ORIGINAL ARTICLE

Asymptomatic bacteriuria among pregnant women with sickle cell trait in Enugu, South Eastern Nigeria

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Abstract

Context: Asymptomatic bacteriuria (ASB) in pregnancy is a major risk factor for developing acute cystitis and pyelonephritis, especially, among women with sickle cell disease. This study compared the prevalence, pattern, and microbiological characteristics of ASB in pregnancy between sickle cell trait (HbAS) and normal hemoglobin AA (HbAA) genotype subjects.

Materials and Methods: Culture and sensitivity of mid-stream urine samples were collected from 300 HbAS women and 300 matched HbAA control at the antenatal clinic of University of Nigeria Teaching Hospital Enugu, Nigeria from August 2010 to December 2011. Analysis was both descriptive and inferential at 95% confidence levels.

Results: Prevalence of ASB in HbAS and HbAA women were 32.7% (98/300) and 32% (96/300) respectively (odd ratio (OR) =1.03 [95% confidence interval (CI) 0.73, 1.45]). *Escherichia coli* was the most common organism isolated in both the HbAS group (56.1%, 55/98) and control group (61.4%, 59/96), (OR = 0.80 [95% CI 0.45, 1.42]). The antibiotics with the highest microbial sensitivity were ciprofloxacin 90.8% (89/98) and gentamicin 100% (98/98) for HbAS and HbAA women respectively.

Conclusions: The prevalence of ASB in pregnant women with HbAS in Enugu, Nigeria was high and did not vary significantly from that of woman with HbAA. Therefore, pregnant women irrespective of their sickle cell status would benefit from routine screening for ASB.

Key words: Asymptomatic bacteriuria, Enugu-Nigeria, pregnant women, sickle cell trait

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Introduction

Pregnant women with sickle cell trait (HbAS) are thought to have a greater propensity for the development of asymptomatic bacteriuria (ASB), acute cystitis and pyelonephritis than pregnant women with normal hemoglobin AA (HbAA) genotype.[1] The term asymptomatic bacteriuria (ASB) refers to the presence of a positive urine culture in an individual in the absence of clinical signs and symptoms of urinary tract infection.[2] The diagnosis of this condition requires voided urine specimens and isolation of at least 10^5 colony forming units per milliliter of the same bacterial strain.[3] It has been shown that pregnancy does not increase the risk of ASB,[4] rather it enhances its progression to symptomatic disease;[5] therefore, ASB in pregnancy is a major risk factor for developing symptomatic urinary tract infection during pregnancy.[6] This complication is more common in pregnancy because of the relative obstruction by the gravid uterus and the dilatory effect of progesterone on the urinary collecting tracts;[4] thus, leading to multiplication and ascending of the bacteria to the upper urinary tract. Furthermore, although the HbAS is often considered to be benign, conditions such as hypoxia, hyperviscosity, dehydration, and acidosis may enhance sickling of red blood cells.[7] This increases the risk of vaso-occlusion particularly in the kidneys, where the relatively anoxic, acidotic and

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hypertonic milieu favor hemoglobin S polymerization and hemolysis as evidenced by elevated lactate dehydrogenase levels in the blood of such patients.[7] Furthermore, serum free iron released from sickle erythrocytes in the circulation leads to the accumulation of free iron in the urine increasing the risk of infection.[7] It is obvious therefore that maternal bacteriuria may be associated with increased maternal and fetal morbidity, and this risk may be higher for HbAS pregnant women. This study compared the prevalence of ASB, the pattern of bacterial agents and their antimicrobial susceptibility between pregnant women with HbAS and their HbAA counterpart.

Materials and Methods

This is a cross-sectional analytical study of two cohorts of consenting singleton pregnant women at the University of Nigeria Teaching Hospital (UNTH), Enugu, Nigeria, and Mother of Christ Specialist Hospital, Enugu, from August 2010 to December 2011. The study group was made of 300 consecutive women with HbAS while the control group comprised of 300 women with HbAA matched for age, parity, and gestational age groups. After recruiting an eligible woman for the study group, the next antenatal attendee with HbAA who matched the selected participants was recruited as the control. Exclusion criteria included sickle cell anemia, history of diabetes mellitus, symptoms of urinary tract infections or renal disease, history of antibiotics use or urethral catheterization within 2 weeks prior to the study. Hemoglobin electrophoresis was used for the sickle cell genotyping of pregnant women. Ethical approval for this study was obtained from the Health Research Ethics Committee of UNTH Enugu.

Following informed consent, each study participant was educated on how to collect a urine sample. Clean-catch midstream urine sample from each participant was collected into a sterile boric acid universal bottles after antero-posterior swabbing of the vulva using sterile gauze soaked in normal saline.[5,8,9] Each sample collection was supervised by one of the three nurses trained for the procedure. The urine samples were sent to the microbiology laboratory within one hour of collection. Each urine sample was thoroughly mixed by gentle shaking; afterward, a loop-full (using a standard wire loop) was streaked onto Blood agar, Cysteine Lactose Electrolyte Deficient medium and MacConkey Agar, and incubated aerobically at 37°C for 24 h.[9] Counts of 10^5 organisms or more per milliliter of the urine samples were considered significant.[3] Such colonies were identified using standard methods thus: Colonial morphology, Gram reactions, sugar fermentation, catalase test, coagulase test, arginine deaminase test, oxidase test, indole, and urea hydrolysis test.[9,10] Sensitivity was determined using Kirby-Bauer disc diffusion technique.[11] The data obtained was analyzed by descriptive and inferential statistics using SPSS computer software version 16.0. Proportions were compared with Chi-square test and a P value of < 0.05 was considered statistically significant.

Participants' social classes were determined using their education status and their husbands' occupation.[12]

Enugu State is located in the South-East geo-political zone of Nigeria and it has a population of over 3 million.[13] A study among students in the state showed a HbAS prevalence of 11%.[14]

The UNTH Enugu is a teaching hospital owned by the Federal Government of Nigeria. The average antenatal attendance (first visits and revisits) of the hospital is 795 women/month. On the other hand, the Mother of Christ Specialist Hospital, Enugu is a faith based specialist hospital located in the capital city of Enugu State. Its average antenatal attendance is 703 women/month.

Results

The age range of the study and control groups was 15-49 years with a mean of 28.7 ± 5.0 years and 27.9 ± 4.8 years respectively ($P = 0.765$). The modal age group for both groups was 25-29 years.

Ninety eight urine samples from the study group showed significant culture as against 96 urine samples from the HbAA group, which gave ASB prevalence of 32.7% and 32.0% respectively. The observed difference was not statistically significant (odd ratio (OR) =1.03 [95% confidence interval (CI) 0.73, 1.45]).

Seven different types of bacteria were identified during the study; 4 (57.1%) out of these were isolated at varying proportions from both the HbAS and HbAA groups while the remaining 3 (42.9%) were isolated only from the urine samples from the control group [Table 1].

Table 1: Distribution of organisms isolated in the case and control groups

Organism	Positive culture (%)		*P* value	OR (95% CI)
	Cases (HbAS)	Control (HbAA)		
Escherichia coli	55 (56.1)	59 (61.4)	0.47	0.80 (0.45, 1.42)
Staphylococcus aureus	33 (33.7)	25 (26.0)	0.27	1.44 (0.78, 2.68)
Klebsiella	6 (6.1)	2 (2.1)	0.28	3.07 (0.60, 15.58)
Enterobacter	4 (4.1)	2 (2.1)	0.68	2.0 (0.36, 11.18)
Citrobacter	0 (0.0)	4 (4.2)	0.06	-
Streptoccocus faecalis	0 (0.0)	2 (2.1)	0.24	-
Salmonella	0 (0.0)	2 (2.1)	0.24	-
Total	98 (100.0)	96 (100.0)	-	-

HbAS=Sickle cell trait; HbAA=Hemoglobin AA

Furthermore, *Escherichia coli* was the most common organism isolated in both the HbAS group (56.1%, 55/98) and control group (61.4%, 59/96); but the difference was not significant (OR = 0.80 [95% CI 0.45, 1.42]). Details of the distribution of bacterial isolates in the two groups are shown in Table 1. The antibiotics with the highest microbial sensitivity were ciprofloxacin (90.8%, 89/98) and gentamicin (100.0%, 98/98) for HbAS and HbAA groups respectively. On the other hand, ampiclox (2.0%, 1/98) and amoxicillin (2.1%, 2/96) had the least microbial sensitivity for the study and control groups respectively. Details of the antibiotics' microbial sensitivity are shown in Tables 2 and 3.

When participants were stratified according to socio-economic class [Table 4], significant differences in the prevalence of ASB were observed between the HBAS group and the control group, in class 1 (28.2% vs. 55.2%, OR = 0.32 [95% CI 0.16, 0.64]); and class 4 (37.9% vs. 20.7%, OR = 2.34 [1.04, 5.24]). For the remaining social classes, the prevalence of ASB did not vary significantly between the two groups [Table 4].

Discussion

The modal age group of study participants was 25-29 years, which may suggest that it is the most reproductive age group for the pregnant women with HbAS in the study area. Previous reports on ASB in pregnancy noted wide variation of the prevalence ranging from 7% to 86.6%,[2,5,6,9,15-23] therefore, the prevalence of 32% found in this study may not be unexpected. The ASB prevalence in this study is lower than the findings from a related study by Thurman *et al.* in United States of America, which showed the prevalence of 47.5% and 46.9% among HbAS and HbAA respectively.[1] As in this study, the proportion of women with ASB was higher among the HbAS group when compared to the HbAA group, but the difference was not significant.[1] However, these two study findings did not support the

Table 2: Antibiotic sensitivity pattern of organism isolated from cases (HbAS)

Antibiotics	*Escherichia coli* (*n*=55)	*Staphylococcus aureus* (*n*=33)	*Klebsiella spp* (*n*=6)	*Enterobacter spp* (*n*=4)	Total isolatessensitive (*n*=98)	Percent sensitive (%)
Ciprofloxacin	54	28	6	4	92	93.9
Gentamicin	55	32	0	2	89	90.8
Chloramphenicol	42	0	6	2	50	51.0
Nitrofurantoin	28	4	0	0	32	32.7
Ofloxacin	8	24	0	0	32	32.7
Tetracycline	14	4	0	2	20	20.4
Cephalexin	8	10	0	0	18	18.4
Erythromycin	10	5	0	0	15	15.3
Cotrimoxazole	8	4	0	2	14	14.3
Ampicillin	2	0	6	4	12	12.2
Augmentin	0	8	0	0	8	8.2
Amoxycillin	0	6	0	0	6	6.1
Ceftriazone	0	6	0	0	6	6.1
Ampiclox	0	1	0	0	1	1.0

HbAS=Sickle cell trait, Key: "0"=Resistant organism

Table 3: Antibiotic sensitivity pattern of organism isolated from control (HbAA)

Antibiotics	*Escherichia coli* (*n*=59)	*Staphylococcus aureus* (*n*=25)	*Klebsiella spp* (*n*=2)	*Enterobacter spp* (*n*=2)	*Citrobacter spp.* (*n*=4)	*Streptococcus faecalis* (*n*=2)	*Salmonella* (*n*=2)	Total isolates sensitive (*n*=96)	Percentsensitive (%)
Gentamicin	59	25	2	2	4	2	2	96	100.0
Ciprofloxacin	52	22	2	2	4	2	2	86	89.6
Chloramphenicol	44	0	0	2	2	0	2	50	52.1
Nitrofurantoin	38	0	0	2	0	0	0	40	41.7
Ofloxacin	2	16	0	0	0	0	0	18	18.8
Cotrimoxazole	12	4	0	0	0	0	0	16	16.7
Cefuroxime	13	13	0	0	0	2	0	15	15.6
Erythromycin	2	12	0	0	0	0	0	14	14.6
Tetracycline	10	0	0	0	0	2	0	12	12.5
Cephalexin	2	10	0	0	0	0	0	12	12.5
Ampicillin	6	0	0	0	2	0	2	10	10.4
Augmentin	0	8	0	0	0	0	0	8	8.3
Amoxycillin	0	2	0	0	0	0	0	2	2.1

Key: "0"=Resistant organism, HbAA=Hemoglobin AA

Table 4: Distribution of participants by socioeconomic class

Social class	Cases (HbAS) (%)		Control (HbAA) (%)		*P* value	OR (95% CI)
	Frequency	Positive culture	Frequency	Positive culture		
1	85 (23.8)	24 (28.2)	58 (19.3)	32 (55.2)	0.002	0.32 (0.16, 0.64)
2	59 (19.7)	14 (23.7)	82 (27.3)	20 (24.4)	1.000	0.96 (0.44, 2.11)
3	80 (26.7)	31 (38.8)	88 (29.4)	28 (31.8)	0.419	1.36 (0.72, 2.56)
4	66 (22.0)	25 (37.9)	58 (19.3)	12 (20.7)	0.049	2.34 (1.04, 5.24)
5	10 (3.3)	4 (40.0)	14 (4.7)	4 (28.6)	0.673	1.67 (0.30, 9.27)
Total	300 (100.0)	98 (32.7)	300 (100.0)	96 (32.0)	0.861	1.03 (0.73, 1.45)

HbAS=Sickle cell trait; HbAA=Hemoglobin AA

report of a systematic review on hemoglobinopathy, which showed that the risk of bacteriuria was higher among pregnant women with hemoglobinopathies.[24] Furthermore, an earlier study had identified a lower ASB prevalence for the HbAS when compared with HbAA women (13.0% vs. 9.0%) and in this case, the observed difference was statistically significant.[25] This report was supported by a more recent study which showed that the prevalence of ASB among pregnant women with HbAS were significantly higher than that of HbAA women (13.9 vs. 10.8).[26] A critical review showed these two studies actually influenced the conclusion of the systematic review with respect to bacteriuria. Previous studies on ASB in pregnancy had shown a trend towards higher prevalence of ASB among women from lower socioeconomic classes;[8,15-18] this trend seemed to be the case among HbAS women in this study, but the pattern within the HbAA group was not definite. Furthermore, though this study showed that the prevalence of ASB did not vary between HbAS and HbAA women in general, appreciable differences seem to exist within the socio-economic classes [Table 4] for instance, within the socio-economic class one, pregnant women with ASB were about 3 times more likely to be HbAA when compared with HbAS women; conversely, women in class 4 who had ASB were about 2 times more likely to be HbAS than HbAA. Further studies are required to study the actual effect of socioeconomic status on ASB in pregnancy. Likewise, subsequent studies on the relationship between HbAS and ASB should control for socio-economic status. As expected, *E. coli* was the most common organism isolate from both study and control groups in this study. This finding is in keeping with the reports of previous studies on the subject,[1,5,8,17,18,20,21] except the study from Jos, Nigeria which recorded *Staphylococcus aureus* as the most common organism while *E. coli* was not isolated.[9] Furthermore, this study did not identify any statistical difference between the frequencies of *E. coli* isolated in both groups which is probably because *E. coli* is a fecal flora in human that also colonizes the periurethral area, thereby causing an ascending infection of the urinary tract.[27] In the decreasing order of frequency, the other organisms isolated from both groups included *S. aureus*, *Klebsiella* spp., and *Enterobacter.* Similar organisms and those of the same families were isolated in previous studies.[1,5,6,16,18,22] This study suggests that ASB in HbAS women were less likely to be due to *E. coli* when compared to ASB in HbAA women [Table 1]. On the other hand, the odds of ASB in HbAS women due to *S. aureus*, was higher than that of HbAA women, though the observed difference was not significant. The microorganism pattern observed in this study will help in the determination of effective antibiotics for ASB prophylaxis among pregnant women.

It is not clear why *Citrobacter, Streptococcus faecalis* and *Salmonella* spp. were isolated in the HbAA group only; a larger sample sized study may help confirm whether HbAS is protective against these organisms. Furthermore, bacteria isolated in both groups of this study were most sensitive to gentamicin and ciprofloxacin, but least sensitive to amoxycilin [Tables 3 and 4]. However, the observed sensitivity pattern in this study is at variance with the findings of earlier reports from the study area;[5,18] for instance, Ezeome *et al.* reported least microbial sensitivity to Ciprofloxacin among other drugs.[5] This change in pattern underscores the need for continuous monitoring of bacterial sensitivity pattern in our environment where antibiotics are procured freely over the counter. Unfortunately, the antibiotics to which the organisms isolated in this study were most sensitive to, fall into the category C of the United States Food and Drug Administration classification of antibiotics for the treatment of pregnant women with ASB.[28]

It is concluded that the prevalence of ASB among pregnant women in Enugu, Nigeria is high. Furthermore, pregnant women with HbAS do not have higher odds of developing ASB when compared to their counterparts with normal hemoglobin. Therefore, considering the known effects of ASB on pregnancy outcome, there is the need to initiate routine screening and treatment of ASB among pregnant women in the study area.

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