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# Navigating the Pain, Psychosocial and Racial Dynamics of Hospitalized Patients with Sickle Cell Disease

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## Abstract

Hospital readmissions are receiving more attention because of the implications on cost and quality of care. Many researchers and clinicians believe that a substantial number of readmissions are preventable as evidenced by the significant reductions achieved after the Hospital Readmission Reduction Program mandated by the Affordable Care Act. While sickle cell disease is not currently one of the diseases designated for inclusion in the Hospital Readmission Reduction Program, some of the lessons learned addressing hospital structural characteristics and processes of care can be applied to this population.

Acute worsening of chronic pain is the predominant clinical presentation of patients with sickle cell disease to the hospital. Pain and the measurement of pain is subjective and there are no clearly defined objective clinical criteria or biomarkers to validate or refute the presence of acute sickle cell pain crisis. The current epidemic of nonmedical opioid use and medical opioid abuse combined with racial unrest and governmental oversight in the US worsens a well-known atmosphere of mistrust on the part of both clinicians and patients with sickle cell disease. These dynamics force the need for a paradigm change in management of these patients.

## Key words

Ethnicity; Hospitalized; Readmission; Opiates; Pain; Sickle cell disease

## Introduction

Sickle cell disease (SCD) is the most common inherited disease in African Americans and occurs in 1 of every 625 live births to African-American couples. Even though it is more common in African Americans, the disease also occurs in Arabic, Hispanic, Native Americans and Caucasians and is currently believed to have a prevalence of 100,000 in the US. Although well described as a multiorgan system disease, the primary reason for

admission for the majority patients with SCD is acute pain crisis [1]. Most individuals self-treat these episodes at home with infrequent admissions occurring on average, 1.5 times per year and patients with 3 or more admissions per year have a lower 5-year survival rate [2]. There is however a subpopulation of patients who are termed “high utilizers” and “extremely high utilizers” that are admitted to the hospital more frequently—some as often as several times a month over successive years [3,4]. Many of these patients are quite ill and require high doses of narcotics while admitted and at discharge and attract the most attention and frustration of clinicians. This is the group on which this review is most focused.

## Acute on Chronic Pain

Sickle Cell disease is and its associated complications are a heterogeneous condition with genetic and non-genetic modifiers of disease severity. The complex cascade of events leading to painful episodes culminates in HgbS polymerization and vaso-occlusion and is the primary reason for admission to the hospital [5]. Because most clinicians have used the term “crisis” to describe these acute episodes, and chronic pain to describe such complications as ischemic extremity ulcers or avascular necrosis, there is the perception that most sickle cell patients have pain free periods. The Landmark Pain in Sickle Cell Epidemiology Study (PiSCES) used patient’s self-description of pain and demonstrated that on average, most patients experienced pain over half of their days (56% of patient days) and daily pain was present in a third of patients with only 15% endorsing rarely having pain [6]. Most of the pain described by their cohort was not considered a crisis and patients spent less than 5% of patient days in emergency departments or hospitals. The high Emergency Department (ED) utilizers (3 or more ED visits per year) had higher pain scores, worse lab values and a lower quality of life.

Another visible measure of a painful crisis, health care utilization, was a strong predictor of mortality in the Cooperative Study of Sickle Cell Disease of the 70s and 80s. Patients with 3 or more admissions per year had a lower 5-year survival rate. But again, one of the limitations of this study is the self-reported

endorsement of pain and the well acknowledged more liberal prescribing of narcotics [7].

There are many well described precipitants of painful episodes and include infection, emotional stress, overexertion, changes in barometric pressure, temperature and wind but in many instances, an identifiable precipitant is not found. Pain can be generalized or migratory but most often localized to extremities, back, chest or joints. Depending on the precipitant, most painful episodes last 5-10 days but can be as long as several weeks [8,9]. When a painful crisis lasts longer than seven days, it is very important for clinicians to search for more malicious causes of bone pain such as avascular necrosis, osteomyelitis and compression fractures or deformities. When a bone crisis lasts for weeks, engagements of a hematologist (if not already involved) and an exchange transfusion may be required.

Physical exam can demonstrate joint effusions, fever, leukocytosis, tachycardia or sources of infection in about 50% of patients early in the course of an acute pain crisis, serial lab studies are more useful. There are no objective physical or laboratory findings to confirm the existence of an acute pain episode at initial presentation [10,11]. Reticulocytes are always present in varying degrees and quantity does not correlate with the existence or severity of an acute pain episode [12]. Sickled red blood cells are always found in circulation and the LDH and bilirubin are variably elevated depending on the timing and relationship to an individual's baseline. A congruent history in a patient at risk for an acute pain crisis is the sole definitive diagnostic criteria.

All pain is felt to be worsened by major psycho-social issues but this is consistently and well documented in individuals with SCD [13-15]. Like other chronic diseases that manifest in childhood (rheumatoid arthritis, cystic fibrosis), many sickle cell disease patients require frequent prolonged hospitalizations during childhood and adolescence that are barriers to education and the attainment of developmental milestones. These and other developmental and cognitive skills (communication, coping, trust, independence) are necessary to develop autonomy that leads to effective socialization and participation in civil society [15,16].

Many patients with SCD were initially exposed to intravenous opioids during childhood with subsequent escalating doses secondary to tolerance requiring much larger doses of opiates than most clinicians are comfortable with. Of course, there is dependence and in some cases addiction further complicating the clinical interaction. As improvement in care has extended survival into adulthood, inpatient non-pediatric clinicians will care for more of these patients [17,18].

The overzealous treatment of non-cancer pain increased sharply in the mid to late 90s but is most notably documented from 1999 to 2010 when the number of opioid prescription quadrupled in the US [19-22]. National awareness intensified in 2005 -2010 and the amount of opioids prescribed began to decrease in 2011 but still in 2015 was found to be triple the amount in 1999 and almost 4 times the amount prescribed in Europe [20,23,24].

The Centers for Disease Control (CDC) guidelines published in 2016 recommend that the long-term use of opioids outside of active cancer, palliative and end of life care should be discouraged. These guidelines were suggested for primary care and outpatient populations over the age of 18 and with pain lasting longer than 3 months [25]. The directives also encourage the use of non-pharmacologic interventions and a multidisciplinary approach to caring for patients with chronic pain. Risk factors for abuse were identified as those who obtain overlapping prescriptions from multiple providers, take high daily doses of pain meds, have mental illness or a history of alcohol or substance abuse, those living in rural areas or of a lower socio-economic class. The SCD patient population is not specifically addressed.

Multiple studies have shown that many pts with SCD have achieved some level of success in controlling pain with non-pharmacologic therapies. The range of efficacy has been recorded across many studies as achieving from 50% to 70% of participants achieving some level of improvement by utilizing such therapies as biofeedback, prayer, massage, relaxation, cognitive behavioral therapy, hypnosis acupuncture and certain herbal therapies [26-29]. While researchers noted benefits in adults and children, the younger patients seemed to achieve the highest levels of improvement with nonpharmacological therapies. Most studies had significant limitations such as being underpowered and lacking methodological mechanisms to control for the effects of socioeconomic status, levels of formal education, racial and cultural bias and ongoing use of pain medications. After several years of collaboration, the National Heart Lung and Blood Institute (NHLBI) published an expert panel report of evidence-based guidelines for the care of people with SCD in 2014. They concluded that there is a general lack of research in the area of nonpharmacological management of pain in persons with SCD, and that further randomized controlled trials are needed to determine the roles of alternative and supplemental therapies for the management of pain [30].

## Frequency of Hospitalization

Hospital readmissions in the U.S. have received growing attention because of implications on cost and quality of care. In 2012, the Hospital Readmission Reduction Program (HRRP) was enacted as a component of the Affordable Care Act to incentivize hospitals to reduce readmissions. Currently the HRRP monitors Medicare readmission rates for heart failure, acute myocardial infarction, pneumonia, acute exacerbation of chronic obstructive pulmonary disease, coronary artery bypass surgery and total hip arthroplasty and total knee arthroplasty. Sickle Cell Disease is not currently one of the diseases monitored. According to recent data, the program is working as readmission rates have dropped in every state except one since the program's enactment [31]. Lessons learned indicate that usually there is a complex interplay of personal, medical/psychiatric and social factors that determine whether patients successfully recover or cope with their condition following a hospital stay or experience deterioration that leads to readmission [32,33]. Much data show that multiple socio-demographic features of the patient (age, race, gender, literacy, income) and the

community (primary care provider, geographic location, resource supplies) contribute to hospital admissions. These factors also contribute to readmission but are additive to conditions that occur during the hospital stay such as poor processes of care (care coordination, assessment for food insecurity, service utilization, adequate length of stay, safety net status) [33,34]. The SCD population is not usually impacted by choices of post-discharge care since most of these patients are discharged home but these socio-demographic factors along with processes of care and hospital mortality outcomes are often used as an indicator of the quality of hospital care.

In 2010, persons with SCD had the highest hospital readmission rate of any disease [35]. Individuals with sickle cell disease account for approximately 113,000 hospital admissions annually in the United States, at a cost of approximately \$500 million. Most patients with SCD manage their acute and chronic pain at home with occasional admissions on average 1.5 times a year [4,18,36]. However, there is a well described subpopulation of patients admitted as often as several times a month and deemed "high utilizers" that account for the largest portion of hospital resources associated with care of these patients. Included in this population is a subset deemed "very high utilizers" which have been hospitalized greater than once per week [1,3,4,37,38].

Several studies have shown that high utilizers across the spectrum appear to be more ill and complex than non-high utilizers and had more complications prior to and during the period of high utilization [39,40]. One group did a retrospective review and found that SCD patients from lower socio-economic areas were at a higher risk of readmission (54% readmitted over the study period compared to 28% for those of the least deprived group) and higher inpatient mortality amongst those readmitted [41]. However, most studies were unable to reliably predict which complications or patterns of illness were associated with higher utilization of resources. The one complication associated with persistent high utilization was bacteremia but given the high rate of invasive procedures in this population, it is possible for bacteremia to be more a consequence than a cause. Notably, sustained high utilization rather than the more common transient course seemed more closely related to substance abuse and mood disorders than to complications of the disease [39].

Another group studied patients with the highest costs and the most admissions at a large academic medical center in San Francisco [42]. In their study, "high admit" patients were defined as those responsible for the top decile of admissions, and were grouped into equal-sized high- and low-cost cohorts. The high-admission/high-cost group represented 5% of all patients, 25% of all costs, and 16% of all admissions. These patients were hospitalized primarily for medical conditions (78%) and had a high 30-day readmission rate (47%). The high-admission/low-cost group accounted for 5% of all patients, 12% of all admissions, and 7% of all costs. These patients were also predominantly admitted for medical conditions (87%), with the most common admitting diagnoses representing respiratory, gastrointestinal, and cardiovascular conditions [42].

The role of psychiatric illness and addiction in the frequency of hospitalizations is still unsettled. While many studies have associated mood disorders ranging from mania to major depressive disorder as predictors of higher utilization of resources, the literature is very inconclusive due to the research methods used and the populations studied [13,14,39]. Depression has been stated to be a predictor of higher utilization but when defined as a major depressive disorder as characterized in the Diagnostic and Statistical Manual of Mental Disorders (DSM), the association is not statistically significant [14,40]. Major depression is however more prevalent in individuals with SCD when compared to the African American population without SCD and is associated with worsened pain and greater opioid use.

The major obstacle to determining the role of psychiatric illness in any chronic disease is to assess the level of independence of the psychiatric disorder from the consequences of the underlying disorder. In a disease known to cause clinical and subclinical ischemic neurologic deficits, superimposed on the chronic use of opioids and being a member of a vulnerable subpopulation, it is almost methodologically impossible to tease out the true prevalence of native psychiatric disorders. This does not mean we should not try to understand the role of psychiatric disorders (native or induced) in pain, the use of opioids and the frequency of hospitalizations in individuals with sickle cell disease.

## Psychosocial and Racial Dynamics

In the US, individuals with SCD are vulnerable both because they are almost always members of a racial or ethnic minority group who are defined by the Food and Drug Administration as having an "orphan" disease (less than 200,000 people). Whether an African American, an African from Kenya or an Indian from India, the present environment of racial dynamics in the US must be considered as potentially influencing the ability to care for patients with sickle cell disease [43,44].

Superimposed on the care of this group is the mistrust between patients and clinicians surrounding the use of opioid analgesics and the well documented racial and ethnic bias experienced by minority patients treated for pain in emergency departments. Whether unconscious bias or explicit racism multiple studies have identified disparities in pain treatment due to one's ethnicity in children and adults. One retrospective cohort study at a large urban emergency department in Atlanta, Georgia reviewed records for a forty-month period in the mid-1990s to identify all black and white patients discharged from the emergency department with a diagnosis of isolated long bone fracture [45]. The study consisted of 217 patients, of whom 127 were black and 90 were white. The study found that the white patients were significantly more likely than black patients to receive analgesics (74% vs. 57%,  $p=0.01$ ) despite similar records of pain complaints in the medical record. This study reinforced Todd's 1993 study at the Southern California Academic Center in the city of Los Angeles where Hispanics with isolated long-bone fractures were twice as likely as non-Hispanic whites to receive no pain medication [46].

A more recent study published in *JAMA Pediatrics* in 2015, found stark disparities in pain management in emergency departments in children diagnosed with appendicitis. Researchers found that black patients were far less likely to receive opioids than white ones (12% vs. 34%) [47].

After examining 60 million death certificates issued by the CDC between 1990 and 2014, a group of analysts found that death rates for Non-Hispanic Whites increased for virtually all adult age groups under 65 [48,49]. The highest death rates nationally after 2009, 23% was for whites without a high school education between the ages 25-34 and three times the rate for Whites between the ages of 35-44. Drug overdoses (primarily heroin and newer synthetic opiates are felt to be the primary cause [50]. Comparable death rates for Blacks and Non-White Hispanics continue to drop [49].

The prevailing opinion as to the etiology and driving forces behind the opioid epidemic is that this new generation of opiate users began using legal pain relievers such as fentanyl, oxycodone, hydrocodone or morphine that were obtained with or without prescriptions and graduated to illicit opiates-usually heroin [51-53]. Indeed, in a recent survey 75% of heroin addicts admitted to starting out using prescription drugs and nearly 90% of the people who tried heroin for the first time in the past decade were white. And a growing number are middle-class or wealthy [50,54].

So, even though the painkiller-to-heroin transition is predominantly a rural and small town epidemic affecting mostly whites, many clinicians are afraid to prescribe large quantities of opioids to patients with SCD for fear of state sanctions and contributing to the crisis [55].

## Conclusion

Hospital readmissions are due to a complex interplay of personal, medical/psychiatric and negative social factors-many of which are more prevalent in the sickle cell disease population. While many of these socio-demographic features of patients and the communities in which they live in contribute to hospital admissions and readmissions, they are additive to conditions that occur during the hospital stay such as poor processes of care and transitions of care. All SCD patients identified as high utilizers or very high utilizers should undergo screening for access to primary care providers, adequate nutrition and transportation. When these patients are hospitalized, adequate length of stay, care coordination, equitable care and service utilization should be emphasized. At discharge, transition to a suitable post-discharge care environment and self-management capabilities should be assessed.

There are no objective clinical findings or biomarkers to validate or disprove the existence of an acute sickle cell pain crisis. Serial exams and laboratory studies are more useful in helping to define the etiology and manage the course of a patient's acute pain crisis. Sickle cell disease is a heterogeneous condition with some patients experiencing little pain and very few interactions with the health care system and others deemed

high and very high utilizers because of their very frequent hospitalizations. Even though SCD patients have not been associated with the painkiller-to-heroin transition identified as complicit in the current opioid epidemic, they are clearly at risk for addiction and abuse. Societal, governmental and medical attitudes surrounding the use of opiates has created a paradigm shift in how all chronic pain not associated with cancer or end-of-life care is managed. Clinicians should not be encouraged or forced to use archaic and subjective pain scales in an attempt to render these patients pain free. As recommended by the 2016 CDC guidelines, prescriptions for opiates to treat chronic pain should be written by one prescriber and only for 3 days for patients presenting to emergency departments.

SCD patients should be referred to and encouraged to seek out practitioners engaged in controlling pain with non-pharmacologic therapies. Many of these therapies have been shown to have varying levels of success in the treatment of pain but in most patients studied, there was some level of improvement. Available evidence shows non-pharmacological therapies to be most effective in younger SCD patients so parents and pediatricians should be targeted with educational material, classes and other supportive tools that reinforce alternative therapies for the management of pain.

The higher prevalence of psycho-social issues, the legacy of discrimination and ethnic disparities in analgesic practice combined with bilateral mistrust complicates the clinical interaction between many SCD patients and clinicians. Knowledge of SCD pathophysiology as well as the social, cultural and ethnic dynamics involved in caring for this population is required to give contemporary and compassionate care.

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