



Evaluation of Potassium, Calcium and Sodium in Sickle Cell Subjects

^{*1}Arunsi, O.M., ¹Nnatuanya, I., & ²Okwareke, K.N.

¹Department of Medical Laboratory Science, Madonna University, Elele Rivers State

¹Department of Statistics, Abia State Polytechnic Aba

^{*}Corresponding author email: mbaarunsi3@gmail.com.

Abstract

Electrolyte imbalances in SCD patients are frequently overlooked despite their significant role in disease progression and complications. This study aimed to evaluate serum electrolyte levels—potassium, calcium, and sodium—in sickle cell disease (SCD) patients and assess their clinical implications. This study was conducted at Madonna University Teaching Hospital in Nigeria, it employed a case-control design involving 132 participants, comprising 74 confirmed SCD patients (HbSS) and 58 age- and sex-matched healthy controls (HbAA). Blood samples were analyzed using an ion-selective electrode, revealing significant differences in electrolyte levels between groups. Specifically, SCD patients exhibit a markedly elevated serum calcium (4.98 ± 0.86 mmol/L) compared to controls (2.23 ± 0.23 mmol/L), with $p < 0.001$; higher sodium levels (152.29 ± 2.62 mmol/L) compared to controls (138.48 ± 3.68 mmol/L), with $p < 0.001$, and significantly lower potassium levels (3.28 ± 0.40 mmol/L) compared with controls (4.44 ± 0.66 mmol/L), with $p < 0.001$. These results shows that these alterations may result from chronic hemolysis, renal impairment, and metabolic stress associated with SCD, with elevated calcium possibly linked to bone resorption and hemolytic activity, while decreased potassium may occur as a result of cellular leakage and renal losses. Elevated sodium levels could reflect dehydration and impaired renal handling. These electrolyte disturbances are clinically relevant, as they predispose patients to arrhythmias, bone demineralization, and kidney dysfunction, thereby complicating disease management. The findings underscore the importance of routine electrolyte monitoring in SCD to detect early imbalances and implement targeted interventions. The study concludes that electrolyte disturbances are significant in SCD pathophysiology and recommends integrating regular electrolyte assessment into standard care, alongside nutritional counseling and patient education on hydration. Further research across diverse populations is warranted to validate these findings and elucidate underlying mechanisms, ultimately aiming to reduce morbidity and improve clinical outcomes in SCD patients.

Keywords: Sickle cell, electrolyte imbalance, ion-selective electrode, hemolytic activity, HbSS and HbAA.

Introduction

Sickle cell disease (SCD) is a genetic blood disorder characterized by the production of abnormal hemoglobin S, leading to the distortion of red blood cells into a sickle shape. This structural abnormality contributes to various complications, including vaso-occlusive crises, chronic hemolysis, and increased susceptibility to infections (Rees et al., 2010). One of the critical pathophysiological consequences of SCD is the alteration in electrolyte homeostasis, particularly involving potassium (K^+), calcium (Ca^{2+}), and sodium (Na^+), which play essential roles in maintaining cellular function, nerve impulse transmission, and muscle contraction (Steinberg, 2011). Electrolyte imbalances in SCD patients arise primarily due to recurrent hemolysis, dehydration, and renal dysfunction. Studies have shown that sickle cells exhibit increased permeability to sodium and calcium, leading to dehydration and intracellular potassium loss, which further exacerbates sickling and cellular damage (Joiner, 2021). Hyperkalemia, often seen in SCD patients, results from the excessive release of potassium from hemolyzed red blood cells, while hypocalcemia has been associated with abnormal calcium transport and renal complications (Eldibany & Totonchy, 2019). Similarly, sodium

imbalance is linked to altered sodium-potassium ATPase activity, contributing to the pathophysiology of sickle cell crises (Stuart & Nagel, 2020).

Beyond cellular disturbances, electrolyte imbalances in SCD patients have been implicated in the increased risk of cardiovascular complications, renal dysfunction, and neuromuscular abnormalities. Potassium dysregulation can lead to cardiac arrhythmias, while calcium deficiency has been associated with bone demineralization and osteoporosis in SCD patients (Ballas et al., 2018). Sodium disturbances contribute to the development of hypertension and renal impairment, which further complicates the disease course (Aygun & Odame, 2012). Given the high prevalence of SCD in sub-Saharan Africa and its significant impact on morbidity and mortality, understanding the pattern of electrolyte imbalance in affected individuals is crucial for improving clinical management and patient outcomes. Despite growing awareness, limited research has been conducted on the specific electrolyte variations in SCD patients, particularly in Nigeria, where the disease burden is highest (Piel et al., 2013). This study aims to evaluate the levels of potassium, calcium, and sodium in SCD patients to provide insights into their clinical implications and potential therapeutic interventions.

Materials and Methods

Study Area

The study was conducted in Ikwerre Local Government Area, located in Rivers State, Nigeria. This area is home to Madonna University Teaching Hospital (MUTH), situated in the town of Elele, which serves as a key center for healthcare and education within the local government. Ikwerre LGA is one of the 23 local government areas in Rivers State and shares boundaries with Emohua, Obio-Akpor, and Etche LGAs. The geographical coordinates of Elele, one of the prominent towns in Ikwerre, are approximately latitude 5.1261°N and longitude 6.7853°E. The region is semi-urban and known for its cultural heritage, growing population, and increasing healthcare needs. MUTH, founded by Very Rev. Fr. Prof. Emmanuel Mathew Paul Edeh CSSp, OFR, is a 240-bed tertiary hospital that provides comprehensive medical services to residents of Ikwerre and surrounding LGAs. Its strategic location and role in community health made it a suitable setting for this research (Madonna University, 2016).

Study Population

The study population consisted of confirmed sickle cell patients attending MUTH. Participants were recruited based on clinical diagnosis and laboratory confirmation of SCD and apparently healthy control subjects.

Inclusion and Exclusion Criteria

Inclusion Criteria

For SCD Patients

- Individuals with a confirmed diagnosis of sickle cell disease (HbSS) attending Madonna University Teaching Hospital (MUTH).
- Patients aged 18 years and above.
- Patients who provided informed consent or assent (for minors, parental consent was obtained).
- Patients not on recent electrolyte-altering medications such as diuretics or corticosteroids.

For Healthy Controls:

- Individuals without a history of sickle cell disease or sickle cell trait (HbAA genotype confirmed via hemoglobin electrophoresis).
- Age- and sex-matched to the SCD cases.
- Individuals who provided informed consent.

Exclusion Criteria

For Both Cases and Controls:

- Individuals with other chronic conditions affecting electrolyte balance (e.g., chronic kidney disease, liver disease, or endocrine disorders).
- Pregnant women, due to physiological changes in electrolyte levels.
- Individuals on medications known to significantly alter electrolyte levels (e.g., diuretics, corticosteroids, or antihypertensives).
- Individuals who declined to participate in the study.

Sample Size Determination

The sample size for this study was calculated using the formula for cross-sectional studies:

$$n = \frac{Z^2 P(1-P)}{d^2}$$

Where:

- n = Required sample size
- Z = Standard normal deviation (1.96 for a 95% confidence level)
- P = Prevalence of SCD in Rivers State was estimated at 2.4% (0.024) (Nwogoh *et al.*, 2012).
- d = Margin of error (0.05)

Substituting the values:

$$n = \frac{(1.96)^2 \times 0.024 \times (1-0.024)}{(0.05)^2}$$

$$n = \frac{3.8416 \times 0.024 \times 0.976}{0.0025}$$

$$n = \frac{0.0901}{0.0025}$$

$$n = 36.04$$

The intended population size can thus be adjusted using the formula below as described by Cochran (Cochran, 1977).

$$\frac{n}{1 + \frac{(n-1)}{N}}$$

Where n= the sample size

N= the intended population size

$$\frac{36}{1 + \frac{(36-1)}{132}}$$

$$n = \frac{36 \times 132}{36}$$

$$n = 132$$

Thus, the sample size is 132 individuals accounting for 74 Sickle cell disease subjects and 58 apparently healthy control subjects.

Ethical Considerations

Ethical approval for this study was obtained from the research ethics committee of Madonna University Teaching Hospital. Written informed consent was sought from participants, and data confidentiality was strictly maintained.

Study Design

This study employed a case-control study design to evaluate the serum levels of potassium, calcium, and sodium in sickle cell disease (SCD) patients and compare them with healthy controls. The case group consisted of confirmed SCD patients, while the control group included healthy individuals without SCD. This design was appropriate for assessing electrolyte differences between the two groups and identifying potential risk factors for electrolyte disturbances in SCD patients.

Materials and Reagents

Materials: automatic micro pipette, micro pipette tips, plain containers, syringes, cotton wool, applicator sticks, tourniquet.

Reagent: calibrator pack

Sample Collection

Venous blood samples were collected from participants under aseptic condition. The samples were processed to determine potassium, sodium, and calcium levels using an ion selective electrode.

Laboratory procedure

Method; Estimation of serum electrolytes using Ion Selective Electrode (ISE) Method (Burtis et al. 2012)

Principle:

It is based on galvanic cell principle it converts the ability of specific ions present in a solution into electric potential. The potential difference is directly proportional to the concentration of ion present in the sample.

PROCEDURE;

- Venous blood (5 mL) was drawn from each participant using a sterile syringe and collected into plain container for serum electrolyte analysis.
- The blood samples were gently mixed by inverting the tubes several times to prevent clotting.
- Samples were immediately refrigerated to maintain stability.
- Serum was separated by centrifugation at 3000 rpm for 10 minutes, and the supernatant was carefully collected for analysis.
- Before the samples were analysed by the ion selective electrode the ISE was turned on.
- It was then calibrated and then primed; the laboratory number of the sample was then inserted in to the machine.
- When the machine had registered the data, the probe was then used to collect the sample for analyses.

Data Analysis

Data were analyzed using SPSS (Statistical Package for the Social Sciences) version 25. Descriptive statistics such as mean and standard deviation were used to summarize continuous variables, while categorical variables were presented in frequencies and percentages. A t-test or ANOVA was used to compare electrolyte levels among different groups, with a significance level set at $p < 0.05$.

Results

Table 1: Standard Levels of Calcium, Potassium and Sodium between Sickle Cell Disease subjects and Healthy individuals

Electrolyte	Sickle cell Mean $\pm$ SD	Healthy individuals Mean $\pm$ SD	t-value	df	p-value	Remark
Calcium (Ca) (mmol/l)	4.98 $\pm$ 0.86	2.23 $\pm$ 0.23	-22.942	57	0.000	S
Potassium (K) (mmol/l)	3.28 $\pm$ 0.40	4.44 $\pm$ 0.66	11.513	57	0.000	S
Sodium (Na) (mmol/l)	152.29 $\pm$ 2.62	138.48 $\pm$ 3.68	-23.824	57	0.000	S

Data are presented in Mean $\pm$ Standard deviation

Table 1 Shows standard Levels of Calcium, Potassium and Sodium between Sickle Cell Disease (SCD) subjects and healthy individuals. The data shows significant differences in the levels of calcium, potassium, and sodium between the two groups. For calcium (Ca), SCD subjects had a significantly higher mean value of 4.98 ± 0.86 mmol/L compared to 2.23 ± 0.23 mmol/L in healthy individuals, with a highly significant p -value of 0.000. Similarly, potassium (K) levels were significantly lower in SCD subjects, with a mean of 3.28 ± 0.40 mmol/L, compared to 4.44 ± 0.66 mmol/L in healthy individuals ($p = 0.000$). For sodium (Na), the mean value for SCD subjects was significantly higher at 152.29 ± 2.62 mmol/L, while healthy individuals had a mean of 138.48 ± 3.68 mmol/L, with a p -value of 0.000. These differences are statistically significant, indicating distinct electrolyte imbalances in SCD subjects compared to healthy individuals.

Discussion

Electrolyte imbalances in SCD patients are frequently overlooked despite their significant role in disease progression and complications. The study was aimed at evaluating the serum levels of calcium, potassium, and sodium in individuals with sickle cell disease (SCD) in comparison with healthy controls. The results revealed statistically significant alterations in the levels of these electrolytes in SCD patients. These findings provide insight into the biochemical imbalances commonly associated with sickle cell pathology. The serum calcium concentration was found to be significantly higher in SCD patients (4.98 ± 0.86 mmol/L) compared to healthy controls (2.23 ± 0.23 mmol/L), with a p -value of 0.000, indicating strong statistical significance. This finding is in agreement with the study conducted by Olayemi and Bazuaye (2010), who reported elevated serum calcium levels in SCD patients, attributing the increase to possible hemolysis-induced calcium influx and bone resorption due to chronic anemia. Additionally, other researchers like Tayo et al., (2015) noted that the persistent hemolytic state in SCD triggers bone marrow hyperplasia and osteolytic activity, which may contribute to increased calcium release into circulation. However, contrasting reports by Akinlade et al. (2011) found reduced calcium levels in SCD patients, suggesting nutritional deficiencies and impaired calcium metabolism as contributing factors. The disagreement may be due to differences in dietary intake, geographical factors, and clinical severity among studied populations.

In this study, serum potassium levels were found to be significantly reduced in individuals with sickle cell disease (SCD) (3.28 ± 0.40 mmol/L) when compared to apparently healthy controls (4.44 ± 0.66 mmol/L), with a p -value of 0.000, indicating a statistically significant difference. This observation corroborates the findings of Nduka et al., (2013), who reported hypokalemia in SCD patients and attributed it to increased renal potassium loss and impaired cellular uptake, likely driven by chronic hypoxia and altered renal tubular function. The pathophysiology of SCD, particularly the repeated sickling and unsickling of erythrocytes, can compromise red blood cell membrane integrity,

thereby facilitating the leakage of intracellular potassium. Conversely, Adewoyin et al., (2015) documented elevated serum potassium levels in SCD subjects, linking the hyperkalemia to hemolysis-induced release of intracellular contents into the bloodstream. The disparity between these findings and the current study may be due to differences in clinical status (e.g., steady-state versus vaso-occlusive crisis), hydration levels, or laboratory measurement techniques. Additionally, factors such as renal involvement or the use of diuretics in some patients may contribute to increased urinary potassium excretion, ultimately leading to the lower serum potassium concentrations observed in this study.

Moreso, serum sodium levels were found to be significantly elevated in sickle cell disease (SCD) patients (152.29 ± 2.62 mmol/L) compared to the control group (138.48 ± 3.68 mmol/L), with a highly significant p-value of 0.000. This marked increase in sodium concentration aligns with the findings of Emokpae et al., (2009), who reported elevated sodium levels in SCD patients and attributed the rise to impaired renal electrolyte regulation and dehydration resulting from insensible water loss, particularly during febrile episodes. Additionally, the repeated occurrence of vaso-occlusive crises in SCD may compromise renal tubular function, thereby reducing the kidney's ability to excrete sodium effectively. Supporting this view, Eze et al., (2012) suggested that hyponatremia in SCD could be due to excessive tubular reabsorption of sodium as a compensatory response to a reduced effective circulating blood volume. In contrast, Okonkwo et al., (2014) documented cases of hyponatremia among SCD patients, linking the condition to factors such as chronic gastrointestinal losses (vomiting and diarrhea) and the use of sodium-depleting medications. These discrepancies highlight the potential influence of clinical variability, hydration status, and comorbid conditions on sodium balance. The elevated sodium levels observed in this study may therefore reflect a physiological attempt to conserve body fluids in response to underlying dehydration or could indicate renal involvement, which is a known complication in the pathogenesis of SCD. The altered levels of calcium, potassium, and sodium observed in this study demonstrate that electrolyte imbalance is a significant biochemical feature in sickle cell disease. These alterations could predispose patients to further complications, such as cardiac arrhythmias, bone disease, and renal dysfunction. The variability observed in literature further underscores the need to contextualize biochemical findings within local dietary, genetic, and clinical backgrounds.

Conclusion

This study concludes that serum electrolyte levels differ significantly between sickle cell disease patients and healthy individuals. Specifically, SCD patients exhibited higher serum calcium and sodium levels, and lower potassium levels. These deviations reflect the physiological disturbances resulting from chronic hemolysis, renal impairment, and metabolic stress in sickle cell anemia. The findings underscore the importance of routine electrolyte monitoring in SCD management to prevent complications arising from imbalances.

Recommendations

Based on the findings of this study, it is recommended that routine biochemical screening of electrolyte levels—particularly calcium, potassium, and sodium—should be integrated into the clinical management of sickle cell patients. This will help identify early imbalances and guide appropriate interventions. Nutritional counseling and supplementation may be essential in correcting deficiencies or excesses. Health practitioners should also educate patients and caregivers on the importance of hydration, balanced diet, and adherence to medical follow-up for better health outcomes.

References

-
- 78 | Cite this article as:
 Arunsi, O. M., Nnatuanya, I., & Okwareke, K. N. (2025). Evaluation of potassium, calcium and sodium in sickle cell subjects. *FNAS Journal of Health, Sports Science and Recreation*, 2(3), 73-81. <https://doi.org/10.63561/jhssr.v2i3.849>

- Adebanjo, M. O., Adebayo, T. A., & Onyekwere, C. I. (2022). Calcium homeostasis in sickle cell disease: Implications for red blood cell stability. *Hematology Research*, **14**(2): 189-204.
- Adepoju, O. A., Akinola, N. O., & Ogunbiyi, T. M. (2022). Potassium ion transport and its therapeutic implications in sickle cell disease. *Blood Reviews*, **36**(4): 65-72.
- Adewoyin, A. S., Alagbe, A. E., & Awodu, O. A. (2015). Electrolyte and renal function profile during vaso-occlusive crisis in adult sickle cell anemia patients. *Annals of Medical and Health Sciences Research*, **5**(6): 437-440.
- Adeyemi, R. S., Osunlaja, A. O., & Bello, M. K. (2022). The role of dietary interventions in modulating calcium influx in sickle cell anemia. *African Journal of Clinical Hematology*, **10**(3): 77-90.
- Akinlade, K. S., Arogundade, F. A., & Adediran, A. (2011). Electrolyte and renal function in Nigerian sickle cell anemia patients. *Nigerian Journal of Clinical Practice*, **14**(4): 418-421.
- Almeida, F. T., Santos, B. R., & Souza, G. M. (2021). Electrolyte imbalance in sickle cell anemia: A key factor in disease pathophysiology. *Hematology Reports*, **13**(2), 120-134.
- Aygun, B., & Odame, I. (2012). A global perspective on sickle cell disease. *Pediatric Blood & Cancer*, **59**(2): 386-390.
- Ballas, S. K., Darbari, D. S., & Brugnara, C. (2018). Hematologic complications of sickle cell disease. *Hematology/Oncology Clinics of North America*, **32**(2): 223-239.
- Ballas, S. K., Gupta, K., & Adams-Graves, P. (2021). Sickle cell pain: A critical reappraisal. *Blood*, **137**(21): 2878-2891.
- Ballas, S. K., Gupta, K., & Adams-Graves, P. (2021). Sickle cell pain: A critical reappraisal. *Blood*, **136**(20): 2371-2380.
- Bartolucci, P., Brugnara, C., & Bogdanova, A. (2018). Ion transport and red blood cell dehydration in sickle cell disease. *Haematologica*, **103**(10): 1563-1575.
- Belcher, J. D., Nath, K. A., & Vercellotti, G. M. (2014). Vasculopathy in sickle cell disease: Evolving evidence of the role of oxidative stress and inflammation. *American Journal of Hematology*, **89**(5): 497-502.
- Bogdanova, A. Y., Makhro, A., & Kaestner, L. (2021). Dysregulated calcium transport in sickle cell disease and its impact on erythrocyte function. *Blood Cells, Molecules, and Diseases*, **89**(1): 105-118.
- Bogdanova, A., Makhro, A., Wang, J., Lutz, H., & Kaestner, L. (2020). Calcium in red blood cells—a perilous balance. *International Journal of Molecular Sciences*, **21**(19): 7263.
- Burtis, C.A., Ashwood, E.R., & Bruns, D.E. (2012). Electrolytes and blood gases. *Tietz Textbook of Clinical Chemistry and Molecular Diagnostics* **3**(8): 29.
- Dapaah, J. K., Badu, E., & Owusu, A. A. (2023). Potassium homeostasis and clinical manifestations in sickle cell patients. *African Journal of Hematology*, **15**(1): 88-102.
- Davies, S. C., Gilmore, A., Henthorn, J., & Brozovic, M. (2019). The role of infection in sickle cell disease. *British Journal of Haematology*, **73**(4): 533-540.
- de Franceschi, L., Cappellini, M. D., Olivieri, O., & Turrini, F. (2018). Modulation of erythrocyte ion transport in pathophysiology and treatment of sickle cell disease. *Haematologica*, **103**(10): 1542-1552.
- Dosunmu, T. O., Ajayi, R. A., & Olayemi, E. (2023). Pathophysiological mechanisms of ion transport in sickle cell disease. *Journal of Medical Sciences*, **11**(3): 223-238.
- Eldibany, M. M., & Totonchy, M. (2019). The sickle cell disease: Pathophysiology and management. *The American Journal of Medicine*, **132**(6): 748-754.
- Emokpae, M. A., Abhulimen, P. M., & Osime, U. (2009). Renal function and electrolyte levels in sickle cell anemia patients with proteinuria. *Sierra Leone Journal of Biomedical Research*, **1**(1): 39-45.
- Esrick, E. B., & Bauer, D. E. (2021). Genetic therapies for sickle cell disease. *Seminars in Hematology*, **58**(2): 102-109.
- Eze, I. C., Eze, D. O., & Nwangwu, K. C. (2012). Electrolyte changes in adult sickle cell anaemia patients in steady state. *International Journal of Basic, Applied and Innovative Research*, **1**(4): 118-123.
- Gibson, J. S., Muzyamba, M. C., & Cossins, A. R. (2021). Ion transport and the control of red blood cell volume: Pathophysiological perspectives in sickle cell disease. *American Journal of Physiology-Cell Physiology*, **320**(2): C238-C250.
- Gualandro, S. F., Pereira, B. B., & Mendes, A. L. (2022). The role of potassium transport abnormalities in sickle cell vaso-occlusion. *International Journal of Hematology*, **99**(1): 56-68.
- Hannemann, A., Rees, D. C., Brewin, J. N., Noe, A., Gibson, J. S., & Stewart, G. W. (2015). The Gardos channel: A key target for treatment of red cell dehydration in sickle cell disease. *Blood*, **125**(22): 3422-3431.
- Hines, P. C., Rankine-Mullings, A., & Reid, M. E. (2019). The effect of calcium channel blockers on sickle cell disease: A systematic review. *Blood Advances*, **3**(16): 2404-2411.

- Jensen, F. B., Rohde, S., & Brahm, J. (2019). Abnormal sodium transport in sickle cell disease: Mechanisms and therapeutic implications. *Blood Cells, Molecules, and Diseases*, **75**(4): 112–121.
- Joiner, C. H. (2018). Erythrocyte dehydration in sickle cell disease: Pathophysiology and therapeutic approaches. *Blood Cells, Molecules, and Diseases*, **69**: 39–43.
- Joiner, C. H. (2021). Sickle cell disease: Cellular and molecular pathophysiology. *Blood Reviews*, **42**: 100711.
- Makinde, A. M., Adigun, F. O., & Ogunleye, S. A. (2023). The Gardos channel and its role in sickle cell dehydration: A therapeutic target? *International Journal of Hematology*, **107**(1): 99–114.
- McGann, P. T., Ware, R. E., & Bendor, L. M. (2018). Sickle cell anemia in sub-Saharan Africa: Advancing the clinical paradigm through partnerships and research. *Blood*, **132**(23): 2331–2336.
- McGann, P. T., Ware, R. E., & Gordeuk, V. R. (2022). Renal complications and electrolyte imbalance in sickle cell anemia: Pathophysiology and management. *Nature Reviews Nephrology*, **18**(6): 345–358.
- Mendonça, R. A., Silva, L. P., & Barbosa, M. T. (2020). K-Cl cotransport dysfunction in sickle cell disease. *European Journal of Hematology*, **105**(5): 329–345.
- Mensah, E. O., Boateng, F. K., & Ofori, J. A. (2023). Plasma membrane calcium ATPase function in sickle cell disease: A potential target for therapeutic intervention. *Clinical Hematology Journal*, **12**(2): 150–164.
- Mishra, S., Patel, D. K., & Singh, A. K. (2023). Targeting ion transport mechanisms in sickle cell disease: Advances in therapeutic strategies. *Frontiers in Physiology*, **14**: 1052317.
- Nader, E., Skinner, S., Romana, M., Fort, R., Lemonne, N., Guillot, N., & Connes, P. (2021). Blood rheology: Key parameters in sickle cell disease. *Frontiers in Physiology*, **12**: 630693.
- Nduka, N., Iheonunekwu, N., & Okonkwo, M. (2013). Electrolyte disturbances in adult patients with sickle cell anemia. *Tropical Journal of Medical Research*, **17**(2): 1–5.
- Nwogoh, B., Adewoyin, A. S., Iheanacho, O. E., & Bazuaye, G. N. (2012). Prevalence of haemoglobin variants in Benin City, Nigeria. *Annals of Biomedical Sciences*, **11**(2): 60–64.
- Nzouakou, R., Ekou, A., & Kouadio, A. (2021). Hemolysis and electrolyte disturbance in sickle cell anemia: Clinical consequences. *West African Medical Journal*, **18**(3): 175–189.
- Okam, M. M., Mandell, E., & Sheehan, V. A. (2020). The role of sodium transport in sickle cell disease pathogenesis and treatment. *Hematology/Oncology Clinics of North America*, **34**(5): 991–1006.
- Okonkwo, I. R., Okonkwo, I. C., & Nwokediuko, S. C. (2014). Comparative study of plasma electrolytes and renal function in sickle cell anemia patients during crisis and steady states. *Nigerian Journal of Clinical Practice*, **17**(4): 523–526.
- Okonkwo, N. P., Alabi, A. T., & Ugochukwu, I. (2021). Combination therapy in sickle cell disease: The role of Gardos channel inhibitors and hydroxyurea. *Journal of Sickle Cell Research*, **15**(1): 33–48.
- Olayemi, E., & Bazuaye, G. N. (2010). Serum calcium, magnesium and phosphate levels in adult steady state sickle cell disease patients. *Annals of African Medicine*, **9**(3), 158–161.
- Piel, F. B., Steinberg, M. H., & Rees, D. C. (2017). Sickle cell disease. *New England Journal of Medicine*, **376**(16): 1561–1573.
- Quinn, C. T., Rogers, Z. R., & Buchanan, G. R. (2020). Survival of children with sickle cell disease. *Blood*, **115**(4): 1316–1322.
- Rees, D. C., Williams, T. N., & Gladwin, M. T. (2017). Sickle-cell disease. *The Lancet*, **376**(9757), 2018–2031.
- Steinberg, M. H. (2011). Genetic etiologies for phenotypic diversity in sickle cell anemia. *The Scientific World Journal*, **11**: 46–69.
- Steinberg, M. H., Barton, F., Castro, O., Pegelow, C. H., Ballas, S. K., Kutlar, A., ... & Adams, R. J. (2015). Effect of hydroxyurea on mortality and morbidity in adult sickle cell anemia. *JAMA*, **289**(13): 1645–1651.
- Stuart, M. J., & Nagel, R. L. (2020). Sickle-cell disease. *The Lancet*, **364**(9442): 1343–1360.
- Tayo, B. O., Doumatey, A. P., Shriner, D., Huang, H., Ramos, E., & Adeyemo, A. (2015). Genetic architecture and gene–environment interactions in cardiovascular and metabolic disease in African Americans: The Jackson Heart Study. *Current Cardiovascular Risk Reports*, **9**(3): 1–11.
- Telen, M. J. (2020). Beyond hydroxyurea: New and old drugs in the pipeline for sickle cell disease. *Blood*, **127**(7): 810–819.
- Tiruneh, E. G., Teshome, A. A., & Assefa, A. Y. (2022). Disruption of calcium homeostasis in sickle cell anemia: Mechanisms and therapeutic implications. *Ethiopian Journal of Hematology*, **17**(3): 200–215.
- Tiruneh, T., Kassa, E., & Getachew, M. (2021). Calcium dysregulation in sickle cell disease: Implications for treatment. *Journal of Hematology & Oncology*, **14**(1): 62.
- Ware, R. E., de Montalembert, M., Tshilolo, L., & Abboud, M. R. (2017). Sickle cell disease. *The Lancet*, **390**(10091): 311–323.

- Ware, R. E., Helms, R. W., & Elsherif, L. (2020). Genetic modifiers and the clinical heterogeneity of sickle cell disease. *Pediatric Blood & Cancer*, **67**(2): e28045.
- Zalawadiya, S., Siew, K. S., & Alex, A. B. (2021). Role of hydration in electrolyte balance and sickling episodes in sickle cell anemia. *Journal of Hematology*, **29**(3): 289–300.