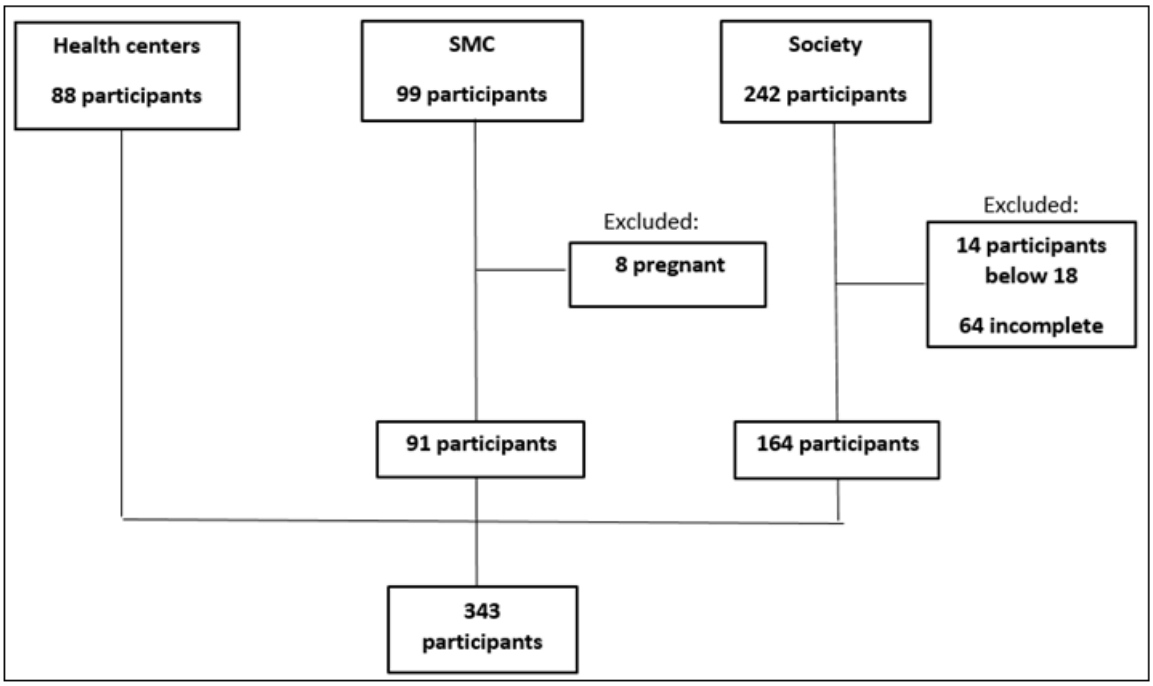

Fig-2:

A total of 429 participants responded to the questionnaire. Of these, 8 were pregnant, 14 were below 18 and 64 incomplete questionnaires were excluded (Figure-1).

Theremaining 343 sickle cell anemia individuals were included in our study. The majority of the sample were recruited through the survey monkey 164 (47.8%). The rest of the sample from SMC outpatient clinic 91 (26.5%) and from local health centers 88 (25.7%) (Table-1).

Socio-demographic and clinical characteristic of the participants

The males represent 199 (58%) of the sample. Majority of the respondents (84.6%) were aged below 40 years . A total of 207 (60.4%) were married. Almost half of respondents had attained higher education level 179(52.2%), 127 (37%) had completed secondary school and only 37(10.8%) had educational status up to intermediate or below. More than half of the individuals 182(53.1%) were unemployed (Table-1).

Most of the participants 147(42.9%) visited emergency more than 6 times last year due to sickle cell crisis. A total of 63(18.4%) attended the emergency between 4-6 times, 96(28%) attended between 1-3 times while 37(10.8%) did not need to visit the emergency at all during the past year (Table-2).

With regards to the frequency of hospitalization due to sickle crisis during the last year, most of the participants 139(40.5%) were admitted around 1-3 times, 95(27.7%) got admitted 4-6 times, 50(14.6%) required more than 6 times admissions and 59(17.2%) required no hospitalization. From our participants 188(54.8%) required ICU admission during their life time (Table-2).

With respect to local health center visits per week for analgesic injection, 105(30.6%) attended the health center more than 5 times, on the other hand 133(38.8%) required none. While 81(23.6%) visited 1-2 times per week and 24(7%) visited the local health center around 3-4 times per week for analgesic injection (Table-2).

The majority of the study sample 294(85.7%) had sickle cell anemia related complication (Table 2).

From 343 participants 53.9% were depressed, 70.8% had anxiety and 51.6% were stressed (figure-1).

Using the DASS21 scale the severity of depression, anxiety and stress was assessed. 11.4%, 22.2%, 9% and 11.4% were mild, moderate, severe and extremely severely depressed respectively (figure-2).

In ascending order of severity, 7.9%, 22.7%, 12.2% and 28% were mild, moderate, severe and extremely severely anxious (figure-3).

Mild, moderate, severe and extremely severely stressed respectively were 16.3%, 13.7%, 12.8% and 8.7% (figure-4).

Participants were included from outpatient clinics, health centers and the society (survey monkey) but no significant difference was found with regard to depression, anxiety and stress (P-value 0.318, 0.223 and 0.891 respectively). For that reason we dealt with them as a single group (Table-3).

Association between Depression, Anxiety and Stress and Socio-demographic Data of participants

In this study, several sociodemographic factors of sickle cell anemia were assessed. With regard to association of sickle cell anemia with gender 98 (49.2%) males and 87 (60.4%) females were depressed, 132 (66.3%) males and 111 (77.1%) females had anxiety and 97 (48.7%) males and 80 (55.6%) females had stress. There was a strong statistically significant association between sickle cell anemia and gender with regards to depression and anxiety (P-value 0.041 and 0.031, respectively) (Table-3).

In relation to educational level, depression 28(75.7%), anxiety 29(78.4%) and stress 22(59.5%) was more among those with intermediate degree or below. Of those having secondary degree, 72(56.7%) were depressed, 97(76.4%) had anxiety and 68(53.5%) were stressed. Of those holding collage degree 85(47.5%) had depression, 117(65.4%) had anxiety and 87(48.6%) had stress. Sickle cell anemia and educational level in relation to depression was statistically significant (P-value 0.005) but were not significant for anxiety (p-value0.065) and stress (p-value 0.417) (Table-3).

From the unemployed, 110 (60.4%) were depressed, 139 (76.4%) had anxiety and 100 (54.9%) were stressed. There was a statistically significant relation between sickle cell anemia and work status with regards to depression (P-value 0.01) and anxiety (P-value 0.017). No statistically significant relation was seen for stress (P-value 0.188) (Table-3).

Regarding the habits of the participants, smokers were statistically significantly depressed (P-value 0.032), but anxiety(P-value 0.335) and stress(P-value 0.072) were not statistically significant (Table 3).

On the other hand, age, marital status and the presence of other chronic diseases had no statistically significant association with depression, anxiety and stress in sickle cell anemia (Table-3).

It was seen that patients visiting the emergency frequently due to sickle cell anemia crisis had a statistically significant association with depression and stress, (p-value 0.008 and 0.001 respectively). However, no significant association was seen with anxiety (p-value 0.056) (Table-4).

Regarding hospital admissions for SCD crisis, a statistically significant association was found for depression (p-value 0.005), anxiety (p-value 0.047) and stress (p-value 0.008). On the other hand, there was no significant association between the number of ICU admissions, number of visits to the local health center for analgesia and complications of SCD with depression, anxiety and stress (Table-4).

Regarding medication use, Morphine sulfate tablet (MST) and antidepressants had a statistically significant association with depression (p-value 0.003 and <0.001respectively), anxiety (p-value 0.033 and 0.002 respectively) and stress (p-value 0.018 and <0.001 respectively). Use of Diazepam and Codeine phosphate hemihydrate/ paracetamol tablet (codalgin) had a statistically significant association with anxiety (p-value 0.024 and 0.017 respectively) and stress (p-value 0.029 and 0.038 respectively). However, these two medications did not have a statistically significant association with depression (p-value 0.056 and 0.106 respectively). Furthermore, there was no statistically significant association between paracetamol, Ibuprofen, Naproxen, Diclofenac sodium and Hydroxyurea and depression, anxiety and stress (Table-4).

Table-1: General and Demographical Data of Sickle Cell Anemia Patients in the Kingdom of Bahrain

		n	%
Source of data	Outpatient clinic	91	26.5%
	Health center	88	25.7%
	Society	164	47.8%
Gender	Male	199	58.0%
	Female	144	42.0%
Age	<30	146	42.6%
	30-39	144	42.0%
	40-49	39	11.3%
	>=50	14	4.1%
Marital status	Single	118	34.4%
	Married	207	60.4%
	Divorced / Widowed	18	5.2%
Educational level	Intermediate or below	37	10.8%
	Secondary	127	37.0%
	College	179	52.2%
Work status	Unemployed	182	53.1%
	Employed	161	46.9%
Smoking		109	31.8%
Chronic disease		108	31.5%

Table-2: Clinical Characteristics of Sickle Cell Anemia Patients in the Kingdom of Bahrain

		n	%
Emergency visit due to SCD crisis during the last year	None	37	10.8%
	1-3 times	96	28.0%
	4-6 times	63	18.4%
	>6 times	147	42.9%
Admission due to SCD crisis during last year	None	59	17.2%
	1-3 times	139	40.5%
	4-6 times	95	27.7%
	>6 times	50	14.6%
ICU admission ever in life		188	54.8%
Current use of medication Use of Panadol (Paracetamol)		255	74.3%
Use of Brufen (Ibuprufen)		153	44.6%
Use of Naproxen		182	53.1%
Use of MST (Morphine sulfate tablet)		140	40.8%
Use of Valium (Diazepam)		33	9.6%
Use of Hydroxyurea		63	18.4%
Use of Antidepressant		28	8.2%
Use of Voltaren (Diclofenac sodium)		148	43.1%
Use of Codalgin (Codeine phosphate hemihydrate/ paracetamol)		133	38.8%
Number of visits to local health center per week for analgesic injections	None	133	38.8%
	1-2 times	81	23.6%
	3-4 times	24	7.0%
	>=5	105	30.6%
Complication		294	85.7%

Table-3: Association between Depression, Anxiety and Stress and Socio-demographic data in Sickle Cell Anemia Patients in the Kingdom of Bahrain

		Depression			**Anxiety**			**Stress**		
		Normal	**Depressed**	**P-value**	**Normal**	**Anxious**	**P-value**	**Normal**	**Stressed**	**P-value**
		n (%)	n (%)	P-value	n (%)	n (%)	P-value	n (%)	n (%)	P-value
Source of data	Outpatient clinic	47 (51.6%)	44 (48.4%)	0.318	22 (24.2%)	69 (75.8%)	0.223	46(50.5%)	45 (49.5%)	0.891
	Health center	42 (47.7%)	46 (52.3%)		23 (26.1%)	65 (73.9%)		42 (47.7%)	46 (52.3%)	
	Society	69 (42.1%)	95 (57.9%)		55 (33.5%)	109 (66.5%)		78 (47.6%)	86 (52.4%)	
Gender	Male	101 (50.8%)	98 (49.2%)	**0.041**	67 (33.7%)	132 (66.3%)	**0.031**	102 (51.3%)	97 (48.7%)	0.213
	Female	57 (39.6%)	87(60.4%)		33 (22.9%)	111 (77.1%)		64 (44.4%)	80 (55.6%)	
Age	<30	68 (46.6%)	78 (53.4%)	0.98	45 (30.8%)	101 (69.2%)	0.749	67(45.9%)	79 (54.1%)	0.506
	30-39	67 (46.5%)	77 (53.5%)		41 (28.5%)	103 (71.5%)		76(52.8%)	68 (47.2%)	
	40-49	17(43.6%)	22 (56.4%)		9 (23.1%)	30 (76.9%)		16(41.0%)	23 (59.0%)	
	>=50	6 (42.9%)	8 (57.1%)		5 (35.7%)	9 (64.3%)		7 (50.0%)	7 (50.0%)	
Marital status	Single	52 (44.1%)	66 (55.9%)	0.842	32 (27.1%)	86 (72.9%)	0.797	57 (48.3%)	61 (51.7%)	0.506
	Married	98(47.3%)	109 (52.7%)		62 (30.0%)	145 (70.0%)		99 (47.8%)	108 (52.2%)	
	Divorced / Widowed	8 (44.4%)	10 (55.6%)		6(33.3%)	12 (66.7%)		10 (55.6%)	8 (44.4%)	
Educational level	Intermediate or below	9 (24.3%)	28 (75.7%)	**0.005**	8 (21.6%)	29 (78.4%)	0.065	15 (40.5%)	22 (59.5%)	0.417
	Secondary	55 (43.3%)	72 (56.7%)		30 (23.6%)	97 (76.4%)		59(46.5%)	68 (53.5%)	
	College	94 (52.5%)	85 (47.5%)		62 (34.6%)	117 (65.4%)		92(51.4%)	87 (48.6%)	
Work status	Unemployed	72 (39.6%)	110 (60.4%)	**0.01**	43 (23.6%)	139(76.4%)	**0.017**	82 (45.1%)	100 (54.9%)	0.188
	Employed	86 (53.4%)	75 (46.6%)		57 (35.4%)	104 (64.6%)		84 (52.2%)	77 (47.8%)	
Smoking		41 (37.6%)	68 (62.4%)	0.032	28 (25.7%)	81 (74.3%)	0.335	45 (41.3%)	64 (58.7%)	0.072
Chronic disease		48 (44.4%)	60 (55.6%)	0.683	26 (24.1%)	82 (75.9%)	0.16	48 (44.4%)	60(55.6%)	0.321

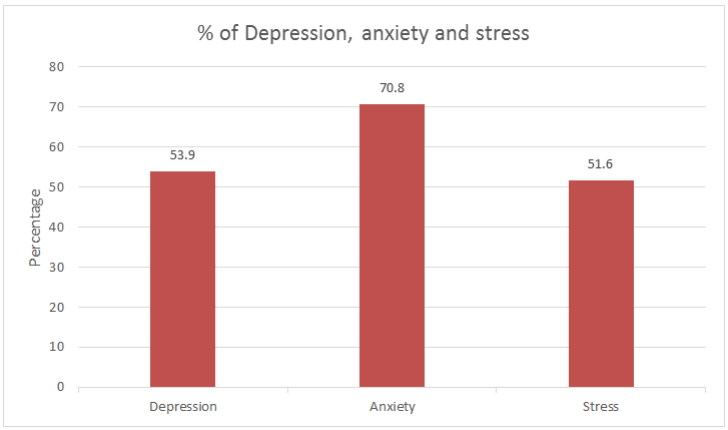

Fig-3: % of Depression, Anxiety and Stress in SCD Patients of Bahrain

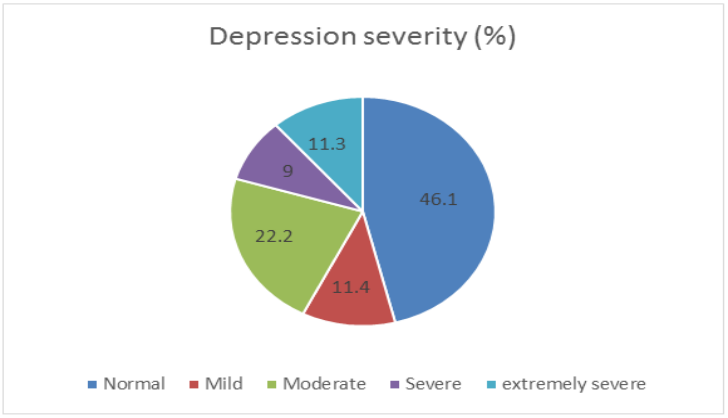

Fig-4: Severity of Depression(%) in SCD Patients of Bahrain

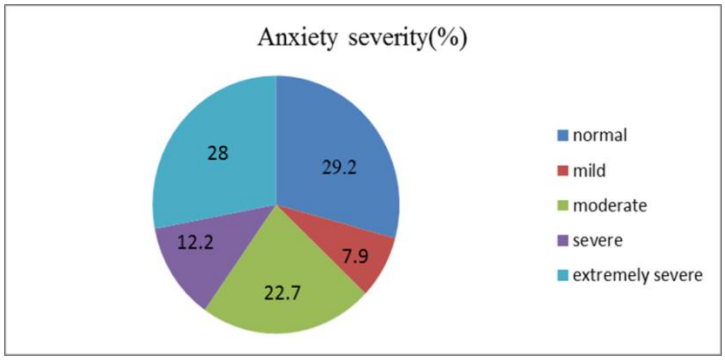

Fig-5: Severity of Anxiety (%) in SCD Patients of Bahrain

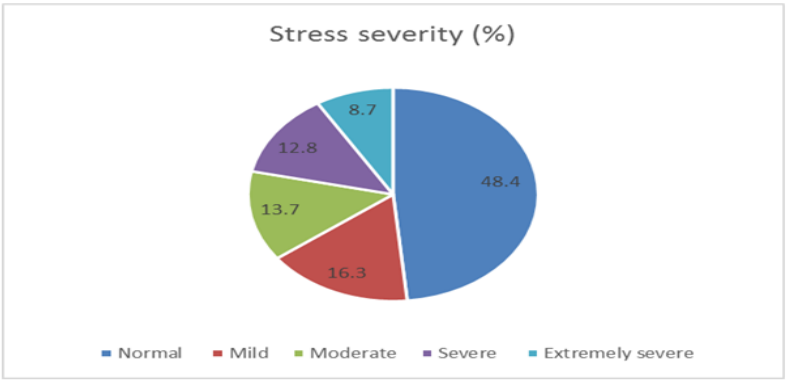

Fig-6: Severity of Stress (%) in SCD Patients of Bahrain

Table-4: Association between Depression, Anxiety and Stress and Clinical Characteristics of SCD Patients in the Kingdom of Bahrain

		Depression		**p-value**	**Anxiety**		**p-value**	**Stress**		**p-value**
		Normal	**Depressed**		**Normal**	**Anxious**		**Normal**	**Stressed**	
		N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Emergency visit due to SCD crisis during the last year	None	20 (54.1%)	17 (45.9%)	**0.008**	15 (40.5%)	22 (59.5%)	0.056	23 (62.2%)	14 (37.8%)	**0.001**
	1-3 times	52 (54.2%)	44 (45.8%)		32(33.3%)	64 (66.7%)		53 (55.2%)	43 (44.8%)	
	4-6 times	34 (54.0%)	29 (46.0%)		21 (33.3%)	42 (66.7%)		37 (58.7%)	26 (41.3%)	
	>6 times	52 (35.4%)	95 (64.6%)		32 (21.8%)	115 (78.2%)		53 (36.1%)	94 (63.9%)	
Admission due to SCD crisis during last year	None	35 (59.3%)	24 (40.7%)	**0.005**	25 (42.4%)	34 (57.6%)	**0.047**	36 (61.0%)	23 (39.0%)	**0.008**
	1-3 times	72 (51.8%)	67 (48.2%)		42 (30.2%)	97 (69.8%)		75 (54.0%)	64 (46.0%)	
	4-6 times	33 (34.7%)	62 (65.3%)		22 (23.2%)	73 (76.8%)		37 (38.9%)	58 (61.1%)	
	>6 times	18 (36.0%)	32 (64.0%)		11 (22.0%)	39 (78.0%)		18 (36.0%)	32 (64.0%)	
ICU admissions ever		90 (47.9%)	98 (52.1%)	0.459	49 (26.1%)	139 (73.9%)	0165	90 (47.9%)	98 (52.1%)	0.831
Current use of medication Use of Panadol		117 (45.9%)	138 (54.1%)	0.908	74 (29.0%)	181 (71.0%)	0.925	122 (47.8%)	133 (52.2%)	0.727
Use of Brufen		64 (41.8%)	89 (58.2%)	0.158	38 (24.8%)	115 (75.2%)	0.114	69 (45.1%)	84 (54.9%)	0.273
Use of Naproxen		85 (46.7%)	97 (53.3%)	0.801	48 (26.4%)	134 (73.6%)	0.228	88 (48.4%)	94 (51.6%)	0.986
Use of MST		51 (36.4%)	89 (63.6%)	**0.003**	32 (22.9%)	108 (77.1%)	**0.033**	57 (40.7%)	83 (59.3%)	**0.018**
Use of Valium		10 (30.3%)	23 (69.7%)	0.056	4 (12.1%)	29 (87.9%)	**0.024**	10 (30.3%)	23 (69.7%)	**0.029**
Use of Hydroxyurea		35 (55.6%)	28 (44.4%)	0.094	18 (28.6%)	45 (71.4%)	0.910	31 (49.2%)	32 (50.8%)	0.887
Use of Antidepressant		4 (14.3%)	24 (85.7%)	**<0.001**	1 (3.6%)	27 (96.4%)	**0.002**	3 (10.7%)	25 (89.3%)	**<0.001**
Use of Voltaren		64 (43.2%)	84 (56.8%)	0.361	42 (28.4%)	106 (71.6%)	0.783	64 (43.2%)	84 (56.8%)	0.096
Use of Codalgin		54 (40.6%)	79 (59.4%)	0.106	29 (21.8%)	104 (78.2%)	**0.017**	55 (41.4%)	78 (58.6%)	**0.038**
Number of visits to local health centre per week for analgesic injections	None	72 (54.1%)	61 (45.9%)	0.076	48 (36.1%)	85 (63.9%)	0.139	76 (57.1%)	57 (42.9%)	0.073
	1-2 times	34 (42.0%)	47 (58.0%)		19 (23.5%)	62 (76.5%)		36 (44.4%)	45 (55.6%)	
	3-4 times	12 (50.0%)	12 (50.0%)		5 (20.8%)	19 (79.2%)		11 (45.8%)	13 (54.2%)	
	>=5	40 (38.1%)	65 (61.9%)		28 (26.7%)	77 (73.3%)		43 (41.0%)	62 (59.0%)	
Complication		134 (45.6%)	160 (54.4%)	0.658	82 (27.9%)	212 (72.1%)	0.207	140 (47.6%)	154 (52.4%)	0.480

DISCUSSION

Sickle cell disease is a chronic condition characterized by chronic pain and end organ complications. Studies have shown that affected people have psychiatric and social difficulties along with poorer functioning and quality of life compared to controls [10].

In Bahrain, previously a study was conducted comparing quality of life of sickle cell disease patients to patients with other chronic diseases and disease free

individuals. Respondents with SCD scored significantly lower than the other two groups [14]. However depression, anxiety and stress were not studied specifically.

Our findings showed that 53.9% of recruited sickle cell disease patients were depressed. This is higher than the previously mentioned study held in Washington DC in 2003 which showed a prevalence of depression of 44% [18]. This may be attributed to the fact that our study included all SCD patients irrespective of when was their last vaso-occlusive attack but their study excluded patients with vaso-occlusive crisis in the past one month of data collection.

The anxiety prevalence in our study was 70.8%. which is similar to the results of a study done on adolescents with SCD in the kingdom of Bahrain [13], this study showed significantly higher proportion of severe-extremely severe anxiety (P<0.002) among adolescents with sickle cell disease [13].

It's worth mentioning that previously no study has looked into stress and sickle cell anemia in adults. Our study showed a stress prevalence of 51.6%. This which is much higher than a study done in Malaysia on diabetic patients with stress prevalence of 12.5%, using the same instrument as ours, i.e., DASS 21 [19]. This can be attributed to the fact that sickle cell disease patients suffer from pain. As seen in our results, patient who were on analgesia (MST, codalgin) were found to have stress. Furthermore, a similar study done at Bahrain in 2010 on SCD adolescents also showed significantly high prevalence of stress (P=0.001), which was not related to VOC attacks [13].

Studying the demographic factors, we observed a statistically significant relationship between female gender and unemployment for development of depression and anxiety. Those who had lower educational level were only found to be significantly depressed. Other studies have also established that patients more likely to be depressed among those with low family income, less than high school education and females, even after controlling for disease severity [18]. However, our study also indicates that such factors may also be a cause for anxiety. Psychological complications in patients with SCD mainly result from the impact of pain and symptoms on their daily lives and society's attitudes towards them [7].

In regards to the clinical characteristics of sickle cell disease patients and their relation to the development of depression, anxiety and stress, our results concur with previous studies in some of the tested variables. Our results showed that visiting the emergency department frequently due to sickle cell anemia crisis had a statistically significant association with depression and stress, while hospital admissions for SCD crisis was significantly associated with depression, anxiety and stress. These variables reflects the disease severity in these patients.

This is consistent with the work of other studies who found that persons with sickle cell disease are at risk for depression and other psychological impairments that negatively impact on medical outcomes. These findings suggest that SCD patients should be evaluated routinely for depressive symptoms in addition to being evaluated for medical problems associated with the disease [10, 9].

Regarding medication use, Morphine sulfate tablet and antidepressants had a statistically significant association with depression anxiety and stress.

The significant association of antidepressants and depression is explainable as patients who use antidepressants are likely to be diagnosed with depression (P-value 0.001). Similarly, patients who were anxious and stressed where found to be on anxiolytic medication (i.e. Diazepam) (P-value 0.024). This is in accordance to the results of earliest studies suggesting that antidepressants help control both pain and depression [8].

Patients who are taking opiates and sedatives have medication related psychological complications. We believe that this is applicable to sickle cell disease patients who encounter chronic pain and several acute painful crisis.

According to our study, there was no significant association of Paracetamol, Ibubrufen, Naproxen, Diclofenac sodium and Hydroxyurea with depression, anxiety and stress [18]. This is inconsistent with other study which showed that Hydroxyurea users were more likely to be depressed than those patients who did not use hydroxyurea. This may be attributed to the fact that Hydroxyurea is responsible for decreasing the disease severity and frequency of vaso occlusive attacks [18].

Our study has some limitations that may affect the interpretation of results. The sample recruitment was convenient in order to get a representative sample size as there is no official number or registry of sickle cell disease patient to attempt randomization.

We could not compare our findings with healthy controls not suffering from sickle cell disease, and further studies are needed in this aspect.

The collected data was self-reported and this could contribute to recall bias. The patients previous medical records were not explored.

Additionally, the impact of vaso-occlusive crisis independently on depression, anxiety and stress needs to be studied further.

CONCLUSION

According to our results, the prevalence of depression was (53.9%), anxiety (70.8%) and stress (51.6 %) among the studied population.

As these symptoms are highly correlated, they should be considered together when managing sickle cell disease patients. Our findings could help primary care physicians identify and screen high risk sickle cell patients for mental disorders. Socio-demographic factors like female gender, low educational level and unemployment could be predictors for depression, anxiety and stress.

Among the clinical characteristics, frequent visiting of emergency department, number of hospital admission and use of certain medications (MST, antidepressants, anxiolytics) was significantly associated with depression, anxiety and stress. Psychological interventions should be incorporated into protocols for the management of patients with SCD and offered as standard care.

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