

Original Article

# Prevalence of Asymptomatic Bacteriuria in Children with Sickle Cell Disease

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**Abstract** - Background: Asymptomatic bacteriuria (ASB) is a common finding in pediatric patients including children with sickle cell (SCD); those children have a great risk of symptomatic urinary tract infections and associated serious Sequelae. Materials and Methods: An observational descriptive study (cross-sectional) was conducted for a period of one year (May 2022 to May 2023) at Tishreen University Hospital in Lattakia-Syria. The study included a group of children with sickle cell anemia who underwent a screening for bacteriuria. Results: A total of 95 children, of which 66.3% were male, and 33.7% were female, with a mean age of 6.7±3.1 years, were enrolled. The prevalence of ASB was 6.3%, and *Escherichia coli* (*E.coli*) was the most dominant germ (50%), followed by *proteus*, *staphylococcus aureus*, and *klebsiellae* on average 16.7% of each of them without the presence of significant difference ( $p>0.05$ ). There was no significant correlation between age ( $p: 0.1$ ), sex ( $p: 0.9$ ), and occurrence of ASB. Conclusion: Asymptomatic bacteriuria is a prevalent condition in children with sickle cell anemia without any significant association with demographic characteristics, including age and sex.

**Keywords** - Asymptomatic bacteriuria, Children, Prevalence of sickle cell anemia, Syria.

## 1. Introduction

Sickle cell disease(SCD) is considered one of the most frequent genetic disorders in red blood cells (RBCs) that results from a mutated form of hemoglobin S(HbS) [1,2,3]. It can be either heterozygous (two different alleles for HbS and another beta-globin, especially beta-thalassemia) or homozygous (two identical alleles for HbS). The incidence of SCD varies according to ethnicity (mostly present in blacks and also detected in eastern Mediterranean and Middle Eastern populations but with much less frequency) [4, 5]. Clinical manifestations of SCD begin early in infancy and childhood, with the most common feature - the vaso-occlusive crisis - which results from microcirculation obstruction by sickled red blood cells when deoxygenated hemoglobin polymerizes and forms crystals, resulting in ischemic injury to organs. In addition, chronic hemolytic anemia is usually present [6, 7, 8, 9, and 10].

Asymptomatic bacteriuria (ASB) is defined as the presence of one or more species of bacteria in the urine at quantitative counts  $\geq 10^5$  colony-forming units CFU/ml. The prevalence of ASB is approximately 3% in school-age children and decreases to 1% in older children [11, 12, 13]. SCD is a complex genetic disorder associated with multiple clinical manifestations, including increased susceptibility to bacterial and viral infections due to immunity dysfunction. Renal manifestations range from some tubular and glomerular functional

abnormalities to gross anatomic alterations of kidneys and urinary tract infections [14, 15]. Many supposed mechanisms predispose to urinary tract infections, including dysfunction of the immune system and spleen (including splenic opsonization and the inability to concentrate and acidification of urine) that lead to an increase in the incidence and frequency of infections [16, 17, 18, 19, 20, 21]. The absence of national studies in Syria about the prevalence and the importance of ASB in children with SCD prompts us to carry out this study in order to reveal this serious phenomenon that could serve in the early prediction of future expected renal complications and sequels in such children with SCD. Therefore, the aims of this study were: 1- to investigate the prevalence of asymptomatic bacteriuria in children with a diagnosis of SCD. 2- To determine the association between the presence of bacteriuria and the demographic characteristics of the patients.

## 2. Patients and Methods

### 2.1. Study Population

A cross-sectional observational descriptive study was conducted in all pediatric patients with SCD seen at the Pediatric General Clinic, Tishreen University Hospital, over one year from April 2022 to April 2023.

Inclusion Criteria were as follows: Children of both sexes aged 2 to 12 years with proven diagnosis of SCD. Exclusion Criteria: Patients with one of the following: fever, a clinical



history that supposes the presence of urinary tract infection (sudden need to urinate, pain in the flank, dysuria, and incontinence), congenital urological malformations, and use of antibiotic in the last 72 hours.

Complete history, review of systems, physical examination, and laboratory and radiology investigations of the urinary tract were performed. Urine samples were obtained for analysis in all patients to demonstrate the presence of asymptomatic bacteriuria.

### 3. Statistical Analysis

Statistical analysis was performed using IBM SPSS version 20. Basic Descriptive statistics included means, standard deviations (SD), median, frequency, and percentages. The chi-square test examined the relationships and comparisons between the two groups. All the tests were considered significant at a 5% type I error rate ( $p < 0.05$ ),  $\beta$ : 20%, and power of the study: 80%.

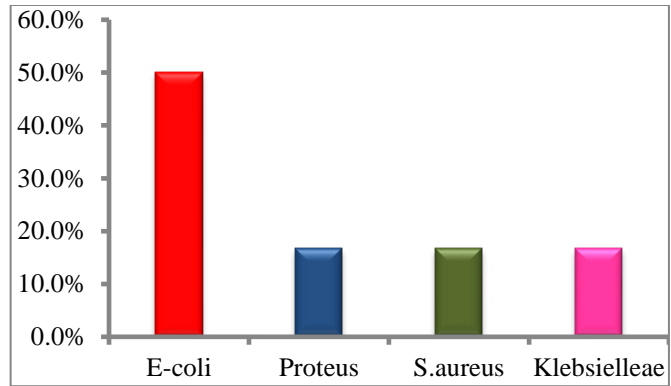
### 4. Results

The baseline characteristics of patients are shown in Table (1). Among the 95 study participants, 66.3% were males and 33.7% were females, with an average age of children was  $7.6 \pm 3.1$  years. Age group 3-6 years represented the most frequent age group (38.9%), followed by 6-9 (34.7%), 9-12 (14.8%), and 0-3 (11.6%). The overall prevalence of positive urinalysis was 9.5% (9/95), and isolation of bacteria was detected only in 6 cases (6.3%).

Table 1. Demographic characteristics of the study population

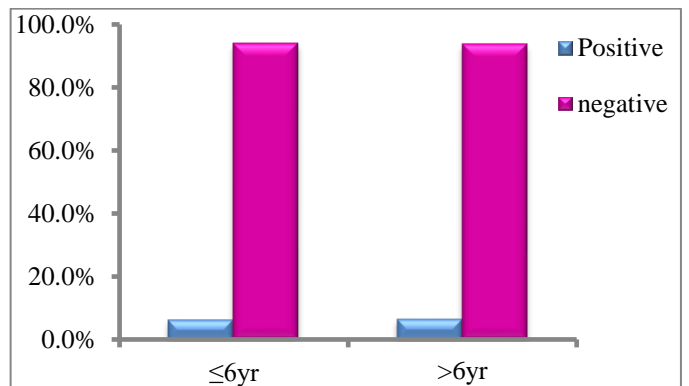
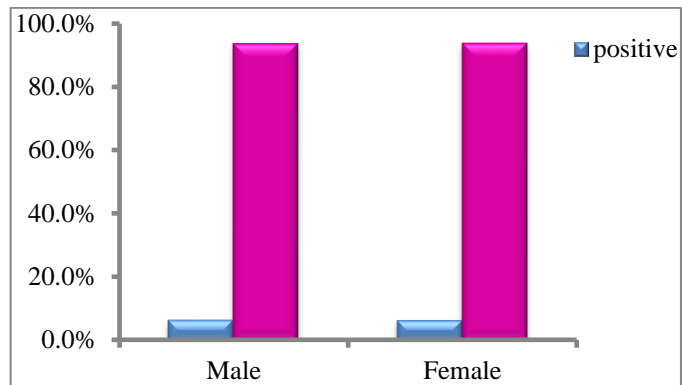
Variables	Results
<b>Age (years)</b>	$7.6 \pm 3.1$ (Range 2.3-12 year)
<b>Age groups (n, %)</b>	
0-3	11(11.6%)
3-6	37(38.9%)
6-9	33(34.7%)
9-12	14(14.8%)
<b>Sex</b>	
Male	63(66.3%)
Female	32(33.7%)
<b>Urinalysis</b>	
Positive	9(9.5%)
Negative	86(90.5%)
<b>Urine culture</b>	
Positive	6(6.3%)
Negative	89(93.7%)

As shown in graph (1), Escherichia coli (E.coli) represented the most frequently isolated bacteria in 3 cases (50%), followed by proteus, staphylococcus aureus, and Klebsiellae on average 16.7% of each of them which was detected only in females.



Graph 1. Distribution of isolated bacteria according to sex

As shown in Graph (2&3), bacteriuria was detected in 4 males (6.3%) and 2 females (6.2%),  $p = 0.9$ . There was no significant difference in the occurrence of bacteriuria according to age; 6.2% in children younger than 6 years versus 6.4% in children older than 6 years,  $p = 0$ .



Graph 2&3 Association between bacteriuria and demographic characteristics of the study population

### 5. Discussion

Asymptomatic bacteriuria can have a significant impact on children and affect the outcome of pediatric patients if untreated. Asymptomatic bacteriuria (ASB) is benign except in certain medical conditions such as pregnancy, immunosuppression, and children with SCD, so understanding the association between the two conditions would improve the

outcome. To our current knowledge, there are limited studies regarding the prevalence of bacteriuria in children with SCD.

Significant bacteriuria may be either symptomatic or asymptomatic. The former defines urinary tract infection with common symptoms such as dysuria, pyuria, etc.

In asymptomatic bacteriuria (ASB) the symptoms of urinary tract infection are absent, and some of the associated risk groups of ASB include elderly people and patients with diabetes, bladder catheters, and Sickle Cell Disease (SCD).

The prognostic significance of ASB is based on the fact that it could lead to an increased risk of pyelonephritis and renal impairment in certain medical conditions such as diabetes mellitus and pregnancy. Several bacterial organisms have been implicated in bacteriuria, but the common ones include *Escherichia coli* and *Staphylococcus* spp. In ASB,

Alterations in host-pathogen interaction may be responsible for the absence of symptoms despite the presence of urinary pathogens (15)

The result of the current study revealed that approximately two-thirds of patients were males, and age groups 3-6 and 6-9 years represented the most frequent groups, which sample characteristics might explain because the incidence of sickle cell anemia is not gender related as it is transmitted as an autosomal recessive disorder. Urine culture was positive in 6.3% of the patients without the presence of any symptoms, which might be related to the predisposition for urinary tract infections in patients with sickle cell anemia due to papillary necrosis, renal inability to concentrate, and acidification of urine, which promote bacteria growth. In addition, alterations in host-pathogen interactions might be responsible for asymptomatic cases. Many pathogens were isolated from urine samples, and *E. coli* represented the most frequent pathogen without significant difference, which might be explained by abnormalities in the immune system in patients, predisposing them to grow another type of bacteria. There was no significant correlation between bacteriuria and patient demographic variables, including age and sex ( $p > 0.05$ ), despite the predominance of urinary tract infections usually seen in females due to urinary tract anatomy and deficiency in the response of secretory IgA in urinary tract mucosa. The results of the current study are consistent with the previous studies.

Chukwu et al. (2011) demonstrated in a study conducted in Nigeria for one year, which included 100 patients with sickle cell anemia compared with 100 healthy children, that the prevalence of asymptomatic bacteriuria was 6% in patients versus 2% in healthy patients. Bacteriuria was detected more frequently in females than males, and *E. coli* represented the most frequently isolated organism. This finding disagrees with the current study regarding the high frequency of urinary tract infections in females (22).

Adegoke et al (2013) showed in a study conducted in Nigeria for one year, which included 196 patients with sickle cell anemia that the prevalence of asymptomatic bacteriuria was 6.6%, which was observed more frequently in older children ( $p:0.04$ ), females ( $p:0.003$ ) especially in presence of pyuria and *E.coli* represented the most frequent isolated organism. This finding disagrees with the current study regarding the association between age and sex with bacteriuria. (23).

Musonda et al. (2020) demonstrated in a study conducted in Zambia for one year, which included 78 children with proven diagnoses of sickle cell anemia that the prevalence of asymptomatic bacteriuria was 25%, and the most frequent isolated organisms were staphylococcus, streptococcus, proteus, and *E.coli*. This finding disagrees with the current study regarding the high prevalence of bacteriuria and frequency of isolated pathogens, which might be explained by the characteristics of the study population. (24)

Abdel Kader et al. (2021) demonstrated in a study conducted in Egypt for one year, which included 30 children with proven diagnoses of sickle cell anemia, that the prevalence of asymptomatic bacteriuria was 16.7% and the most frequent isolated organism was staphylococcus followed by *E.coli* and streptococcus. This finding disagrees with the current study regarding the high prevalence of bacteriuria and frequency of isolated pathogens, which might be explained by the small sample size and immune alterations that predispose patients to infection by another organism rather than *E. coli* (25).

In summary, ASB in SCD patients emphasizes the importance of frequent urinalysis and culture in infants and children as early detection of ASB and the regular follow-up of patients to improve the outcome.

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