Patient-reported vaso-occlusive events, their associated pain severity, and impact of sickle cell disease on fatigue and quality of life: a real-world survey in the United States

PS2179

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BACKGROUND

Sickle cell disease and vaso-occlusive events

- Sickle cell disease (SCD) is an inherited blood disorder characterized by a gene mutation producing sickle hemoglobin (HbS)[1]
  - HbS polymerization results in red blood cell sickling and downstream effects including hemolysis, anemia, and vaso-occlusive events (VOEs)
- VOEs are a significant complication of SCD and are instances of acute severe pain occurring in various parts of the body[2]
  - These vary in severity and can result in life-threatening complications[3]
- Fatigue is a core symptom associated with SCD, experienced by many patients on a daily basis[4,5]
  - SCD has a significant impact on quality of life (QoL), with pain (both acute and chronic) and fatigue as the hallmark symptoms[5]
- Key aspects of the real-world patient experience with VOEs and the humanistic burden of SCD remain under-researched, including the spectrum of patient-reported VOEs and their impact on fatigue and health-related QoL (HRQoL)

AIM

To investigate patient-reported VOEs, fatigue, and HRQoL of adults with SCD in the United States (US)

METHODS

- Data were analyzed from the Adelphi Real World patient-reported survey of patients with SCD, completed in the US from June to September 2024
  - The survey was cross-sectional, with elements of retrospective data collection, whereby patients were asked about their current and previous experiences (e.g. in the previous 12 months)
- Adult patients (≥18 years) with physician-diagnosed SCD were recruited from patient advocacy groups and patient panels (**Figure 1**)
- The survey captured patient demographics, clinical characteristics including VOE history, details from the most recent VOE, and validated patient-reported outcomes (PROs) (**Table 1**)
  - Using questions from the Adult Sickle Cell Quality of Life Measurement Information System (ASCQ-Me) Pain Episode Frequency and Severity measure, patients rated their VOE pain severity from 0 (no pain) to 10 (worst pain imaginable) and reported where they sought medical assistance (if any)
- Subgroup analyses were conducted on the most recent self-reported hemoglobin (Hb) level (<8 g/dL and ≥8 g/dL) and the number of VOEs experienced in the 12 months prior to the survey (0–3 VOEs and ≥4 VOEs), to evaluate SCD-related pain, fatigue, and HRQoL
- Data were summarized descriptively

Figure 1: Study patient inclusion criteria

Patient inclusion criteria

- Physician-diagnosed sickle cell disease
- Resides in the United States
- Adult (aged ≥18 years)

Table 1: PRO measures included

ASCQ-Me Pain Episode Frequency and Severity measure	5-item instrument measuring the frequency of sickle cell pain events in the last 12 months, as well as the timing, severity, level of interference, and duration of the last attack; items were summarized individually
Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue scale, version 4	13-item measure to assess fatigue and its impact on daily activities and function over a 7-day recall period; score range of 0–52; higher scores indicate lower fatigue
EuroQoL 5-Dimensions 5-Levels (EQ-5D-5L) and EuroQol visual analog scale (VAS)	The EQ-5D-5L measures patients' health status and QoL through 5 dimensions and a VAS, where patients rank their health on a scale of single increments ranging from 1 to 100; responses from the 5 dimensions are transformed into a utility value ranging from −0.573 to 1 using the US value set; for both the utility value and VAS, higher scores indicate better health

ASCQ-Me, Adult Sickle Cell Quality of Life Measurement Information System; EQ-5D-5L, Euro-QoL 5-Dimensions 5-Levels; FACIT, Functional Assessment of Chronic Illness Therapy; PRO, patient-reported outcome; QoL, quality of life; VAS, visual analog scale.

RESULTS

Patient characteristics

- Overall, 217 patients were included in the study
- Patient characteristics are reported in **Table 2**
- In the 3 months prior to the survey, 82% (n=177) of patients experienced at least 1 VOE ; these patients reported the number of VOEs in the last 3 months managed in each location (**Table 3**)
  - Patients managed VOEs in multiple locations during this period, with a mean (standard deviation [SD]) of 2.6 (1.3) locations
  - Patients managed the highest number of VOEs at home (mean [SD]: 3.1 [2.7]), followed by the emergency room (ER; 1.6 [2.4]) and the inpatient setting (1.3 [2.0])
  - Based on this survey question, 94% (n/N=167/177) reported experiencing ≥1 VOE managed at home, 59% (n=104) experienced ≥1 VOE managed at the ER, and 50% (n=89) experienced ≥1 VOE managed with an inpatient hospital admission (**Table 3**)
    - The survey did not collect whether multiple settings were used per VOE

Table 2: Patient characteristics at time of survey

	Overall (N=217)
Age (years), mean (SD)	36.9 (10.1)
Female, n (%)	190 (88)
Ethnicity, n (%)	
Black/African American	203 (94)
White	4 (2)
Native Hawaiian or Pacific Islander	3 (1)
Other[a]	7 (3)
Number of VOEs experienced in the past 12 months, n (%)	
≥4	121 (56)
3	34 (16)
2	34 (16)
1	14 (6)
0	14 (6)
Time since last VOE, n (%)	
>5 years	7 (3)
1–5 years	7 (3)
7–11 months	20 (9)
1–6 months	64 (29)
1–3 weeks	44 (20)
<1 week	40 (18)
I have one right now	35 (16)
Patient's most recent Hb level (g/dL)[b], n (%)	162 (74.7)
Mean (SD)	7.3 (2.0)
Patients with Hb level <8 g/dL, mean (SD), n=100	5.9 (1.0)
Patients with Hb level ≥8 g/dL, mean (SD), n=62	9.4 (1.3)
Patients receiving DMTs[c] at time of survey, n (%)	143 (66)

[a]Responses provided for ethnicity response option of "Other" were: African Indigenous American, biracial, Caribbean American, Haitian American, Jamaican, Panamanian, and West Indian. [b]Patients were asked to report their most recent Hb level. If the patient had received a blood transfusion in the 2 months prior to the survey for their SCD, they were asked to report their Hb level before their most recent transfusion. [c]DMTs include hydroxyurea, L-glutamine, crizanlizumab, and voxelotor. DMT, disease-modifying therapy; Hb, hemoglobin; SCD, sickle cell disease; SD, standard deviation; VOE, vaso-occlusive event.

Table 3: Patient-reported locations of where VOEs were managed in last 3 months[a]

	Overall (N=177)[b]
Number of patients with at least 1 VOE managed at the following locations in the last 3 months, n (%)	
At home	167 (94)
In the emergency room	104 (59)
In inpatient admission	89 (50)
In a doctor's office/center	42 (24)
In urgent care or outpatient clinics	41 (23)
At day hospital	35 (20)
Number of VOEs managed per location in the last 3 months, mean (SD)	
At home	3.1 (2.7)
In the emergency room	1.6 (2.4)
In inpatient admission	1.3 (2.0)
In a doctor's office/center	0.6 (1.5)
In urgent care or outpatient clinics	0.6 (1.6)
At day hospital	0.5 (1.3)

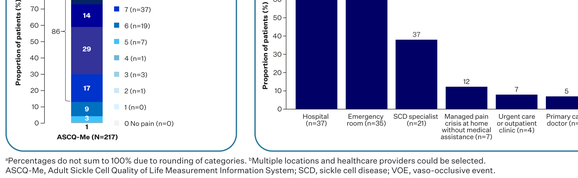
[a]Patients reported the number of VOEs in the last 3 months managed in each location. The survey did not collect whether multiple locations were used per VOE. [b]Total number of patients with at least 1 VOE in the last 3 months.
SD, standard deviation; VOE, vaso-occlusive event.

Patient-reported VOE pain descriptors and locations

- All patients (N=217) were asked to describe their pain experiences when having a VOE via a multi-select option list[a]
  - The most prevalent descriptors for VOE included acute extreme pain in certain areas, which included the chest, back, extremities, and joints (94%); impact on the patient's ability to walk (75%); and acute pain that cannot be controlled with pain medications (60%) (**Figure 2**)

[a]Pain experience when having a VOE was described generally; no specific time frame was required.

Figure 2: Description of VOEs



[a]Responses provided by patients as "Other" included acute chest syndrome, fatigue, bone pain, and feeling light-headed. VOE, vaso-occlusive event.

Patient-reported most recent VOE

- On an 11-point pain severity scale, where a score of 10 is the worst pain imaginable, 86% (n/N=186/217) of patients rated their most recent VOE pain as 7 or greater (**Figure 3a**)
- Of these 186, 31% (n=57) reported their pain as 10 (worst pain imaginable)
  - 88% (n/N=50/57) of these patients sought medical care from various locations and healthcare providers, including the hospital (65%, n=37), the emergency room (61%, n=35), and/or with an SCD specialist (37%, n=21) (**Figure 3b**)
  - 12% (n/N=7/57) of these patients only managed their VOE at home without medical assistance
- 83% of patients with 0–3 VOEs in the last 12 months, and 88% of patients with ≥4 VOEs in the last 12 months reported severe pain (defined as a pain score of 7 or greater) during their most recent VOE (**Table 4**)
  - Of the patients who experienced 0–3 VOEs and ≥4 VOEs in the last 12 months, 28% (n/N=27/96) and 25% (n/N=30/121), respectively, rated their most recent VOE as the worst pain imaginable
- High pain severity was also reported in patients with Hb levels <8 g/dL (92%) and ≥8 g/dL (81%; **Table 4**)
  - Among those patients with a self-reported Hb level (n=162), 29% (n/N=29/100) of patients with Hb <8 g/dL reported the worst pain imaginable (pain level of 10) during their most recent VOE; this was 16% (n/N=10/62) for patients with Hb ≥8 g/dL

Patient-reported most recent VOE pain severity and location care was received for worst pain imaginable

Figure 3a: Patient-reported most recent VOE pain severity[a]

Figure 3b: Location care was received for patients who reported the worst pain imaginable during their most recent VOE[b]

[a]Percentages do not sum to 100% due to rounding of categories. [b]Multiple locations and healthcare providers could be selected.
ASCQ-Me, Adult Sickle Cell Quality of Life Measurement Information System; SCD, sickle cell disease; VOE, vaso-occlusive event.

Table 4: ASCQ-Me—severity of pain experienced during most recent VOE[6,a]

ASCQ-Me pain rating	Overall (N=217)	Most recent Hb level		Number of VOEs experienced in the past 12 months	
		<8 g/dL[b] (n=100)	≥8 g/dL[b] (n=62)	0–3 VOEs (n=96)	≥4 VOEs (n=121)
0 (no pain), n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
1–3 (mild), n (%)	4 (2)	1 (1)	2 (3)	2 (2)	2 (2)
4–6 (moderate), n (%)	27 (12)	7 (7)	10 (16)	14 (15)	13 (11)
7–10 (severe), n (%)	186 (86)	92 (92)	50 (81)	80 (83)	106 (88)

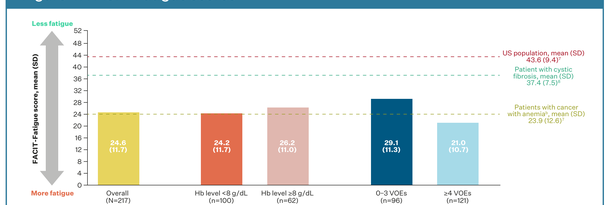
[a]ASCQ-Me Pain Episode Frequency and Severity item 3. Question: "Using any number from 0 to 10, where 0 is no pain and 10 is the worst pain imaginable, how severe was your pain during your last pain attack (crisis)?" Scale given as 0 = no pain to 10 = worst pain imaginable, with a pain level of 7–10 considered severe. [b]Full base for patients who answered their current/most recent Hb level was n=162; n=55 patients did not provide an answer here. ASCQ-Me, Adult Sickle Cell Quality of Life Measurement Information System; Hb, hemoglobin; VOE, vaso-occlusive event.

Patient-reported outcomes

- Patients with SCD had low scores (high disease burden) on the FACIT-Fatigue scale, EQ-5D-5L utility, and VAS scores regardless of Hb or VOE stratifications. The scores were below the published US population norms[7–9], indicating worse fatigue and HRQoL, with patients in the ≥4 VOEs subgroup having the worst outcomes (**Figures 4** and **5, Table 5**)[b]
- These scores were further contextualized using findings from literature[c] in patients with cystic fibrosis and patients with cancer with anemia (respectively; **Figures 4** and **5**)

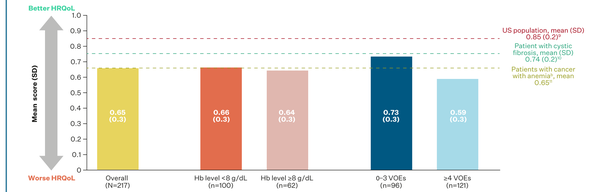
[b]Mean (SD) FACIT-Fatigue score for patients with cancer with anemia reported as 23.9 (12.6)[7]. [c]Anemia was defined as Hb level ≤11.0 g/dL.

Figure 4: FACIT-Fatigue scores[a]



[a]FACIT-Fatigue scores range from 0 to 52, with higher scores representing improved QoL and reduced fatigue. [b]Anemia was defined as Hb level ≤11.0 g/dL. FACIT, Functional Assessment of Chronic Illness Therapy; Hb, hemoglobin; QoL, quality of life; SD, standard deviation; US, United States; VOE, vaso-occlusive event.

Figure 5: EQ-5D-5L utility score



EQ-5D-5L, Euro-QoL 5-Dimensions 5-Levels; Hb, hemoglobin; HRQoL, health-related quality of life; SD, standard deviation; US, United States; VOE, vaso-occlusive event.

Table 5: Mean EQ-VAS scores (SD)[a]

EQ-VAS score	Overall (N=217)	Most recent Hb level before transfusion		Number of VOEs experienced in the past 12 months	
		Hb <8 g/dL (n=100)	Hb ≥8 g/dL (n=62)	0–3 VOEs (n=96)	≥4 VOEs (n=121)
Mean (SD)	64.1 (20.7)	60.0 (21.1)	69.6 (18.1)	70.1 (18.3)	59.3 (21.2)

[a]EQ-5D-5L scores range from 1 to 100, with lower scores indicating worsened health status and reduced HRQoL. EQ-5D-5L, EuroQoL 5-Dimensions; EQ-VAS, EuroQoL visual analog scale; Hb, hemoglobin; HRQoL, health-related quality of life; SD, standard deviation; VOE, vaso-occlusive event.

CONCLUSIONS

- **Patients with SCD experience frequent and severe VOEs**
- **Patients frequently managed their VOEs at home; however, the majority of the most painful VOEs were managed within a healthcare setting**
- **Patients with SCD, regardless of Hb levels or VOE frequency, experience worse fatigue and impaired HRQoL relative to a general US population; scores were comparable to those of patients with cystic fibrosis and patients with cancer with anemia (respectively); worse scores were reported in those who experience more VOEs**
- **There is an unmet need for patient-centered therapeutic approaches that address SCD-associated pain and fatigue, and improve HRQoL for individuals living with SCD**

Limitations

- The results from this survey may not be generalizable to all patients with SCD because participation was influenced by the patient's willingness to complete the survey
- Recall bias, a common limitation of surveys, may have affected the quality of the data obtained from patients and is dependent on how accurately patients were able to recall and report information

Acknowledgments: We would like to thank the patients for taking part in this study and providing the information included

Data collection was undertaken by Adelphi Real World (Bollington, UK) as part of an independent survey entitled the Adelphi SCD Disease Specific Programme™.

All data are the intellectual property of Adelphi Real World. Agios Pharmaceuticals, Inc. subscribed to this survey and did not influence the original survey through either contribution to the design of questionnaires or data collection

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Disclosures: Medical writing assistance was provided by Amy Hall, MSc, of Adelphi Group, Macclesfield, UK, funded by Agios Pharmaceuticals, Inc.

OC has received consultancy fees from Agios Pharmaceuticals, Inc., Novo Nordisk, and Pfizer. **EC, HI, SLai, RS, and SLibby** are employees of Adelphi Real World. **MJS** is a researcher contractor at Sick Cells. **AV** is Co-Founder and President of Sick Cells. **JM, PW, AY,** and **CC** are employees and shareholders of Agios Pharmaceuticals, Inc. **NS** has received consulting fees from Agios Pharmaceuticals, Inc., bluebird bio, Novo Nordisk, Pfizer, and Vertex Pharmaceuticals; research funding from Pfizer; and speaker fees from Alexion, Emmaus Pharmaceuticals, and Pfizer.

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Presented at the European Hematology Association, June 12–15, 2025, Milan, Italy