# Clinical, Hematological and Biochemical Characteristics of Sickle Cell Trait: A Cross-Sectional Study

Original Article

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## ABSTRACT

**Background:** Sickle cell disease (SCD) is a widespread inherited hemoglobin disorder caused by a single amino acid substitution in the beta-globin gene. Sickle cell trait (SCT), where only one allele carries the mutation, is often seen as benign, though growing evidence suggests clinical symptoms can emerge under certain conditions.

**Aim of the Work:** To assess the clinical presentations, hematological profiles, and biochemical markers of SCT individuals attending Pediatric Hematology specialized clinics at Cairo University and Misr University for Science and Technology.

**Patients and Methods:** This cross-sectional research enrolled 60 Egyptian SCT subjects (50% male, median age 8 years), with full medical histories, clinical examinations, and laboratory investigations recorded.

**Results:** Half of the participants were symptom-free, while 50% displayed symptoms like abdominal pain (28.3%) and painful crises (26.7%). Strong familial aggregation (88.3%) and parental consanguinity (61.7%) were noted. Symptoms were often triggered by exertion, infection, or dehydration. Symptomatic subjects showed significantly lower mean red cell count, hemoglobin (Hb), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) ($p$ =0.036, 0.001, 0.008, 0.019, and 0.029 respectively), and higher reticulocytes, and c-reactive protein (CRP) ($p$ = 0.021 and 0.044 respectively), indicating that symptomatic subjects experienced significant anemia, hemolysis, and inflammation. Additionally, Alanine transaminase (ALT) levels were significantly lower in symptomatic subjects ($p$ = 0.011), suggesting liver enzyme variations between both groups. On the other hand, other variables did not show significant differences.

**Conclusion:** Despite its reputation as a benign condition, SCT can lead to clinical symptoms and hematological abnormalities, necessitating awareness, careful monitoring, and tailored care for affected individuals.

**Key Words:** Clinical and hematological characteristics, egyptian, sickle cell trait.

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## INTRODUCTION

Sickle cell disease (SCD) is recognized globally as the most common inherited hemoglobinopathy, resulting from a point mutation where glutamic acid is replaced by valine in the beta-globin gene [1]. Individuals with one mutated and one normal beta-globin gene are considered to have sickle cell trait (SCT) [2].

Typically, SCT is classified as a carrier condition with minimal clinical consequences. Nonetheless, individuals with SCT may develop symptoms under environmental stressors such as low oxygen levels, high altitude, intense physical exertion, or significant dehydration, attributed to red cell sickling and microvascular obstruction [3].

Emerging evidence connects SCT with increased risks of complications like splenic infarctions, renal pathologies, venous thromboembolism, and exertional injuries[4-6]. Biochemical markers including raised bilirubin, lactate dehydrogenase (LDH), and reticulocyte counts have also been reported in symptomatic cases.

Enhanced identification and clinical understanding of SCT are essential for effective prevention strategies, counseling, and management plans.

## AIM OF THE WORK

This study aims to investigate the clinical symptoms, hematological indices, and biochemical markers in SCT

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individuals attending Pediatric Hematology Specialized Clinics at Cairo University and Misr University for Science and Technology.

## PATIENTS AND METHODS

A cross-sectional study was performed on 60 SCT subjects (50% male, median age 8 years) fulfilling defined criteria between January and June 2024. Subjects were recruited from Pediatric Hematology Specialized Clinics.

Inclusion Criteria: Egyptian individuals diagnosed with SCT (confirmed via hemoglobin electrophoresis and/or high-performance liquid chromatography showing adult hemoglobin (HbA) > Sickle hemoglobin (HbS), with HbS typically ≤45%). Only steady-state subjects with no acute illness or recent blood transfusion were included.

Exclusion Criteria: Non-Egyptians, SCD patients {sickle ccell anemia (HbSS), hemoglobin sickle C disease (HbSC), Hemoglobin S beta thalassemia(HbSβ-thalassemia)}, recently transfused individuals, or those with chronic inflammatory/infectious diseases were excluded.

Medical histories emphasized pain crises, anemia, abdominal symptoms, transfusion history, and exposure to triggers and family history that clarified if patients had similar conditions in other family members and parental consanguinity so in our study Thirty-seven (61.7%) of our subjects gave a history of parental consanguinity, fifty-three (88.3%) had a similar condition in the family (a family member with sickle cell trait including siblings and parents). Thorough review of medical record with special emphasis on complete physical and general examination, Anthropometric measurements, system examination (neurological, respiratory, abdominal and skeletal examination) for any associated manifestations. Laboratory tests included complete blood counts, reticulocyte counts, bilirubin levels, LDH, AST, ALT, serum creatinine, CRP, ferritin, urinalysis, and Hb electrophoresis.

## ETHICAL CONSIDERATIONS

The study was approved by the Ethics Committee of the Faculty of Medicine, Misr University for Science & Technology Hospital (2022/0075) with number FWA00025577 and date May 31, 2023 and by Department Councils, Faculty of Medicine, Cairo University and Misr University for Science & Technology. A written informed consent/assent was obtained from all subjects and/or legal guardians before enrollment in the study. All conducted procedures complied with the Helsinki Declaration, of 1964, and any subsequent revisions or similar ethical norms.

Statistical analysis: Data were coded and entered using the statistical package for the Social Sciences (SPSS) version 23 (IBM Corp., Armonk, NY, USA). Data were summarized using mean, standard deviation, median, interquartile range (IQR), minimum, and maximum in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data, and according to their distribution, the suitable test was used. Data were explored for normality using Kolmogorov-Smirnov and Shapiro-Wilk Tests. The confidence interval was set to 95% and the accepted margin of error was set to 5%. *P-values* less than 0.05 were considered statistically significant.

## RESULTS

Our study included 60 consecutive SCT subjects (50% were males) with a median age at enrollment of 8 years (IQR of 3 to 28 years) diagnosed either in the context of screening of family members of an affected SCD patient or having presenting symptom/s and followed up at the Pediatric Hematology Specialized Clinic.

Descriptive Data: Demographic and baseline laboratory data of studied subjects are illustrated in (Table 1) Thirty-eight (63.3%) of our studied subjects belonged to pediatric age (≤ 18 years). The median age at diagnosis was 7 years (IQR of 3 to 27 years). Most of our subjects resided in Giza and Cairo (55% and 21.7% respectively), had at least one affected family member (88.3%) and showed a high positive consanguinity rate (61.7%). Five (8.3%) of our subjects were hypertensive (on antihypertensive drugs), 3 (5%) were diabetic, and one (1.7%) had immune thrombocytopenia. Two (3.3%) had splenomegaly, and one (1.7%) had hepatomegaly. At baseline, the mean hemoglobin (Hb) level of our studied subjects was 10.5 ± 1.17 gm/dL and the mean HbS at diagnosis was 36.9 ± 4.94%. The mean value of mean corpuscular volume (MCV) was 68.9 ± 6.99 fl where 26 of the studied subjects had microcytosis (MCV < 75 fl), 6 of them had associated evidence of iron deficiency while the remaining 20 had normal serum ferritin levels and within normal Minor adult hemoglobin (HbA2) range (query coinheritance of alpha thalassemia for which molecular genetic study was not feasible). None of our subjects showed evidence of albuminuria or hematuria on their urine analysis.

**Table 1:** Demographic and laboratory data of studied SCT subjects (*n* = 60).

| | | Studied subjects (*n*=60) | |
|---|---|---|---|
| | | *N* | % |
| Age (years) | Mean ± SD | 16.1 ± 14.4 | |
| | Median (IQR) | 8 (3-28) | |
| | Range | 0.80 – 50.0 | |
| Age at diagnosis (years) | Mean ± SD | 13.74 ± 13.9 | |
| | Median (IQR) | 7 (3-27) | |
| | Range | 0.1 – 49.0 | |
| Age groups | < 6 years | 24 | 40.0 |
| | 6 - ≤ 12 years | 11 | 18.3 |
| | 13 - ≤ 18 years | 2 | 3.3 |
| | > 18 years | 22 | 36.7 |
| Gender | Male | 30 | 50 |
| | Female | 30 | 50 |
| Residence | Cairo | 13 | 21.7 |
| | Giza | 33 | 55 |
| | Menoufia | 4 | 6.7 |
| | Fayoum | 9 | 15.0 |
| | Beni-Suef | 1 | 1.7 |
| Similar affected family member | | 53 | 88.3 |
| Childhood/ adulthood | Adults | 22 | 36.7 |
| | Child | 38 | 63.3 |
| Parental Consanguinity | | 37 | 61.7 |
| RBCs ($\times 10^6$/L) | Mean ± SD | 4.5 ± 0.36 | |
| | Range | 2.15 – 6.03 | |
| Hb (gm/dL) | Mean ± SD | 10.36 ± 1.73 | |
| | Range | 4.7 – 14.4 | |
| Hct (%) | Mean ± SD | 31.07 ± 4.73 | |
| | Range | 11.8 – 45.8 | |
| MCV (fl) | Mean ± SD | 68.24 ± 6.10 | |
| | Range | 50.9 – 88.3 | |
| MCH (pg) | Mean ± SD | 23.1 ± 2.33 | |
| | Range | 17.0 – 30.5 | |
| MCHC (g/dL) | Mean ± SD | 33.48 ± 3.08 | |
| | Range | 26.3 – 42.7 | |
| WBCs ($\times 10^3$/cmm) | Mean ± SD | 7.91 ± 2.17 | |
| | Range | 3.9 – 19.4 | |
| PLTs ($\times 10^3$/cmm) | Mean ± SD | 370.7 ± 165.76 | |
| | Range | 144 – 833 | |
| Reticulocytes (%) | Mean ± SD | 1.76 ± 1.38 | |
| | Range | 0.38 – 6.7 | |
| TSB (mg/dL) | Mean ± SD | 0.29 ± 0.22 | |
| | Range | 0.03 – 5.3 | |
| DSB (mg/dL) | Mean ± SD | 0.08 ± 0.08 | |
| | Range | 0 – 0.6 | |

| | | |
|---|---|---|
| LDH (U/L) | Mean ± SD | 181.63 ± 53.96 |
| | Range | 123 – 517 |
| AST (U/L) | Mean ± SD | 27.85 ± 8.43 |
| | Range | 12 – 55 |
| ALT (U/L) | Mean ± SD | 14.52 ± 7.30 |
| | Range | 8 – 46 |
| Serum creatinine (mg/dL) | Mean ± SD | 0.45 ± 0.13 |
| | Range | 0.3 – 1.32 |
| CRP | Mean ± SD | 2.25 ± 1.16 |
| | Range | 1 – 5 |
| Serum ferritin (ng/ml) | Mean ± SD | 39.35 ± 21.13 |
| | Range | 17 – 90 |
| HbA1 (%) | Mean ± SD | 60.29 ± 6.67 |
| | Range | 46.9 – 81.5 |
| HbA2 (%) | Mean ± SD | 2.73 ± 0.55 |
| | Range | 1.6 – 3.5 |
| HbS (%) | Mean ± SD | 35.79 ± 5.70 |
| | Range | 16.3 – 44.0 |
| HbF (%) | Mean ± SD | 0.39 ± 0.56 |
| | Range | 0 – 1.6 |

SD: Standard deviation; N: Number; SCT: Sickle cell trait; BMI: Body mass index; RBCs: Red blood cells; Hb: Hemoglobin; Hct: Hematocrit; MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; WBCs: White blood cells; PLTs: Platelets; TSB: Total serum bilirubin; DSB: Direct serum bilirubin; LDH: Lactate dehydrogenase; AST: Aspartate aminotransferase; ALT: Alanine transaminase; CRP: C-reactive protein; HbA1: Major adult hemoglobin; HbA2: Minor adult hemoglobin; HbS: Sickle hemoglobin; HbF: Fetal hemoglobin IQR: Interquartile range. Using: $X^2$= Chi- Square test.

(Table 2) shows the clinical manifestations of our SCT subjects. While half of our cohort were asymptomatic and detected during family members screening, 50% were symptomatic. The most common presenting symptoms were abdominal pain (28.3%), and painful crises (26.7%) [defined as severe pain in the arms, legs, joints, back, or chest necessitating medical attention and with no other explanation] for which one subject needed hospital admission and the others required emergency department visits where they received IV fluids and analgesics then were prescribed non-steroidal anti-inflammatory drugs as home treatment. Further disease-related manifestations among the studied subjects are shown in

(Table 2) Seventeen subjects (28.3%) had painful crisis at a mean age of 13.6 ± 12.13 years. Notably, 6 subjects (10%) had severe acute anemia that required transfusions at a mean Hb of 5.78 gm/dl., with a minimum of one transfusion and a maximum of 4 transfusions per lifetime. None had gall bladder stones, hematuria, venous thromboembolism, leg ulcers, priapism, or ocular symptoms.

Intense physical activity, infection, and dehydration were the most common triggers precipitating symptoms (38.3%, 33.4%, and 6.7% respectively) and were also the main precipitating factors for painful crises (58.8%, 52.9%, and 41.2% respectively). Low oxygen tension or high altitude did not seem to contribute to presenting symptoms among our subjects.

**Table 2:** Clinical manifestations among the studied SCT subjects ($n$ = 60).

| | Studied subjects ($n$=60) | |
|---|---|---|
| | N | % |
| Initial Presenting Symptoms | | |
| Asymptomatic | 30 | 50 |
| Abdominal pain | 17 | 28.3 |
| Painful crisis* | 16 | 26.7 |
| Anemia manifestations (pallor, easy fatigability) | 8 | 13.4 |
| Acute hemolysis (pallor/jaundice/dark urine) | 6 | 10 |
| Disease-related manifestations | | |
| Painful crises* | 17 | 28.3 |
| Abdominal pain | 17 | 28.3 |
| Fever/Infections | 7 | 11.7 |
| Clinical jaundice | 6 | 10 |
| Anemia requiring transfusions | 6 | 10 |
| Headaches | 3 | 5.0 |

N: Number; SCT: Sickle cell trait
* Painful crisis defined as severe pain in the arms, legs, joints, back, or chest necessitating medical attention with no other explanation

Comparing the hematological and biochemical profiles between symptomatic and asymptomatic subjects (Table 3), symptomatic subjects showed significantly lower mean red cell count, Hb, HCT, MCV, MCH ($p$ =0.036, 0.001, 0.008, 0.019, and 0.029 respectively), and higher reticulocytes, and CRP ($p$ = 0.021 and 0.044 respectively), indicating that symptomatic subjects experienced significant anemia, hemolysis, and inflammation. Additionally, ALT levels were significantly lower in symptomatic subjects ($p$ = 0.011), suggesting liver enzyme variations between both groups. On the other hand, other variables did not show significant differences.

Using Spearman correlation coefficients for various hematological and biochemical variables in symptomatic subjects, Hb level showed a highly significant negative correlation (r = -0.379, $p$ = 0.003), suggesting that lower Hb levels are linked to increased symptoms while HCT, MCV, and MCH displayed moderate significant correlations ($p < 0.05$), hinting at the role of red blood cell indices in symptomatic presentations. By contrast, other variables, including white blood cell count, platelet count, hemolysis indicators, CRP and fetal hemoglobin do not show significant correlations, suggesting limited influence on symptom status in this cohort (data not shown).

**Table 3:** Comparison of hematological and biochemical profiles among symptomatic and asymptomatic SCT subjects (*n*=60).

| | | Symptomatic (*N*=30) | Asymptomatic (*N*=30) | Test value | *P-value* |
|---|---|---|---|---|---|
| RBCs ($\times 10^6$/L) | Mean±SD | 4.27 ± 1.02 | 4.72 ± 0.51 | 2.171 | 0.036* |
| | Range | 2.15 – 6.03 | 3.74 - 5.6 | | |
| Hb (gm/dL) | Mean±SD | 10.04 ± 2.46 | 11.78 ± 1.18 | 3.504 | 0.001** |
| | Range | 4.7 – 14.4 | 9.8 – 14.4 | | |
| Hct (%) | Mean±SD | 30.79 ± 6.79 | 34.70 ± 3.85 | 2.736 | 0.008** |
| | Range | 11.8 – 45.8 | 29.1 – 44.3 | | |
| MCV (fL) | Mean±SD | 72.75 ± 8.96 | 77.76 ± 7.05 | 2.407 | 0.019* |
| | Range | 50.9 – 86.9 | 62.3 – 88.3 | | |
| MCH (pg) | Mean±SD | 24.48 ± 3.27 | 26.13 ± 2.33 | 2.246 | 0.029* |
| | Range | 17 – 30.1 | 21.6 – 30.5 | | |
| MCHC (gm/dL) | Mean±SD | 33.29 ± 3.07 | 33.79 ± 1.45 | 0.807 | 0.423 |
| | Range | 26.3 - 42.7 | 31.2 - 36.9 | | |
| WBCs ($\times 10^3$/L) | Mean±SD | 7.87 ± 2.97 | 7.97 ± 2.19 | 0.141 | 0.889 |
| | Range | 3.9 – 19.4 | 5.0 - 14.0 | | |
| PLTs ($\times 10^3$/L) | Mean±SD | 334.53 ± 150.63 | 348.33 ± 139.85 | 0.368 | 0.714 |
| | Range | 144 – 803 | 151 – 833 | | |
| Reticulocytes (%) | Mean±SD | 2.12 ± 1.65 | 1.35 ± 0.71 | 2.364 | 0.021* |
| | Range | 0.38 – 6.70 | 0.40 – 4.0 | | |
| TSB (mg/dL) | Mean±SD | 0.65 ± 1.17 | 0.26 ± 0.17 | 1.793 | 0.078 |
| | Range | 0.04 – 5.3 | 0.03 – 0.8 | | |
| DSB (mg/dL) | Mean±SD | 0.12 ± 0.12 | 0.07 ± 0.07 | 1.856 | 0.069 |
| | Range | 0 – 0.6 | 0 - 0.3 | | |
| LDH | Mean±SD | 187.90 ± 83.16 | 179.73 ± 43.86 | 0.476 | 0.636 |
| | Range | 123 – 517 | 123 – 284 | | |
| AST | Mean±SD | 26.47 ± 10.30 | 27.0 ± 8.51 | 0.219 | 0.828 |
| | Range | 12 – 54 | 13 – 55 | | |
| ALT | Mean±SD | 12.70 ± 3.23 | 16.73 ± 7.74 | 2.634 | 0.011* |
| | Range | 8 – 22 | 9 – 46 | | |
| Serum creatinine (mg/dL) | Mean±SD | 0.53 ± 0.21 | 0.51 ± 0.13 | 0.347 | 0.730 |
| | Range | 0.30 – 1.32 | 0.30 - 0.80 | | |
| CRP | Mean±SD | 2.23 ± 1.28 | 1.67 ± 0.80 | 2.057 | 0.044* |
| | Range | 1 – 5 | 1 – 3 | | |
| Serum Ferritin (ng/mL) | Mean±SD | 47.70 ± 20.51 | 47.75 ± 24.05 | 0.005 | 0.996 |
| | Range | 17 – 90 | 17 – 80 | | |
| HbA1 (%) | Mean±SD | 60.35 ± 6.25 | 58.51 ± 7.00 | 1.071 | 0.288 |
| | Range | 53.3 - 81.5 | 46.9 – 80.0 | | |
| HbA2 (%) | Mean±SD | 2.94 ± 0.48 | 2.77 ± 0.46 | 1.425 | 0.160 |
| | Range | 1.9 – 3.5 | 1.6 – 3.4 | | |
| HbS (%) | Mean±SD | 36.41 ± 5.59 | 37.38 ± 4.24 | 0.765 | 0.447 |
| | Range | 16.3 – 44.0 | 25.0 – 44.0 | | |
| HbF (%) | Mean±SD | 0.35 ± 0.53 | 0.16 ± 0.44 | 1.520 | 0.134 |
| | Range | 0 - 1.5 | 0 – 1.6 | | |

SD: Standard deviation; N: Number; SCT: Sickle cell trait; RBCs: Red blood cells; Hb: Hemoglobin; Hct: Hematocrit; MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; WBCs: White blood cells; PLTs: Platelets; TSB: Total serum bilirubin; DSB: Direct serum bilirubin; LDH: Lactate dehydrogenase; AST: Aspartate aminotransferase; ALT: Alanine transaminase; CRP: C-reactive protein; HbA1: Major adult hemoglobin; HbA2: Minor adult hemoglobin; HbS: Sickle hemoglobin; HbF: Fetal hemoglobin. Using: $X^2$= Chi- Square test; when appropriate *p-value* >0.05 is insignificant; **p-value* <0.05 is significant.

## DISCUSSION

Sickle cell trait (SCT) is an inherited hematological disorder resulting from the presence of a single mutated hemoglobin S (HbS) gene inherited from one parent, while the other gene encodes normal hemoglobin A (HbA)[8]. In contrast to sickle cell disease (SCD), where both hemoglobin genes are abnormal, SCT is usually considered a milder condition. Most individuals with SCT remain asymptomatic and have a normal lifespan; however, under certain conditions, clinical manifestations similar to SCD — such as hemolytic anemia, painful crises, and organ involvement — can occur. These events are often triggered by dehydration, strenuous physical activity, infections, or exposure to hypoxic environments [9].

Although traditionally regarded as benign, increasing evidence has highlighted that SCT can present with various clinical, hematological, and biochemical abnormalities. Several studies have identified a risk of complications including splenic infarction, exertional rhabdomyolysis, renal impairment, and venous thromboembolism (VTE) in individuals with SCT[10]. Furthermore, elevated reticulocyte counts, bilirubin, and lactate dehydrogenase (LDH) levels have been associated with hemolysis in symptomatic patients [11].

In this cross-sectional study, we aimed to characterize the clinical, hematological, and biochemical profiles of 60 SCT subjects attending the Pediatric Hematology Specialized Clinics of Cairo University and Misr University for Science and Technology. Among the studied cohort, half were symptomatic at the time of presentation, while the other half were asymptomatic, diagnosed incidentally during routine family screenings. Among symptomatic patients, abdominal pain and painful crises were the most frequently reported symptoms (28.3% each). Intense physical exertion, infections, and dehydration were identified as the main precipitating factors (38.3%, 33.4%, and 6.7%, respectively) and were major contributors to painful crises (58.8%, 52.9%, and 41.2%, respectively).

While SCT is generally considered a benign carrier state, there are documented reports of clinical complications, though acute presentations remain rare[12–15]. To our knowledge, few studies have documented a 50% symptomatic rate among SCT patients, as observed in our cohort. These findings align with those reported by Moez and Younan, who screened schoolchildren in Siwa Oasis and found that 50% of SCT carriers exhibited symptoms[16]. Similarly, Vargas-Hernández and colleagues reported systemic complications in 52.9% of SCT patients, mostly precipitated by altitude change, physical activity, infections, or travel[3]. Conversely, ***Khaled et al.*** found a lower symptomatic rate (12.8%) in their cohort, with anemia being the predominant clinical feature[17].

The majority of SCT individuals maintain a higher proportion of HbA compared to HbS (approximately 30–40% HbS), which generally protects against sickling events. However, factors such as oxygen desaturation, changes in intracellular pH, and alterations in 2,3-diphosphoglycerate levels can modify HbS polymerization kinetics [14]. Genetic factors also play a role; co-inheritance of conditions like pyruvate kinase deficiency, hereditary spherocytosis, or glucose-6-phosphate dehydrogenase (G6PD) deficiency can contribute to symptomatic presentations[18–21]. Additionally, dominant HbS variants (Hb Jamaica Plain, HbS Antilles, HbS São Paulo) are associated with greater sickling tendencies even in heterozygotes[22–24]. Other rare genetic mechanisms, including βS/β++-thalassemia or uniparental disomy of chromosome 11, may also result in symptomatic disease [25–27]. In our study, only hematological phenotyping was performed; molecular diagnostics were not available.

Environmental and physiological stressors such as intense exertion, dehydration, infection, and hypoxia are recognized triggers of sickling complications in SCT [4,5,28]. In our cohort, intense physical activity was the leading trigger for symptoms (38.3%) and painful crises (58.8%). Although SCT is traditionally seen as benign, its risk during high-intensity exercise is increasingly recognized. Hemorheological changes, including increased blood viscosity, reduced red cell deformability, and endothelial activation, have been reported during exertion [29–32]. When exercise is combined with altitude exposure, dehydration, or hyperthermia, serious complications such as heatstroke, arrhythmias, splenic infarction, and even sudden death may occur [33]. Exercise-induced systemic acidosis, through elevated lactate levels, lowers hemoglobin's oxygen affinity (Bohr effect), promoting early oxygen release and HbS polymerization, thereby favoring sickling [34].

Among our SCT subjects, the most common clinical manifestations included painful crises and abdominal pain (28.3% each), followed by fever and infections (11.7%), jaundice (10%), and anemia requiring transfusion (10%). Headache was a less common symptom (5%). These findings reinforce that although SCT is milder than SCD, it still carries a risk for significant morbidity, underscoring the need for appropriate clinical monitoring.

Our findings are consistent with those of ***Vargas-Hernández et al.***, who reported abdominal pain and fever as predominant symptoms among symptomatic SCT patients[3]. Similarly, ***Tsaras et al.*** highlighted that SCT could result in complications, particularly under physiologic stress [28].

Acute hemolysis occurred in six (10%) of our SCT patients, a rare presentation that should raise suspicion of concurrent conditions. G6PD deficiency, which impairs

erythrocyte resistance to oxidative stress, can exacerbate hemolysis and has been reported to occur independently or alongside SCD [35,36]. Previous studies have shown that individuals with concurrent SCT and G6PD deficiency may experience increased hemolytic susceptibility [37].

Comparison between symptomatic and asymptomatic SCT subjects revealed that symptomatic individuals had significantly lower red cell indices (Hb, HCT, MCV, MCH) and higher reticulocyte counts, indicating low-grade ongoing hemolysis. In contrast, ***Vargas-Hernández et al.*** found no significant differences in these indices but did observe higher leukocyte counts, bilirubin, LDH, and CRP levels in symptomatic patients [3].

Microcytosis was detected in 26 (43.3%) of our SCT patients; six had confirmed iron deficiency, while the remaining 20 had normal ferritin and HbA2 levels, suggesting other causes such as alpha-thalassemia. ***Khaled et al***. also reported lower red cell parameters among SCT individuals compared to controls [17]. ***Jaber et al.*** found microcytosis in 85.26% of SCT patients, with iron deficiency accounting for the majority, and alpha-thalassemia co-inheritance suspected in non-iron-deficient cases [38].

Correlation analysis revealed significant negative associations between symptomatology and hematological parameters (Hb, HCT, MCV, MCH), suggesting that anemia may contribute to the clinical manifestations in symptomatic SCT individuals.

## CONCLUSION

This study challenges the notion of sickle cell trait (SCT) as entirely benign, showing that half of the cohort had symptoms like abdominal pain, painful crises, anemia, and acute hemolysis. Symptomatic individuals exhibited lower hemoglobin, higher reticulocytes, and elevated inflammation markers. Anemia was significantly linked to symptoms, highlighting the need for closer monitoring for early diagnosis, and individualized patient management to prevent complications.

## DECLARATIONS

## AVAILABILITY OF DATA AND MATERIALS

The data sets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

## COMPETING INTERESTS

The authors declare that they have no competing interests.

## FUNDING

This work was self-funded by the authors.

## AUTHORS CONTRIBUTIONS

M. El-Ghamrawy conceptualized the study, supervised data collection, and analyzed the results. Y.M.M. Selim drafted the manuscript and supervised data collection. M.S.E.M. Abdel Kader oversaw the revisions. R.M.S. Yousef collected data and interpreted the results. All authors critically revised the manuscript for important intellectual content and approved the final version of the manuscript.

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# الخصائص الاكلينيكية و الدموية و الكيميائية لسمة فقر الدم المنجلي: دراسة مقطعية

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**المقدمة:** يُعد مرض الخلايا المنجلية (SCD) هو اضطراب وراثي شائع في الهيموجلوبين ناتج عن استبدال حمض أميني واحد في جين بيتا-جلوبين. بينما يُعتبر حاملو الصفة المنجلية (SCT) – حيث يحملون نسخة واحدة من الجين المتحور – عادةً غير عرضيين، إلا أن الأدلة المتزايدة تشير إلى ظهور أعراض سريرية في ظروف معينة.

**هدف الدراسة:** تقييم المظاهر السريرية، والملامح الدموية، والعوامل الكيميائية الحيوية لدى الأفراد حاملي الصفة المنجلية المراجعين لعيادات أمراض دم الأطفال المتخصصة في جامعة القاهرة وجامعة مصر للعلوم والتكنولوجيا.

**المرضى والطرق:** شملت هذه الدراسة المقطعية 60 فردًا مصريًا حاملاً للصفة المنجلية (50% ذكور، متوسط العمر 8 سنوات)، مع تسجيل التاريخ الطبي الكامل، والفحوصات السريرية، والتحاليل المخبرية.

**النتائج:** كان نصف المشاركين دون أعراض، بينما ظهرت أعراض مثل آلام البطن (28.3%) ونوبات ألمية (26.7%) لدى 50%. لوحظ تجمع عائلي قوي (88.3%) وزواج الأقارب (61.7%). غالبًا ما تم تحفيز الأعراض بالجهد البدني أو العدوى أو الجفاف. أظهر الأفراد العرضيون انخفاضًا معنويًا في متوسط عدد كريات الدم الحمراء، والهيموجلوبين (Hb)، والهيماتوكريت (HCT)، ومتوسط حجم الكرية (MCV)، ومتوسط هيموجلوبين الكرية (MCH) (قيم 0.019 ،0.008 ،0.001 ،0.036 = p، و0.029 على التوالي)، مع ارتفاع في الخلايا الشبكية وبروتين سي التفاعلي (CRP) (قيم $p = 0.021$ و0.044 على التوالي)، مما يشير إلى وجود فقر دم، وتحلل دموي، والتهاب لدى الأفراد العرضيين. بالإضافة إلى ذلك، كانت مستويات إنزيم ألانين ترانساميناز (ALT) أقل بشكل ملحوظ لدى الأفراد العرضيين ($p = 0.011$)، مما يشير إلى اختلافات في إنزيمات الكبد بين المجموعتين. بينما لم تظهر متغيرات أخرى فروقًا ذات دلالة إحصائية.

**الاستنتاج:** على الرغم من اعتبار الصفة المنجلية حالة غير عرضية، إلا أنها قد تؤدي إلى أعراض سريرية واختلالات دموية، مما يستدعي التوعية، والمراقبة الدقيقة، ورعاية مخصصة للأفراد المتأثرين.