

Emotional Distress, Barriers to Care, and Health-Related Quality of Life in Sickle Cell Disease

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ABSTRACT

- **Objective:** Emotional distress may adversely affect the course and complicate treatment for individuals with sickle cell disease (SCD). We evaluated variables associated with physical and mental components of health-related quality of life (HRQL) in SCD in the context of a biobehavioral model.
- **Methods:** We conducted a cross-sectional cohort study of 77 adults with SCD (18–69 years; 60% female; 73% Hgb SS) attending an urban, academic medical center. We measured emotional distress (Patient Health Questionnaire–9, Generalized Anxiety Disorder 7-item scale), clinical complications and utilization, barriers to health care, sociodemographics and HRQL (SF-36 Health Survey). We developed models predictive of physical and mental HRQL by conducting stepwise regression analyses.
- **Results:** Sample prevalence of moderate to severe depression and anxiety symptoms was 33% and 36%, respectively; prevalence of impaired physical and mental HRQL was 17% and 16%, respectively. Increased symptoms of depression, older age, and ≥ 3 emergency department visits in the previous 12 months were independently associated with lower ratings of physical HRQL, controlling for anxiety and sex. Increased symptoms of depression were independently associated with lower ratings of mental HRQL, controlling for barriers to care, insurance status, lifetime complications of SCD, and sex.
- **Conclusion:** Emotional distress is an important contributor to both physical and mental HRQL for adults with SCD, although sociodemographic variables and barriers to care must also be considered. Innovative approaches that integrate mental health interventions with SCD clinical care are needed.

Emotional distress, including symptoms of depression and anxiety, may adversely affect the course and complicate the treatment of chronic physical conditions [1]. For patients with sickle cell disease (SCD), a group of inherited red blood cell conditions, symptoms of depression and anxiety are more prevalent compared with rates found in the general population [2–8]. The most common symptom of SCD is acute pain events, and other complications range from mild to life-threatening, including anemia, increased risk of infection, acute chest syndrome, stroke, skin ulcers, and pulmonary hypertension [9]. Depression in adults with SCD has been associated with increased sickle cell vaso-occlusive pain events, poor pain control, multiple blood transfusions, and prescription of the disease-modifying therapy hydroxyurea [4]. Adults with SCD and comorbid depression and anxiety had more daily pain and greater distress and interference from pain compared with those who did not have comorbid depression or anxiety [10]. Patients have linked emotional distress and episodes of illness [11], and research has found a relation between pain episodes and depression [12]. In a diary study, negative mood was significantly higher on pain days compared with non-pain days [13].

Studies examining the consequences of emotional distress on health-related quality of life (HRQL) for patients with SCD are emerging. Depressed adults with SCD rated their quality of life on the SF-36 Health Survey [14] as significantly poorer in all areas compared with non-depressed adults with SCD [15]. In regression models, depression was a stronger predictor of SF-36 scores than demographics, hemoglobin type, and pain measures. In a multi-site study [16], 1046 adults with

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SCD completed the SF-36. Increasing age was associated with significantly lower scores on all subscales except mental health, while female sex additionally contributed to diminished physical function and vitality scale scores in multivariate models [16]. The presence of a mood disorder was associated with bodily pain, and diminished vitality, social functioning, emotional role, and the mental component of HRQL. Medical complications other than pain were not associated with impaired HRQL. Anie and colleagues [17,18] have highlighted the contributions of sickle cell–related pain to diminished mood and HRQL, both in the acute hospital phase and 1 week post discharge.

A comprehensive literature review of patient-reported outcomes for adults with SCD revealed broad categories of the impact of SCD and its treatment on the lives of adults [19]. Categories included pain and pain management, emotional distress, poor social role functioning, diminished overall quality of life, and poor quality of care. Follow-up individual and group interviews with adults with SCD ($n = 122$) as well as individual interviews with their providers ($n = 15$) revealed findings consistent with the literature review on the major effects of pain on the lives of adults with SCD, interwoven with emotional distress, poor quality of care, and stigmatization [19].

In the present study, our goal was to describe variables associated with physical and mental HRQL in SCD within the context of the recently published comprehensive conceptual model of broad clinical and life effects associated with SCD [19]. The present analysis uses an existing clinical database and evaluates the effects of the relations between clinical complications of SCD, emotional distress, health care utilization, and HRQL. Our model includes barriers to health care that might prevent vulnerable patients from accessing needed health care services. Sociodemographic variables including ethnic and racial minority status and lower socioeconomic status and educational attainment may create barriers to health care for patients with SCD, as they do for individuals with other chronic conditions [20–23]. Over 60% of patients with SCD are on public insurance [24] and can have difficulties with accessing quality health care [25]. Negative provider attitudes and stigmatization when patients are seeking care for acute pain episodes have been highlighted by patients as major barriers to seeking health care [19,26–28]. In a qualitative study, 45 youth with SCD reported that competing school or peer-group

activities, “feeling good,” poor patient-provider relationships, adverse clinic experiences, and forgetting were barriers to clinic attendance [29]. Limited research suggests that barriers to accessing health care are associated with poorer HRQL [30,31]; however no studies were identified that directly evaluated the relation between barriers to care and HRQL for populations with SCD.

We hypothesized that clinical complications of SCD, including pain, and barriers to accessing health care would be independently associated with the physical component of HRQL for adult patients with SCD, controlling for demographic variables. Further, we hypothesized that emotional distress, clinical complications of SCD, and barriers to accessing health care would be independently associated with the mental component of HRQL for adult patients with SCD, controlling for demographic variables.

METHODS

Patient Recruitment

Participants were 18 years and older and were a subgroup selected from a larger prospective cohort enrolled in the Sickle Cell Disease Treatment Demonstration Program (SCDTDP) funded by the Health Resources and Services Administration (HRSA). As 1 of 7 SCDTDP grantees, our network collected common demographic, disease-related, and HRQL data as the other grantees to examine sickle cell health and health care [32]. Enrollment at our site was $n = 115$ from birth through adult, with data collection occurring at baseline in 2010 and annually through 2014. Participants were eligible for enrollment if they had any confirmed diagnosis of SCD and if they were seen at any facility treating SCD in the San Francisco Bay Area region. Interpreter services were available where English was a second language; however, no participant requested those services. The data collection site was an urban comprehensive sickle cell center. Participants were recruited through mailings, posted flyers, or were introduced to the project by their clinical providers. The institutional review boards of the sponsoring hospitals approved all procedures. This report describes analyses from the baseline data collected in 2010 and excludes pediatric patients under the age of 18 years, as we developed our conceptual model based on the adult SCD literature.

Procedures

Patients directly contacted the project coordinator or were introduced by their health care provider. The proj-

ect coordinator explained the study in more detail, and if the patient agreed to participate, the project coordinator obtained their informed consent. Participants completed the study materials in a private space in the clinic immediately after or were scheduled for a separate visit at a convenient time and location. Participants with known or observed difficulties with reading completed the questionnaires as an interview. We allowed participants who were unable to complete the forms in one visit to take them home or schedule a follow-up visit to complete them. We asked participants who took the questionnaires home to return them within 2 business days and provided them with a stamped addressed envelope. Participants were compensated with gift cards for their involvement.

Measures

Demographics and Clinical Characteristics

Participants completed an Individual Utilization Questionnaire created for the SCDTDP grantees [32], either as an interview or in paper and pencil format. Participants indicated their age, race and ethnicity, education level, type of insurance, and annual household income. They indicated the type of SCD, number of hospital days and emergency department (ED) visits in the previous 12 months, disease-modifying therapies including hydroxyurea or transfusions, and lifetime incidence of sickle cell-related complications. Complications included pain, acute chest syndrome, fever, severe infection, stroke, kidney damage, gallbladder attack, spleen problems and priapism. Medical data was verified by reviewing medical records when possible; the clinical databases in the hematology/oncology department at the sponsoring hospital are maintained using Microsoft SQL Server, a relational database management system designed for the enterprise environment. However, not all of the participating institutions were linked via this common clinical database or by an electronic health record at the time the study was conducted.

Barriers to Care

We modified a checklist of barriers to accessing health care for patients with a range of chronic conditions [33] to create a SCD-specific checklist [34]. The final checklist consists of 53 items organized into 8 categories including insurance, transportation, accommodations and accessibility, provider knowledge and attitudes, social support, individual barriers such as forgetting or difficulties understanding instructions, emotional barriers

such as fear or anger, and barriers posed by SCD itself (eg, pain, fatigue). Participants check off any applicable barrier, yielding a total score ranging from 0 to 53. The checklist overall has demonstrated face validity and test-retest reliability (Pearson $r = 0.74$, $p < 0.05$).

Depressive Symptoms

Adults with SCD completed the PHQ-9, the 9-item depression scale of the Patient Health Questionnaire [35]. The PHQ-9 is a tool for assisting primary care clinicians in assessing symptoms of depression, based on criteria from the *Diagnostic and Statistical Manual 4th edition* (DSM-IV [36]). The PHQ-9 asks about such symptoms as sleep disturbance and difficulty concentrating over the past 2 weeks with scores ranging from 0 (Not at all) to 3 (Every day). The total symptom count is based on the number of items in which the respondent answered as “more than half of days” or greater, and scores are categorized as reflecting no (< 10), mild (10–14), moderate (15–19) or severe (≥ 20) symptoms of depression. Respondents indicate how difficult the symptoms make it for them to engage in daily activities from 0 (Not difficult at all) to 3 (Extremely difficult). The sensitivity and diagnostic and criterion validity of the PHQ-9 have been established [37]. The internal consistency of the PHQ-9 is high, with $\alpha > 0.85$ in several studies and 48-hour test-retest reliability of 0.84. The PHQ has been used widely, including with African-American and Hispanic populations, and with individuals with chronic conditions [38].

Symptoms of Anxiety

Participants completed the Generalized Anxiety Disorder 7-item (GAD-7) questionnaire for screening and measuring severity of generalized anxiety disorder [39]. The GAD-7 asks about such symptoms as feeling nervous, anxious, or on edge over the past two weeks. Scores from all 7 items are added to obtain a total score [40]. Cut-points of 5, 10, and 15 represent mild, moderate, and severe levels of anxiety symptoms. Respondents indicate how difficult the symptoms make it for them to engage in daily activities from 0 (Not difficult at all) to 3 (Extremely difficult). The internal consistency of the GAD-7 is excellent ($\alpha = 0.92$). Test-retest reliability is also good (Pearson $r = 0.83$) as is procedural validity (intraclass correlation = 0.83). The GAD-7 has excellent sensitivity and specificity to identify generalized anxiety disorder [41].

Health-Related Quality of Life

Participants completed the SF-36, which asks about the patient's health status in the past week [14]. Eight subscales include physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional and mental health. Two summary measures, the Physical Component Summary and the Mental Component Summary, are calculated from 4 scales each. Use of the summary measures has been shown to increase the reliability of scores and improve the validity of scores in discriminating between physical and psychosocial outcomes [14]. Higher scores represent better HRQL, with a mean score of 50 (SD = 50) for the general population. Internal consistency estimates for the component summary scores are $\alpha > 0.89$, item discriminant validity estimates are greater than 92.5% and 2-week test-retest reliability was excellent. Scores on the SF-36 have been divided into categories of HRQL functioning [42,43]. Participants in the impaired to very impaired category have scores \leq mean - 1 SD while participants with average to above average functioning have scores $>$ mean - 1 SD.

The SF-36 has been used extensively in observational and randomized studies for a range of illness conditions. In SCD, some aspects of HRQL as measured by the SF-36 improved for adult patients who responded to hydroxyurea [44]. Participants in the Pain in Sickle Cell Epidemiology Study scored lower than national norms on all SF-36 subscales except psychosocial functioning [45]. HRQL decreased significantly as daily pain intensity increased [45]. Further, women reported worse bodily pain compared with men [46].

Data Analyses

All biostatistical analyses were conducted using Stata 13 [47]. Continuous variables were examined for normality with measures of skewness and peakedness. All variables satisfied the assumptions of normality with the exception of barriers to health care and ED utilization. The variable barriers to health care was transformed using a square root transformation, resulting in a more normally distributed variable. ED utilization was dichotomized as 0-2 versus 3 or more ED visits in the previous 12 months, based on the distribution of utilization in the sample. The cutpoint of ≥ 3 annual ED visits is consistent with other literature on SCD clinical severity [48].

Descriptive statistics were computed to include means, standard deviations and frequencies. Sociodemographic

variables (age, sex, insurance status [public or private] and income) were examined as potential covariates using Pearson correlations and *t* tests. Associations among emotional distress (anxiety and depression symptoms), clinical complications and ED utilization, barriers to health care, and the outcomes of the Physical and Mental Component Summary scores from the SF-36 were examined using Pearson correlations. We conducted stepwise regression with forward selection to determine models predictive of physical and mental HRQL. We tested the addition of each chosen variable (anxiety symptoms, depression symptoms, clinical complications, ED utilization, barriers to health care, age, sex, insurance status, and income), adding the variables (if any) that were most correlated with the outcome, and repeated the process until the model was not improved. A significance level of 0.05 was used for all statistical tests.

RESULTS

Demographic and Clinical Characteristics

Table 1 shows the demographic characteristics of the 77 participating adults with SCD. Sixty percent were female. Patients ranged in age from 18 to 69 years, with a mean age of 31.6 (SD = 13.1) years. Consistent with the general SCD population, participants were predominantly black/African American. Over 66% of families reporting had a median household income of less than \$30,000 annually, although the mean household size was 3 to 4 persons. The majority of the participants (57%) had some college and beyond, although 14% had not completed high school. Over 80% of participants were on public insurance.

The majority of patients (73%) were diagnosed with Hgb SS disease and the most common lifetime complication was pain, reported by almost all of participants (Table 1). The next most common complication was fever, followed by acute chest syndrome. Twenty-seven percent of participants were currently on the disease-modifying therapy hydroxyurea, while 61% had a lifetime history of transfusion therapy. These data were verified with information from the clinical database for 73 participants (95%).

The median number of ED visits in the previous year was 1 (range, 0-50), with 19 patients (25%) with zero visits. The median number of hospital days in the previous year was 13 (range, 0-81). Twenty-nine patients (38%) had no hospital days in the previous year. These data were verified with information from the clinical database for 53 participants (69%), since hospital and ED

Table 1. Characteristics of Study Participants ($n = 77$): Subgroup from Larger Cohort Study

Age in years, mean \pm SD	31.6 \pm 13.1
Female sex, n (%)	46 (60)
Race/ethnicity, n (%)	
Hispanic/Latino	7 (9)
Black/African American	68 (90)
Other	1 (1)
Household size, mean \pm SD	3.4 \pm 2.2
Annual household income, n (%) [*]	
Less than \$30,000	38 (49)
\$30,000 or greater	19 (25)
Insurance status, n (%)	
Public insurance	63 (82)
Private insurance	14 (18)
Education level, n (%)	
High school graduate or less	33 (43)
Some college or beyond	44 (57)
Hemoglobin type, n (%)	
Hgb SS	51 (73)
Hgb SC	16 (23)
Hgb S beta zero	2 (3)
Other	1 (1)
Lifetime # of clinical complications, mean \pm SD [†]	8.1 \pm 1.1
Specific complications n (%) [‡]	
Pain	76 (99)
Fever	67 (87)
Acute chest syndrome	67 (87)
Infection	53 (69)
Gall bladder attack	46 (60)
Stroke	16 (21)
Spleen problems	26 (34)
Kidney disease	20 (26)
Skin ulcers	9 (12)
Eye damage	21 (27)
Dactylitis	20 (26)
Current hydroxyurea therapy, n (%)	21 (27)
Lifetime history of transfusion therapy, n (%)	47 (61)

*Total does not add up to 100% due to non-responses.

[†]Total number of potential complications = 11. Priapism was included on the original questionnaire but excluded from this analysis given that only men can be affected.

[‡]Patients could endorse multiple complications.

visits occurred at institutions not always linked with the clinical databases at the sponsoring hospitals.

Emotional Distress, Barriers to Care, and Health-Related Quality of Life

The mean score for the sample on the PHQ-9 was 7.2 (SD = 5.6, $\alpha = 0.86$, Table 2). The prevalence of moderate to severe symptoms of depression (ie, scores ≥ 10) was 33% ($n = 25$). Twelve patients with moderate to severe symptoms (48%) reported that symptoms of depression created some difficulty in work, daily activities, or relationships, while 10 patients (40%) reported very much to extreme difficulty in work, daily activities, or relationships due to depression symptoms.

The mean score on the GAD-7 was 7.9 (SD = 6.0, $\alpha = 0.90$, Table 2). The prevalence of moderate to severe symptoms of anxiety (scores ≥ 10) was 36.4% ($n = 28$). Fourteen patients with moderate to severe symptoms (50%) reported that anxiety symptoms created some difficulty in work, daily activities, or relationships. Twelve patients (43%) reported that symptoms created very much to extreme difficulty in work, daily activities, or relationships. Fifteen patients (29%) with moderate to severe symptoms of anxiety or depression exhibited comorbid anxiety and depression.

The mean Physical Component Summary score on the SF-36 was 53.6 (SD = 24.1, $\alpha = 0.94$, Table 2). The prevalence of impaired to very impaired HRQL in the physical domain was 17% ($n = 13$). The mean Mental Component Summary score on the SF-36 for the sample was 50.1 (SD = 23.7, $\alpha = 0.93$), with a prevalence of 16% ($n = 12$) in the impaired to very impaired range for HRQL in the mental domain.

The mean number of barriers from the barriers checklist was 9.2 (SD = 10.1) out of 53 possible. Sixty-five participants (86%) reported at least 1 barrier to accessing health care (Table 2). The most frequently cited barriers to care were provider knowledge and attitudes, followed by transportation, insurance, and access to services (eg, hours and location of services). Less frequently cited barriers to care were individual barriers, including memory, health literacy and motivation, as well as those related to SCD itself, ie, fatigue and pain.

Sociodemographic Variables, Emotional Distress, and Health-Related Quality of Life

Symptoms of anxiety and depression were highly correlated with one another, as would be expected ($r = 0.75$, $P < 0.001$). Physical and mental HRQL were significantly correlated with symptoms of depression ($r = -0.67$, $P < 0.001$ for physical HRQL component and $r = -0.70$ for mental HRQL component, $P < 0.001$), with impaired HRQL in

Table 2. Health-Related Quality of Life, Emotional Distress, and Barriers to Care: Descriptive Statistics ($n = 77$)

Dependent Variables	Mean \pm SD (Range)
Health-Related Quality of Life – SF-36	
Physical Component	53.6 \pm 24.1 (3.1 – 100)
Mental Component	50.1 \pm 23.7 (3.1 – 100)
Independent Variables	Mean \pm SD (Range)
Emotional distress	
Depression Symptoms – PHQ-9	7.2 \pm 5.6 (0 – 22)
Anxiety Symptoms – GAD-7	7.9 \pm 6.0 (0 – 20)
Barriers to care	9.2 \pm 10.1 (0 – 51)
	<i>n</i> (%)*
Provider knowledge & attitudes	44 (58.0)
Transportation	43 (56.6)
Insurance	41 (53.9)
Access to services/adequate accommodations	39 (51.3)
Social, family and caregiver support	34 (44.7)
Emotional barriers (eg, worry, anger, embarrassment)	31 (40.8)
Individual barriers (eg, memory, health literacy, motivation)	28 (36.8)
Barriers related to sickle cell disease (fatigue, pain)	24 (31.6)

*One or more barriers reported in each category.

both domains correlated with greater symptoms of depression. Physical and Mental Component Summary scores were significantly correlated with symptoms of anxiety ($r = -0.58$, $P < 0.001$ for the physical component and $r = -0.62$ for the mental component, $P < 0.001$), with impaired HRQL in both domains correlated with greater symptoms of anxiety. Ratings of difficulty with daily functioning from depressive symptoms were correlated with impaired HRQL in the physical ($r = -0.46$, $P < 0.01$) and mental domains ($r = -0.52$, $P < 0.001$). Ratings of difficulty with daily functioning from anxiety symptoms were also correlated with impaired HRQL in the physical ($r = -0.58$, $P < 0.001$) and mental domains ($r = -0.63$, $P < 0.001$). Reports of more barriers to health care were significantly correlated with reports of more depressive and anxiety symptoms ($r = 0.53$, $P < 0.001$ and $r = 0.48$, $P < 0.001$), with lower Mental Component Summary scores ($r = -0.43$, $P < 0.05$), and with more ED visits in the past year ($r = 0.43$, $P < 0.05$).

Relations Between Independent Variables and Outcomes

Results of regression analyses (Table 3) indicated that a model including depression symptoms, age, ED utilization, anxiety symptoms and sex predicted the physical

component of HRQL ($R^2 = 0.55$, $F(5, 66) = 15.8$, $P < 0.001$). Increased symptoms of depression, older age and 3 or more ED visits in the previous 12 months were independently associated with lower ratings of physical HRQL, controlling for anxiety and sex. A model including depression symptoms, barriers to care, insurance status, lifetime complications of SCD and sex predicted the mental component of HRQL ($R^2 = 0.56$, $F(5, 66) = 16.7$, $P < 0.001$). Increased symptoms of depression were independently associated with lower ratings of mental HRQL, controlling for barriers to care, insurance status, lifetime complications of SCD, and sex.

DISCUSSION

Results of this study showed that as expected, symptoms of depression were independently associated with the mental component of HRQL, controlling for other variables. Symptoms of depression were also independently associated with the physical component of HRQL. The effect size for both models was moderate but comparable to effect sizes of other studies of predictive models of physical and mental HRQL in SCD [49]. Our findings were consistent with previous literature, with older age and increased ED utilization independently associated with lower ratings of physical HRQL, with sex and

Table 3. Results of Stepwise Forward Regression Models Predicting Physical and Mental HRQoL*

	Model 1	Model 2
	R ² = 0.55	R ² = 0.56
	Physical HRQL (n = 72)	Mental HRQL (n = 72)
Dependent variables	β ± SE	β ± SE
Depression symptoms	-1.61 ± 0.55 [†]	-2.31 ± 0.39 [†]
Age	-0.53 ± 0.16 [†]	-
Emergency department utilization	-10.5 ± 4.34 [‡]	-
Anxiety symptoms	-0.93 ± 0.51	-
Sex	-6.26 ± 4.07	-6.45 ± 4.22
Lifetime complications	-	3.11 ± 1.80
Barriers to health care	-	-2.24 ± 1.39
Private insurance	-	9.08 ± 5.20
Income	-	-

*The variables age, sex, income (< \$30,000 or ≥ \$30,000), insurance status (public or private), the square root of barriers to care, number of lifetime complications, scores on anxiety (GAD-7) scale and scores on depression (PHQ-9) scales were allowed to enter into an empty model in order of significant contribution to the variance in physical or mental HRQL (SF-36 scores) respectively. Variables were allowed to enter into the model until a significance level of P = 0.20 was reached.

[†]P < 0.01

[‡]P < 0.05

anxiety symptoms entering into the predictive model [15–18,44,45]. Contrary to our hypotheses, barriers to accessing health care were not independently associated with physical or mental HRQL but did contribute to the model for mental HRQL, as did clinical complications and private insurance status.

While our sample was similar to previous samples in mean age and percentage of women participants, our patients reported significantly higher physical HRQL scores, and a wider range of HRQL scores (eg, 53.6, SD = 24.1 compared with 39.6, SD = 10.0 [16]). The mean Physical Component Summary score was in fact similar to the general population mean of 50. This may reflect improvements in quality of care and subsequent overall improved patient health and HRQL given that these data were collected in year 2 of the HRSA SCDT-DP. As an SCDTDP grantee, we implemented goals to improve coordination of service delivery and to increase access to care. However, it should also be considered that there was a selection bias in our study, in favor of those with better HRQL. Nevertheless, as already noted, our findings are consistent with previous literature with regard to inter-relations between variables, ie, associations between lower physical HRQL ratings and symptoms of depression, older age, and increased ED utiliza-

tion [15]. Future studies in SCD that directly evaluate reported access to a medical home in relation to HRQL are needed to assess the impact of access to care and care coordination on HRQL ratings.

Our use of a data collection tool that focused on lifetime rather than acute history of complications may have contributed to our failure to find a relation between clinical manifestations and physical HRQL. Further, we were not able to assess the effects of pain separately from other complications, since almost every participant reported a lifetime history of pain. However, our findings were consistent with those of researchers who have found psychosocial and sociodemographic factors, versus clinical manifestations, to be major influences on both physical and mental HRQL for individuals with SCD and other chronic and life-threatening conditions [15, 16, 50]. Our confidence is increased in this finding, given that we were able to verify self-reports of clinical manifestations with our clinical database. Our results contribute to the developing body of knowledge that emphasizes the importance of understanding the broad impact on the lives of adults of living with SCD, not just the physical symptomatology.

There has been limited research on barriers to accessing health care as associated with HRQL for SCD

populations. Health care barriers have been identified for ethnic minorities, even within patient-centered medical homes, with minority status moderating the effect of barriers to care on HRQL [30]. Our findings that barriers to health care were correlated with depression and anxiety symptoms, mental HRQL, and greater ED utilization support the need to view SCD care within a biobehavioral framework. Health care provider negative attitudes and lack of knowledge were the most frequently cited barriers for adults in our study, particularly in the context of ED and inpatient care. These findings are similar to other studies that have highlighted the impact of these provider variables on quality of care [26,51]. We were not able to separate out effects of ethnic minority status, given that our patients were predominantly African American.

Contributors to poor HRQL that have been identified in SCD are poverty [42] and public insurance status [49]. While over half of our participants had family incomes of less than \$30,000, despite a mean household size of 3 members, we did not find that income contributed to either of our models predicting physical or mental HRQL. Over half of our patients were well educated, which could have moderated the effect of their low incomes, but we did not measure other potential moderators such as active coping and supportive relationships [19]. These analyses were beyond the scope of our existing database, but future studies are needed on such resilience factors and processes. Our adults were predominantly on public insurance and we did find that private insurance status was positively associated with higher ratings of mental HRQL, consistent with other SCD research [49]. Taken together, our findings underscore the importance of considering the interplay between emotional distress, sociodemographic and clinical factors and quality of care in order to address risk factors for poor patient-reported outcomes [52,53].

There have not been previous reports of symptoms of emotional distress in SCD using the PHQ-9 and GAD-7, but both measures have been used widely for depression and anxiety screening, including with African-American populations. We selected these over other measures for their brevity, free availability, and psychometric properties. Our prevalence of moderate to severe depression and anxiety symptoms in the present study was similar to what has been found using other tools [2–8]. The PHQ-9 and GAD-7 also provide ratings of symptom interference on daily functioning, and we found that these ratings were associated with impaired physical and

mental HRQL. Given that there generally are limited mental health resources in the communities where individuals with SCD reside and are treated, ratings of emotional distress and HRQL can be taken together to stratify those patients with the most immediate need for interventions. Further, screening can be used for early detection with the goal to intervene and prevent the progression of symptoms of emotional distress to long-term, disabling mental health disorders [54]. There is a need for innovative and cost-effective strategies for assessment and treatment of mental health symptoms and disorders for patients with SCD. One model for evidence-based practice in the management of emotional distress for patients with in SCD is the collaborative care model.

The collaborative care model integrates physical and mental health care in the patient-centered medical home and focuses on treating the whole person and family [55]. In this model, a care management staff (eg, nurse, social worker, psychologist) is integrated with the primary care team. The care management staff, in consultation with a psychiatrist, provides evidence-based care coordination, brief behavioral interventions, and support for other treatments, including medications. The effectiveness of collaborative care programs has been demonstrated for ethnic minority and safety net populations such as the SCD population, which is disproportionately low-income and on public insurance [56, 57]. Future research with SCD populations should investigate such interventions as the collaborative care model that addresses both emotional distress and barriers to care.

Limitations

Our results need to be interpreted with caution given the small sample size and the potential bias introduced by non-random sampling. In addition, as our patients are from an urban setting, findings might not generalize to rural populations. This study was cross sectional so no inferences can be made with regard to causality and temporal relations between anxiety symptoms, barriers to care, and HRQL. Our strategy for measuring total clinical complications and barriers to care conserved power but it was not possible to evaluate if specific complications or barriers may have exerted a greater impact on HRQL compared with others. Similarly, other studies have examined specific domains of HRQL, while we limited our analysis to the Physical and Mental Component Summary scores. The utilization questionnaire was designed to assess only lifetime complications, not complications more proximal to the HRQL ratings.

Patient-reported outcomes, now widely accepted as outcome measures, elicit patients' descriptions of the impact of their condition on their day-to-day lives [34, 58–60]. However, measures of mental health symptoms and HRQL may be subject to recall bias, measurement error, and confounding [61,62]. Nevertheless, a range of studies support the idea that mental health symptoms and HRQL are distinct constructs, and that patients with physical and mental health symptoms are vulnerable to lower ratings of HRQL [63,64]. Disease-modifying therapies such as hydroxyurea can contribute to improved ratings of HRQL [44,65], but we were not able to evaluate the contribution of hydroxyurea to HRQL as it appears to have been underutilized in our sample.

Conclusion

We evaluated emotional distress and other variables in the context of a biobehavioral model of HRQL outcomes for adults with SCD. Integrating the patient's perspective of the impact of the disease and its treatment with assessment of clinical indications is critical to implementing and evaluating effective therapies [25]. However, there are conceptual challenges in determining what actually contributes to HRQL from the patient's perspective in the context of genetic disorders such as SCD [50]. Our findings highlight the importance of incorporating comprehensive psychosocial screening in order to support optimal HRQL in SCD. Providers may be reluctant to include such screening if, as is often the case, mental health services are difficult to access. Models such as the collaborative care model, which include mental health interventions within the sickle cell center or primary care provider's office, should be implemented. Barriers to care and HRQL should also be routinely evaluated for patients with SCD. Use of disease-specific tools, such as the Adult Sickle Cell Quality of Life measurement system [66], may increase the specificity needed to detect differences within adults with SCD and improvements related to interventions, whether medical or psychosocial. Contributors to HRQL in SCD go beyond clinical manifestations to include psychological and social factors, as well as provider and health system variables. Research conducted within the framework of a comprehensive conceptual model of broad clinical and life effects associated with SCD can inform clinical applications that ultimately enhance HRQL for patients with SCD.

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