Health Science Reports

WILEY

Health Science Reports
Open Access

ORIGINAL RESEARCH OPEN ACCESS

Haemato-Urological Profile and Asymptomatic Urinary Tract Infection in Ghanaian Steady-State Sickle Cell Disease Patients: A Case-Control Study

Stephen Twumasi[1] | Richard Owusu Ansah[2] | Samuel Essien-Baidoo[3] | Laud Anthony W. Basing[1] | Alexander Yaw Debrah[1] | Enoch Odame Anto[1,4] | Allwell Adofo Ayirebi[5,6] | Rebecca Asiamah-Broni[1] | Waldemer Attivor[1] | Eric Twum Ameyaw[1] | Gabriel Addai Manu[1] | Edward Afriyie[7] | Thomas Kwabena Gyampomah[7] | Joseph Nkrumah Opoku[8] | Prince Kwadwo Amoafo[9] | Samuel Kelvin Owusu[7] | Vincent Akwai[7] | Matthew Talmang[7] | Amos Mensah[7] | Isaac Kusi-Amponsah[7] | Angela Opoku[7] | Lilian Antwi Boateng[1]

[1]Department of Medical Diagnostics, Faculty of Allied Health Sciences, College of Health Sciences, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana | [2]Genomic and Infectious Diseases Laboratory, Faculty of Allied Health Sciences, College of Health Sciences, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana | [3]University of Health and Allied Sciences, Ho, Ghana | [4]School of Medical and Health Sciences, Edith Cowan University, Perth, Australia | [5]Kuntanase Government Hospital, Bosomtwe, Kumasi, Ghana | [6]Medicare College of Applied Sciences, Kumasi, Ghana | [7]Laboratory Directorate, Komfo Anokye Teaching Hospital, Kumasi, Ghana | [8]Laboratory Department, Emena Diagnostic Center, Emena, Kumasi, Ghana | [9]Laboratory Department, Suntreso Government Hospital, Kumasi, Ghana

Correspondence: Stephen Twumasi (stwumasi7116@gmail.com) | Lilian Antwi Boateng (akosboak@yahoo.com)

Received: 19 November 2024 | **Revised:** 27 February 2025 | **Accepted:** 27 March 2025

Keywords: asymptomatic | bacteria culture | bacteriuria | sickle cell disease | urinalysis | urinary tract infection

ABSTRACT

Background and Aims: Due to the reduction in immunity caused by auto-splenectomy and the consequent opsonic antibody shortage, patients with SCD are more susceptible to encapsulated organism infections, especially asymptomatic urinary tract infection (ASM-UTI). This study investigated the prevalence of ASM-UTI and compared urine and hematology parameters among SCD patients in Ghana to their healthy counterparts.

Methods: In this study, 104 SCD participants (cases) and 80 non-SCD (HbAA) controls were recruited. Participants' information was thoroughly documented using a well-structured questionnaire and patient case records. To achieve the study's aims, a mid-stream urine in a cleaned dry aseptic urine capped container and venous blood were collected for laboratory analysis.

Results: The prevalence of ASM-UTI among SCD participants and non-SCD (HbAA) individuals were 22 (21.2%) and 18 (22.5%) respectively. Among the 22 (21.2%) SCD individuals with ASM-UTI, 64% were HbSS and 36% were HbSC. *S. aureus* 15 (8.2%) accounted for the majority of the organisms isolated with the larger proportion 9(60.0%) isolated from the SCD patients. There was a statistical difference between SCD with ASM-UTI, without ASM-UTI, and non-SCD (HbAA) with respect to urine appearance ($p = 0.047$), proteinuria ($p = 0.024$), leukocyte ($p < 0.0001$). Significantly high total WBC ($p < 0.0001$), low platelets ($p < 0.0001$), and low hemoglobin ($p < 0.0001$) in SCD with ASM-UTI compared to non-SCD (HbAA) with ASM-UTI were also observed. Major risk factors associated with ASM-UTI includes a cloudy urine appearance, a positive (+1 and +2) urine leukocytes and positive (+1) urine bilirubin compared to having a clear urine appearance, negative leukocyte, and a negative bilirubin.

Conclusion: This study has shown ASM-UTI to be common in adult SCD participants with higher rate in females. It has also showed that ASM-UTI can exist alongside other clinical states such as anemia, microalbuminuria, hematuria and proteinuria which are characteristics of kidney disease which can trigger crises in SCD participants.

1 | Introduction

A urinary tract infection (UTI), is defined as a bacterial infection of the urinary tract with a culture-proven infection (greater than 100,000 CFU/mL in a clean catch midstream urine) linked to acute-onset symptoms, including hematuria, dysuria with varying degrees of increased urinary urgency and frequency, and new or worsening incontinence [1]. Due to the reduction in immunity caused by autosplenectomy and the consequent opsonic antibody shortage, patients with sickle cell disease (SCD) are more susceptible to encapsulated organism infections, especially UTIs [2]. From a changed blood picture to symptoms such leukocytosis, elevated platelets, and decreased hematocrit and hemoglobin [3], SCD is linked to a number of consequences, including kidney issues. Hyposthenuria, or decreased capacity to concentrate urine, is a common early observation in SCD patients for urinary abnormalities. It is less severe and manifests later in sickle cell trait and SCD patients. Hyposthenuria causes nocturia and polyuria. The result of sickling in the vasa recta obstructing countercurrent exchange in the inner medulla appears to impair free water reabsorption. On the other hand, antidiuretic hormone production and the capacity to dilute urine persist in patients with SCD. The unaltered resorptive capability of the cortical nephrons' superficial loops of Henle, which are nourished by peritubular capillaries as opposed to the most severely impacted vasa recta, is responsible for the retention of normal urine diluting capacity [2]. Changes in urine concentration, or hyposthenuria, are the first signs of kidney disease in SCD [4]. Papillary necrosis and renal infarction might result from more severe ischemia. Usually presenting as painless gross hematuria, papillary necrosis can be made worse by a blockage or UTI. Severe segmental or whole renal infarctions may result in fever, discomfort in the flanks or abdomen, nausea, vomiting, and even renin-mediated hypertension [2]. Hematuria is a prevalent problem among SCD patients. Though it can occasionally be hemorrhagic and challenging to treat, it is usually benign, painless, and self-limiting. Sickled red blood cells (RBCs) that block vascular access in the renal medulla and cause blood cell extravasation appear to be the etiology of hematuria [5]. The “nutcracker phenomenon” and the left renal vein's greater length have been implicated in the left-sided origin of hematuria. It is thought that asymptomatic bacteriuria, which causes ASM-UTIs in SCD patients, is increased by abnormalities in kidney function. This explains why sickle cell affects the distribution and kind of bacteria that cause UTIs [6]. These UTIs can either be asymptomatic (having no acute symptoms) or symptomatic (having bacteriuria and symptoms such dysuria, pyuria, and frequent urine) [7]. In people with SCD, a delay in diagnosis and, consequently, in the implementation of suitable treatment may result in scarring and eventual renal impairment, which may trigger a crisis and cause deadly septicemia [8]. However, little information is available regarding the prevalence of asymptomatic UTIs among SCD patients in Ghana. Therefore, this study aimed to investigate the prevalence of asymptomatic UTI and compared urine and hematology parameters among SCD patients in Ghana.

2 | Materials and Methods

2.1 | Study Design, Duration, and Study Setting

The present study utilized a case-control design and was carried out at the Komfo Anokye Teaching Hospital (KATH), the Suntreso Government Hospital and the Kumasi South Government Hospital from November 25, 2023 to August 31, 2024. The KATH is located at Bantama, Kumasi, Ashanti Region, Ghana. It is the sole tertiary healthcare facility in the Ashanti Region and the second-largest hospital in Ghana. Kumasi South Hospital and Suntreso Government Hospital are also located at Atonsu Agogo and North Suntreso respectively. These facilities are situated in the Kumasi Metropolis in the Ashanti Region of Ghana. They are 24-hour working health facilities that boast of services like laboratory, scan, obstetrics and gynecology They also have sickle cell clinics from where SCD participants were recruited for the study.

2.2 | Ethical Clearance and Informed Consent

The Komfo Anokye Teaching Hospital (KATH IRB/AP/175/23) and Kwame Nkrumah University of Science and Technology's (CHRPE/AP/1037/23) committees on human research and publication ethics approved the study. Once the study participants had received a thorough explanation of the study's objectives, advantages, risks, and right to withdraw at any time in both English and the local dialect (primarily Twi), their written consent was requested.

2.3 | Study Participants

Participants in the study were first given an explanation of the study's purpose with the help of a medical doctor, which included urine and blood sampling, data gathering and laboratory testing. After that, 104 SCD patients and 80 non-SCD (HbAA) individuals were recruited. Known SCD patients who were registered at the Kumasi South Government Hospital and Komfo Anokye Teaching Hospital's sickle cell clinic in Ghana were included in the study. Before SCD patients were recruited, expert hematologists in the selected hospitals evaluated them based on their clinical histories and determined that they were eligible for the study. Additionally, participants with sickle cell disease who had symptoms of an acute illness (fever or need for an urgent care center referral), a clinically suspected UTI, severe hematuria, or symptoms suggestive of a sickle cell pain crisis were excluded. Healthy individuals were recruited from the laboratory units of these health facilities.

SCD individuals who were above eighteen (18) years were included in the study. SCD individuals with a history of diabetes mellitus, arterial hypertension, neoplastic, cardiovascular, renal, lung or endocrine disease as well as cancer patients were excluded from the study. Also, subjects who had symptomatic infections, pregnant women, individuals with G6PD defects and other known hemolytic disease aside SCD were excluded. Controls were individuals who were normal for hemoglobin phenotypes (HbAA). Non-SCD (HbAA) individuals without history of

diabetes mellitus, arterial hypertension, neoplastic, cardiovascular, inflammatory, renal, lung and endocrine diseases and currently not on any medication were included. Before recruitment, both patients and controls fasted for 8 to 12 h.

2.4 | Data Collection

A well-structured questionnaire and patient case records were used to document key demographic and clinical history data about the participants. When wearing light clothing, weight was estimated to the nearest 0.1 kg, and height was estimated to the nearest centimeter without shoes. Height was measured using a ruler that was fixed to the wall. Weight was measured using a bathroom scale manufactured by Zhongshan Camry Electronic Co. Ltd in Guangdong, China.

2.5 | Blood Sampling and Analysis

Blood samples were collected following standard protocol [9]. One (1) milliliter (ml) (venous blood) were collected into K3 EDTA tube. Participants were directed to collect a mid-stream urine in a cleaned dry aseptic urine capped container. They were instructed to void the first part of the urine flow to fall into the toilet bowl before they collected about 1 to 2 ounces of urine, then void the rest into the toilet bowl. The urine sample was used for urinalysis, bacteria culture and UACR.

2.6 | Laboratory Assay

To confirm the phenotypes in all participants, cellulose acetate electrophoresis at pH 8.9 followed by high-performance liquid chromatography (Bio-Rad variant II dual program hemoglobin testing) were performed and results reported as HbSS, HbSC and HbAA. Full Blood Estimation was done using five (5)-part Automated Hematology Analyzer XN-550 (XN-550; Sysmex Corporation, Kobe Japan) following standard protocol [10]. Urine albumin-to-creatinine (UACR) was analyzed with the VITROS 5600 Integrated System. The 10-parameter urine strip for urine biochemistry was obtained from Shenzhen Render Bio-tech Co. Ltd.

2.7 | Urine Macroscopy, Microscopy and Culture

Urine Macroscopy: This consisted of appearance, color and biochemistry of the urine. The urine sample collected from participants were analyzed within 1 h after collection. The color (eg. straw, amber, reddish, dark etc.) of the urine was recorded, then the urine was shaken to determine the appearance (e.g. Clear, hazy, cloudy etc.). The urine was poured into 10 ml plane centrifuge tube and urine strips with 10 parameters (pH, specific gravity, glucose, ketones, bilirubin, urobilinogen, blood, protein, nitrite and leukocyte) was dipped to check the biochemical components of the urine based on color reactivity [11].

Urine Microscopy: The urine was centrifuged for 3–5 min at 3000 revolutions per minute. The supernatant was discarded and a drop of the deposit was placed on a clean dried slide and cover slip placed on it. The slide was examined with MICROSTAR IV microscope. Examination was done with ×10 and ×40 objective lens. The deposit was observed for pus cells, red blood cells, yeast cells, bacteria cells, casts, crystals and epithelial cells [11].

Urine culture: Briefly, 10 μl inoculation loop was heated in a burning flame, allowed to cool and dipped into the collected urine. The loop was then streaked on cystine-lactose-electrolyte deficient (CLED) agar and incubated for 24 to 48 h under aerobic condition. Pathogen or bacteria identification was done when colony count exceeded 100,000 CFU/ML [12]. The bacteria identified was confirmed with repeated cultures as well as biochemical testing. Confirmed organisms were recorded and analyzed.

2.8 | Definition of Asymptomatic Bacteriuria or ASM-UTI

In a culture of a midstream urine specimen taken from a patient during the review visit, the presence of at least 10^5 colony forming units of a urinary tract pathogen per milliliter of urine was considered probable asymptomatic bacteriuria. When two or more successive cultures showed evidence of asymptomatic bacteriuria caused by the same urinary tract pathogen, it was considered a verified episode of asymptomatic bacteriuria. If more than two urinary tract pathogens were grown in a sample, even in modest amounts, it was considered to be grossly contaminated [13]. Only confirmed asymptomatic bacteriuria were recorded and analyzed in this study.

2.9 | Statistical Analysis

The study's data was entered and cleaned in Microsoft Excel (2016). Data were exported into R programming Language version 4.2.3 and Statistical Package for Social Sciences (SPSS) version 26.0 for statistical analysis. All categorical variables were presented as frequencies with percentages and graphically with bar charts. Again, The Chi square test was appropriately used to assess the significance of association between categorical variables. Kruskal-Wallis test was also computed to assess the median differences between more than two independent variables and it was followed by pairwise comparison test to determine the significant pairs within the groups using the Bonferroni correction for multiple test *p*-values. *p-values* less than 0.05 were considered statistically significant for all statistical analyzes.

3 | Results

3.1 | Sociodemographic Characteristics of Study Participants

A total of 104 SCD patients (46 males and 58 females) and 80 healthy individuals were recruited for this study. For the SCD participants, seventy-four 74 (71.2%) were HbSS and thirty 30 (28.8%) were HbSC. They were all in steady state based on their clinical status assessed by hematologists. Age varied significantly ($p < 0.001$) across the groups as majority (40.8%) of the participants were between 21 and 30 years, with females having a

higher percentage across study groups with respect to gender ($p = 0.022$). Again, the study found significant difference in the distribution of marital status ($p < 0.001$), BMI ($p < 0.001$), educational background ($p < 0.001$) and alcohol intake ($p = 0.012$) among cases and non-SCD (HbAA) as larger proportion of the participants were single (73.4%), underweight (60.9%), in Senior High school (46.7%), and rarely take in alcohol (89.1%) respectively. Although, there was no significant difference in the distribution of occupation ($p = 0.191$) and Tobacco intake ($p = 0.138$), majority of participants were unemployed (44.6%) and rarely take in tobacco (98.4%) (Table 1).

3.2 | Prevalence of ASM-UTI Among Study Participants

The prevalence of ASM-UTI among SCD patients was assessed to know and understand the scope and ASM-UTI

TABLE 1 | Sociodemographic characteristics of study participants.

Variables	Total 184 (100%)	Cases		Control AA 80 (43.5%)	*p*-value
		SC 30 (16.3%)	SS 74 (40.2%)		
Age group					**< 0.001**
< 20	47 (25.5)	9 (19.1)	29 (61.7)	9 (19.1)	
21–30	75 (40.8)	13 (17.3)	30 (40.0)	32 (42.7)	
31–40	33 (17.9)	1 (3.0)	12 (36.4)	20 (60.6)	
41–50	22 (12.0)	7 (31.8)	2 (9.1)	13 (59.1)	
> 50	7 (3.8)	0 (0.0)	1 (14.3)	6 (85.7)	
Gender					**0.022**
Male	66 (35.9)	12 (18.2)	34 (51.5)	20 (30.3)	
Female	118 (64.1)	18 (15.3)	40 (33.9)	60 (50.8)	
Marital status					**0.001**
Single	135 (73.4)	22 (16.3)	66 (48.9)	47 (34.8)	
Married	47 (25.5)	8 (17.0)	8 (17.0)	31 (66.0)	
Divorced	2 (1.1)	0 (0.0)	0 (0.0)	2 (100.0)	
Educational background					**< 0.001**
Non formal	2 (1.0)	0 (0.0)	0 (0.0)	2 (100.0)	
Basic	41 (22.3)	5 (12.2)	6 (14.6)	30 (73.2)	
SHS	86 (46.7)	11 (12.8)	48 (55.8)	27 (31.4)	
Tertiary	55 (29.9)	14 (25.5)	20 (36.4)	21 (38.2)	
Occupation					0.191
Unemployed	82 (44.6)	13 (15.9)	38 (46.3)	31 (37.8)	
Formal	31 (16.8)	3 (9.7)	15 (48.4)	13 (41.9)	
Informal	71 (38.6)	14 (19.7)	21 (29.6)	36 (50.7)	
BMI					**< 0.001**
Normal (18.5–24.9 kg/m)	9 (4.9)	2 (22.2)	7 (77.8)	0 (0.0)	
Underweight (< 18.5 kg/m)	112 (60.9)	23 (20.5)	55 (49.1)	34 (30.4)	
Overweight (25–29.9)	60 (32.6)	4 (6.7)	11 (18.3)	45 (75.0)	
Obese (≥ 30 kg/m)	3 (1.6)	1 (33.3)	1 (33.3)	1 (33.3)	
Tobacco intake					0.138
Irregular	3 (1.6)	0 (0.0)	0 (0.0)	3 (100.0)	
Rarely	181 (98.4)	30 (16.6)	74 (40.9)	77 (42.5)	
Alcohol intake					**0.012**
Regular	3 (1.6)	0 (0.0)	0 (0.0)	3 (100.0)	
Irregular	17 (9.2)	1 (5.9)	3 (17.6)	13 (76.5)	
Rarely	164 (89.1)	29 (17.7)	71 (43.3)	64 (39.0)	

Note: *p*-values were computed with Chi-Square test.
Abbreviation: BMI, body mass index.

burden in SCD population. The prevalence of ASM-UTI among the 104 patients and the 80 non-SCD (HbAA) individuals was comparable ($p = 0.858$), with 22 (21.2%) and 18 (22.5%) having asymptomatic ASM-UTI, respectively, Figure 1A. Among the 22 (21.2%) SCD individuals with ASM-UTI, 64% were HbSS and 36% were HbSC as shown in Figure 1B. Again, the prevalence of ASM-UTI among SCD patients was stratified by age and gender to ascertain age and gender-specific vulnerabilities among SCD patients. Although, the distribution of ASM-UTI across the age groups and gender was not statistically significant ($p = 0.682$) and ($p = 0.092$) respectively, it was revealed that, ASM-UTI was more prevalent in females 16 (72.7%) compared to their male counterparts 6 (27.3%), and the age groups < 20 10(44.5%) followed by 21-30 9(40.9%) however, it was less prevalent in adults above 50 years (Figures 2A and 3A). Also, ASM-UTI was more prevalent in HbSS females (66.7%) and males (62.5%) compared to HbSC females (33.3%) and males (37.5%) among SCD patients with ASM-UTI. Again, HbSS with age groups < 20 (70%) and 21–30 (66.7%) had a higher prevalence as compared to their HbSC age groups, although age groups 31–40 and 41–50 in both HbSS and HbSC patients had equal ASM-UTI prevalence (Figures 2B and 3B).

3.3 | Distribution of Isolated ASM-UTI Organisms Among Cases and Non-SCD (HbAA)

Of the 184 urine samples cultured, 144 (78.3%) showed no bacterial growth. *S. aureus* 15 (8.2%) accounted for the majority of the organisms isolated with the larger proportion 9 (60.0%) being isolated from the SCD patients (Figure 4A). *Klebsiella spp*. 10 (5.4%) were the second most common organisms isolated, with 5 (50.0%) isolated from both cases and non-SCD (HbAA) each. Nine (4.9%) of the isolates were also *E. coli*, with 5 (55.6%) being isolated from the non-SCD (HbAA). The least isolated organism was *Candida spp*., which were mostly recovered from SCD patients 4 (66.7%), as illustrated Figure 4B.

3.4 | Comparative Analysis of Urological and Hematological Profile Among SCD Patients and Non-SCD (HbAA)

Chi-square and Kruskal-Wallis tests were computed to determine the association between categorical and continuous urological and hematological parameters of participants. Significant differences were followed by pairwise comparison test to determine the significant pairs within the group using the Bonferroni correction for multiple test *p*-values. Majority of the participants had clear urine 164 (89.1%) with 16 (8.7%) having hazy urine. Larger proportion of those with hazy urine were SCD without ASM-UTI 11 (68.85%) with 2 (50.0%) of those with cloudy urine being SCD with ASM-UTI. The distribution of urine appearance across the groups was statistically significant ($p = 0.047$). The distribution of urine protein across the groups was statistically significant ($p = 0.024$) with majority being negative 129 (70.1%) and 55 (29.9%) also having traces to positive (+3). Majority of those who had traces to positive (+3) were SCD without ASM-UTI 35 (63.6%) followed by SCD with ASM-UTI 9 (16.4%). A similar trend was observed for urine leukocyte ($p < 0.001$), urine bilirubin ($p = 0.009$), urine urobilinogen

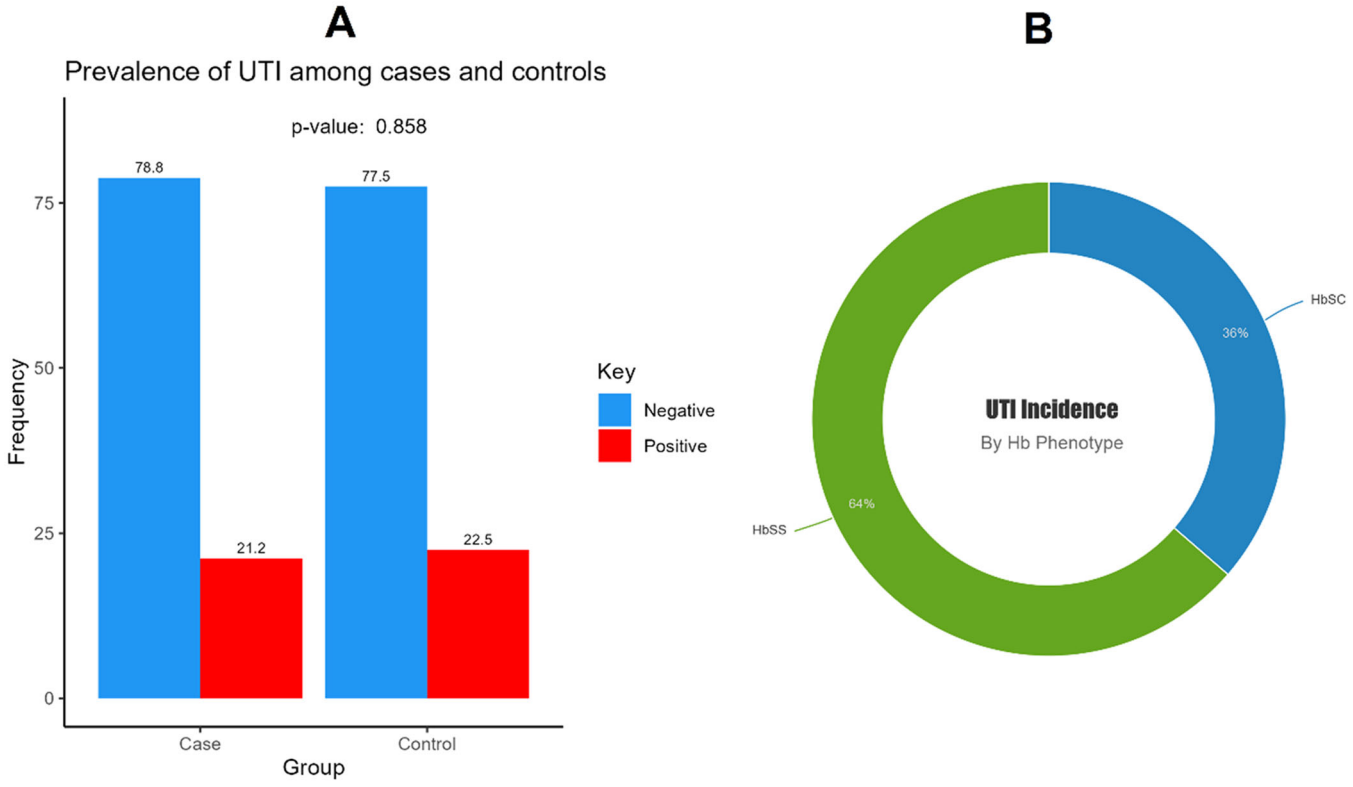

FIGURE 1 | Prevalence of ASM-UTI among study participants. (A) A bar chart displaying the prevalence of ASM-UTI among cases and non-SCD (HbAA). (B) A pie chart displaying the prevalence of ASM-UTI among SCD patients.

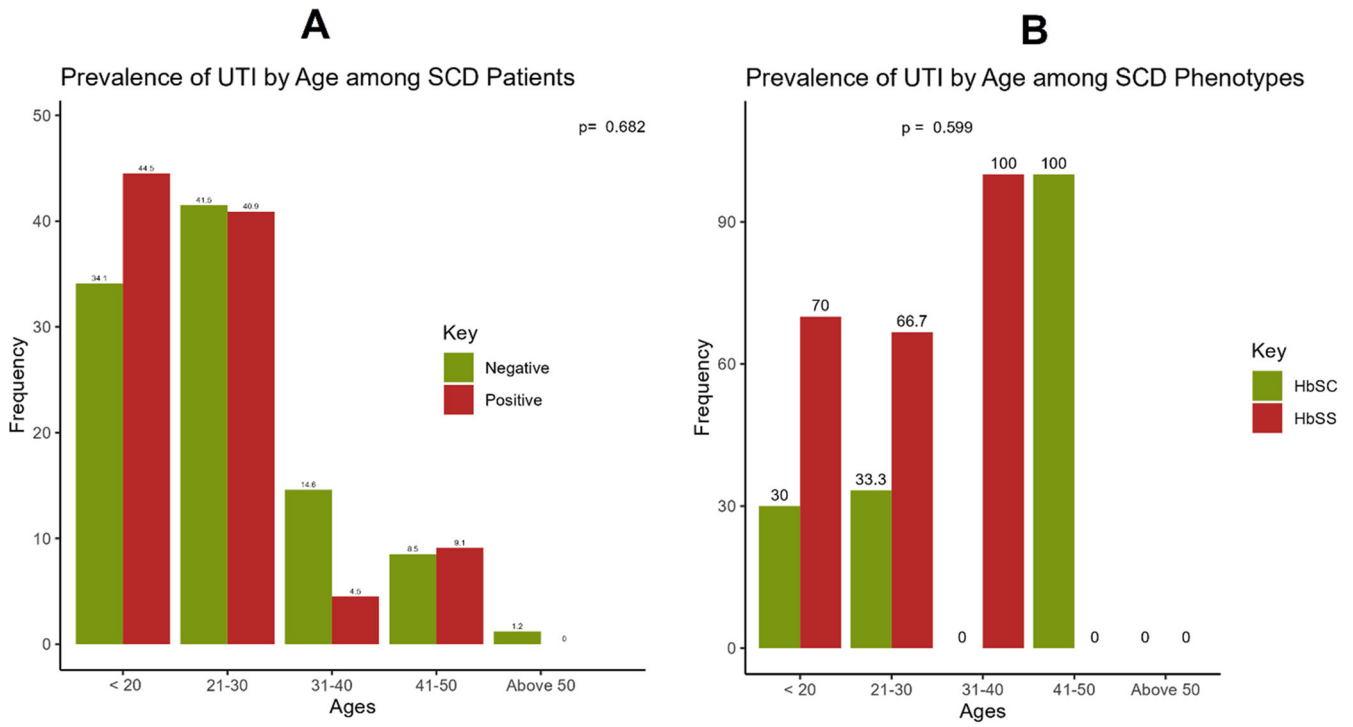

FIGURE 2 | Prevalence of ASM-UTI by age SCD Patients. (A) A bar chart displaying the prevalence of ASM-UTI by age among SCD patients. (B) A bar chart displaying the prevalence of ASM-UTI by age among SCD phenotypes.

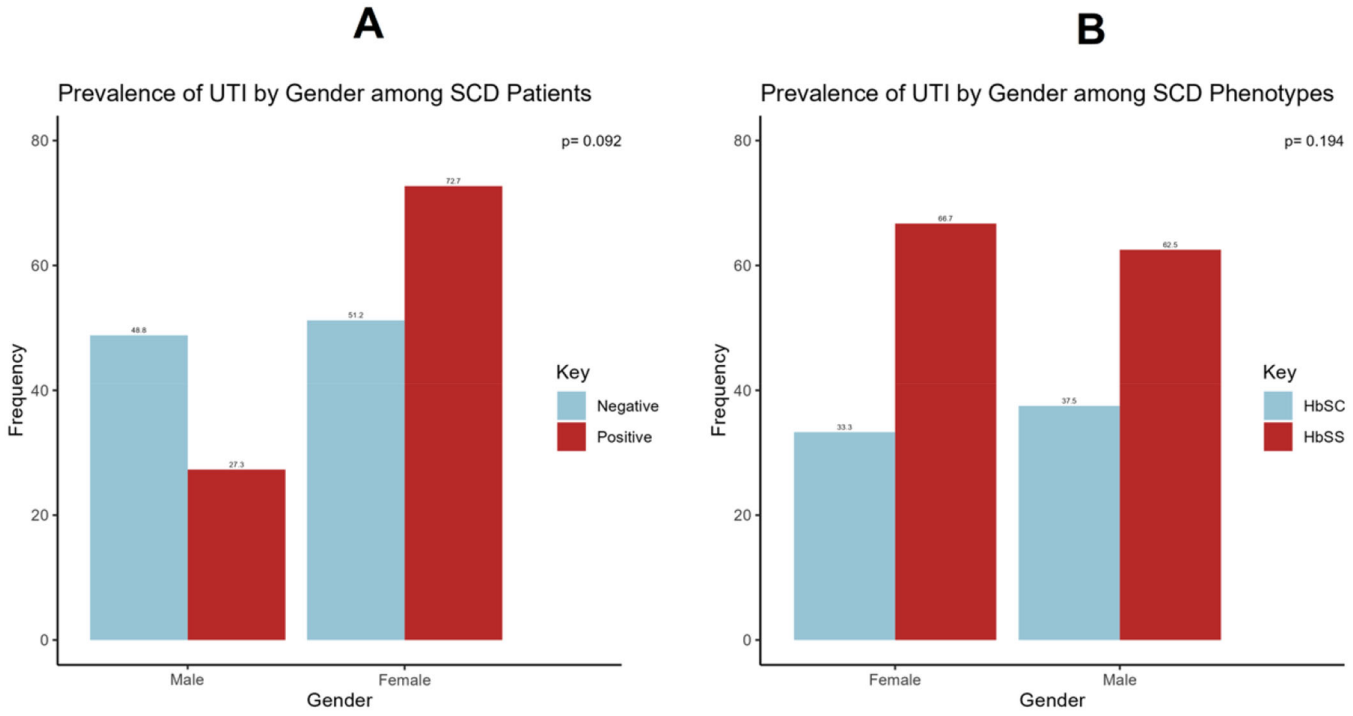

FIGURE 3 | Prevalence of ASM-UTI by gender SCD Patients. (A) A bar chart displaying the prevalence of ASM-UTI by gender among SCD patients. (B) A bar chart displaying the prevalence of ASM-UTI by gender among SCD phenotypes.

($p < 0.001$), urine blood ($p = 0.001$) and urine crystals ($p < 0.001$). Pus cells was high in participants with ASM-UTI especially in SCD with ASM-UTI compared to non-SCD (HbAA) with ASM-UTI (11.5 vs 10.0 respectively, $p < 0.001$). A similar trend was observed in urine epithelial cells (12.00 vs 10.5 respectively, $p < 0.001$). Again, participants with ASM-UTI had reduced RBC, HB and platelets counts compared to their counterparts with no ASM-UTI ($p < 0.001$ and $p = 0.026$ respectively). Although all participants had averagely normocytic cells (84.1 fL, $p = 0.019$), however, non-SCD (HbAA) individuals with ASM-UTI had increased MCV (83.8 vs 81.4 respectively) than those with no ASM-UTI and SCD with ASM-

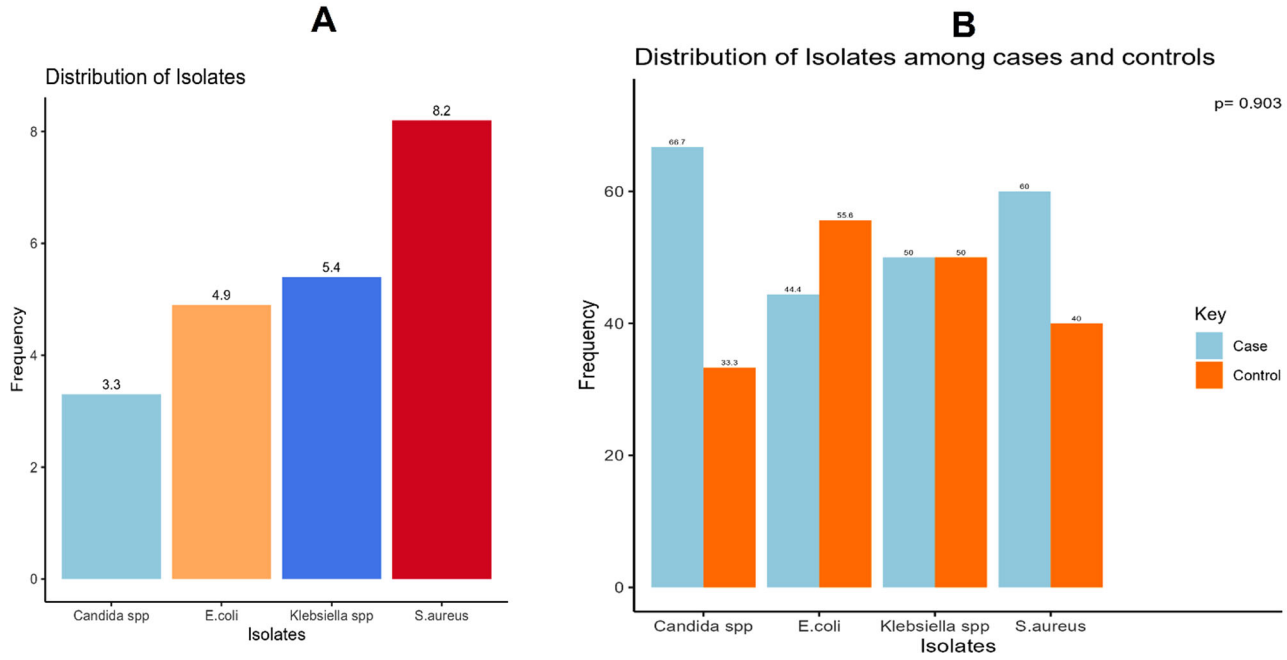

FIGURE 4 | Distribution of isolated ASM-UTI organisms. (A) Distribution of isolated ASM-UTI organisms; (B) distribution of isolated ASM-UTI organisms among cases and non-SCD (HbAA).

UTI too had reduced MCV (86.8 vs 87.1) than those with no ASM-UTI. A similar trend was also observed for MCH ($p = 0.001$), WBC count ($p < 0.001$), absolute neutrophils count ($p = 0.004$). Absolute eosinophils count ($p = 0.001$) were seen to be high in control individuals with no ASM-UTI compared to non-SCD (HbAA) with ASM-UTI (0.10 vs 0.07 respectively), however, it was high in SCD with ASM-UTI compared to SCD with no ASM-UTI (0.17 vs 0.13). A similar trend was observed for absolute lymphocytes count ($p < 0.001$). Participants with ASM-UTI had reduced monocytes compared to their counterparts with no ASM-UTI especially when control with ASM-UTI was compared to SCD with ASM-UTI (0.5 vs 0.6 respectively, $p < 0.05$). Although not statistically significant ($p = 0.228$), however, microalbuminuria (UACR) was high in SCD with ASM-UTI compared to their counterparts SCD without ASM-UTI (22.2 vs 18.9 respectively), and low in non-SCD (HbAA) with ASM-UTI compared to those with no ASM-UTI (17.1 vs 24.0 respectively) (Table 2).

3.5 | Risk Factors of ASM-UTI Among SCD Patients

In a univariate and multivariate logistic regression computed to know the risk factors of ASM-UTI among SCD patients, it was observed that, having a cloudy urine appearance had a significantly increased odd (8.11, $p = 0.042$) of having ASM-UTI in SCD compared to a clear urine appearance. Again, having a positive (+1) and positive (+2) urine leukocytes and positive (+1) urine bilirubin had a significantly increased odd (7.65, $p = 0.001$), (9.50, $p = 0.001$) and (3.39, $p = 0.019$) respectively of having ASM-UTI in SCD compared to a negative urine leukocyte. It was also observed that for any unit increase in the pus cells count, epithelial cells count, MCHC, absolute lymphocytes and basophils counts, the odds of testing positive for ASM-UTI in SCD significantly increased (1.21, $p < 0.001$), (1.31, $p < 0.001$), (1.24, $p = 0.046$), (1.42, $p = 0.023$) and (149.3, $p = 0.021$) respectively. Also, for any unit increase in RBC count ($p = 0.033$), and HCT ($p = 0.027$), the odds of testing positive for ASM-UTI in SCD significantly reduced 0.59 and 0.92 respectively. However, after adjusting for confounding variables in the adjusted odds ratio, epithelial cells count was significantly associated with ASM-UTI in SCD for any unit increase in urine epithelial cells count (1.46, $p = 0.007$), while having a hazy urine appearance was also significantly associated with reduced odd (0.10, $p = 0.034$) of having ASM-UTI in SCD compared to having clear urine appearance. The relation between all other variables was not statistically significant ($p > 0.05$) (Table 3).

4 | Discussion

One of the most common infectious diseases, UTIs, have a significant negative impact on society's health and economy. The traditional definition of asymptomatic UTI, also known as asymptomatic bacteriuria, is the identification of a particular quantitative count of bacteria in a urine sample that has been properly collected from a person who does not exhibit any symptoms or indicators of a UTI [14].

According to studies conducted by Ohene Frimpong et al. [15] and Ephraim et al. [16] from Ghana, the majority of SCD patients had HbSS variants, followed by HbSC variants. A similar trend was observed in this current study. HbSS patients are known to have severe form of SCD and this account for more clinic visits than other SCD phenotypes. The higher female-to-male proportion in this study may be due to the better health-

TABLE 2 | Comparative analysis of urological and hematological profile among SCD patients (cases) and non-SCD (HbAA)(controls).

Variables	Total 184 (100%)	Control 80 (43.5%)		Cases 104		*p*-value
		Negative 62 (77.5%)	Positive 18 (22.5%)	Negative 82 (78.8%)	Positive 22 (21.2%)	
Appearance						**0.047**
Clear	164 (89.1)	59 (36.0)	17 (10.4)	70 (42.7)	18 (11.0)	
Hazy	16 (8.7)	3 (18.8)	0 (0.0)	11 (68.8)	2 (12.5)	
Cloudy	4 (2.2)	0 (0.0)	1 (25.0)	1 (25.0)	2 (50.0)	
Color						0.160
Straw	160 (87.0)	60 (37.5)	14 (8.8)	68 (42.5)	18 (11.3)	
Amber	23 (12.5)	2 (8.7)	4 (17.4)	13 (56.5)	4 (17.4)	
Deep Amber	1 (0.5)	0 (0.0)	0 (0.0)	1 (100.0)	0 (0.0)	
Proteinuria						**0.024**
Negative	129 (70.1)	55 (42.6)	14 (10.9)	47 (36.4)	13 (10.1)	
Trace	20 (10.9)	2 (10.0)	0 (0.0)	14 (70.0)	4 (20.0)	
Positive (+1)	29 (15.8)	5 (17.2)	4 (13.8)	16 (55.2)	4 (13.8)	
Positive (+2)	5 (2.7)	0 (0.0)	0 (0.0)	4 (80.0)	1 (20.0)	
Positive (+3)	1 (0.5)	0 (0.0)	0 (0.0)	1 (100.0)	0 (0.0)	
Leukocyte						**< 0.001**
Negative	105 (57.1)	45 (42.9)	2 (1.9)	54 (51.4)	4 (3.8)	
Trace	14 (7.6)	6 (42.9)	1 (7.1)	5 (35.7)	2 (14.3)	
Positive (+1)	43 (23.4)	8 (18.6)	9 (20.9)	16 (37.2)	10 (23.3)	
Positive (+2)	22 (12.0)	3 (13.6)	6 (27.3)	7 (31.8)	6 (27.3)	
Glucose						0.781
Negative	182 (98.9)	61 (33.5)	18 (9.9)	81 (44.5)	22 (12.1)	
Positive (+1)	1 (0.5)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Positive (+3)	1 (0.5)	0 (0.0)	0 (0.0)	1 (100.0)	0 (0.0)	
Bilirubin						**0.009**
Negative	153 (83.2)	60 (39.2)	17 (11.1)	61 (39.9)	15 (9.8)	
Trace	3 (1.6)	0 (0.0)	0 (0.0)	3 (100.0)	0 (0.0)	
Positive (+1)	26 (14.1)	2 (7.7)	1 (3.8)	16 (61.5)	7 (26.9)	
Positive (+2)	2 (1.1)	0 (0.0)	0 (0.0)	2 (100.0)	0 (0.0)	
Urobilinogen						**< 0.001**

(Continues)

TABLE 2 | (Continued)

Variables	Total 184 (100%)	Control 80 (43.5%)		Cases 104		*p*-value
		Negative 62 (77.5%)	Positive 18 (22.5%)	Negative 82 (78.8%)	Positive 22 (21.2%)	
Negative	143 (77.7)	60 (42.0)	18 (12.6)	49 (34.3)	16 (11.2)	
Trace	7 (3.8)	0 (0.0)	0 (0.0)	7 (100.0)	0 (0.0)	
Positive (+1)	24 (13.0)	2 (8.3)	0 (0.0)	18 (75.0)	4 (16.7)	
Positive (+2)	8 (4.3)	0 (0.0)	0 (0.0)	7 (87.5)	1 (12.5)	
Positive (+3)	2 (1.1)	0 (0.0)	0 (0.0)	1 (50.0)	1 (50.0)	
Ketone						0.153
Negative	180 (97.8)	60 (33.3)	16 (8.9)	82 (45.6)	22 (12.2)	
Positive (+1)	2 (1.1)	1 (50.0)	1 (50.0)	0 (0.0)	0 (0.0)	
Positive (+2)	2 (1.1)	1 (50.0)	1 (50.0)	0 (0.0)	0 (0.0)	
Blood						**< 0.001**
Negative	169 (91.8)	62 (36.7)	14 (8.3)	74 (43.8)	19 (11.2)	
Trace	4 (2.2)	0 (0.0)	3 (75.0)	1 (25.0)	0 (0.0)	
Positive (+1)	10 (5.4)	0 (0.0)	1 (10.0)	6 (60.0)	3 (30.0)	
Positive (+2)	1 (0.5)	0 (0.0)	0 (0.0)	1 (100.0)	0 (0.0)	
Nitrite						0.061
Negative	182 (98.9)	62 (34.1)	17 (9.3)	82 (45.1)	21 (11.5)	
Positive (+1)	2 (1.1)	0 (0.0)	1 (50.0)	0 (0.0)	1 (50.0)	
Casts						0.069
Negative	176 (95.7)	62 (35.2)	18 (10.2)	75 (42.6)	21 (11.9)	
Positive (+1)	8 (4.3)	0 (0.0)	0 (0.0)	7 (87.5)	1 (12.5)	
Crystals						**< 0.001**
Negative	173 (94.0)	62 (35.8)	18 (10.4)	76 (43.9)	17 (9.8)	
Positive (+1)	8 (4.3)	0 (0.0)	0 (0.0)	6 (75.0)	2 (25.0)	
Positive (+2)	3 (1.6)	0 (0.0)	0 (0.0)	0 (0.0)	3 (100.0)	
SG	1.01 (1.01–1.01)	1.01 (1.00–1.01)	1.01 (1.01–1.01)	1.01 (1.01–1.01)	1.01 (1.01–1.01)	0.997
Pus Cells	4.00 (2.00–11.00)	1.00 (1.00–4.00)	10.00 (8.25–14.00)	4.00 (2.00–11.00)	11.50 (9.00–16.25)	**< 0.001**[a,b,c,f]
EC	5.00 (2.00–11.00)	2.00 (1.00–5.00)	10.50 (5.75–12.00)	5.00 (3.00–11.00)	12.00 (10.00–14.00)	**< 0.001**[a,b,c,f]
pH	6.00 (5.00–6.50)	6.00 (5.00–7.63)	6.00 (5.00–8.00)	6.00 (5.75–6.63)	6.25 (5.75–6.63)	0.780

(Continues)

TABLE 2 | (Continued)

Variables	Total 184 (100%)	Control 80 (43.5%)		Cases 104		*p*-value
		Negative 62 (77.5%)	Positive 18 (22.5%)	Negative 82 (78.8%)	Positive 22 (21.2%)	
Hematobiochemical						
RBC (10^6/uL)	3.80 (2.73–4.40)	4.35 (3.94–4.91)	4.30 (3.74–4.66)	2.97 (2.44–3.85)	2.83 (2.61–4.27)	**< 0.001**[b,c,d,e]
HB (g/dL)	10.15 (8.4–11.90)	11.70 (10.55–13.10)	11.80 (10.73–13.10)	8.65 (7.60–10.13)	9.65 (8.33–10.78)	**< 0.001**[b,c,d,e]
HCT (%)	29.70 (24.60–35.70)	35.30 (30.63–39.50)	35.50 (31.60–37.03)	25.30 (22.60–29.65)	26.60 (22.93–31.48)	**< 0.001**[b,c,d,e]
MCV (fL)	84.10 (76.73–90.40)	81.40 (76.03–85.45)	83.80 (80.05–88.45)	87.05 (76.73–95.90)	86.80 (73.93–96.95)	**0.019**[b]
MCH (pg)	28.50 (25.90–30.90)	27.55 (24.98–29.15)	28.75 (27.63–32.70)	29.70 (26.45–32.70)	29.50 (25.80–34.10)	**0.001**[b,c]
MCHC (g/dL)	34.50 (32.70–35.70)	33.60 (32.50–34.63)	34.40 (33.13–35.40)	35.00 (32.70–36.40)	36.10 (34.38–37.10)	**< 0.001**[b,c]
WBC (10^3/uL)	7.11 (5.37–9.46)	5.63 (4.94–7.01)	6.27 (5.12–7.28)	8.88 (6.69–10.87)	7.96 (6.53–10.07)	**< 0.001**[b,c,d]
LYMPH (10^3/uL)	2.69 (2.03–3.60)	2.15 (1.74–2.68)	2.14 (1.87–2.58)	3.34 (2.48–4.08)	3.48 (2.90–3.93)	**< 0.001**[b,c,d,e]
MONO (10^3/uL)	0.60 (0.45–0.83)	0.56 (0.43–0.66)	0.51 (0.39–0.61)	0.73 (0.47–0.99)	0.61 (0.45–-1.00)	**0.009**[b]
NEUT (10^3/uL)	3.35 (2.54–4.96)	2.97 (2.05–3.88)	3.21 (2.55–4.45)	4.22 (2.73–5.27)	3.67 (2.87–5.073)	**0.004**[b]
EO (10^3/uL)	0.12 (0.06–0.22)	0.10 (0.05–0.21)	0.07 (0.38–0.12)	0.13 (0.07–0.24)	0.17 (0.09–0.28)	**0.001**[d,e]
BASO (10^3/uL)	0.04 (0.03–0.07)	0.03 (0.02–0.04)	0.03 (0.02–0.04)	0.05 (0.04–0.09)	0.09 (0.05–0.12)	**< 0.001**[b,c,d,e]
PLT	256.50 (205.50–354.75)	248.00 (206.50–286.75)	236.50 (217.25–290.50)	309.50 (213.00–418.00)	219.50 (150.50–358.25)	**0.026**
UACR	21.15 (8.08–36.78)	24.02 (12.16–44.94)	17.10 (6.40–37.42)	18.94 (7.22–34.84)	22.16 (3.92–36.41)	0.228

Note: p-values for all categorical variables were computed with Chi-Square test and that of continuous variables with Kruskal-Wallis test, values are presented as median (inter-quartile ranges) for continuous variables and frequency (%) for categorical variables.

Abbreviations: BAS; basophil; EC; epithelial cells; EOS; eosinophil; fl; femtolitre; g/dL; gram per deciliter; HB; hemoglobin; HCT; hematocrit; LYMPH; lymphocyte; MCV; mean cell volume; MCH; mean cell hemoglobin; MCHC; mean cell hemoglobin concentration; MON; monocyte; NEUT; neutrophil; pg; picogram; PLT; platelet; RBC; red blood cell; SG; specific gravity; uL; microliter; WBC; white blood cell.

[a]Statistical association ($p < 0.05$) between ASM-UTI-negative non-SCD (HbAA) and ASM-UTI-positive non-SCD (HbAA).

[b]Statistical association ($p < 0.05$) between ASM-UTI-negative non-SCD (HbAA) and SCD ASM-UTI-negative.

[c]Statistical association ($p < 0.05$) between ASM-UTI-negative non-SCD (HbAA) and SCD ASM-UTI-positive.

[d]Statistical association ($p < 0.05$) between ASM-UTI-positive non-SCD (HbAA) and SCD ASM-UTI-negative.

[e]Statistical association ($p < 0.05$) between ASM-UTI-positive non-SCD (HbAA) and SCD ASM-UTI-positive.

[f]Statistical association ($p < 0.05$) between SCD ASM-UTI-negative and SCD ASM-UTI-positive.

TABLE 3 | Univariate and multivariate logistic regression for risk factors of ASM-UTI among SCD patients.

	SCD ASM-UTI positive			
Variable	**cOR (95% C.I)**	***p*-value**	**aOR (95% C.I)**	***p*-value**
Age group				
< 20*	—	—		
21–30	0.51 (0.18–1.35)	0.174		
31–40	0.12 (0.01–0.95)	0.045		
41–50	0.37 (0.07–1.86)	0.227		
> 50	0.00 (0.00–0.00)	0.999		
Gender				
Female*	—	—		
Male	0.64 (0.24–1.72)	0.373		
Marital status				
Single*	—	—		
Married	0.26 (0.06–1.14)	0.073		
Divorced	0.00 (0.00–0.00)	0.999		
BMI				
Normal (18.5–24.9 kg/m) *	—	—		
Underweight (< 18.5 kg/m)	0.50 (0.09–2.65)	0.415		
Overweight (25–29.9)	0.32 (-0.05–1.96)	0.217		
Obese (≥ 30 kg/m)	1.75 (0.10–30.84)	0.702		
Appearance				
Clear*	—	—	—	—
Hazy	1.16 (0.24–5.62)	0.853	0.10 (0.01–0.84)	**0.034**
Cloudy	8.11 (1.08–61.16)	**0.042**	3.73 (0.21–65.16)	0.367
Proteinuria				
Negative*	—	—		
Trace	2.23 (0.65–7.68)	0.203		
Positive (+1)	1.43 (0.43–4.75)	0.561		
Positive (+2)	2.23 (0.23–21.49)	0.488		
Positive (+3)	0.00 (0.00–0.00)	> 0.99		
Leukocyte				
Negative*	—	—	—	—
Trace	4.21 (0.70–25.45)	0.118	1.41 (0.18–10.99)	0.742
Positive (+1)	7.65 (2.25–26.03)	**< 0.001**	0.98 (0.15–6.56)	0.984
Positive (+2)	9.50 (2.40–37.29)	**< 0.001**	0.73 (0.06–9.55)	0.811
Bilirubin				
Negative *	—	—	—	—
Trace	0.00 (0.00–0.00)	0.999	0.00 (0.00–0.00)	0.999
Positive (+1)	3.39 (1.23–9.37)	**0.019**	1.44 (0.29–7.24)	0.655
Positive (+2)	0.00 (0.00–0.00)	0.999	0.00 (0.00–0.00)	0.999
Urobilinogen				
Negative*	—	—		
Trace	0.00 (0.00–0.00)	0.999		
Positive (+1)	1.59 (0.48–5.23)	0.448		

(Continues)

TABLE 3 | (Continued)

Variable	SCD ASM-UTI positive			
	cOR (95% C.I)	*p*-value	aOR (95% C.I)	*p*-value
Positive (+2)	1.13 (0.13–9.82)	0.909		
Positive (+3)	7.94 (0.47–133.19)	0.150		
Blood				
Negative*	—	—		
Trace	0.00 (0.00–0.00)	0.999		
Positive (+1)	3.38 (0.81–14.20)	0.096		
Positive (+2)	0.00 (0.00–0.00)	> 0.99		
Nitrite				
Negative*	—	—		
Positive (+1)	7.67 (0.46–127.20)	0.155		
Pus cells	1.21 (1.11-–1.32)	**< 0.001**	0.99 (0.79–1.25)	0.947
EC	1.31 (1.17–1.47)	**< 0.001**	1.46 (1.11–1.93)	**0.007**
PH	1.08 (0.73–1.58)	0.715		
Hematobiochemical				
RBC (10^6/uL)	0.59 (0.37–0.96)	**0.033**	0.77 (0.21–2.86)	0.699
HB (g/dL)	0.84 (0.68–1.03)	0.088		
HCT (%)	0.92 (0.86–0.99)	**0.027**	0.96 (0.78–1.18)	0.693
MCV (fL)	1.01 (0.98–1.05)	0.407		
MCH (pg)	1.06 (0.98–1.15)	0.162		
MCHC (g/dL)	1.24 (1.00–1.53)	**0.046**	1.14 (0.90–1.43)	0.279
WBC (10^3/uL)	1.10 (0.96–1.26)	0.167		
LYMPH (10^3/uL)	1.42 (1.05–1.92)	**0.023**	1.52 (0.91–2.55)	0.113
MONO (10^3/uL)	1.13 (0.36–3.57)	0.837		
NEUT (10^3/uL)	1.02 (0.82–1.27)	0.839		
EO (10^3/uL)	4.60 (0.92–22.86)	0.062		
BASO (10^3/uL)	149.30 (2.10–10606.53)	**0.021**	3.13 (0.01–791.32)	0.686
PLT	1.00 (0.99–1.00)	0.247		
UCAR	0.99 (0.96–1.01)	0.211		

Abbreviations: aOR; adjusted odd ratio; BAS; basophil; cOR; crude odd ratio; EC; epithelial cells; EOS; eosinophil; fl; femtolitre; g/dL; gram per deciliter; HB; hemoglobin; HCT; hematocrit; LYMPH; lymphocyte; MCH; mean cell hemoglobin; MCHC; mean cell hemoglobin concentration; MCV; mean cell volume; MON; monocyte; NEUT; neutrophil; pg; picogram; PLT; platelet; RBC; red blood cell; uL; microliter; WBC; white blood cell.

seeking habits of females as compared to males and the fact that women generally live longer than men do in most populations [17]. In Ghana, the life expectancy (in years) for a male at birth is 61.0 and for a female is 63.9, per WHO data released in 2015 [18]. This may also explain the higher female-to-male ratio reported in this study. Interestingly, most of SCD patients were single which agrees with a study done by Adzika et al., (2017) who reported that 88.9% SCD patients in Ghana are unmarried [19] and the fact that SCD people are already living with stress and fear including fear of marriage and fear of having children [20].

The overall prevalence of asymptomatic UTI was found to be 22.1% in SCD patients and 22.5% in non-SCD (HbAA). In line with our findings, Asinobi et al. [21] reported asymptomatic UTI to be 21.6% in SCD and 15.8% in non-SCD (HbAA). Again, Mava et al. [22] also found that 26% SCD and 20.4% non-SCD (HbAA) had asymptomatic UTI in their studies in Nigeria. However, Donkor et al., [7], in Ghana reported the prevalence of asymptomatic ASM-UTI in SCD and non-SCD (HbAA) to be 17.3% and 8.2% respectively which are below the prevalences reported in this study. The differences in prevalences reported could be attributed to the age, phenotypes and geographical locations of participants. This study only recruited adult steady state HBSS and HbSC participants whereas previous studies reported different ages and phenotypes. The variations in prevalences implies that there are more elements at play than the variations in immunological state between SCD and non-SCD (HbAA) individuals. Inadequate personal hygiene, cultural and religious cleaning customs, and other elements could be contributing factors.

SCD participants with HbSS had a higher prevalence of asymptomatic ASM-UTI (13.5% of the overall SCD participants) which is lower than the prevalences in sickle cell anemia (HBSS) studies done by Akinbami et al. [23] (44.4%) and Iwalokun et al. [24] (14.6%) in Nigeria. Different geographical locations, sample size and personal hygiene of participants could explain the heterogenous prevalences observed. ASM-UTI was high among female participants (72.7%) which agrees with SCD studies done in Ghana and Nigeria [21, 25–27]. For example, Donkor et al. [7] in Ghana reported a higher prevalence (26.5% in SCD vs 11.8% in non-SCD (HbAA) in females than males (2.4% in SCD and 2.4% in non-SCD [HbAA]). This has been linked to the short female urethra with its closeness to the anal canal, which facilitates easier contamination and ascending.

This study reported high incidence of *Candida spp* and *Staphylococcus aureus* in SCD patients than in non-SCD (HbAA) patients with ASM-UTI. In the same vein, *Klebsiella spp* had equal distribution rates in both SCD and non-SCD (HbAA) with ASM-UTI. *E. coli* was however decreased in the SCD group than the non-SCD (HbAA) group with ASM-UTI. Generally, there was high incidence of *Staphylococcus aureus* (coagulase-positive) in both cases and non-SCD (HbAA) with ASM-UTI, this is inconsistent with a similar study done by Donkor et al. [7] in Ghana, who reported coagulase-negative *Staphylococcus spp* as the most common organism isolated in both SCD and non-SCD (HbAA), although the isolated organisms are from the same species but have different biochemical enzyme activity [7]. These observations are consistent with several studies [26–30]. *Staphylococcus aureus* (13.8%) was common in a study by Mava et al. with predominance of *E. coli* (27.7%) and *Klebsiella spp* (24.6%) in same study which varies from distribution of isolates observed in this present study. In an adult and children sickle cell anemia study done by Musonda et al., [6], *Staphylococcus aureus* (32%) was the most common isolate followed by *Klebsiella spp* (16%) which is comparable to this present study. The variations of predominant isolates may be due to fact participants in this study were older than that of studies done by Mava et al. as well as differences in geographical locations. The diverse organisms isolated in SCD patients were also reported by Donkor et al. in Ghana which agrees with this study.

This study reported similarities among study groups with respect to urine pH, and specific gravity which is in line with the findings from Anto et al. [25] study. Moreover, 9.6% SCD patients and 1.3% non-SCD (HbAA) individuals with ASM-UTI tested positive to blood, an indication of gross hematuria. This is similar to a study done by Akinbami et al. [23] who reported 7% gross hematuria in SCD participants with ASM-UTI. Increased blood viscosity, microthrombi, and papillary necrosis brought on by sickling of red blood cells cause structural alterations that ultimately culminate in hematuria [31]. Although either kidney can cause hematuria, left-sided renal bleeding has been seen to be more common [31].

Increased levels of microalbuminuria in SCD with ASM-UTI compared to non-SCD (HbAA) with ASM-UTI (22.2 vs 17.1) indicates that ASM-UTI is associated with kidney disease and even worsen when it occurs in SCD participants [24]. Again, compared to SCD with ASM-UTI and non-SCD (HbAA) with ASM-UTI, this study reported high proteinuria (16.4% vs 7.3%), leukocyte (22.8% vs 20.3%), hematuria (20.0% vs 26.6%), crystalluria (45.5% vs 0.0%), pus cells (11.5 vs 10.0), and epithelial cells (12.0 vs 10.5) among SCD with ASM-UTI than non-SCD (HbAA) with ASM-UTI. Though, there are limited studies to compare these values to, an adult sickle cell anemia study done by Akinbami et al. [23] showed high proteinuria (19%) and hematuria (7%) in SCD patients with ASM-UTI.

In comparison to the control group with ASM-UTI, SCD patients with ASM-UTI had lower RBC (2.8 vs. 4.3) and platelet counts (219.5 vs. 236.5), but higher WBC (8.0 vs. 6.3) and absolute neutrophil counts (3.7 vs. 3.2). Comparing them to SCD without ASM-UTI, however, showed that all of these values were lower in SCD with ASM-UTI. The lower WBC and neutrophils demonstrated by SCD with ASM-UTI may be attributed to the fact that SCD patients experience chronic inflammation and infections including ASM-UTI [32]. In a similar study by Musonda et al. [6] most of the patients had Hb (50% having moderate anemia and 50% having severe anemia) lower than the WHO recommended reference range (11 g/dl for females and 13 g/dl for males) [33] which is comparable to the current observation.

The average hemoglobin (9.7 ± 1 g/dL) in SCD participants reported in this study is consistent with a study done in Zambia (8 ± 1 g/dL) [6] which might be due to persistent hemolysis of red blood cells as a result of red cell membrane injury [34]. Here, too, the development of anemia in SCD participants with or without ASM-UTI is influenced by the reduced erythropoietin response and decreased red cell survival that are linked to SCD [3]. Also, platelets and WBC levels were high in participants with ASM-UTI groups which may be due to the fact ASM-UTI is an inflammatory disease and even get worse when it happens in SCD patients which is in line with a study done by Musonda et al. [6]. Crystalluria were high in SCD with ASM-UTI compared to other participant groups. Likewise, epithelial cells, and pus cells were increased in SCD with ASM-UTI compared to non-SCD (HbAA) with ASM-UTI, indicating the contribution of inflammatory conditions associated with SCD in ASM-UTI [6].

In this study, the major risk factors associated with ASM-UTI are cloudy urine, positive leukocyte, positive bilirubin, pus cells, epithelial cells, blood lymphocyte and basophils. A known risk factor for sickle cell disease is recurrent infection, which is linked to leucocyturia reported in this study [35]. A significant cause of morbidity in individuals with SCD is UTIs, which can aggravate anemia, produce septicemia, and trigger crises. Reducing morbidity requires early diagnosis and suitable treatment [21, 22]. The strength of this study is that, this is the first attempt to investigate risk factors associated with ASM-UTI in SCD and the haemato-urological profile of steady-state SCD with ASM-UTI in Ghana. The main limitation of this study is that we were unable to monitor the SCD patients to determine outcome of asymptomatic ASM-UTI as symptomatic ASM-UTI or not. Hence, further studies required to confirm that the progression of asymptomatic ASM-UTI leads to symptomatic ASM-UTI. If this is the case, early screening and treatment for asymptomatic ASM-UTI in SCD patients may be required due to the increased risk of asymptomatic

ASM-UTI among SCD patients as demonstrated by this study. Another limitation is that because there were few SCD patients with ASM-UTI, we were unable to stratify the haemato-urological variables and associated risk factors by SCD phenotypes (HbSS and HbSC). A large data with high ASM-UTI prevalence in SCD is therefore necessary to determine the hematological and urological variables in each HbSS and HbSC patient.

5 | Conclusion

This study has shown that asymptomatic ASM-UTI is common in adult SCD participants and normal healthy individuals with higher rate in females. Routine screening of SCD participants is therefore recommended. This study also showed that ASM-UTI can exist alongside other clinical conditions such as anemia, microalbuminuria, hematuria, proteinuria which are characteristics of kidney disease and can trigger crises in SCD participants. Lastly, this study demonstrated that the major risk factors associated with ASM-UTI in SCD participants are leucocyturia, urine cloudiness and bilirubinuria.

Author Contributions

Stephen Twumasi: conceptualization, investigation, writing – original draft, methodology, validation, visualization, writing – review and editing, software, formal analysis, project administration, data curation, supervision, resources. **Richard Owusu Ansah:** conceptualization;, methodology, software, writing – review and editing, writing – original draft. **Samuel Essien-Baidoo:** writing – review and editing, writing – original draft. **Laud Anthony W Basing:** conceptualization, investigation, writing – review and editing, writing – original draft. **Alexander Yaw Debrah:** writing – review and editing. enoch odame anto: writing – review and editing. **Allwell Adofo Ayirebi:** writing – review and editing, writing – original draft. **Rebecca Asiamah-Broni:** writing – review and editing. **Waldemer Attivor:** writing – review and editing. **Eric Twum Ameyaw:** writing – review and editing. **Gabriel Addai Manu:** investigation, writing – review and editing. **Edward Afriyie:** writing – review and editing. **Thomas Kwabena Gyampomah:** writing – review and editing, investigation, conceptualization. **Joseph Nkrumah Opoku:** writing – review and editing. **Prince Kwadwo Amoafo:** investigation, writing – review and editing. **Samuel Kelvin Owusu:** investigation, writing – review and editing. **Vincent Akwai:** investigation, writing – review and editing. **Matthew Talmang:** investigation, writing – review and editing. **Amos Mensah:** investigation, writing — review and editing. **Isaac Kusi-Amponsah:** investigation, writing – review and editing. **Angela Opoku:** investigation, writing – original draft, writing – review and editing. **Lilian Antwi Boateng:** conceptualization, investigation, writing – original draft, writing – review and editing, visualization, validation, methodology, project administration, supervision.

Acknowledgments

We are grateful for the immense contributions of the staff of Komfo Anokye Teaching Hospital, Suntreso Government Hospital and Kumasi South Hospital for their warm reception, not forgetting our participants. Special thanks to the serology department of Komfo Anokye Teaching Hospital on their support in storage of samples. The author(s) received no financial support for the research, authorship and or/publication of this article.

Consent

The authors have nothing to report.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The authors confirm that the data supporting the findings of this study are available within the article. Data and materials for study are available upon request from the corresponding authors.

Transparency Statement

The lead author Stephen Twumasi, Lilian Antwi Boateng affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

References

1. J. Anger, U. Lee, A. L. Ackerman, et al., "Recurrent Uncomplicated Urinary Tract Infections in Women: AUA/CUA/SUFU Guideline," *Journal of Urology* 202, no. 2 (2019): 282–289.

2. E. V. Lerma, "Sickle Cell Nephropathy." *Nephrology Secrets* (Elsevier, 2012), 356–361.

3. C. Antwi-Boasiako, I. Ekem, M. Abdul-Rahman, et al., "Hematological Parameters in Ghanaian Sickle Cell Disease Patients," *Journal of Blood Medicine* 9 (2018): 203–209.

4. S. T. Miller, W. C. Wang, R. Iyer, et al., "Urine Concentrating Ability in Infants With Sickle Cell Disease: Baseline Data From the Phase III Trial of Hydroxyurea (Baby Hug)," *Pediatric Blood & Cancer* 54, no. 2 (2010): 265–268.

5. P. Saborio and J. I. Scheinman, "Sickle Cell Nephropathy," *Journal of the American Society of Nephrology* 10, no. 1 (1999): 187–192.

6. T. Musonda, M. Zulu, M. Samutela, et al., "Leucocytosis and Asymptomatic Urinary Tract Infections in Sickle Cell Patients at a Tertiary Hospital in Zambia," *Anemia* 2020, no. 1 (2020): 1–5.

7. E. Donkor, J. Osei, I. Anim-Baidoo, and S. Darkwah, "Risk of Asymptomatic Bacteriuria Among People With Sickle Cell Disease in Accra, Ghana," *Diseases* 5, no. 1 (2017): 4.

8. Y. Mava, M. Bello, J. Ambe, and S. Zailani, "Antimicrobial Sensitivity Pattern of Organisms Causing Urinary Tract Infection in Children With Sickle Cell Anemia in Maiduguri, Nigeria," *Nigerian Journal of Clinical Practice* 15, no. 4 (2012): 420–423.

9. G. Lima-Oliveira, G. Lippi, G. L. Salvagno, G. Picheth, and G. C. Guidi, "Laboratory Diagnostics and Quality of Blood Collection," *Journal of Medical Biochemistry* 34, no. 3 (2015): 288–294.

10. K. Uchihashi, T. Morikawa, Y. Hamaguchi, et al, "XN-L Series," *Sysmex Journal International* 25, no. 1 (2015): 1–5.

11. A. L. Komaroff, "Diagnostic Decision: Urinalysis and Urine Culture in Women With Dysuria," *Annals of Internal Medicine* 104, no. 2 (1986): 212–218.

12. H. Sinawe and D. Casadesus Urine Culture. 2020.

13. V. Cumming, S. Ali, T. Forrester, K. Roye-Green, and M. Reid, "Asymptomatic Bacteriuria in Sickle Cell Disease: A Cross-Sectional Study," *BMC Infectious Diseases* 6 (2006): 46.

14. L. E. Nicolle, S. Bradley, R. Colgan, J. C. Rice, A. Schaeffer, and T. M. Hooton, "Infectious Diseases Society of America Guidelines for the Diagnosis and Treatment of Asymptomatic Bacteriuria in Adults," *Clinical Infectious Diseases* 40 (2005): 643–654.

15. K. Ohene-Frempong, J. Oduro, H. Tetteh, and F. Nkrumah, "Screening Newborns for Sickle Cell Disease in Ghana," *Pediatrics* 121, no. Suppl_2 (2008): S120–S121.

16. R. K. D. Ephraim, D. N. M. Osakunor, O. Cudjoe, et al., "Chronic Kidney Disease is Common in Sickle Cell Disease: A Cross-Sectional Study in the Tema Metropolis, Ghana," *BMC Nephrology* 16 (2015): 75.

17. A. E. Thompson, Y. Anisimowicz, B. Miedema, W. Hogg, W. P. Wodchis, and K. Aubrey-Bassler, "The Influence of Gender and Other Patient Characteristics on Health Care-Seeking Behaviour: A QUALICOPC Study," *BMC Family Practice* 17 (2016): 38.

18. W. H. Organization, Global Health Observatory Data Repository: By Category. Medical Doctors 2021, https://appswhoint/gho/data/nodemainHWFGRP_0020.

19. V. A. Adzika, F. N. Glozah, D. Ayim-Aboagye, and C. S. K. Ahorlu, "Socio-Demographic Characteristics and Psychosocial Consequences of Sickle Cell Disease: The Case of Patients in a Public Hospital in Ghana," *Journal of Health, Population, and Nutrition* 36 (2017): 4.

20. M. Kilonzi, D. L. Mwakawanga, F. F. Felician, et al., "The Effects of Sickle Cell Disease on the Quality of Life: A Focus on the Untold Experiences of Parents in Tanzania," *International Journal of Environmental Research and Public Health* 19, no. 11 (2022): 6871.

21. A. O. Asinobi, O. J. Fatunde, B. J. Brown, K. Osinusi, and N. A. Fasina, "Urinary Tract Infection in Febrile Children With Sickle Cell Anaemia in Ibadan, Nigeria," *Annals of Tropical Paediatrics* 23, no. 2 (2003): 129–134.

22. Y. Mava, J. P. Ambe, M. Bello, I. Watila, and V. A. Nottidge, "Urinary Tract Infection in Febrile Children With Sickle Cell Anaemia," *West African Journal of Medicine* 30, no. 4 (2011): 268–272.

23. A. Akinbami, S. Ajibola, I. Bode-Shojobi, et al., "Prevalence of Significant Bacteriuria Among Symptomatic and Asymptomatic Homozygous Sickle Cell Disease Patients in a Tertiary Hospital in Lagos, Nigeria," *Nigerian Journal of Clinical Practice* 17, no. 2 (2014): 163–167.

24. B. A. Iwalokun, S. O. Iwalokun, S. O. Hodonu, O. A. Aina, and P. U. Agomo, "Evaluation of Microalbuminuria in Relation to Asymptomatic Bacteruria in Nigerian Patients With Sickle Cell Anemia," *Saudi Journal of Kidney Diseases and Transplantation: An Official Publication of the Saudi Center for Organ Transplantation, Saudi Arabia* 23, no. 6 (2012): 1320–1330.

25. E. O. Anto, C. Obirikorang, E. Acheampong, et al., "Renal Abnormalities Among Children With Sickle Cell Conditions in Highly Resource-Limited Setting in Ghana," *PLoS One* 14, no. 11 (2019): e0225310.

26. E. Barrett-connor, "Bacterial Infection and Sickle Cell Anemia: An Analysis of 250 Infections in 166 Patients and a Review of the Literature," *Medicine* 50, no. 2 (1971): 97–112.

27. A. M. Elbashier and G. A. Badu, "Pattern of Bacteriuria in Patients With Sickle Cell Disease in Qatif Central Hospital," *Saudi Medical Journal* 12, no. 2 (1991): 121–124.

28. M. Ajasin and R. Adegbola, "Asymptomatic Bacteriuria in Children With Sickle Cell Anaemia," *Nigerian Journal of Paediatrics* 15 (1988): 19–25.

29. R. Akuse, "Variation in the Pattern of Bacterial Infection in Patients With Sickle Cell Disease Requiring Admission," *Journal of Tropical Pediatrics* 42, no. 6 (1996): 318–323.

30. O. Hu, O. Ba, I. Bc, and N.-O. Nu, "Prevalence of Asymtomatic Bacteriuria Among Nursery School Children," *Nigerian Journal of Paediatrics* 20, no. 4 (1993): 84–88.

31. T. Masekoameng Sickle Cell Trait and Targeted Genomic Variants in Chronic Kidney Disease an African Cohort. 2019.

32. N. Conran and J. D. Belcher, "Inflammation in Sickle Cell Disease," *Clinical Hemorheology and Microcirculation* 68, no. 2–3 (2018): 263–299.

33. J. Murphy, *Haemoglobin Concentrations for the Diagnosis of Anaemia and Assessment of Severity. Vitamin and Mineral Nutrition Information System*. World Health Organization, 2002).

34. D. Allan, A. R. Limbrick, P. Thomas, and M. P. Westerman, "Release of Spectrin-Free Spicules on Reoxygenation of Sickled Erythrocytes," *Nature* 295, no. 5850 (1982): 612–613.

35. I. Okpala, "Steady-State Platelet Count and Complications of Sickle Cell Disease," *Hematology Journal* 3, no. 4 (2002): 214–215.