# Evaluation of the renal function among sickle cell patients: a cross-sectional study

Talal Qadah,[1,2] Anwar Refaei[1,2]

[1]Department of Medical Laboratory Sciences, Faculty of Applied Medical Sciences, King Abdulaziz University, Jeddah; [2]Hematology Research Unit, King Fahad Medical Research Center, King Abdulaziz University, Jeddah, Saudi Arabia

## ABSTRACT

This cross-sectional study aimed to explore the implications and effects of hematological and kidney function patterns in individuals with sickle cell disorder (SCD) residing in the Jazan Region of Saudi Arabia. In this study, a cohort of individuals (including sickle cell anemia patients, sickle cell trait carriers, and control subjects) at Abu-Arish General Hospital with a total of 172 sickle cell anemia patients, 70 patients with sickle cell traits, and 91 control subjects is evaluated. A 5 mL sample of venous blood was collected into ethylenediaminetetraacetic acid (EDTA) anticoagulated tubes and serum gel separator tubes for hematological tests and biochemical analysis, respectively. Hematological assays were performed in EDTA. Red blood cell (RBC) parameters were recorded. Renal function tests were conducted to determine serum analytes, including sodium, potassium, urea, and creatinine. The dimension autoanalyzer determined biochemical parameters. High-performance liquid chromatography was performed. The predominant variant observed in sickle cell anemia cases was sickle hemoglobin, accounting for 67.4% of the cases, whereas hemoglobin A1 constituted 22.4% of the cases. SCD patients exhibited elevated levels of white blood cells, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, red cell distribution width, and platelets. Conversely, they displayed decreased levels of RBC, hemoglobin, hematocrit, and mean corpuscular volume. In addition, SCD patients demonstrated higher serum electrolyte levels compared to control subjects. Conversely, serum urea and creatinine levels were lower in SCD patients compared to control subjects. In conclusion, SCD patients commonly exhibit compromised kidney function. It is recommended that such patients be provided with comprehensive health education pertaining to their overall well-being and strategies for mitigating the risk of renal impairment.

Correspondence: Talal Qadah, Department of Medical Laboratory Sciences, Faculty of Applied Medical Sciences, King Abdulaziz University, 21589 Jeddah, Saudi Arabia.
Tel.: +966 (0) 55 554 0081.
E-mail: thqadah@kau.edu.sa

Key words: sickle cell disorders, hemoglobinopathy, renal, creatinine, urea.

Contributions: both authors made a substantial intellectual contribution, read and approved the final version of the manuscript, and agreed to be accountable for all aspects of the work.

Conflict of interest: the authors declare that they have no conflicts of interest to be reported with this study.

Ethics approval and consent to participate: ethical approval was obtained from the Jazan Health Ethics Committee with reference number 2112.

Informed consent: all patients were notified that their involvement in the study was voluntary, and signed informed consent was obtained from the participants themselves or from the parents of child participants.

Availability of data and materials: the data used to support the findings of this study are available from the corresponding author upon request.

Funding: none.

Acknowledgments: Abu-Arish General Hospital at Jazan Region, Saudi Arabia for providing full support through accessing the laboratory facilities and equipment.

Received: 25 November 2024.
Accepted: 27 November 2024.


*Licensee PAGEPress, Italy*
*Italian Journal of Medicine 2025; 19:1868*
*doi:10.4081/itjm.2025.1868*



## Introduction

Sickle cell disorder (SCD) is the most common pathological mono-genic and is inherited as an autosomal recessive pattern. It is estimated that about 72,000 people are affected in the form of sickle cell anemia (SCA), and 2 million are carriers (trait) in the USA.[1] SCD occurs due to the presence of a change in one nucleotide in the β-globin gene of hemoglobin (Hb), converting glutamic acid to valine at location six of the β-chain. This, in turn, leads to the synthesis of sickle hemoglobin (HbS) instead of the standard HbA.[2] The involvement of vital organs in the pathophysiological pathway of SCD is considered a predisposing factor to red blood cell (RBC) sickling. Moreover, kidney function abnormality is a common complication seen in SCA patients, such as impaired ability

of urinary concentration, abnormal acidification of urine, abnormal potassium excretion, and glomerular filtration rate. Also, hematuria, proteinuria, renal papillary necrosis, and gradual renal impairment may occur. Therefore, it is essential to assess and monitor the renal function of high-risk patients, for example, those with SCD.

The majority of prior research has documented a correlation between SCA and parental consanguinity. These studies have consistently found that consanguineous marriages are linked to an increased likelihood of offspring being affected by inherited blood disorders, including SCA. In the Kingdom of Saudi Arabia (KSA), there is a significant incidence of consanguineous marriage, exceeding 50%. The rates of marriage among first-degree relatives range from 40% to 50%.[3]

Jazan Region is a prominent region located in the southern part of the KSA, known for its prevalent practice of consanguineous marriage. Therefore, it is anticipated that regions with a high prevalence of inherited blood disorders, such as SCD, have a higher incidence of these conditions. Prior research has examined the renal functions of SCD in several parts of Saudi Arabia; however, there is limited knowledge regarding the Jazan Region. Hence, this study aimed to address the existing information gap about the scope of renal impairment in patients with SCD. The research endeavors to enhance our current comprehension and awareness of the inherent patterns and characteristics of SCD by assessing the renal function of all participants.

This study aimed to assess the hematological changes and biochemical renal function patterns in a group of SCD patients who live in the Jazan Region, in the southwestern part of KSA. The study included patients with any of the two clinical forms of SCD, namely SCA or sickle cell trait (SCT). Patients' renal function was assessed by determining serum biochemical analytics, including Na, K, urea, and creatinine. This study is expected to increase our understanding and current knowledge of the natural behavior of SCD.

Furthermore, the renal functioning of individuals with SCD was examined for both mild and severe manifestations of SCD to identify the predominant Hb types observed among SCD individuals in the Jazan Region. This research draws attention to the hematological alterations linked to SCD. As a result, it seeks to identify the alterations in serum electrolyte levels observed in instances with SCD.

## Materials and Methods

This study employed a case-control study design. The study was conducted in Abu-Arish General Hospital, located in Abu-Arish City, Jazan Region, situated in the southwestern region of Saudi Arabia. The participants in this study consisted of individuals diagnosed with SCD who were registered at Abu-Arish General Hospital. The study encompassed a total of 333 individuals, consisting of 172 patients diagnosed with SCA with Hb SS, 70 patients with sickle cell characteristics (Hb AS), and 91 subjects with HbAA who were selected as the control group. *Supplementary Table 1* presents both the inclusion and exclusion criteria.

The inclusion criteria for this study were that only patients from Saudi Arabia, regardless of gender, were eligible for inclusion. The exclusion criteria for this study encompass pregnant women as well as patients experiencing acute conditions, such as sickle pain crises and urinary tract infections. Individuals who possessed SCT and healthy control participants who exhibited renal disorders were not included in the study.

The research was conducted over 12 months. Demographic information, including age and gender, was collected from each participant. A 5 mL sample of venous blood was obtained from each participant, using ethylenediaminetetraacetic acid (EDTA) anticoagulated tubes for hematological testing and serum gel separator tubes for biochemical analysis. The specimens were analyzed within the laboratory facilities of Abu-Arish General Hospital. Hematological analyses were conducted using EDTA, encompassing the complete blood count (CBC) and high-performance liquid chromatography (HPLC) techniques, specifically targeting individuals lacking documentation of their Hb type in their medical records.

The characteristics of RBC, including RBC count, Hb concentration, hematocrit (HCT), mean corpuscular volume (MCV), and platelet count, were documented and subsequently compared to the corresponding values seen in the control group. Renal function tests were performed to assess serum analytes, including as sodium, potassium, urea, and creatinine.

The process of HPLC was utilized to ascertain the carriers and affected individuals identified during the premarital screening test. Individuals diagnosed with SCT exhibited nearly an equal proportion of two Hb types, specifically HbA and HbS. Conversely, individuals affected by SCA predominantly displayed the HbS type.

The hematological assays conducted on control patients consisted of CBC and screening tests for SCD, specifically the "solubility test". The analysis of the CBC was conducted using an automated equipment called XN100, manufactured by Sysmex (Kobe, Japan). The determination of Hb levels was performed using HPLC models, namely VARINAT 2 by BioRad (Hercules, CA, USA). The serum gel separator tubes were subjected to centrifugation at a speed of 1500 revolutions per minute for 3 minutes, ensuring that this process was completed within 2 hours of sample collection. The levels of Na, K, urea, and creatinine in all individuals were measured using automated equipment (Unicel DXC600, Backman, Brea, CA, USA).

### Statistical analysis

Data were collected using Excel 2019 software (Microsoft, Redmond, WA, USA), while the statistical analysis of data was performed using the Statistical Package for Social Sciences (IBM, Armonk, NY, USA). Quantitative variables were described as means and standard deviations (SD) and the comparisons were made by applying the independent variables unpaired *t*-test. On the other hand, qualitative variables were described as frequency and percentage, and the comparisons were made by applying the chi-square ($c^2$) test. If p-values were less than 0.05, they were considered statistically significant.

The research acquired ethical approval from the Jazan Health Ethics Committee with reference number 2112 to perform the current research. All participants were explicitly notified that their involvement in the study was entirely voluntary, and signed informed consent was obtained from the participants themselves or from the parents of child participants.

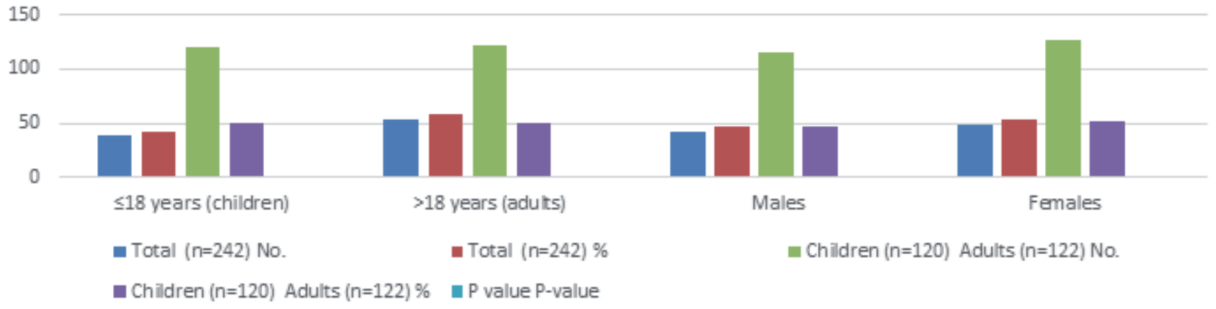


**Figure 1.** Personal characteristics of control subjects and cases with sickle cell disorder.

## Results

The inclusion of essential organs in the pathophysiological pathway of SCD is seen as a contributing cause to the sickling of RBC. Nephropathy is a prevalent condition associated with SCA, characterized by impaired urinary concentration, aberrant urine acidity, abnormal potassium excretion, and altered glomerular filtration rate. In addition, it is important to note that the presence of hematuria, proteinuria, renal papillary necrosis, and progressive renal dysfunction may manifest in certain cases. Hence, it is imperative to evaluate and track renal functioning in those at a heightened risk, such as those with SCD. Based on the results of prior research, SCD has been found to impact renal function.

Figure 1 presents the personal characteristics of the participants which illustrates that about half of the participants in both the control and patient groups were over the age of 18, with percentages of 58.2% and 50.4%, respectively. The proportion of female participants exceeded that of male participants in both study groups, with percentages of 53.8% and 52.5%, respectively.

There were no statistically significant differences seen between the two study groups in terms of age (p=0.202) and gender (p=0.824).

The findings of the study further indicate that HbS accounted for the majority of SCA cases (67.4%), with HbA1 being the second most prevalent type (22.4%) (*Supplementary Table 2*). HbF and HbA2 constituted smaller proportions, with percentages of 6.3% and 3.9%, respectively. There were statistically significant variations observed in the Hb% between children and adults for HbA1 and HbF (p=0.012 and p<0.001, respectively).

Figure 2 presents the distribution of SCA cases, indicating that out of 172 cases, 71.07% (n=123) were diagnosed in children and adults with Hb SS, while 28.93% (n=49) were identified in individuals with Hb AS. Specifically, among the Hb SS cases, 93 were children and 79 were adults, whereas among the Hb AS cases, 27 were children and 43 were adults.

The analysis of personal characteristics among control subjects and individuals diagnosed with SCA (Hb SS) reveals that about half of the participants in both groups were above the age of 18 (58.2% and 50.4%, respectively). The proportion of female participants was somewhat higher than that of male participants in both study groups, with percentages of 53.8% and 52.5%, respectively. There were no statistically significant differences seen between the two study groups in terms of age (p=0.202) and gender (p=0.824).

The analysis of personal characteristics among individuals with SCA, categorized by their Hb type, reveals a notable disparity in the distribution of children. Specifically, the proportion of children is considerably higher among cases with Hb SS compared to those with Hb AS (54.1% and 38.6% respectively, p=0.029). The proportion of men was higher in individuals with Hb SS compared to those with Hb AS (52.9% and 34.3%, respectively, p=0.009).

*Supplementary Table 3* presents the results of the blood composition of male control participants and male individuals diagnosed with SCD.

Male SCA patients had considerably lower white blood cell (WBC) counts than controls. Patients had a higher WBC count (mean±SD: 13.02±5.87) compared to controls (7.26±1.61), with p<0.001. Patients had significantly lower RBC counts (mean±SD: 3.7±1.1) compared to controls (5.16±0.6), p<0.001. Notably, controls had higher Hb and HCT than patients. Patients and controls had Hb levels of 9.2±2.09 and 12.62±1.65, respectively, with p<0.001. Average HCT levels were 28.01±6.96 for patients and 40.02±4.02 for controls (p<0.001). Patients had lower MCV than controls (77.13±10.0 *vs*. 77.94±7.14, p=0.630). Mean corpuscular hemoglobin (MCH) levels were somewhat higher in patients (25.4±3.76 *vs*. 24.61±3.32, p=0.232) compared to controls. Patients exhibited considerably higher mean corpuscular hemoglobin concentration (MCHC) than controls (33.05±2.27 *vs*. 31.44±1.89, p<0.001). Patients had a substantially greater mean red cell distribution width (RDW) than controls (19.31±4.0 *vs*. 14.11±1.89, p<0.001). Patient platelet counts were substantially higher than controls (408.11±173.32 *vs*. 304.36±68.76, p<0.001).

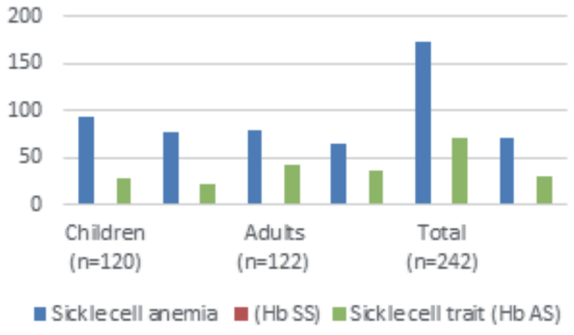


**Figure 2.** Sickle cell disorder, according to types of hemoglobin.

Our study also revealed significant blood profile differences (mean±SD) between males with Hb SS and Hb AS. WBC counts were significantly higher in Hb SS cases (14.51±5.60) compared to Hb AS cases (7.36±2.45), p<0.001. RBC count was significantly lower in Hb SS cases (3.35±0.87) compared to Hb AS cases (5.02±0.86), p<0.001.

Hb SS patients had lower Hb and HCT than Hb AS patients. Hb levels averaged 8.47±1.40 for Hb SS and 11.96±2.03 for Hb AS, p<0.001. Hb SS had a mean HCT of 25.5±4.52 and Hb AS 37.51±6.39, p<0.001. MCV was somewhat greater in Hb SS patients compared to Hb AS patients (77.48±10.55 *vs*. 75.79±7.59, p=0.462 The levels of MCH differed considerably between SCD (Hb SS) and trait (Hb AS) (25.8±3.95 *vs*. 23.9±2.47, p=0.027). SCA (Hb SS) was linked to a greater MCHC than SCT (Hb AS) (33.31±2.37 *vs*. 32.04±1.52) compared to Hb AS patients, Hb SS patients had substantially greater mean RDW (20.59±3.23 *vs*. 14.45±2.7, p<0.001) and higher platelet count (mean±SD: 419.83±171.19 *vs*. 363.67±177.79, p=0.159).

SCD female patients had a considerably higher WBC count (10.74±4.7 *vs*. 7.29±1.71, p<0.001) than female controls. Patients showed significantly reduced RBC counts (3.94±0.95 *vs*. 4.84±0.73, p<0.001) compared to controls. Patients exhibited significantly lower Hb and HCT readings compared to controls (9.43±1.62 and 12.49±1.8 for Hb, p<0.001; 29.37±5.65 and 38.78±5.02 for HCT, p<0.01). Cases had a significant decrease in MCV compared to controls (76.13±10.45 *vs*. 80.78±6.35, p=0.004). Patients showed significantly lower MCH levels than controls (24.52±3.97 *vs*. 25.88±2.53, p=0.028). Patients showed slightly higher MCHC than controls (32.17±2.44 *vs*. 32.04±1.69) (p=0.739). Compared to controls, the patient exhibited a substantially higher RDW (18.49±4.08 *vs*. 14.1±1.81, p<0.01) and a considerably higher platelet count (348.19±161.74 *vs*. 284.65±101.1).

*Supplementary Table 4* illustrates the mean and SD of serum electrolyte levels, specifically sodium and potassium, for both control subjects and individuals diagnosed with SCA. The results indicate that the levels of sodium in the serum were substantially elevated in the cases compared to the control participants (137.43±3.27 and 136.68±2.4, respectively, p=0.046). Patients had substantially higher serum levels of potassium compared to the control participants (4.14±0.52 and 3.91±0.54, respectively, p=0.009). Similarly, the result indicates serum electrolyte levels, specifically sodium and potassium, between individuals with Hb SS and those with Hb AS. The result reveals that serum levels of sodium and potassium were lower among cases with Hb SS than those with Hb AS (137.18±3.26 and 138.06±3.24, respectively, p=0.059, for sodium, and 4.12±0.54 and 4.19±0.46, respectively, p=0.339 for potassium)

The comparison of serum concentrations of sodium and potassium in two distinct groups showed the following: the cases and the control participants indicated that "serum sodium concentrations" for the group of patients exhibited an average serum sodium level of 137.43 mmol/L, with a standard variation of 3.27. The control group had an average serum sodium level of 136.68 mmol/L, with a SD of 2.4. The statistical significance, as indicated by the p-value, suggests that there was a statistically significant disparity in serum sodium levels between the cases and control patients, as evidenced by a p-value of 0.046. This finding implies that the elevated levels of serum sodium observed in the cases group are unlikely to be attributed to random variation and may instead be linked to the specific illness or factor under investigation.

Considering the quantification of "potassium concentrations in serum", it was revealed that the group classified as "cases" exhibited an average serum potassium level of 4.14 mmol/L, with an SD of 0.52. The "control group" exhibited an average serum potassium level of 3.91 mmol/L, accompanied by an SD of 0.54.

*Supplementary Table 5* presents the mean and SD of serum electrolyte levels, specifically sodium and potassium, for both control participants and individuals diagnosed with sickle cell anemia (Hb SS patients).

Higher serum sodium levels were seen in cases compared to controls (137.18±3.26 *vs*. 136.68±2.4, p=0.200). Cases reported significantly higher potassium levels in their serum compared to controls (4.12±0.54 vs. 3.97±0.49, p=0.034). Compared to controls, cases appear to have significantly higher serum potassium levels, suggesting an effect of causation. Although there was a tendency for serum sodium levels to be greater in cases, this trend did not achieve statistical significance at the p-value that was calculated.

The study found substantial variations in sodium and potassium levels between SCT (Hb AS) patients and controls. Mean serum sodium levels were significantly higher in SCT cases (138.06±3.24) compared to controls (136.68±2.4) (p=0.002). Patients had significantly higher potassium levels in their serum compared to controls (4.19±0.46 *vs*. 3.97±0.49, p=0.005).

Figure 3 shows that plasma levels of urea were slightly lower among cases than control subjects (3.10±2.27 and 2.99±1.52, respectively, p=0.056). Serum levels of creatinine were significantly lower among cases than control subjects (41.36±22.07 and 59.15±18.88, respectively, p<0.001). The urea/creatinine ratio was significantly higher among cases than control subjects (90.34±75.12 and 60.7±24.53, respectively, p=0.008).

Similarly, the plasma levels of urea were lower among cases with Hb SS than those with Hb AS (2.95±1.52 and 3.09±1.54, respectively, p=0.496). Serum levels of creatinine were significantly lower among cases with Hb SS than those with Hb AS (37.94±23.19 and 49.77±16.34, respectively, p<0.001). The urea/creatinine ratio was significantly higher among cases with Hb SS than those with Hb AS (98.51±81.76 and 70.24±50.64, respectively, p=0.008).

The plasma levels of urea were significantly lower among cases than control subjects (2.95±1.52 and 3.32±1.09, respectively, p=0.037). Serum levels of creatinine were significantly lower among cases than control subjects (37.94±23.19 and 59.15±17.85, respectively, p<0.001). The urea/creatinine ratio was significantly higher among cases than control subjects (98.51±75.12 and 60.7±24.53, respectively, p<0.001).

Finally, the plasma levels of urea were lower among cases than control subjects (3.09±1.54 and 3.32±1.09, respectively, p=0.269). Serum levels of creatinine were significantly lower among cases than control subjects (49.77±16.34 and 59.15±17.85, respectively, p=0.001). The urea/creatinine ratio was higher among cases than control subjects (70.24±50.64 and 60.7±24.53, respectively, p=0.118).

To summarize, individuals diagnosed with Hb SS demonstrate decreased levels of serum creatinine and an increased ratio of urea to creatinine when compared to both control subjects and individuals with Hb AS. The variations in the area levels have a reduced degree of prominence and may not con-

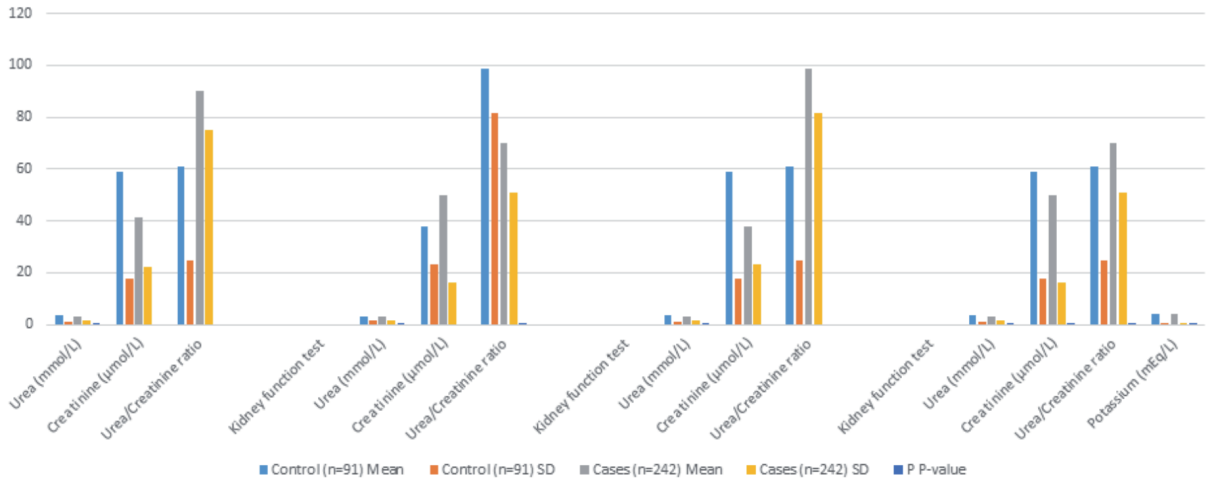


**Figure 3.** Serum electrolytes (sodium and potassium) levels (mean ± standard deviation) of participant control subjects and cases with sickle cell anemia and "cases with Hb SS compared with those with Hb AS (sickle cell trait)", "control subjects and Hb SS cases with sickle cell anemia" and "control subjects and Hb AS cases with sickle cell trait".

sistently demonstrate statistical significance. The observed fluctuations in urea and creatinine levels had potential clinical importance, perhaps serving as indicators of abnormalities in kidney function among people afflicted with SCA.

## Discussion and Conclusions

Rare Hb variations seldom symptomatize. Mutations in the Hb cause SCA.[4] In Jazan, Saudi Arabia, this study assessed SCD patients' renal function. Jazan SCD individuals have mostly HbS. Despite rare HbF and HbA2, 25% had HbA1. Children and adults had different Hb. According to Steinberg,[5] 75% of late-stage fetal Hb is HbF. Late-infancy Hb is 1%. SCA takes 5-10 years to manufacture Hb from fetal to adult. At 10, Arab-Indian haplotype patients have 17% fetal Hb. Pagana *et al*. described how Hb electrophoresis distinguishes normal and abnormal HbS.[6] HbA1 is >95%, HbA2 is 2-3%, and HbF is 1-2% of adult Hb. HbF creates 50-80% of infant Hb. HbF drops 1-2% in 6 months. HbS and HbA are increased in sickle cell patients. Patients with SCA have HbS and HbF but not HbA. Automatic HPLC detects hemoglobinopathy (Figure 4). Interpreting Hb electrophoresis data requires considering family history, serum iron levels, RBC shape, Hb levels, HCT, and indices.[7]

The sickle cell rate was 71.07%. Only 28.93% have sickle cell AS. Sickle cell was more common in children (54.1%) than adults (45.9%). The SCT group had 38.6% fewer children than adults (61.4%). Significant age differences (p=0.029). Males (52.9%) outweighed females (47.1%) in sickle cell. Men were 34.3% of SCT patients and women were 65.7%. Gender differences were significant (p=0.009). Gibson and Rees report 25% SCT in Africa and 60% in Saudi Arabia.[8] SCD is more common in Eastern and Southwestern

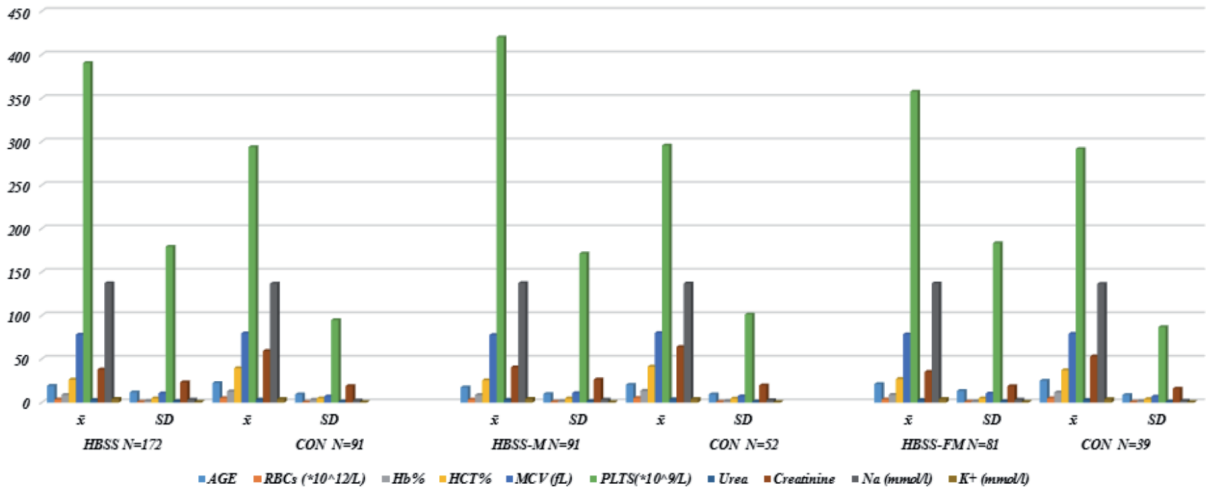


**Figure 4.** Mean differences of sickle cell anemia. Hb SS *vs.* control (con); Hb SS male (M) *vs.* con; Hb SS female (FM) *vs.* con.

Saudi Arabia.[9] In a similar vein, when examining the notable disparities in the blood composition between female control subjects and female cases with SCA, it was observed that the count of WBC was significantly higher among the cases compared to the control subjects. Conversely, the count of RBC was significantly lower among the cases compared to the control subjects, as depicted in Figure 5.

By location, SCT affects 2-27% and illness 2.6%. This study's sickle cell illness prevalence gap between patients and trait carriers may be attributable to recruiting. Not communities, but hospitals choose participants. High morbidity and mortality induce SCD and trait age differences. SCD is autosomal recessive, hence Ceglie *et al.* reported no gender difference in incidence.[10] Jit *et al.* found that sex hormones influenced children less than adults.[11] The current study compared SCD patients' hematological parameters to controls. The study included males and females. SCD increased WBC numbers, MCH, MCHC, RDW, and platelets. RBC, Hb, HCT, and MCV fell. Controls had higher hematological differences than SCT patients.

This study aligns with the one by Antwi-Boasiako *et al.*, which showed lower Hb and RBC counts in SCD patients.[12] Sickle cell patients have decreased Hb and MCV, as Meshram *et al*. discovered.[13] SCD increases platelet and red cell dispersion. Sickle cell illness produces hemolysis after 12-14 days of RBC life.[14] Thus, they have lower Hb and RBC levels than healthy people.

The sickness boosts platelets and WBC. They may have spleen issues such as sequestration, hyposplenism, autosplenectomy, or inflammation. Ahmed *et al*. revealed that repeated infections or medication adverse effects can cause leukocytosis in sickle cell patients.[15] Regular WBC tests reveal sickle cell causes, therapies, and crises.

According to Mombo *et al.*,[16] doctors in rural and remote areas without Hb electrophoresis can screen neonates for SCA with hemogram. The screening criteria include Hb level below 8.5 g/dL and leukocytic count exceeding 9.5×109/L, 84.4% sensitivity, 97.8% specificity, and 97.4% PPV. Wazir indicated that peripheral blood films are cheap, rapid, and easy to diagnose and detect sickle cells.[17] SCT requires Hb electrophoresis and sickling test.

The study aimed to evaluate the characteristics of Hb type SCA (Hb SS) in male control subjects and male cases with SCA. The analysis focused on examining the blood picture of the participants. In general, individuals with Hb SS and Hb AS exhibit notable differences in their WBC and RBC counts. Specifically, cases with Hb SS tend to have much higher WBC counts compared to cases with Hb AS, but patients with Hb SS tend to have significantly lower RBC counts compared to cases with Hb AS (Figure 6). The study aimed to compare the differences in the findings of individuals with SCT (Hb AS) and control subjects. The blood picture of male participants with SCT was compared to that of male control subjects. The results indicated that the count of WBC was higher among individuals with SCT compared to control subjects. Conversely, the count of RBC was lower among individuals with SCT compared to control subjects. The levels of Hb and HCT were found to be lower in the cases compared to the control participants, as depicted in Figure 6.

SCD patients had higher prothrombin, partial thromboplastin, and international normalized ratios than trait and control individuals. There was no statistical difference between SCT patients and controls. This study confirms the findings by Raffini *et al*.[18] Researchers attributed these findings to SCD-related hepatic dysfunction. SCD patients commonly develop liver fibrosis and hepatic dysfunction, researchers observed. Sickled erythrocyte sinusoidal occlusion, anoxia damages the liver and bile ducts. Patients with SCA and trait had greater blood sodium and potassium than controls.[19]

Sickle cell patients had higher serum potassium than controls.[20,21] Statistics showed no blood salt change. Potassium ion migration from intracellular to external regions raises the sickle cell serum potassium. Dysfunction of RBC membranes. Intravenous potassium and repeated blood transfusions raise serum potassium in sickle cell patients.

In a similar vein, when examining the notable disparities in blood composition between female control subjects and female patients with SCT, it was observed that the count of

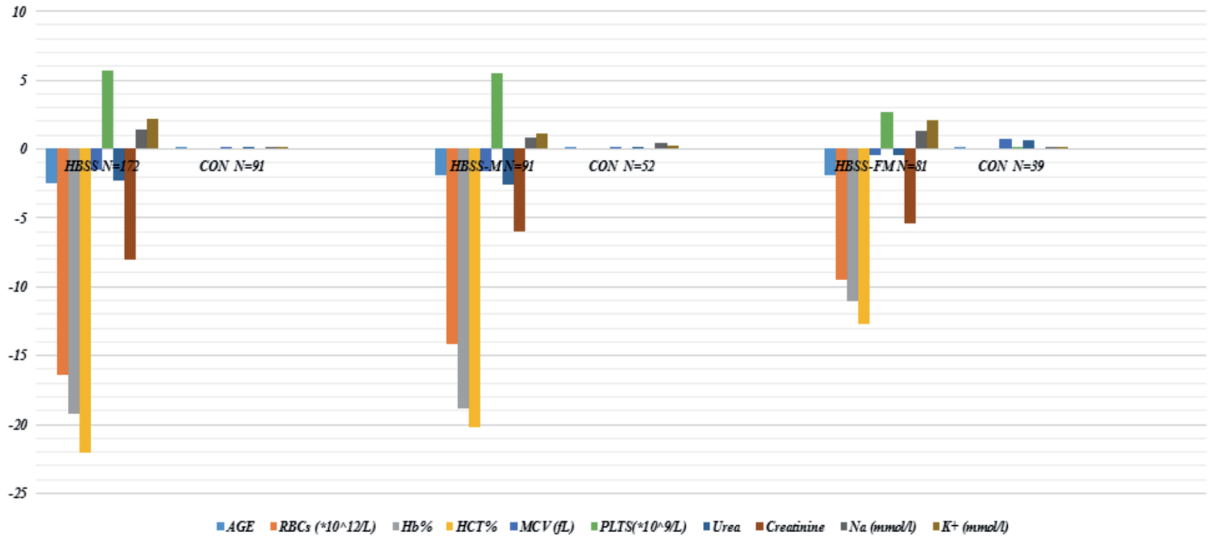


**Figure 5.** Significant differences of sickle cell anemia. Hb SS *vs.* control (con); Hb SS male (M) *vs.* con; Hb SS female (FM) *vs.* con.

WBC was higher among the cases compared to the control subjects. Conversely, the count of RBC was lower among the cases in comparison to the control individuals. The patients exhibited a substantial decrease in Hb and HCT levels compared to the control participants. The MCV exhibited a statistically significant decrease in cases compared to control patients, as illustrated in Figure 7.

Pandey *et al.* suggested metabolic issues induce SCA.[22] Abdulrahman considered SCD a major public health issue in Saudi Arabia, especially in the East.[23] Nephropathy sickles RBC by impairing glomerular filtration, tubular function, and electrolyte metabolism. SCD decreases potassium excretion and increases sodium intake. Despite infrequent hyperkalemia, hemolytic crises boost potassium. Renal collecting duct ischemia may affect tubular potassium secretion and excretion. SCD patients had lower serum urea and creatinine than controls but adequate potassium elimination. SCA patients showed lower serum creatinine and urea than controls, supporting the findings by Aloni *et al.*[24] In SCA, hepatic dysfunction lowers urea and muscle mass lowers creatinine, as noted by Al-Naama.[25] Abdulrahman revealed that SCA elevates tubular creatinine.[23] Thus, creatinine clearance may boost GFR significantly. Aleem said SCA lowers serum creatinine to low normal. Low creatinine can lower clearance.

## Study limitations

The present study employed a cross-sectional research design, which is commonly utilized for hypothesis development rather than hypothesis testing. In addition, the diagnostic evaluation necessitated more funding to conduct all necessary tests and procedures, hence presenting a financial barrier for

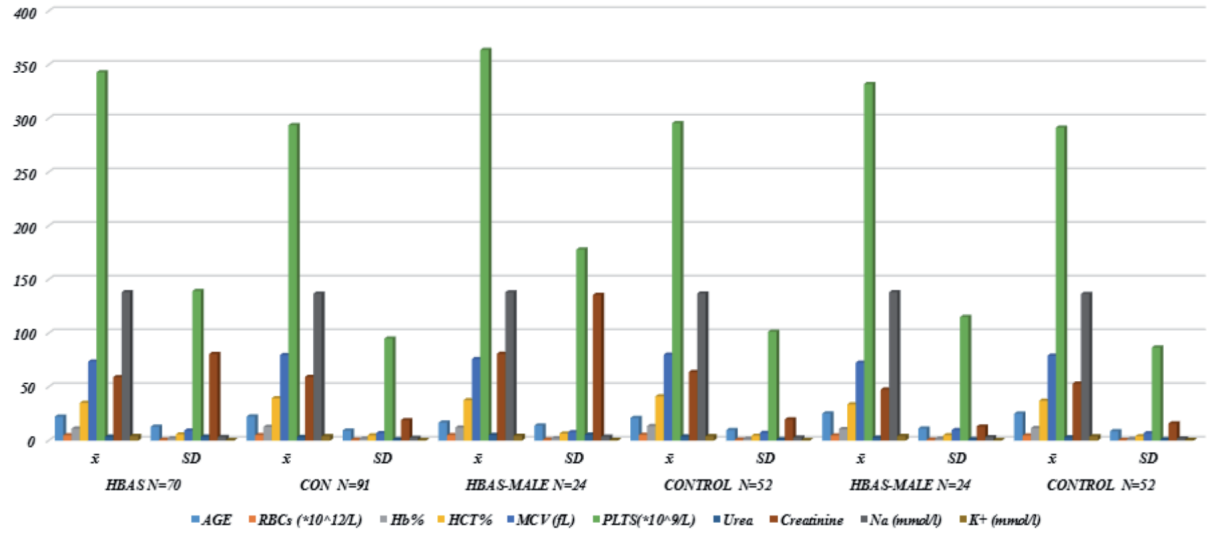


**Figure 6.** Mean differences of sickle cell anemia. Hb AS *vs.* control (con); Hb AS male (M) *vs.* con; Hb AS female (FM) *vs.* con.

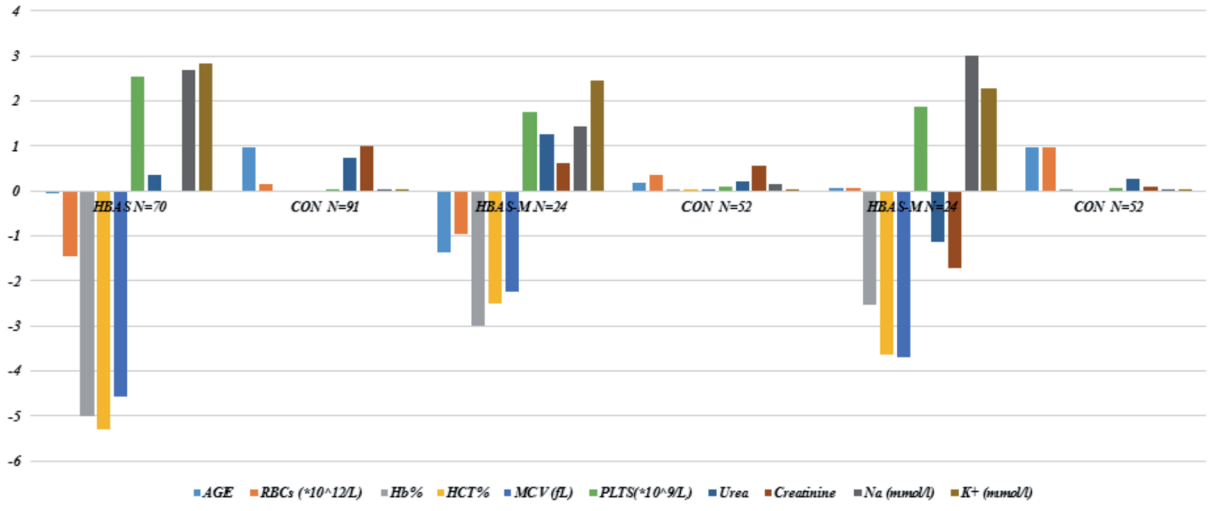


**Figure 7.** Significant differences of sickle cell anemia Hb AS *vs.* control (con); Hb AS male (M) *vs.* con; Hb AS female (FM) *vs.* con.

researchers. Many laboratory examinations exhibited limitations, such as the exclusion of chloride, magnesium, and phosphate in the testing of electrolytes, whereas only sodium and potassium were assessed. Furthermore, some crucial tests assessing renal function were omitted, such as serum cystatin C, β2-microglobulin, retinol-binding protein, glomerular filtration rate, and albuminuria screening.

## References

1. Creary M, Williamson D, Kulkarni R. Sickle cell disease: current activities, public health implications, and future directions. J Women's Health 2017;16:575-82.
2. Okwi AL, Byarugaba W, Ndugwa CM, et al. An update on the prevalence of sickle cell trait in Eastern and Western Uganda. BMC Blood Disord 2010;10:5.
3. Zaini R. Sickle-cell anemia and consanguinity among the Saudi Arabian population. Arch Med 2016;8:15.
4. Mandal AK, Mitra A, Das R. Sickle cell hemoglobin. Subcell Biochem 2020;94:297-322.
5. Steinberg MH. Fetal hemoglobin in sickle hemoglobinopathies: high HbF genotypes and phenotypes. J Clin Med 2020;9:3782.
6. Pagana KD, Pagana TJ, Pagana TN. Mosby's diagno. stic & laboratory test reference. 14th ed. St. Louis, MO, USA: Elsevier; 2018. https://www.amazon.com/Mosbys-Diagnostic-Laboratory-Test-Reference/dp/0323609694
7. Hoffman R, Benz EJ, Silberstein LE, et al. Hematology: basic principles and practice. 2017. Available from: https://mayoclinic.elsevierpure.com/en/publications/hematology-basic-principles-and-practice.
8. Gibson JS, Rees DC. How benign is the sickle cell trait? EBioMedicine 2016;11:21-2.
9. Jastaniah W. Epidemiology of sickle cell disease in Saudi Arabia. Ann Saudi Med 2011;31:289-93.
10. Ceglie G, Di Mauro M, Tarissi De Jacobis I, et al. Gender-related differences in sickle cell disease in a pediatric cohort: a single-center retrospective study. Front Mol Biosci 2019;6:140.
11. Jit BP, Mohanty PK, Purohit P, et al. Association of fetal hemoglobin level with the frequency of acute pain episodes in sickle cell disease (HbS-only phenotype) patients. Blood Cells Mol Dis 2019;75:30-4.
12. Antwi-Boasiako C, Ekem I, Abdul-Rahman M, et al. Hematological parameters in Ghanaian sickle cell disease patients. J Blood Med 2018;9:203-9.
13. Meshram AW, Bhatkulkar PA, Khare R, Pazare K. Hematological indices & electrolyte status in sickle cell disease at the rural hospital of Central Maharashtra. Int J Med Sci Public Health 2014;3:1410-2.
14. Omoti, CE. Hematological values in sickle cell anemia in steady state and during vaso-occlusive crisis in Benin City, Nigeria. Ann Afr Med 2005;4:62-7.
15. Ahmed AE, Ali YZ, Al-Suliman AM, et al. The prevalence of abnormal leukocyte count, and its predisposing factors, in patients with sickle cell disease in Saudi Arabia. J Blood Med 2017;8:185-91.
16. Mombo LE, Mabioko Mbembo G, Bisseye C, et al. Hematological values in steady state sickle cell anemia patients and matched hemoglobin AA controls in a rural area of Eastern Gabon. Nigerian Postgrad Med J 2019;26:13-7.
17. Wazir ZU. Peripheral blood picture of sickle cell anemia. Gomal J Med Sci 2017;15(4):184.
18. Raffini LJ, Niebanck AE, Hrusovsky J, et al. Prolongation of the prothrombin time and activated partial thromboplastin time in children with sickle cell disease. Pediatric Blood Cancer 2006;47:589-93.
19. Niebanck AE, Kwiatkowski JL, Raffini LJ. Neutropenia following IVIG therapy in pediatric patients with immune-mediated thrombocytopenia. J Pediatr Hematol Oncol 2005;27:145-7.
20. Meshram P, Pandey BD, Mankhand TR. Extraction of lithium from primary and secondary sources by pre-treatment, leaching and separation: a comprehensive review. Hydrometallurgy 2014;150:192-208.
21. Antwi-Boasiako C, Kusi-Mensah YA, Hayfron-Benjamin C, et al. Serum potassium, sodium, and chloride levels in sickle cell disease patients and healthy controls: a case-control study at Korle-Bu Teaching Hospital, Accra. Biomarker Insights 2019;14:1177271919873889.
22. Pandey S, Sharma A, Dahia S, et al. Biochemical indicator of sickle cell disease: preliminary report from India. Ind J Clin Biochem 2012;27:191-5.
23. Abdulrahman IS. The kidney in sickle cell disease: pathophysiology and clinical review. Hong Kong J Nephrol 2004;6:2-13.
24. Aloni MN, Ngiyulu RM, Gini-Ehungu JL, et al. Renal function in children suffering from sickle cell disease: challenge of early detection in highly resource-scarce settings. PLoS One 2014;9:e96561.
25. Al-Naama LM, Al-Sadoon TA, Al-Sadoon EA. Levels of uric acid, urea, and creatinine in Iraqi children with sickle cell disease. J Pak Med Assoc 2000;50:98-102.

*Online supplementary material:*

*Supplementary Table 1. The inclusion and exclusion criteria.*

*Supplementary Table 2. Results of hemoglobin electrophoresis among cases with sickle cell anemia.*

*Supplementary Table 3. Blood picture of participant male control subjects and male cases with sickle cell disorder.*

*Supplementary Table 4. Serum electrolytes (sodium and potassium) levels of participant control subjects and cases with sickle cell anemia (Hb SS) compared with those with Hb AS.*

*Supplementary Table 5. Serum electrolytes (sodium and potassium) levels of participant control subjects and Hb SS cases with sickle cell anemia as well as control subjects and Hb AS cases with sickle cell trait.*