Assessment of Urine Kidney Injury Molecule-1 as an Early Biomarker for Nephropathy in Sickle Cell Anaemia Patients

Akeem Olayinka Busari[1,2,4,*], Shola Lois Jolayemi[2], Muhammad Bello Ahmad[3], Renata Trentin Perdomo[4]

ABSTRACT

Background: Sickle cell anemia (SCA), a form of sickle cell disorder (SCD), is characterized by chronic hemolytic anemia, recurrent acute and persistent pain episodes, and progressive multiorgan complications. Among these, sickle cell nephropathy (SCN) is a significant and severe complication that may advance to chronic kidney disease (CKD), often beginning asymptomatically in childhood. Despite its clinical relevance, data on the early assessment of renal function in patients with SCA remain limited in Nigeria, hindering timely detection and intervention. This study, therefore, investigates the diagnostic utility of urinary kidney injury molecule-1 (KIM-1) as a biomarker for renal dysfunction in patients with steady-state SCA.

Objective: This study assessed urinary kidney injury molecule 1 as an early biomarker of nephropathy in patients with sickle cell anemia.

Method: This cross-sectional comparative study included ninety participants, comprising forty-five individuals with a normal hemoglobin genotype (HbAA) and forty-five with sickle cell anemia (HbSS). Hemoglobin genotype was determined using cellulose acetate electrophoresis. Serum creatinine levels were measured using the modified Jaffe method, and the estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. Urinary kidney injury molecule-1 (KIM-1) concentrations were assessed using the enzyme-linked immunosorbent assay (ELISA) technique.

Results: This study observed no significant difference in mean age between the HbAA and HbSS groups (14.16 ± 2.54 vs. 13.52 ± 3.33 years; $p = 0.121$). However, the mean body mass index (BMI) was significantly higher in the HbAA group (21.40 ± 1.02 kg/m²) compared to the HbSS group (18.69 ± 2.19 kg/m²; $p = 0.004$). Serum creatinine levels did not differ significantly between the two groups ($p = 0.311$). In contrast, urinary KIM-1 levels were significantly elevated in the HbSS group relative to the HbAA group ($p < 0.001$). In addition, a significant negative correlation was observed between urinary KIM-1 and estimated glomerular filtration rate (eGFR) in both groups, with the correlation being stronger in the HbSS group (HbAA: $r = -0.64$, $p = 0.005$; HbSS: $r = -0.79$, $p = 0.002$).

Conclusion: The findings from this study observed no significant difference in serum creatinine levels between individuals with HbAA and HbSS genotypes. However, urinary KIM-1 concentrations were significantly higher in the HbSS group, with a stronger negative correlation with eGFR. These findings suggest that, while serum creatinine may not be effective in detecting early renal impairment in sickle cell anemia, urinary KIM-1 has promising potential for detecting renal dysfunction in this population.

KEYWORDS

nephropathy; sickle cell anaemia; urinary kidney injury molecule 1

AUTHOR AFFILIATIONS

[1] Laboratório de Biologia Molecular e Cultura Celular, Laboratório de Fluidos Biológicos e Citologia Clínica, Instituto Biosciência/Farmácia-INBIO/FACFAN, Universidade Federal de Mato Grosso do Sul, Campo Grande, Brazil
[2] Department of Medical Laboratory Science, Kwara State University, Malete, Nigeria
[3] Department of Medical Laboratory Science, Bayero University, Kano, Nigeria
[4] Laboratório de Biologia Molecular e Cultura Celular, Laboratório de Fluidos Biológicos e Citologia Clínica, Farmácia-FACFAN, Universidade Federal de Mato Grosso do Sul, Campo Grande, Brazil
* Corresponding author: Laboratório de Biologia Molecular e Cultura Celular, Laboratório de Fluidos Biológicos e Citologia Clínica, Farmácia-Facfan/Instituto de Biosciência, Universidade Federal de Mato Grosso do Sul, Campo Grande, Mato Grosso do Sul, Brazil; busakeem@yahoo.com

Received: 29 June 2025
Accepted: 1 September 2025
Published online: 6 January 2026

Acta Medica (Hradec Králové) 2025; 68(3): 95–100
https://doi.org/10.14712/18059694.2025.27

INTRODUCTION

Sickle cell disorder (SCD) is an autosomal recessive hereditary hemoglobinopathy resulting from a point mutation in the β-globin gene, leading to the production of sickle hemoglobin (HbS) and associated with severe clinical manifestations (1). This mutation involves the substitution of valine for glutamic acid at the sixth position of the β-globin chain, located on the short arm of chromosome 11p15.5 (2). The most common HbS genotype is HbSS, accounting for approximately 69.9% of cases, followed by HbSC (27.2%) and sickle β-thalassemia (2.95%) (3–5). HbSS is characterized by chronic hemolytic anemia, recurrent episodes of severe pain, and progressive end-organ damage throughout life (6).

According to epidemiological studies, SCD predominantly affects individuals of African or Afro-Caribbean descent, with approximately 1 in 12 carrying the sickle cell trait and 1 in 365 Black infants in the United States diagnosed with SCD, accounting for an estimated 100,000 cases nationwide and millions globally (6). Of the approximately 300,000 infants born annually with SCD worldwide, 75% are born in sub-Saharan Africa. Sickle cell anemia (SCA), the homozygous form of SCD, represents the most common monogenic disorder in Africa. In Nigeria, the prevalence of homozygous SCD (HbSS) is estimated at 2–3%, with over 150,000 newborns affected each year (7).

The pathophysiology of SCD is driven by the presence of abnormal hemoglobin (HbS) within red blood cells, which leads to cellular deformation or "sickling" upon deoxygenation. The sickling of red blood cells results from a single nucleotide substitution (adenine to thymine) in the codon for the sixth amino acid of the β-globin gene. This mutation alters the normal glutamic acid codon (GAG) to a valine codon (GTG). Unlike glutamic acid, which is hydrophilic, valine is a hydrophobic amino acid, contributing to the abnormal polymerization of deoxygenated hemoglobin S and subsequent red cell sickling (8). These rigid, sickled cells obstruct the microvasculature, causing vaso-occlusion, which underlies the clinical symptoms and progressive organ damage characteristic of the disease (9).

SCN is a severe complication of SCA, characterized by early, often asymptomatic onset in childhood and a potential progression to chronic kidney disease (CKD) (7). SCN presents a significant challenge in the clinical management of patients with sickle cell anemia, contributing to a reduction in life expectancy by approximately 20 to 30 years. The clinical progression of SCN is age-dependent, with renal dysfunction typically emerging during childhood and gradually advancing to chronic kidney disease and, ultimately, kidney failure by the third or fourth decade of life (10).

Despite its clinical significance, limited research has evaluated renal function in young Nigerian patients with SCA, hindering early detection and timely intervention to reduce associated morbidity and mortality. This study, therefore, investigated the diagnostic utility of urinary KIM-1 as a biomarker for renal dysfunction in individuals with steady-state SCA.

MATERIALS AND METHODS

STUDY DESIGN

This cross-sectional comparative study was carried out to assess the diagnostic value of KIM-1 as an early biomarker to identify tubular nephropathy in sickle cell patients (HbSS) and age-matched non-sickle cell individuals (HbAA).

ETHICAL APPROVAL

This study was approved by the Institutional Review Board of General Hospital, Ilorin, Kwara State, Nigeria, with reference number GHI/ADM/134/VOL.II/387 prior to its commencement. The detailed information regarding the study's objectives, potential benefits, risks, and the autonomy to partake was thoroughly explained to the participants. Also, detailed information about this study was equally explained to the children based on their level of understanding and to their parents and guardians to obtain their explicit and implied consent. In accordance with the Declaration of Helsinki (11), each participant provided verbal and written informed consent prior to the commencement of the study.

SAMPLING TECHNIQUE

Following the detailed explanation of this study to the prospective participants, their informed consent was obtained. Each prospective participant was instructed to aseptically produce a clean-catch spot urine sample that was screened for overt proteinuria to qualify their participation. Those who were qualified were recruited into the study consecutively by convenient random sampling. Sociodemographic information was gathered from the participants using a semi-structured questionnaire. With light clothing and shoes off, each participant's height and weight were recorded to the closest 0.1 m (m) and kilogram (kg), respectively, using a standardized, accurately calibrated Europharma Stadiometer with a weighing scale (measuring station).

INCLUSION CRITERIA

i. Stable-state SCA patients (HbSS) and age-matched non-sickle cell individuals (HbAA) attending General Hospital Ilorin.
ii. Individuals who consented to the study or whose parents/guardians did so.
iii. Individuals without overt proteinuria screened by urinary dipstick technology.

EXCLUSION CRITERIA

i. Individuals who were screened to have overt proteinuria with urine dipstick technology.
ii. Individuals diagnosed with end-stage kidney disease.

SAMPLE COLLECTION AND PROCESSING

Five (5) milliliters of blood samples were collected from each study participant following an aseptic procedure and

dispensed into gel activator bottles. They were packed securely and delivered to the laboratory for processing and analysis. The blood samples were allowed to clot and spun at 3,000 rpm for 5 minutes using a TDL-24 bench-top laboratory centrifuge. Following the centrifugation, the sera were then transferred into sterile plain tubes.

Aliquots of urine samples from participants who were screened negative for overt proteinuria using urine dipstick technology were also transferred into plain tubes for urinary creatinine and kidney injury molecule 1 estimation.

Every participant's sample bottles were appropriately labeled using the same code. All samples were analyzed in duplicate.

LABORATORY ANALYSIS

QUALITATIVE DETERMINATION OF URINARY PROTEINURIA

The qualitative determination of urinary proteinuria was carried out by dipstick technology of Cortez Diagnostics, Inc., urinary protein strips (12) as a screening tool for exclusion. Participants without overt proteinuria were included in the study, while those with overt proteinuria were excluded from the study. The test was based on the "protein error" principle of indicators. When pH is held constant by a buffer, indicator dyes release H^+ ions because of the protein present and change color from yellow to blue-green.

DETERMINATION OF HAEMOGLOBIN GENOTYPE

The hemoglobin genotype was ascertained using the DY-300 Electrophoresis Machine based on the principle of the cellulose acetate electrophoresis separation technique, which was modified by (13). A cellulose acetate membrane or strip serves as a support matrix in cellulose acetate electrophoresis, which separates the hemoglobin components in a sample. An electrophoresis running buffer, kept at a pH of 6.8, is placed inside the electrophoresis tank, submerging the cellulose acetate membrane that has the hemolyzed blood sample and standard controls applied to it. After the machine is turned on, the separation process lasts for 15 minutes. Components of the sample are separated into discrete bands or zones upon completion of the separation process. The hemoglobin genotype in each band is represented by the samples' traits that are either the same as or comparable to those of the controls.

QUALITATIVE ESTIMATION OF SERUM CREATININE

The serum creatinine was quantitatively measured using the creatinine assay kits from ESB Biomedicals, Nigeria, based on the modified Jaffe's colorimetric method (14). The assay was based on the reaction of creatinine with sodium picrate. Creatinine reacts with alkaline picrate, forming a red Janovski complex. The time interval chosen for measurements avoids interference from other serum constituents. The intensity of the color formed is proportional to the creatinine concentration in the sample measured at 520 nm spectrophotometrically.

ESTIMATION OF GLOMERULAR FILTRATION RATE (EGFR)

The CKD-EPI Equation 2021 (15) was used to estimate the glomerular filtration rate (eGFR), which was used to measure kidney function.

$$eGFR = 142 \times \min(Creat/K, 1)^{\alpha} \times \max(Creat/K, 1)^{-1.200} \times 0.9938^{age} \times 1.012 \text{ (if female)}$$

where $K = 0.7$ (female) or 0.9 (male) and $\alpha = -0.241$ (female) or -0.302 (male)

QUANTITATIVE ESTIMATION OF URINARY KIDNEY INJURY MOLECULE-1 (KIM-1)

The enzyme-linked immunoassay (ELISA) method, as described by Jin et al. (16), was used to quantitatively estimate the urinary KIM-1 using the Sun Red (Shanghai, China) kit.

DATA ANALYSIS

Statistical Package for Social Sciences (SPSS) version 20.0 software was used to analyze the data. Mean ± standard deviation was used to present the measured (serum creatinine and urine KIM-1) and sociodemographic (age, weight, height, and BMI) data. The mean variables between HbAA and HbSS were compared using an independent t-test. The Spearman correlation coefficient was used to evaluate the relationship between urinary KIM-1 and eGFR. Statistical significance was set at $p < 0.05$.

Tab. 1 Sociodemographic Distribution of the Study Population.

Parameters	HbAA (n = 45) Mean ± SD	HbSS (n = 45) Mean ± SD	t-value	p-value
Age (years)	14.16 ± 2.54	13.52 ± 3.33	2.303	0.121
Weight (Kg)	42.55 ± 2.62	26.02 ± 4.01	0.123	0.000*
Height (m)	1.41 ± 0.22	1.18 ± 0.12	0.247	0.002*
Body Mass Index (kg/m²)	21.40 ± 1.02	18.69 ± 2.19	0.411	0.004*

kg: kilogram, m: meter, kg/m²: kilogram per meter square, t-value: statistical measure to determine the difference between two means, *sig: $p < 0.05$.

RESULTS

SOCIODEMOGRAPHIC DISTRIBUTION OF THE STUDY POPULATION

The study participants' sociodemographic distribution is presented in Table 1, which also compares the means of four parameters (age, height, weight, and BMI) between those with the HbAA and HbSS genotypes statistically. The HbAA group had a slightly higher mean age (14.16 ± 2.54 years) than the HbSS group (13.52 ± 3.33 years). This difference, however, was not statistically significant (p = 0.121), suggesting that age is similar in the two groups and unlikely to have an impact on other outcomes that were measured. However, the mean weight of individuals with the HbAA genotype was 42.55 ± 2.62 kg, which was significantly higher (p = 0.000) than the mean weight of individuals with the HbSS genotype, which was 26.02 ± 4.01 kg. Similarly, the mean height of 1.41 ± 0.22 m for those with the HbAA genotype was significantly higher than the mean height of 1.18 ± 0.12 m for those with the HbSS genotype (p = 0.002). The mean BMI of the HbAA genotype participants was 21.40 ± 1.02 kg/m², which was significantly higher than the BMI of the HbSS group, which was 18.69 ± 2.19 kg/m² (p = 0.004).

COMPARISON OF THE SERUM CREATININE AND URINARY KIM-1 OF STUDY PARTICIPANTS

Table 2 compares the levels of serum creatinine and urine Kidney Injury Molecule-1 (KIM-1) in participants with normal hemoglobin (HbAA) and sickle cell anemia (HbSS). Although the two groups' serum creatinine levels did not differ significantly (p = 0.311), the HbSS group's mean urinary KIM-1 levels were significantly higher (p = 0.000) than those of the HbAA group.

RELATIONSHIP BETWEEN URINARY KIM-1 AND EGFR OF THE STUDY POPULATION

Table 3 presents the analysis of the relationship between urinary KIM-1 levels and eGFR, which revealed significant negative correlations in both the HbAA and HbSS groups. In the HbAA group, the mean KIM-1 level was 2.44 ± 0.431, and the mean eGFR was 103.52 ± 16.125. The correlation coefficient (r = −0.64, p = 0.005) indicates a significant moderate negative correlation between KIM-1 and eGFR, suggesting that as KIM-1 levels increase, eGFR decreases significantly in this group. In the HbSS group, KIM-1 levels were higher, with a mean of 3.11 ± 0.222, and eGFR was lower, with a mean of 92.54 ± 17.272. The negative correlation was significantly stronger in this group, with a correlation coefficient (r = −0.79, p = 0.002). This strong negative correlation suggests that the increase in KIM-1 levels is associated with a more pronounced decrease in eGFR among individuals with HbSS.

DISCUSSION

SCA is a rare genetic blood condition affecting millions worldwide. Renal complications are common in both adult and pediatric SCA patients, and they pose a serious risk of increasing mortality. Effective renal plasma flow and glomerular filtration rates are higher in young SCD patients but decrease to normal ranges and subnormal levels in young adulthood with advancing age (17, 18). In the SCD population, the prevalence of kidney failure varies between 5 and 18% (10). Nonetheless, 16–27% of the pediatric population has CKD, according to Kidney Disease Improving Global Outcome (KDIGO) criteria (19). KIM-1, a type I transmembrane glycoprotein, is undetectable in normal kidneys, and its level increases in urine as a result of nephrotoxic injury of proximal tubule cells after 12–24 h (20).

As an early biomarker of renal dysfunction, we evaluated the clinical utility of kidney injury molecule-1 (KIM-1) to detect early indicators of renal damage in sickle cell patients prior to the development of overt nephropathy.

In this study, we recruited 90 participants consisting of 45 HbAA participants (age: 14.16 ± 2.54 years, weight: 42.55 ± 2.62 kg, height: 1.41 ± 0.22 m, BMI: 21.40 ± 1.02 kg/m²) and 45 HbSS (age: 13.52 ± 3.33 years, weight: 26.02 ± 4.01 kg, height: 1.18 ± 0.12 m, BMI: 18.69 ± 2.19 kg/m²). Table 1 compares sociodemographic characteristics between HbAA and HbSS genotype

Tab. 2 Comparison of Serum Creatinine and Urinary KIM-1 of the Study Participants.

Parameters	HbAA	HbSS	t-test	p-value
SCr (mg/dl)	0.868 ± 0.093	0.848 ± 0.096	1.019	0.311
Urinary KIM-1 (ng/ml)	2.440 ± 0.431	3.110 ± 0.222	3.741	0.000*

SCr: serum creatinine, mg/dl: milligram per deciliter; Urinary KIM-1: urinary kidney injury molecule, ng/ml: nanogram per milliliter, *sig = p < 0.05.

Tab. 3 Relationship Between KIM and eGFR in the Study Population.

Group	Urinary KIM-1 (ng/ml)	eGFR (ml/min/1.73m²)	n	r-value	p-value
HbAA	2.44 ± 0.431	103.52 ± 16.125	45	−0.64	0.005*
HbSS	3.11 ± 0.222	92.54 ± 17.272	45	−0.79	0.002*

Urinary KIM-1: Urinary Kidney Injury Molecule-1, ng/ml: nanogram per milliliters, eGFR: estimated Glomerular Filtration Rate, ml/min/1.73m²: milliliters per minute per 1.73 squared meters, n: number of participants, r-value: Correlation coefficient, *sig = p < 0.05.

participants. While there was a slight difference in age between the two groups (14.16 ± 2.54 years for HbAA versus 13.52 ± 3.33 years for HbSS), this difference was not statistically significant ($p = 0.121$). This suggests that age did not significantly influence the observed differences between the two groups. In contrast to age, the two groups observed statistically significant differences in weight, height, and BMI ($p < 0.05$ for all comparisons). HbSS participants had significantly lower weight, height, and BMI compared to HbAA participants. The significantly lower weight, height, and body mass index (BMI) observed in HbSS participants compared to their HbAA counterparts might be due to the chronic disease burden and metabolic demands associated with SCA. Individuals with SCA often experience impaired growth and delayed physical development due to a combination of factors, including chronic hemolytic anemia, increased energy expenditure, recurrent vaso-occlusive crises, and suboptimal nutrient utilization. These factors can compromise nutritional status and hinder normal growth trajectories, particularly during critical developmental periods such as childhood and adolescence. These findings are consistent with a previous study by Martins et al. (21) and Rinam et al. (22) that reported delayed physical and sexual development in individuals with SCD, indicating a peripheral cause of hypogonadism, most likely brought on by androgen resistance in SCD patients. These findings underscore the necessity for comprehensive care strategies, including nutritional support and regular growth monitoring, to address growth and developmental challenges in patients with SCA.

Serum creatinine and urinary KIM-1 levels in HbAA and HbSS participants are compared in Table 2. There was no statistically significant difference in the serum creatinine levels of HbAA (0.868 ± 0.093 mg/dL) and HbSS (0.848 ± 0.096 mg/dL) between the two groups ($p = 0.311$). This implies that the levels of conventional indicators of kidney function were similar in the two groups. In sickle cell anemia, glomerular damage is the main cause of renal injury; however, not all patients experience sickle nephropathy at a young age. The need for early biomarkers to predict renal damage and direct prompt intervention is highlighted by the fact that traditional renal parameters, such as creatinine, frequently become abnormal late in the course of the disease. This result is consistent with Tehseen et al. (23), who reported that renal damage is a progressive complication of SCD that starts in childhood and can lead to renal failure and early death in 12% of adults with SCA. Also, it aligns with recent research indicating that standard renal biomarkers, such as serum creatinine, can underestimate kidney dysfunction in SCA patients due to factors like increased tubular secretion and reduced muscle mass, which lower creatinine production and mask early renal impairment (24).

Urinary KIM-1 levels were significantly higher ($p < 0.001$) in HbSS participants (3.11 ± 0.222) than in HbAA participants (2.44 ± 0.431), in contrast to serum creatinine. This underscores the potential of KIM-1 as a biomarker for early renal dysfunction in SCA and emphasizes the limitations of traditional renal markers like serum creatinine, which may not detect early kidney injury in SCA patients due to factors such as increased tubular secretion and reduced muscle mass. This finding is consistent with previous studies (25, 26) that reported KIM-1 as an early biomarker of renal tubular dysfunction in patients with SCD, often occurring prior to significant alterations in glomerular filtration rate. Also, this elevation indicates proximal tubular injury, reinforcing the role of KIM-1 as an early marker of renal damage in SCA (27). These findings suggest urinary KIM-1 is a promising biomarker for the early detection of renal dysfunction in SCA patients, potentially allowing for timely interventions to mitigate progression to chronic kidney disease.

The relationship between estimated glomerular filtration rate (eGFR) and urinary kidney injury molecule-1 (KIM-1) in participants with HbAA and HbSS genotypes is presented in Table 3. A statistically significant negative correlation ($p < 0.05$) was observed between KIM-1 and eGFR in both groups, with a significantly stronger negative relationship observed among individuals with SCA. Moreover, the mean eGFR was significantly lower in the HbSS group compared to the HbAA group, although only a small subset of HbSS participants exhibited an eGFR below 60 mL/min/1.73 m^2. These findings suggest a trend in which increasing urinary KIM-1 levels are associated with declining eGFR, highlighting the potential of KIM-1 as an early biomarker of renal dysfunction.

A study by Niss et al. (28) found that urinary KIM-1 levels were associated with baseline and persistent albuminuria, reinforcing its role as a marker of tubular injury in SCA. Similarly, this observation is consistent with the research by Kasztan et al. (29) in a mouse model of SCA revealed that increased urinary KIM-1 levels occurred early in the disease course, preceding significant declines in eGFR. Markers of tubular damage, including increased urinary KIM-1 excretion, interstitial fibrosis, and brush border loss, occurred before glomerular injury. Their findings also revealed that the severity of long-term renal damage in male HbSS mice was closely associated with the degree of hyperfiltration, suggesting a tubuloglomerular mechanism underlying early kidney injury. Based on the findings from this study, it is suggestive that urinary KIM-1 is a potential earlier biomarker for the detection of SCN.

CONCLUSION

The findings from this study observed no significant difference in serum creatinine levels between individuals with HbAA and HbSS genotypes. However, urinary KIM-1 concentrations were significantly higher in the HbSS group, with a stronger negative correlation with eGFR. These findings suggest that, while serum creatinine may not be effective in detecting early renal impairment in sickle cell anemia, urinary KIM-1 has promising potential for early detection of renal dysfunction in sickle cell anemia patients.

IMPLICATIONS FOR CLINICAL PRACTICE

Based on the findings from this study, urinary KIM-1 can serve as a non-invasive monitoring tool for renal function

in patients with SCA compared to conventional markers like serum creatinine.

REFERENCES

1. Simoneaux R. Whole Genome Sequencing of Pediatric Sickle Cell Disease Patients. Oncol Times. 2019 Feb 5; 41(3): 11–12.
2. Venugopal A, Chandran M, Eruppakotte N, Kizhakkillach S, Breezevilla SC, Vellingiri B. Monogenic diseases in India. Mutat Res Rev Mutat Res. 2018 Apr–Jun; 776: 23–31.
3. Sarat CNF, Ferraz MB, Ferreira Junior MA, et al. Prevalence of sickle cell disease in adults with delayed diagnosis. Acta Paul Enferm. 2019; 32(2): 202–9.
4. Egesa WI, Nakalema G, Waibi WM, et al. Sickle Cell Disease in Children and Adolescents: A Review of the Historical, Clinical, and Public Health Perspective of Sub-Saharan Africa and Beyond. Int J Pediatr. 2022 Oct 8; 2022: 3885979.
5. Uçucu S, Karabıyık T, Azik F. Difficulties in the diagnosis of HbS/beta thalassemia: Really a mild disease? J Med Biochem. 2022 Feb 2; 41(1): 32–9.
6. Brandow AM, Liem RI. Advances in the diagnosis and treatment of sickle cell disease. J Hematol Oncol. 2022 Mar 3; 15(1): 20.
7. Nnaji UM, Ogoke CC, Okafor HU, Achigbu KI. Sickle Cell Nephropathy and Associated Factors among Asymptomatic Children with Sickle Cell Anaemia. Int J Pediatr. 2020 Aug 14; 2020: 1286432.
8. Piccin A, Murphy C, Eakins E. Insight into the complex pathophysiology of sickle cell anaemia and possible treatment. Eur J Haematol. 2019 Apr; 102(4): 319–30.
9. Chinegwundoh FI, Smith S, Anie KA. Treatments for priapism in boys and men with sickle cell disease. Cochrane Database Syst Rev. 2020 Apr 6; 4(4): CD004198.
10. Adebayo OC, Van den Heuvel LP, Olowu WA, Levtchenko EN, Labarque V. Sickle cell nephropathy: insights into the pediatric population. Pediatr Nephrol. 2022 Jun; 37(6): 1231–43.
11. World Medical Association. World Medical Association Declaration of Helsinki. Ethical principles for medical research involving human subjects. Bull World Health Organ. 2001; 79(4): 373–4.
12. Résimont G, Piéroni L, Bigot-Corbel E, Cavalier E, Delanaye P. Urinary strips for protein assays: easy to do but difficult to interpret! J Nephrol. 2021 Apr; 34(2): 411–32.
13. Westermeier R. Electrophoresis in practice: a guide to methods and applications of DNA and protein separations. John Wiley & Sons; 2016 May 16.
14. Tarim EA, Tekin HC. Colorimetric detection of serum creatinine on a miniaturized platform using hue-saturation-value space analysis. Sci Rep. 2024 Aug 21; 14(1): 19441.
15. Lu S, Robyak K, Zhu Y. The CKD-EPI 2021 Equation and Other Creatinine-Based Race-Independent eGFR Equations in Chronic Kidney Disease Diagnosis and Staging. J Appl Lab Med. 2023 Sep 7; 8(5): 952–61.
16. Jin Y, Shao X, Sun B, Miao C, Li Z, Shi Y. Urinary kidney injury molecule-1 as an early diagnostic biomarker of obstructive acute kidney injury and development of a rapid detection method. Mol Med Rep. 2017 Mar; 15(3): 1229–35.
17. Ataga KI, Saraf SL, Derebail VK. The nephropathy of sickle cell trait and sickle cell disease. Nat Rev Nephrol. 2022 Jun; 18(6): 361–77.
18. Elenga N, Yassin MA. Real-world observational study on the long-term effect of L-glutamine treatment on renal parameters of adult and pediatric patients with sickle cell disease. Front Med (Lausanne). 2023 Dec 6; 10: 1243870.
19. Olaniran KO, Eneanya ND, Nigwekar SU, et al. Sickle Cell Nephropathy in the Pediatric Population. Blood Purif. 2019; 47(1–3): 205–13.
20. Ghadrdan E, Ebrahimpour S, Sadighi S, Chaibakhsh S, Jahangard-Rafsanjani Z. Evaluation of urinary neutrophil gelatinase-associated lipocalin and urinary kidney injury molecule-1 as biomarkers of renal function in cancer patients treated with cisplatin. J Oncol Pharm Pract. 2020 Oct; 26(7): 1643–9.
21. Martins PRJ, De Vito FB, Resende GAD, Kerbauy J, Pereira GA, Moraes-Souza H, Figueiredo MS, Verreschi IT. Male sickle cell patients, compensated transpubertal hypogonadism and normal final growth. Clin Endocrinol (Oxf). 2019 Nov; 91(5): 676–82.
22. Doshi RN, Jain A, Saiyad SS, Sayeed MS. Growth Delays and Developmental Challenges in Children with Sickle Cell Disease. Int J Pharm Clin Res. 2024 Oct 31; 16(10): 62–6.
23. Tehseen S, Joiner CH, Lane PA, Yee ME. Changes in urine albumin to creatinine ratio with the initiation of hydroxyurea therapy among children and adolescents with sickle cell disease. Pediatr Blood Cancer. 2017 Dec; 64(12): e26665.
24. Afangbedji N, Jerebtsova M. Glomerular filtration rate abnormalities in sickle cell disease. Front Med (Lausanne). 2022 Oct 21; 9: 1029224.
25. Belisário AR, da Silva AA, Silva CV, et al. Sickle cell disease nephropathy: an update on risk factors and potential biomarkers in pediatric patients. Biomark Med. 2019 Aug; 13(11): 967–87.
26. Laurentino MR, Parente Filho SLA, Parente LLC, da Silva Júnior GB, Daher EF, Lemes RPG. Non-invasive urinary biomarkers of renal function in sickle cell disease: an overview. Ann Hematol. 2019 Dec; 98(12): 2653–60.
27. Neto FD, Santos MJ, Adôrno EV, Ferreira JR, Gonçalves MS, Barbosa CG. Early Urinary Biomarkers of Renal Damage in Sickle Cell Disease Patients. Hematol Transfus Cell Ther. 2024 Oct 1; 46: S72.
28. Niss O, Lane A, Asnani MR, et al. Progression of albuminuria in patients with sickle cell anemia: a multicenter, longitudinal study. Blood Adv. 2020 Apr 14; 4(7): 1501–11.
29. Kasztan M, Fox BM, Lebensburger JD, et al. Hyperfiltration predicts long-term renal outcomes in humanized sickle cell mice. Blood Adv. 2019 May 14; 3(9): 1460–75.