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An Integrative Review of Sickle Cell and Depression

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Abstract

Purpose: Gain insight and knowledge through the exploration of depression among adult patients living with chronic illness such as sickle cell disease. The review focused on defining the prevalence of depression in chronic illness with emphasis on sickle cell. Associated chronic pain, quality of life, disease trajectory and the need for increased screening and treatment for depression in chronic illness such as with those living with sickle cell disease will be evaluated.

Data Sources: A search of the following databases: Cumulative Index to Nursing and Allied Health Literature, Cochrane Library, Ovid/Medline, PubMed and Google Scholar between (2003-2014).

Conclusions: There is a high prevalence of depression among patients living with SCD impacting their pain and quality of life. Additional research is needed to evaluate the use of antidepressants in SCD.

Implications for practice: Health care providers play an essential role in the assessment, and screening for depression. Effective management of these conditions may improve the quality of life of this adult population. Further investigation is warranted to understand the meaning of depression and psychosocial factors in this patient population. Findings from this integrative review may help to provide a clearer understanding of depression and psychosocial factors in adults with sickle cell disease and lead to future research to identify how depression treatment affects pain and quality of life.

Keywords

Sickle cell, Depression, Quality of life, Pain, Disease trajectory

Introduction

Sickle Cell Disease (SCD) refers to a group of genetic hematologic disorders characterized by the production of abnormal hemoglobin S instead of normal hemoglobin A**.** Common types of SCD are: anemia-SS, hemoglobin-SC and S-beta thalassemia. The anemia of SCD fosters increased susceptibility to infection, chronic and intermittent acute pain episodes, and multiple organ system dysfunctions [1]. Due to the distorted and rigid formation of sickled erythrocytes in microcirculation, there is tissue and organ ischemia [2]. Pain is considered the primary SCD symptom, occurring in both chronic and acute crisis [3].

A common hematologic disorder is SCD in the United States (US), affecting approximately 70,000-100,000, most of whom are African-Americans (AA) or Latino. The occurrence rate of SCD is 1 in 5 AAs and 1 in 36,000 Hispanic births [4]. Not limited to the US, SCD affects millions worldwide. Regions of high prevalence include: Africa, Caribbean, South America, Central America, Mediterranean countries (Turkey, Greece, and Italy), India and Saudi Arabia [4].

Impact of the trajectory of sickle cell disease

Uncertainty and unpredictability of the SCD illness trajectory allows for a range of severity of illness. Uncertainty of when crises will occur coupled with pain and life threatening complications, contributes to a reduced quality of life (QOL) and psychological health among those affected. A study of 50 AAs found a higher prevalence of depression among those living with SCD than the general AA community [5]. Mild depression was present in 44% of the participants in comparison to the National Study of American Life which found a 10.4% prevalence of depression in AA [6]. Prevalence rates of depression in US from 2006-2008 among 17,604 AA ranged from 5.0-12.9% (CDC, 2010) [7]. Ward and Mengesha conducted a systematic review of 19 studies regarding AA men and depression and found a prevalence range of 5-10% [8].

The unpredictable trajectory of SCD leads to substantial situational depression. Little is however known about how interventions to treat depression may affect health outcomes for SCD. Prevalence of depression in SCD is comparable to that of other chronic illness and ranges from 18%-44% [3,5,9-13].

The NICE-91 guideline (2009) reported a two-three fold increase in depression among patients with a chronic illness (20-30%) compared to general population (10%) [14]. Rheumatoid Arthritis like SCD has acute and chronic pain episodes and uncertain trajectory with a similar rate of depression ranging from 14-38% [15]. Other common chronic illness such as diabetes mellitus has increased prevalence of co-morbid depression. Patients living with diabetes experience chronic neuropathic pain, multiple organ failure and uncertain trajectory similar to SCD. Ali, Stone, Peters, Davies and Khunti found the prevalence of depression in patients living with diabetes at 18% [16].

Studies of SCD to examine depression, evaluated pain and QOL are limited. Chronicity of illness, pain, stigma, discrimination

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and uncertainty in disease trajectory, overwhelming degree of complications, inadequate care, socioeconomic factors, educational level and social support are some of the complex factors that influence this complex relationship [1,3,12]. The exact cause of depression in SCD may not be entirely known; it may be a result of the underlying process, stigma or may actually be multifactorial [12]. The exact cause and effect relationship between depression and pain is not known, as to how much of the pain experienced in SCD is caused by depression versus whether more pain is causing the depression [3]. Despite the potential for adverse complications associated with comorbid depression, it is still under diagnosed and treated.

Purpose of this review was to analyze the research, gain insight and knowledge of depression in adult patients living with chronic illnesses such as SCD. Information gained by providers through increased understanding of SCD, may facilitate screening and early treatment of depression. Provider efficacy in addressing this life altering condition has a potential to improve health outcomes among those with SCD.

Methods

An integrative review of literature was conducted using Preferred Items for Systematic Reviews and Meta-Analyses (PRISMA) to increase rigor. Databases searches were conducted to identify studies that examined depression and psychosocial factors present among patients with SCD (e.g., CINAHL, Cochrane Library, Ovid/Medline, PubMed and Google Scholar). Search terms utilized were: sickle cell, depression, quality of life, trajectory and pain. The search was limited to studies published in English between 2003-2014 that examined the variables related to depression and psychosocial factors in adult with SCD. Results identified thirty-four articles using this criterion. Fourteen studies were selected for inclusion. Only research articles with adult participants aged 18 or greater diagnosed with SCD, were included. The studies contained variables related to depression and associated factors. Data evaluation to increase rigor and complexity was conducted. The fourteen articles included in this review are summarized in Table 1.

Results

Depression and SCD

Living with the encumbrance of a chronic illness is potentially devastating as SCD may lead to depression [12]. Symptoms of depression and chronic illness are often similar and therefore healthcare providers fail to diagnose depression [3]. The prevalence of depression and its impact on pain and other variables is not limited.

The Pain in Sickle Cell Epidemiology Study (PiSCES) measured the presence of depression and anxiety among N = 232 participants with SCD and examined the relationship that exists with pain, QOL, healthcare utilization and opioid usage by having participants journal daily [9]. Baseline variables of depression, anxiety, and health-related QOL were assessed. Findings were that 27.6% were depressed and had pain more days than participants that were not depressed ($p < 0.001$). Depressed participants reported higher pain, more distress and interference from pain on non-crisis pain days. Additionally, depressed participants reported less physical and a poorer mental QOL [3]. These findings could represent the presence of chronic pain in SCD population which can be predicted by the presence of depression. Despite the absence of a crisis they were having pain almost daily representing chronic pain due to presence of depression.

Hasan et al. studied N = 50 adults with SCD to assess the prevalence of depressive symptoms and determine impact of disease severity and health care usage among participants without a vaso-occlusive crisis for at least one month [5]. These researchers found 44% scored within the mild-severe range for depression and 26% were severely depressed [5]. It was found that depressed patients were more likely to access healthcare services through frequent ED visits ($p = 0.03$) and were subsequently hospitalized for pain crisis (> 5 in 1 year; $p = 0.0003$). The study found gender to be a predictor of depressive symptoms in females ($p = 0.03$), those with > 20 units of blood transfusions ($p = 0.03$), > 5 hospitalizations or ED visits within the previous year ($p=0.03$), less than a high school education ($p = 0.04$), > 5 crises in the previous year ($p = 0.00003$), inadequate social support ($p = 0.02$), family income < 10,000/year ($p = 0.001$) and use of Hydroxyurea ($p = 0.03$) as a proxy of SCD severity. These results highlight the

Table 1: Overview of Studies

Authors; Year of Publication & Level of Evidence (LOE)	Study Design	Sample	Purpose	Instruments	Results
Levenson et al., [9] LOE 4	Prospective cohort of PiSCES Project; Longitudinal study. Data collected from daily diary entries up to 6 months regarding sickle cell pain intensity, distress, interference, whether in SCD crisis or not, healthcare and opioid utilization. Variables include demographics, sickle cell genotype, lab data, HR-QOL, depression and anxiety	n = 232 SCD, aged 18 years or older. Enrolled in community settings and medical centers in Virginia.	To examine prevalence of depression & anxiety, determine relationship with pain (crisis and non-crisis), distress from pain, life interference, QOL, opioid usage and healthcare utilization.	Health Related QOL assessed via Medical Outcome Study 36 items short form (MOS SF-36) survey. Use of PHQ (Patient Health Questionnaire) for measurement of depression and anxiety. Combined major depressive syndrome and other depressive syndrome into one category of depression.	n = 64 (27.6%) were depressed. Significant association between depression and more days of pain ($p < 0.001$). Depression associated with higher mean pain, distress from pain and interfered with life on days when no crisis present.
Hasan, S.P., Hashmi, S., Alahassen, M., Lawson, W. and Castro, O. LOE 4 [5]	Quantitative study using questionnaires. Collected data including demographics (age, gender, marital status, education level, employment, income), type of SCD, type of SCD, disease severity, pain and health car usage.	Convenience Sample of N = 50; 27 females, 23 males; Age range 21 years to 64 years; mean age 36. Outpatient SC clinic at Howard University Hospital. In stable health for at least a month prior.	Assess prevalence of depressive symptoms; determine if any contribution of demographics, severity of SCD, health care use to depressive symptoms	Beck Depression Inventory (BDI); using a cut-off score of 14-17 as mild and > 20 severe. It is a 21 item self-report scale to measure presence and degree of depression and associated depressive symptoms. Commonly used in primary care for variety of chronic illnesses.	High prevalence (> 44%) of depression in the mild to severe range. Severe depression in n = 13. Depression caused more frequent ED visits and hospitalizations due to crisis. Low-income (< $10,000/yr) $p = 0.001$; educational attainment (less than high school) $p = 0.04$; female, $p = 0.03$; multiple blood transfusions (> 20 units) $p = 0.03$; uncontrolled pain (> 5 crisis in 12 months) $p = 0.001$; poor social support, $p = 0.02$; Hydroxurea prescribed, $p = 0.03$; history of frequent hospitalizations (> 5 in 12 months) $p=0.0003$ and ED visits (> 5 in 12 months, $p =0.03$ was statistically significant in predicting depressive symptoms.

Asnai, M., Fraser, R., Lewis, N. and Reid, M. LOE 4 [11]	Cohort Study; The Jamaica Sickle Cell Cohort Study. Administered questionnaires on socio-demographics (age, sex, marital status, genotype, employment status, and educational attainment), disease severity, depression and loneliness.	N = 277 SCD, mean age 31 years and N = 65 AA without SCD mean age 33.6 years; equal males & females in each subgroup. Participants had SC-SS, SC disease, beta thalassemia	To determine prevalence of depression and factors associated with depression and loneliness in SCD compared to matched AA controls.	SCD group: Demographic questionnaire including questions regarding utilization the SC clinic, frequency of pain crisis, presence of leg ulcers or not. Depression measured using BDI-II using a cut-off score of 17. Loneliness measured using UCLA-8 scale. Abbreviated version of UCLA-20; UCLA 8 highly correlated (r = 0.91) with original. BDI reported:α = 0.95; UCLA reported :α = 0.82 AA group: only socio-demographic questions. BDI-II for depression, and UCLA-8 for loneliness.	Two fold increase in depression in SCD group compared to AA group; 21.6% vs. 9.4%. SCD group increased mean loneliness scores compared to AA group (16.9 ± 5.1vs. 14.95 ± 4.69). SCD group: depression significantly correlated with unemployment (p = 0.01); complication of leg ulcer (p = 0.001), frequent healthcare visits (p = 0.019); uncontrolled pain/multiple crisis (p = 0.035). Loneliness in SCD correlated with unemployment (p = 0.004) and higher educational attainment (p < 0.001) with adjustment of SCD genotype. Whether SCD was present or not, depression was associated with unemployment (p < 0.001) and loneliness was associated with unemployment and lower educational attainment (p = 0.002)
Sogutlu, A., Levenson, J., McClish, D., Rosef, S. and Smith, W. LOE 4 [10]	Prospective cohort of PiSCES Project. Collected baseline demographic data, genotype. Participants used diaries to document daily entries on SCD pain, health care utilization secondary to SCD for up to a 6 months. Used questionnaires to measure SSB and HR-QOL.	Enrolled 308 in PiSCES Project; N = 230 SCD, aged at least 18 years. Mean age 34.4 years. Answered SSB questionnaire. All were from Virginia.	To examine somatic symptom burden (SSB) in SCD and its impact on pain, depression, anxiety, healthcare utilization and QOL.	Baseline data collected: age, gender, income, education, marital status, genotype, if receiving care at SCD center. SSB measured:PHQ-15 abridged to PHQscd (to exclude four common areas of pain in SCD: limb, back, stomach and chest; α = 0.75). Total scores on PHQ-15 range from 0-30; 15 cut-off of high SSB. Study cutoff is score of 11 excluding for 4 common areas of pain. HRQOL measured by: MOS SF-36.	More women had high SSB then men (24.6% vs. 9.1%, p = 0.0033). High SSB noted in n = 42(18.3%) of participants. Prevalence of depression noted n = 64(27.8%); of those n = 24(37.5%) had high SSB. High SSB burden was associated with increased percentage of days with complaints of pain (chronic/non crisis pain). There is no difference between low SSB and high SSB group regarding crisis pain. High SSB group had higher hospitalizations, healthcare utilization related to pain than low SSB (p < 0.05).
Jenerette, C., Funk, M., Murdaugh, C. LOE 4 [12]	Part of a larger cross-sectional descriptive study. Completed questionnaire packet including demographic data. Provided a list of potential complications experience d/t SCD.	Convenience sample of N = 232 AA aged 18 years or older living with SCD. Avg. age 35 yrs. More female than males.	To evaluate depressive symptoms in SCD	Demographic/ Vulnerability/Knowledge Instrument Depression measured using Beck Depression Inventory Fast Screen (BDI-FS). 7 item self-report scale. Shorter version of BDI-II. Completed by n = 221 (95%) of the sample. α was 0.84	Most common symptom reported was lack of pleasure and enjoyment. Least common experienced was suicidal ideation. Reported depression was n = 61(26.3%) compared to n = 70 (32%) scored in depression range on BDI-FS. Found a higher rate of depression in SCD than general population; 9.5%. Significant correlation (p = 0.02) between depressive symptoms on BDI and frequency of pain crises.
Edwards et al. LOE 4 [17]	Cross-sectional survey part of a longitudinal evaluation.	N = 67 AA aged 18-70yrs with SCD. Mean age 36.82 ± 11.47. Males = 30, Females = 37. Recruited from Duke Comprehensive SC Center	Exploration of self-reported depression, suicidal ideation and/or attempts.	Longitudinal Exploration of Medical and Psychosocial Factors in SCD (LEMPFSCD). 700 questions to measure pain, demographics, and 8 validated instruments measuring psychiatric, behavioral and social function. Depression measured using BDI.	A significance (p < 0.0007) was noted for reporting suicidal ideation in n = 19 (29%) of participants. n = 14 (22%) scored in mild or greater range on BDI (score > 14). Self- reporting of depressive symptoms in past 30 days was n=24 (36%). n = 5 (8%) reported previous suicide attempt. Significant association found depression and suicidal ideation (p = 0.02) and previous suicide attempts (p = 0.001).
Smith et al. LOE 4 [20]	Prospective cohort study; part of longitudinal study: PiSCES Project.	N = 232 AA living with SCD. Aged 18 years or older. More females than males.	Examine the prevalence and relationship among self-reported pain in SCD	Daily pain diaries completed for up to 6 months; minimum of 30 days consisting of 31, 017 diary patient days.	n = 125 (54%) self-reported pain on more than half of the days. Chronic pain/daily pain was reported in n = 67 (29%) of participants consisting of > 95% of diary days. In remaining 5% of diary days only n = 32 (14.2%) reported pain. Significance noted as percentage of days with pain increased so did mean pain intensity regardless if crisis, non-crisis or total pain (p<0.001). Substantially lower of days of healthcare utilization (3.5%) vs. 12.7% for crisis pain.

Wellington et al. LOE 4 [21]	Cross-sectional survey of 1st of 5 years of data from a longitudinal study	N = 156 adults aged 18-75 years.	Examine the relationship among somatization, psychopathology and pain in SCD	Longitudinal Exploration of Medical and Psychosocial Factors in SCD (LEMPFSCD). 700 questions to measure pain, demographics, and 8 validated instruments measuring psychiatric, behavioral and social function.	Somatization significantly predicted pain intensity, severity and range of average of pain over time ($p < 0.0001$) Somatization significant predictor of pain ($p < 0.001$)
Imhode, H., Ndom, R. and Ehon, A. LOE 4 [22]	Descriptive study using questionnaires covering 5 sections: QOL, Depression, Social support, Demographics, Self Esteem	N = 52 participants from SC center in Benin City. More male than female (29 vs 23);	Examine how social support, self-esteem, gender and depression would impact QOL among SCD.	Demographics: age, level of education, gender and religious affiliation QOL: adapted from FACT-G scale; higher scores = better QOL. SCD population reported cronbach's $\alpha = 0.73$ Depression: BDI- cut off score of 19 indicates moderate depression. Reported coefficient $\alpha = 0.68$ Social Support: Social Support Scale- coefficient α reported for study = 0.87 Self-Esteem: Self Esteem scale; higher scores above mean = higher self-esteem. Reported coefficient $\alpha = 0.66$	QOL significantly ($p < 0.001$) mutually impacted by self-esteem, depression and social support. Independently, social support significantly ($p < 0.05$) impact QOL. Depression significantly ($p < 0.05$) inversely impacted QOL
Dampier et al. LOE 3 [23]	Clinical Trial: C-Data Project- a clinical database to record 62 SCD related complications. 19 were used in the study.	Non random sample of N = 1046 aged 18-72 years; average age 31.4 years. 545 women, 501 men. 90% Black, non-Hispanic ethnicity. Any genotype of SCD included. Enrolled from nine (9) Comprehensive Sickle Cell Centers	Examine relationship between multiple disease related complications of SCD and reported health related QOL (HR-QOL)	collected health history (Med History I), administered interviews assessing psychosocial and health behavior (Medical History II) HR-QOL: measured by SF-36 version 2 questionnaire. Assess 8 aspects of health: physical functioning, physical role functioning, emotional role functioning, social functioning, pain, mental health, general health and vitality.	Median 4 SCD related complications experienced by participants. As age increased; number of complications markedly increased ($p < 0.001$). Self rating of health status as poor in n = 224 (22%) participants. Increasing age ($p < 0.01$), opioid usage ($p < 0.01$), history of crisis/ vaso-occlusive pain ($p < 0.01$) and asthma ($p < 0.05$) associated with reports of poor health status. All scores on SF-36 lower than mean (50) of general population: general health most decreased. Chronic antidepressant usage: significantly ($p < 0.05$) scores on bodily pain, vitality, social functioning, emotional role, and mental health. Chronic opioid usage decreased all scale scores ($p < 0.01$). Mental health scores only decreased by antidepressant or opioid usage ($p < 0.01$)
Mann-Jiles, V. and Morris, D. LOE 4 [24]	Descriptive study; cross-sectional survey	Convenience sample of N = 62 age 18 years or older. Outpatient hematologic and oncology clinic in urban Midwestern university medical center.	To examine QOL in SCD patients.	Demographic questionnaire QOL scale (QOLS): used 7 point Likert-type scale. Higher scores equate to higher QOL; scores can range from 62-112.	Score ranged from 52-112; Mean QOL scores lower (83.6) compared to general population (90). Spirituality only significant ($p < 0.05$) variable, all others non-significant. No demographic variables, SCD type or personal characteristics had impact on QOL.
Gibson et al. LOE 4 [25]	Descriptive study; cross-sectional survey	N = 143 Jamaican adults age 18 or older diagnosed w/SCD. Mean age: 36.4 ± 12.2 years; 48% male. Outpatient SC Unit at University of West Indies.	Explored relationship of locus of control (LOC), depression and QOL in SCD.	LOC: measured using Multidimensional Health Locus of Control (MHLC). External and Internal LOC. Using Likert-type scale. -external: "doctors", "other people" and "chance" - internal: "internal" Depression: BDI-II QOL: SF-36	No significant association between external LOC and QOL. Internal LOC significantly associated ($p < 0.05$) with higher QOL and decrease depressive symptoms. Depression present in n = 18(13%) of participants External LOC "chance" significant ($p < 0.01$) higher scores compared to RA, chronic pain and DM
Levels of Evidence based upon Melnyk Pyramid http://guides.lib.umich.edu/content.php?pid=25673&sid=1946060					

impact of certain demographic variables and severity of disease as contributors to depression. Availability of social support, education level and socioeconomic status were found to especially impact females. The need for providers to monitor number of transfusions, hospitalization utilization and use of Hydroxurea as predictors of disease severity and a risk of depression may be important. This study confirmed AA with SCD had a higher prevalence of depression than healthy counterparts.

Asnani, et al. assessed the prevalence of and variables associated with depression and loneliness among N = 277 Jamaican adults with SCD compared to an N = 65 AA control group [11]. The prevalence of depression was 21.6%. A two-fold increase was found in comparison to control group at 9.4% [11]. These researchers used a higher cutoff score of 17 for diagnosis of depressive symptoms to increase specificity due to the high somatic symptom burden (fatigue, and loss of energy) associated with SCD.

The PiSCES Project, examined somatic symptom burden (SSB) among adults with SCD (N = 230) who answered SSB questionnaires, to exclude 4 common pain sites of SCD: limb, back, stomach and chest [10]. High SSB was found in 18.3% and occurred more often among women than men ($p = 0.0033$). Analysis found 27.8% were depressed; of those depressed 37.5% had coexisting high SSB ($p \leq 0.0001$). Sogutlu et al. found the high SSB was an indication of more days of chronic pain requiring increase usage of healthcare and corresponded with depression, anxiety and decreased health-related QOL [10]. This study demonstrated the prevalence of somatic symptoms may not be related to the disease process or severity, but are more a comorbidity with depression. There were also more days of chronic pain due to somatization and psychological factors in comparison to crisis pain. Pain associated with a SC crisis was not different between those with high or low SSB. Recognition of these symptoms may be beneficial to health outcomes. Knowledge of the high prevalence of other somatic symptoms besides pain of SCD may influence care of this population and improve QOL.

Depression/depressive symptoms were evaluated among N = 232 AAs with SCD. Participants 26.3% self-reported being depressed. However, 32% had a score which was diagnostic for depression. The most common depressive symptom reported as experienced was lack of pleasure and enjoyment; the least common reported was suicidal ideations [12]. Researchers also reported a correlation ($p = 0.02$) between reported depressive symptoms and frequency of crises. This study demonstrated the high prevalence of depression in SCD and the importance of providers screening and assessing for depressive symptoms.

Edwards et al. explored depression, suicidal ideation and/or attempts in N = 67 AAs diagnosed with SCD. The investigators found that AA's depressive symptoms and suicidal ideation may be challenging to recognize and diagnose due to how their symptoms present [17]. As depressive symptoms that are common in the general population such as: apathy, hopelessness and crying spells were lower in this study however, fatigue and appetite disturbances yielded an overestimation of depression prevalence. Among AA populations, depression carries a stigma and self-measures and perseverance is used to manage it versus seeking treatment [13].

Edwards et al. found 22% of participants depression scores were in the mild or greater range [18]. Self-reporting of depression in the past 30 days occurred in 36% of the participants. Suicide Ideation was assessed and it was found 29% of the participants reported an episode of suicidal ideation, ($p < 0.0007$) and 8% reported an attempt. Those participants that reported suicidal ideation ($p = 0.02$) and/or previous suicide attempts ($p = 0.001$) reported higher levels of depression. The researchers did not find that pain ratings to be impacted by suicidal ideation or attempts (Edwards et al, 2009). These results demonstrate the unique presentation and variation in depressive symptoms among SCD.

SCD and Pain

Pain is a hallmark symptom of SCD and a primary reason for morbidity in SCD [18,19]. Pain can be very debilitating and devastating to those living with SCD. Pain can be acute episodic referred to as "crises" and/or chronic in nature. Acute pain is secondary to ischemia caused by vaso-occlusion from the malformed red blood cells [3]. Little is known about chronic pain in SCD. Taylor et al. found chronic pain was a result of the multiple complications of SCD [19]. Pain and depression in SCD is a complex dynamic relationship; studies discussed previously in this review are applicable to defining pain in SCD [20].

A sub-study of the PiSCES Project examined relationships among self-reported SCD pain. Pain diaries were completed by N = 232 participants defining characteristics of their pain, crisis experienced or not, medication utilized or healthcare utilization [20]. It was found 54% reported pain on greater than half of the days. Pain was reported almost every day in 29% participants. As the percentage of pain days increased so did the intensity of mean pain score ($p < 0.001$). Pain intensity was significantly higher on healthcare utilization days ($p < 0.001$) however, it was not a predictor of crisis. Despite experiencing crisis pain on 12.7% of the days, utilization of healthcare only occurred on 3.5% of the days. This study demonstrated the prevalence and severity of pain in SCD is greater than previously thought and is an expected finding not an exception. Pain was experienced on more days than not, demonstrating chronicity of pain. These results indicate that pain is occurring almost daily, is moderate to severe intensity however, healthcare service was not readily utilized for management of pain at home. Providers may underestimate the prevalence of SCD associated pain resulting in under treatment which can foster untreated depression [20].

Wellington et al. conducted an evaluation of the 1st of 5 years of data that examined the relationships among: somatization, psychopathology and pain among N = 156 adults with SCD [21]. Somatization as defined in the study is the obsessive focus on health or symptoms regardless of cause that often results in neglect of other life priorities. A multidimensional tool was administered that covered pain and eight other validated instruments measuring psychiatric, behavioral and social function. The results found somatization ($p < 0.0001$) predicted pain intensity, severity and length of average pain over time [21]. Somatization was found to be a significant ($p < 0.001$) prediction of depression. Demonstrating that people living with SCD have a tendency to focus excessively on their health or small changes in their health status and somatization may result in experiencing more pain. The providers' early assessment and identification of somatization may result in more effective and efficient interventions geared to improving their psychological function and pain management.

Sogutlu et al. examined the relationship between SSB and found pain is also applicable to depression, among N = 230 participants who answered SSB, health care QOL questionnaires and kept pain diaries [10]. Excessive SSB had significantly higher percentage of days of non-crisis pain (chronic pain), and healthcare utilization for pain but no difference was found regarding crisis associated pain [10]. This study's findings are consistent with others [3,12,22] that examined the depression and pain in SCD and may facilitate understanding of pain in SCD and the complex relationship with depression.

SCD and QOL

Imhonde, Ndom and Edon examined how social support, self-esteem, gender and depression would impact QOL with SCD [22]. A total of N = 52 participants from an SCD center answered a questionnaire with five sections consisting of: demographic variables, QOL scale, depression, social support scale and self-esteem scale. The study measured mental health as depression and self-esteem and social health as closeness with family and friends [21]. Findings revealed QOL was impacted ($p < 0.001$) by self-esteem, depression and social support. Social support was found to have an impact ($p < 0.05$) on QOL, and depression ($p < 0.05$) inversely impacted QOL among SCD [22]. These findings may facilitate providers understanding of QOL in SCD, and the need to allow for interventions to enhance social support, and treatment for depression. Imhonde et al., research on

QOL, suggested that there are four types of social support (affection, emotional/informational, positive social interaction and tangible) that positively impacts QOL [22]. Encouraging social contacts through close relationships with family and friends, participating in social activities and forming friendships through social networks may improve social support, depression and QOL.

Dampier et al, examined the relationship between multiple disease complications of SCD and reported QOL. Adults N = 1046 from SCD Centers answered questions regarding their health history and a questionnaire that measured QOL [23]. The researchers found reporting poor health status was associated with increasing age, opioid usage, history of vaso-occlusive pain ($p < 0.01$) and asthma ($p < 0.05$). Three complications: vaso-occlusive crisis, asthma and avascular necrosis were the complications that lowered the score. Use of chronic antidepressants ($p < 0.05$) decreased scores on bodily pain. Chronic opioids use resulted in diminished scores on all scales. Frequent use of opioids or chronic antidepressants ($p < 0.01$) lowered mental health scores [23]. The patient's perspective of their QOL is impaired by acute and chronic pain more than any of the other disease related complications [23]. In general, SCD is associated with a substantial decrease in QOL. Effective pain management and treatment of depression by providers is needed to improve overall QOL in patients living with SCD.

Mann-Jiles and Morris conducted a study in an outpatient hematology-oncology clinic with N = 62 adults with SCD [24]. A self-reported scale was used, scores could range from 16-112 with higher scores equating to a higher QOL. The mean QOL scores were significantly lower (83.6) in comparison to general healthy population (90). Results of other chronic disease QOLS scores were reported ranged from 61-87; scores were 52-112 in this study. Spirituality was the only variable that was significant ($p < 0.05$) when examining QOL [24]. This study suggests QOL among those living with SCD is impaired; providers should incorporate an assessment of variables that impact patients' QOL to facilitate improved physical and psychological health.

Gibson et al. explored the relationship of locus of control (LOC), depression and QOL in N = 143 Jamaican adults with SCD [25]. The LOC orientation is either external or internal; if ones' perception that life experiences are determined by external factors outside their control this is external. Life experiences which are determined by ones' behavior is defined as internal LOC [26]. The participants answered questions on three scales measuring LOC, depression and QOL. Three subscales; "doctors", "other people", "chance" and "internal"; the first three are measures of external LOC and the last is internal LOC. Depression was present in 13% of the participants. The study revealed ($p < 0.01$) higher scores in the external LOC domains of "chance" compared to other chronic illness (rheumatoid arthritis, chronic pain and diabetes). External LOC domain "other people" was significant ($p < 0.01$) compared to rheumatoid arthritis, pain, diabetes and cancer. Internal LOC had significantly ($p < 0.01$) higher scores than all other compared chronic illness except diabetes. A significant association between external LOC and QOL, however internal LOC was associated ($p < 0.05$) with higher QOL and decreased depressive symptoms. External LOC "other people" was significant ($p < 0.05$) of depressive symptoms [25]. Improving internal LOC and minimizing "other people" LOC may improve QOL and decrease risk of depression. Empowering the patient with choices in clinical decision making provides a sense of autonomy and improves QOL. Assisting patient with finding a balance between over reliance mentally and physically on family and friends and maintaining appropriate levels of contact and support with family, friends and social will be beneficial in decreasing risk of depression.

SCD and disease trajectory

Uncertainty and unpredictability in disease course can hinder those living with SCD and lead to fear, psychosocial and emotional distress. This population is at risk for early death due to acute complications: stroke, osteonecrosis of femoral head, pain episodes, acute chest, multiple organ failure and increased risk of infection and pulmonary hypertension [22,16]. The uncertainty of knowing when or how their death is going to happen and the unpredictability of disease course contributes to a decrease QOL and depression.

Platt et al., conducted a study of deaths and clinical course among N = 3764 patients in the Cooperative Study of SCD (CSSCD). The cause of deaths of n=209 adults who died during the study was evaluated and risk factors for early death was evaluated in n = 964 adults followed for a minimum of 2 years [27]. The researchers found nearly 1/3 of the participants that died did not have clinical evidence of organ failure; death occurred during an acute crisis (pain, acute chest or stroke). Risk for early mortality was the presence of symptomatic disease [27].

Morbidity and mortality are high with SCD, however it has been reduced over the decades due in part to the advances in medical therapy, improved psychosocial support, management of infections and complications and health maintenance [28]. It is estimated that starting in late adolescents 40% of people with SCD will be affected by pulmonary hypertension of which there is a50% mortality within 2 years [2]. The prognosis was estimated by the type and severity of SCD with median age of survival of 42 years of age for males and 48 years of age in female in SCD SS and 60 years and 68 years in SCD-SC [18,28]. Prognosis has improved as patients are now living longer into the 7th and 8th decade [28]. Advances in medical technology and treatments have changed SCD into a chronic illness of childhood extending into adulthood. The improved life expectancy provides opportunity for providers to improve QOL through health maintenance, recognition and treatment of depression and effective chronic and acute pain management, patient and family education. The practitioner's role is key to meeting the challenges of this endeavor.

Discussion

Fourteen articles met inclusion criteria for this integrative review. The review discussed depression, pain, QOL and disease trajectory and impact depression among those living with SCD. A high prevalence of depression was confirmed among SCD ranging from 18-44% [3,5,10-12]. Depression in SCD is more prevalent than in the general AA population, however it is consistent with that of other chronic illness of prevalence of 20-30% [5,11]. Demographic variables such as: education, gender, social support and unemployment are predictive of depression [5,11]. Interventions should be carried out to ensure adequate social support and close and healthy relationship with friends and families to minimize risk for depression. Depression is ($p = 0.02$) associated with frequency of crisis, increased healthcare utilization services and hospitalizations for pain crisis and presence of chronic/near daily pain [3,5,12]. Depressive symptoms may be a challenge to recognize in SCD populations as they present with different symptoms than the general population. Edwards et al., found a significant association between depression and suicidal ideations ($p = 0.04$), suicide attempts ($p = 0.001$) however, in contrast suicidal ideation was the least common reported symptom in the study conducted by Jenerette et al., [17].

Rates of pain may actually be higher than findings of study as patients were staying home and not seeking healthcare even though they had near daily pain. Despite the PiSCES Project predicting the relationships between depression and pain variables it is still unknown if having more pain caused depression or if more pain was a result of the presence of depression [3]. Since depression caused significantly more pain on days when a crisis was not occurring then providers should develop interventions for pain and depression management applicable to outpatient setting and not entirely focused on inpatient setting. Depression results in poorer QOL. There is not much known about QOL in SCD. This can be accomplished by empowering SCD patients to be actively involved in treatment plan and provide choices or options when applicable.

The consistent limitation of all the studies was the self-report nature of the instruments used to measure depression and other variables. Use of self- report relies on the participant to answer

accurately and truthfully. A few of the studies had small sample sizes or used convenience sampling. The tools to measure depression were validated for use in primary care, however the use specifically in vulnerable populations with chronic illness like SCD was not established.

Implications for Practice

Providers play an essential role in the assessment, and screening of depression. Effective management of these conditions may improve QOL. Further investigation is warranted to understand the meaning of depression and psychosocial factors in this patient population. Findings from this review may help to provide a clearer understanding of depression and psychosocial factors in adults with SCD and lead to future research to identify how depression treatment affects pain and quality of life. Providers' first step is the acknowledgement and acceptance that depression is a substantial problem that must be addressed. Early depression screening, identification and treatment of depression are important to improve QOL. Educating patients about depression and its impact on their life and pain management may remove the stigma associated and assist in early treatment of depression.

Conclusion

There is a high prevalence of depression in SCD impacting their pain and quality of life. Additional research is needed in evaluating the use of antidepressants in SCD to determine if QOL and pain is improved. Antidepressants that also treat pain may be most efficacious among those living with SCD. Practitioners are in the best position to treat depression through providing holistic care but not just treating the disease.

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