Poster #EE506

Association of fatigue and acute pain with health care resource utilization and costs in sickle cell disease in the United States

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Patients with SCD with:
acute pain or fatigue

Greater probability of inpatient, outpatient, emergency department, and pharmacy utilization

Acute pain was associated with an average increase of **$6,108** per patient per year

Fatigue was associated with an average increase of **$7,500** per patient per year

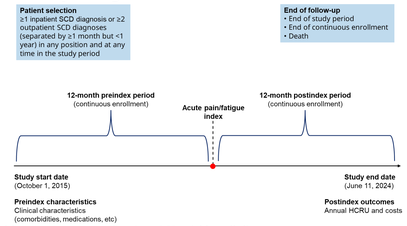
BACKGROUND & AIMS

- Sickle cell disease (SCD) is a debilitating chronic disease that affects millions of people worldwide
- Pain and fatigue are common in SCD: >50% of patients experience pain and >80% experience fatigue daily[1,2]; however, the associated economic burden of these symptoms remains largely unknown
- The aim of this study was to evaluate whether fatigue or acute pain in patients with SCD is associated with increased health care resource utilization (HCRU) and all-cause costs in the United States

MATERIALS & METHODS

- This retrospective, longitudinal cohort analysis used data from patients aged ≥12 years who were diagnosed with SCD between October 1, 2015, and June 21, 2024. Patients were identified using the TriNetX Linked Network claims database and TriNetX Dataworks-USA electronic health record data **(Figure 1)**
  - Inclusion in the study required ≥1 inpatient SCD diagnosis or ≥2 outpatient SCD diagnoses separated by ≥1 month but <1 year
  - Patients with sickle cell trait and those who had gene therapy or stem cell transplantation were excluded from the study
- Two comparisons were conducted with data from (1) patients with vs without acute pain, and (2) patients with vs without fatigue
- Acute pain was defined as an emergency department (ED) or inpatient encounter with an *International Classification of Diseases, Tenth Revision, Clinical Modification* (*ICD-10-CM*) diagnosis code for generic pain or SCD crisis, with intravenous pain medication administered during the encounter or an opioid prescription given within 7 days of the respective encounter
- Fatigue was defined as hemoglobin levels ≤10.0 g/dL (a proxy for fatigue) or an encounter assigned an *ICD-10-CM* diagnosis code for fatigue
- Multivariable regression models were used to estimate incremental annual HCRU and payer costs (2023 US dollars) among patients with fatigue or acute pain compared with controls

Figure 1 Study design



HCRU, health care resource utilization; SCD, sickle cell disease.

RESULTS

Patient characteristics

- A total of 1,966 and 2,220 patients were included in the evaluation of acute pain and fatigue, respectively **(Table 1)**
- In both cohorts, most patients were Black or African American, and the majority were enrolled in Medicaid **(Table 1)**
- SCD-related comorbidities were more prevalent among patients with fatigue compared with those without **(Table 1)**

Table 1 Baseline demographics and clinical characteristics of patients with SCD

	Without acute pain (n=884)	With acute pain (n=1,082)	*P* value	Without fatigue (n=1,260)	With fatigue (n=960)	*P* value
Sex, n (%)						
Female	493 (55.8)	595 (55.0)	.764	640 (50.8)	553 (57.6)	.002
Male	391 (44.2)	487 (45.0)		620 (49.2)	407 (42.4)	
Mean age (SD), y	36.4 (17.5)	32.4 (14.3)	<.001	31.9 (14.9)	35.4 (14.7)	<.001
Race/ethnicity, n (%)						
American Indian or Alaska Native	2 (0.2)	5 (0.5)	<.001	4 (0.3)	2 (0.2)	.050
Asian	16 (1.8)	3 (0.3)		5 (0.4)	10 (1.0)	
Black or African American	664 (75.1)	898 (83.0)		1021 (81.0)	787 (82.0)	
White	114 (12.9)	83 (7.7)		98 (7.8)	88 (9.2)	
Other race	32 (3.6)	33 (3.1)		57 (4.5)	27 (2.8)	
Hispanic or Latino	44 (5.0)	37 (3.4)	.116	39 (3.1)	53 (5.5)	.002
Type of insurance, n (%)						
Commercial	239 (27.0)	191 (17.7)	<.001	265 (21.0)	160 (16.7)	<.001
Medicaid	547 (61.9)	787 (72.7)		865 (68.7)	694 (72.3)	
Medicare Advantage	70 (7.9)	82 (7.6)		75 (6.0)	85 (8.9)	
Unknown	28 (3.2)	22 (2.0)		55 (4.4)	21 (2.2)	
CCI, mean (SD)	0.96 (1.86)	1.04 (1.86)	.004	0.74 (1.41)	1.57 (2.39)	<.001
SCD genotype,[a] n (%)						
Hb-SS	324 (36.7)	733 (67.7)	<.001	665 (52.8)	645 (67.2)	<.001
Hb-SC	171 (19.3)	147 (13.6)		240 (19.0)	101 (10.5)	
Hb-Sβ	23 (2.6)	14 (1.3)		19 (1.5)	17 (1.8)	
Hb-Sβ thalassemia	85 (9.6)	58 (5.4)		95 (7.5)	53 (5.5)	
Not specified	281 (31.8)	130 (12.0)		241 (19.1)	144 (15.0)	
Select SCD-related comorbidities, n (%)						
Anxiety	148 (16.7)	169 (15.6)	.541	176 (14.0)	240 (25.0)	<.001
Asthma	134 (15.2)	248 (22.9)	<.001	233 (18.5)	230 (24.0)	.002
COPD	45 (5.1)	66 (6.1)	.386	49 (3.9)	111 (11.6)	<.001
Depression	63 (7.1)	60 (5.5)	.178	81 (6.4)	100 (10.4)	<.001
Diabetes mellitus	84 (9.5)	89 (8.2)	.361	69 (5.5)	116 (12.1)	<.001
Heart failure	32 (3.6)	51 (4.7)	.277	43 (3.4)	112 (11.7)	<.001
Hyperlipidemia	123 (13.9)	112 (10.4)	.019	109 (8.7)	150 (15.6)	<.001
Hypertension	213 (24.1)	264 (24.4)	.917	278 (22.1)	313 (32.6)	<.001
Obesity	111 (12.6)	162 (15.0)	.140	148 (11.7)	174 (18.1)	<.001
Pneumonia	53 (6.0)	153 (14.1)	<.001	117 (9.3)	219 (22.8)	<.001
Urinary tract infection	71 (8.0)	117 (10.8)	.045	97 (7.7)	168 (17.5)	<.001
Venous thromboembolism	27 (3.1)	63 (5.8)	.005	50 (4.0)	132 (13.8)	<.001
Treatments, n (%)						
ESAs	3 (0.3)	9 (0.8)	.245	5 (0.4)	9 (0.9)	.186
Crizanlizumab-tmca	2 (0.2)	9 (0.8)	.125	14 (1.1)	29 (3.0)	.002
Hydroxyurea	117 (13.2)	281 (26.0)	<.001	246 (19.5)	301 (31.4)	<.001
L-glutamine	2 (0.2)	20 (1.8)	<.001	9 (0.7)	29 (3.0)	<.001
Voxelotor	7 (0.8)	15 (1.4)	.303	14 (1.1)	21 (2.2)	.065
Pain medications[b]	420 (47.5)	890 (82.3)	<.001	787 (62.5)	756 (78.8)	<.001
Transfusions, n (%)	139 (15.7)	274 (25.3)	<.001	234 (18.6)	353 (36.8)	<.001

[a]Hb-SD codes were retained if Hb-SD was the only genotype recorded for the patient; otherwise, the SCD genotype was based on the most frequently recorded diagnosis code. Remaining ties (equal numbers of 2 non–Hb-SD codes) were classified as "multiple/unknown."
[b]Pain medications included in this study were based on expert input and included buprenorphine, benzhydrocodone, butorphanol, codeine, dihydrocodeine, fentanyl (transdermal outpatient, injection use in ED), hydrocodone, hydromorphone, levorphanol, meperidine, methadone, morphine, morphine liposomal, nalbuphine, oliceridine, oxycodone, oxymorphone, pentazocine, propoxyphene (dextropropoxyphene), remifentanil, tapentadol, tramadol, and ketorolac.
CCI, Charlson Comorbidity Index; COPD, chronic obstructive pulmonary disease; ED, emergency department; ESAs, erythropoiesis-stimulating agents; Hb, hemoglobin; SCD, sickle cell disease.

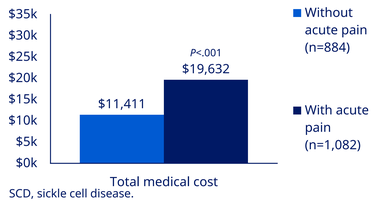
RESULTS (cont'd)

- Across all health care settings, the 12-month unadjusted all-cause HCRU was higher for patients with SCD with acute pain and for patients with fatigue compared with patients with SCD without these symptoms. This difference was most pronounced in the inpatient and ED settings
  - Patients with vs without acute pain: inpatient setting, 62.9% vs 16.4% (*P*<.001); ED setting, 91.9% vs 38.9% (*P*<.001)
  - Patients with vs without fatigue: inpatient setting, 59.7% vs 30.9% (*P*<.001); ED setting, 79.1% vs 55.2%; (*P*<.001)

12-month unadjusted all-cause total health care costs (2023 US dollars)

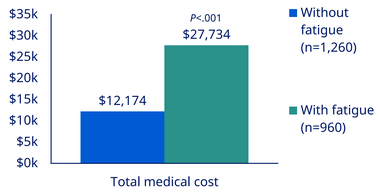
- All-cause total health care costs were significantly higher in patients with acute pain and in patients with fatigue **(Figures 2 & 3)**
  - Total medical costs were 1.7 times higher in the acute pain cohort vs no acute pain **(Figure 2)** and 2.3 times higher in the fatigue vs no fatigue group **(Figure 3)**

Figure 2 12-month unadjusted all-cause total health care costs among patients with SCD with or without acute pain



SCD, sickle cell disease.

Figure 3 12-month unadjusted all-cause total health care costs among patients with SCD with or without fatigue



Regression-adjusted 12-month all-cause total health care costs (2023 US dollars)

- Patients with acute pain had a greater probability of adjusted inpatient, outpatient, ED, and pharmacy utilization than patients without acute pain (all *P*<.001), leading to an additional $6,108 in all-cause cost per patient per year **(Figure 4)**
- Patients with fatigue had a greater probability of adjusted inpatient, outpatient, ED, and pharmacy utilization than patients without fatigue (all *P*<.001), leading to an additional $7,500 in all-cause cost per patient per year **(Figure 5)**
- Additional clinical predictors of significantly higher adjusted all-cause costs for both cohorts included hemoglobin-SD genotype, baseline transfusions, chronic obstructive pulmonary disease, sepsis, and baseline Charlson Comorbidity Index score (all *P*<.05)

Figure 4 12-month regression-adjusted[a] HCRU for patients with acute pain

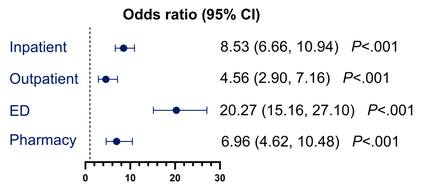
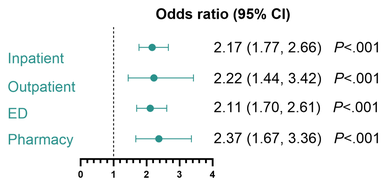


Figure 5 12-month regression-adjusted[a] HCRU for patients with fatigue



[a]Adjusted at baseline for sex, age, race, ethnicity, type of insurance, CCI score, SCD genotype, SCD-related comorbidities, SCD-specific treatments, transfusions, and anxiety or depression.
CCI, Charlson Comorbidity Index; ED, emergency department; HCRU, health care resource utilization; SCD, sickle cell disease.

CONCLUSIONS

- This is the first study to evaluate the associations of pain and fatigue with health care resource utilization and costs among patients with SCD in real-world US settings
- Pain and fatigue were associated with higher inpatient, ED, outpatient, and pharmacy utilization, leading to substantially higher health care costs for patients with SCD
- This study highlights the need for new treatments that address these unmet needs and the associated economic burden

PLAIN LANGUAGE SUMMARY

- **Why does it matter?** Patients with sickle cell disease (SCD) typically experience pain and fatigue; however, how these symptoms affect health care use and associated costs is not well understood
- **How does it work?** This study evaluated the associations of acute pain and fatigue with health care resource utilization (HCRU) and medical costs among individuals with SCD in real-world settings
- **What did we find?** Acute pain and fatigue were associated with a higher likelihood of HCRU and increased medical costs in patients with SCD

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REFERENCES

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2. Batt K, et al. *Blood*. 2023;142(suppl 1):7320-7321. ASH abstract.