Asymptomatic group B streptococcal bacteriuria among pregnant women in Saudi Arabia

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ABSTRACT

This study aims to determine the asymptomatic bacteriuria in pregnancy due to GBS and its antimicrobial sensitivity pattern for planning strategy for the management of these cases and also to determine the relationship between asymptomatic bacteriuria and pyuria. A total of 3863 consecutive urine specimens were collected from 3863 pregnant women with asymptomatic bacteriuria attending the obstetrics and gynaecology department of our hospital over a period of two years. Specimens were processed using standard microbiological procedures. All the subjects were evaluated for bacteriuria. The prevalence of asymptomatic bacteriuria due to group B streptococci (GBS) was 82/3863 (2.1%) among pregnant women in Saudi Arabia. Among these, 69/82 patients (84.2%) had clinical and microbiological features consistent with cystitis, versus 13/82 (15.8%) for pyelonephritis. About 51.2% (42/82) of the patients who had urine analysis performed had positive results based on positive urinary leucocyte esterase and pyuria. Disc-diffusion analysis of all 82 GBS isolates showed that they were highly susceptible to Augmentin and linezolid. Screening for bacteriuria in pregnancy and proper treatment must be considered as an essential part of antenatal care in this community. To prevent asymptomatic bacteriuria complications, all pregnant women should be screened at the first antenatal visit. A negative test for pyuria is not a reliable indicator of the absence of asymptomatic bacteriuria in pregnant women. Further, ongoing surveillance and evaluation of outcomes in pregnancies complicated by GBS bacteriuria is required to optimise maternal and newborn care.

Key words: Antenatal care.
Asymptomatic bacteriuria.
Group B Streptococcus.
Pregnancy.
Pyuria.

Introduction

Urinary tract infections (UTIs) are frequently encountered in the family physician's office. In pregnant women, the incidence of UTI can be as high as 8%.[1,2] Urinary tract infection is the commonest of all bacterial infections, affecting human beings throughout their life span especially in women.[3] Nearly 50% of all women develop symptoms of urinary tract infection at some stage during their life. Urinary tract infection account for more than 7 million visits to physicians and necessitate over 1 million hospital admissions in the USA annually.[3] The urinary tract undergoes profound physiological and anatomical changes during pregnancy facilitating the development of bacteriuria both symptomatic and asymptomatic in women.[4] Symptomatic bacteriuria is the tip of an iceberg of total bacteriuria. Pregnancy is a provocation for the asymptomatic to become symptomatic.[5] About 10% of those with asymptomatic bacteriuria (ABU) develop symptomatic bacteriuria during pregnancy.[6] Symptomatic bacteriuria is easily diagnosed and treated due to its overt symptoms. But asymptomatic bacteriuria is difficult to diagnose and it is more common in pregnant women than non-pregnant women.[7] In pregnancy, 30-40% of untreated pregnant women with asymptomatic bacteriuria develop acute pyelonephritis in late pregnancy.[8,9] Pyelonephritis is associated with significant morbidity during pregnancy for the mother and the fetus. Thus, accurate screening and treatment of bacteriuria regardless of symptoms is important in order to avoid further complications.[10] Anatomic and physiologic changes that occur during the pregnancy increase the risk of pyelonephritis in this period.[10]

Group B *Streptococcus* (GBS) colonisation of the urinary tract in women most likely occurs by an ascending route from the vagina, where GBS can persist asymptomatically. While the overall prevalence of GBS UTI in the adult population remains unclear, GBS bacteriuria during pregnancy occurs at rates of between 1 and 3.5%.[11–13] Many of these episodes represent ABU;[14,15] however, GBS ABU is considered to be a surrogate for heavy maternal colonisation[16,17] and is currently recommended for intrapartum antibiotic chemoprophylaxis.[12,18] In addition, up to 7% of pregnancies may be complicated by GBS UTI, and GBS reportedly accounts for approximately 10% of all cases of pyelonephritis during pregnancy.[19,20]

In pregnancy GBS colonisation causes asymptomatic bacteriuria or UTI. It is a well known cause of puerperal infections with amnionitis, endometritis and sepsis being the most commonly reported infections.[21] Pregnant women who are GBS carriers have the potential to transmit the organism to their newborn infants. There is a spectrum of maternal and fetal GBS infections ranging from asymptomatic colonisation to sepsis. GBS has been implicated in adverse pregnancy outcomes, including premature rupture of membranes (PROM), preterm labour and clinical and subclinical

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chorioamnionitis.[22] GBS is a leading cause of morbidity and mortality among newborns. Universal screening for GBS among women at 35–37 weeks of gestation is more effective than administration of intrapartum antibiotics based on risk factors. Studies indicate that intrapartum prophylaxis of GBS carriers and selective administration of antibiotics to newborns reduce neonatal GBS sepsis by as much as 80-95%.[23]

Women with GBS colonisation are at an increased risk of GBS colonisation in a subsequent pregnancy. Prior GBS colonization should be considered in the algorithm to treat unknown GBS status during term labour.[24] Investigators tried to find out/identify risk factors that may influence the prevalence of GBS, like ethnicity, smoking, maternal age and number of partners. The colonisation rates are incoherent enough to target only high-risk women and may not be an effective strategy.[22,25]

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The Centers for Disease Control and Prevention (CDC) call for antibiotic prophylaxis in women with asymptomatic first trimester bacteriuria because this is a marker for heavy genital tract colonisation, and screening all other women at 35–37 weeks for vaginal and rectal colonisation.[18]

The present study was undertaken to determine the asymptomatic bacteriuria in pregnancy due to GBS and antimicrobial sensitivity pattern for planning strategy for the management of these cases and also to determine the relationship between asymptomatic bacteriuria and pyuria. To the best of knowledge, this reports first study conducted in Saudi Arabia.

Materials and methods

The study was conducted over a period of 2 years on a total of 3863 asymptomatic pregnant females at their first visit in first or second trimester of pregnancy. Informed consent was taken and the pregnant females were counseled regarding the method of collection of clean catch mid stream urine sample. All MSU specimens were submitted for culture upon medical request from the caring gynaecologists. Standard microbiological techniques were used in the culture of all MSU specimens and in the identification of the isolates.[26]

Urine collection

All study subjects were instructed individually about the technique for collecting clean voided midstream urine specimens (posters in the collection areas reinforce the method). Specimens were collected in a sterile wide-mouth screw-capped container with aseptic precautions. The subjects were asked to use the clean-catch method. The samples were immediately transferred to the microbiology laboratory and processed within 1–2 h of collection in the laboratory.

Urine culture

Standard microbiological techniques were used in the culture of all MSU specimens and in the identification of the isolates. They were subjected to semiquantitative culture method. A standard calibrated platinum wire loop delivering 0.001 mL uncentrifuged urine was used to inoculate cysteine lactose electrolyte deficient (CLED) media and sheep blood agar (SBA) plates containing 6% blood. These plates were incubated aerobically at 35-37°C for 18-24 hours.[27] Prolonged incubation was continued for further 24 h if no growth was obtained. The plates were read at the end of the incubation period. The criteria for considering a culture as having a 'significant growth' was the growth of more than 100 colony forming units (cfu) of pure growth/ 1 mL MSU inoculum on the plates corresponding to a colony count of more than 10^5 cfu/mL.[27] Specimens yielding pure growth of GBS only were included in the study.

Urine analysis

Wet preparations were made from centrifuged samples (2000 x*g* for 5 min) and casts, leucocytes and erythrocytes per high power field were reported. A rapid dipstick (Combur 10 test, Boehringer Manheim, Diagnostics and Biochemicals, East Sussex, United Kingdom) was also used to detect pyuria via leucocyte esterase activity.[28]

Antibiotic sensitivity testing

Antibiotic sensitivity testing was performed using the disc-diffusion method on 85-mm sheep blood agar (Oxoid) plates with agar depth of 4 mm. The bacterial suspension prepared for antibiotic sensitivity testing on sheep blood agar was adjusted to the recommended turbidity.[29] The antibiotics tested on each disc were penicillin (10 units), ampicillin (25 μg), trimethoprim-sulphamethoxazole (1.25/23.75 μg), cephalexin (30 μg), amoxicillin-clavulanic acid (20/10 μg), erythromycin (15 μg), clindamycin (2 μg), nitrofurantoin (300 μg), linezolid (30 μg), tetracycline (30 μg) and vancomycin (30 μg). The Clinical Laboratory Standards Institute (CLSI) breakpoints were used for interpretation of susceptibility patterns as sensitive or resistant.[30]

Results

Of 3863 patients, a total of 82 (2.1%) had single-organism GBS bacteriuria with 10^5 cfu/mL concurrent with at least one UTI symptom and were defined as having probable GBS UTI. Among these, 69/82 patients (84.2%) had clinical and microbiological features consistent with cystitis, versus 13/82 (15.8%) for pyelonephritis. None of the 82 cases were associated with an indwelling urinary catheter.

Age distribution

The mean age of the subjects culture-positive for GBS was 46.2±16.8 years. The highest prevalence was recorded in the 46–55 (23.2%) and 15–25 (19.5%) age groups.

Urinalysis

Forty-two (51.2%) patients who had urine analysis performed had positive results based on positive urinary leucocyte esterase and pyuria. The mean WBC reported by UA of the patients positive for GBS was 6.6±10.2 (range 0–50). Most of the study subjects (32 cases, 76.2%) had a low WBC count.

Antibiotic susceptibility report

Disc-diffusion analysis of all 82 GBS isolates showed that they were uniformly susceptible to amoxicillin with clavulanic acid, linezolid and nitrofurantoin. All isolates

Table 1. Antimicrobial susceptibility pattern of positive group B *Streptococcus* isolates from urine cultures.

Antibiotic	Susceptibility	Resistance
Penicillin	40 (48.8%)	42 (51.2%)
Ampicillin	38 (46.3%)	44 (53.7%)
Co-amoxiclav (Augmentin)	80 (97.6%)	2 (2.4%)
Nitrofurantoin	62 (75.6%)	20 (24.4%)
Cephalexin	22 (26.8%)	60 (73.2%)
Co-trimoxazole	13 (15.9%)	69 (84.1%)
Erythromycin	30 (36.6%)	52 (63.4%)
Linezolid	77 (93.9%)	5 (06.1%)
Tetracycline	18 (22.0%)	64 (78.0%)
Clindamycin	31 (37.8%)	51 (62.2%)
Vancomycin	82 (100%)	0

were sensitive to vncomycin (Table 1). A considerable proportion of isolates were resistant to co-trimoxazole (69/82 [84.1%]), tetracycline (64/82 [78.0%]), cephalexin (60/82 [73.2%]), penicillin (42/82[51.2%], ampicillin (44/82 [53.7%]), erythromycin (52/82 [63.4%]) and clindamycin (51/82 [62.2%]).

Discussion

Urinary tract infections are remarkably common in women. Some 20% women in the age range 20–65 years suffer from at least one attack per year, and 50% develop a urinary tract infection within their life time.[31] Not surprisingly, infections of the urinary tract are the most common bacterial infections encountered during pregnancy. These can be both symptomatic and asymptomatic. Asymptomatic bacteriuria during pregnancy is a common and important medical condition, which will result in overt renal infections such as pyelonephirits if not detected and treated.[32] Smaill[33] showed that on average treating seven pregnant women with asymptomatic bacteriuria results in prevention of one episode of pyelonephirits. Ten percent of pregnant women attended in an antenatal clinic had symptomatic urinary tract infections.[5] In another study by Khatun *et al.*,[7] it was found that 30% of clinically healthy pregnant women had asymptomatic bacteriuria.

Group B streptococci continue to be major perinatal pathogens, both for mothers and their infants, and are associated with significant morbidity and mortality, and their attendant cost to society as life-threatening emergency and any delay in treatment may cause death. Early diagnosis and proper management of GBS among pregnant women can bring down the morbidity and mortality substantially. Perinatal infections are one of the fundamental causes of early puerperal complications in mothers and neonates. While different preventive strategies to identify women at risk are being recommended, the optimal strategy depends on the incidence of GBS sepsis and on the prevalence of anogenital GBS colonisation.[34,35]

The uropathogenic potential of GBS prompted the current study to define the clinical and the microbiological features of GBS ABU. Among 3863 patients, 82 showed the pure growth of GBS as a single organism. Thus the prevalence of asymptomatic bacteriuria due to GBS in this study was found to be 2.1%, which agrees with others.[11–13] Findings of the present community-based study indicate that the asymptomatic bacteriuria due to GBS in pregnancy is a major health problem in Saudi Arabia.

The findings of this study indicate that Augmentin and linezolid are highly effective against GBS. This is in agreement with others.[36] It may be due to less use of Augmentin for UTI and linezolid being comparatively a newer introduction and also costly. Another useful oral antibiotic was nitrofurantoin. All the isolates showed 100% sensitivity to vancomycin, which was similar to that reported by others.[37] The organisms showed resistance to currently preferred urinary antibiotics and chemotherapeutic agents such as co-trimoxazole and cephalexin, which is in agreement with other studies.[36,37] Tetracycline was found to be highly resistant, as reported by others.[36,37]

A high rate of resistance to macrolides was observed in this study. These findings are consistent with a recent survey of GBS in the United States where Manning *et al.* demonstrated higher-than-expected frequencies of macrolide resistance among GBS in non-pregnant women.[38] Trends of increasing antibiotic resistance may reflect clonal dissemination and horizontal transfer of resistance genes among GBS, which occurs among certain GBS serotypes.[39]

About 50% of the isolates studied showed resistance to penicillin and ampicillin. Although, penicillin G is the treatment of choice for the prophylaxis and treatment of GBS infection, strains with reduced penicillin susceptibility (GBSRPS; minimum inhibitory concentration [MIC] 0.25–1 μg/mL) have been reported periodically in Japan, the United States and elsewhere since 1994 and are caused mainly by stepwise accumulation of mutations in PBP1a, PBP2b and PBP2x.[40–50] This indicates that urinary pathogens became resistant day by day to the commonly used antibiotics in our country. This may be due to widespread and indiscriminate use of the drugs.

Many studies[31,51–53] have linked pregnancy complications such as hypertensive disorders, low birth weight, premature with symptomatic bacteriuria. Moreover, for the last two decades, asymptomatic bacteriuria has also been identified as a risk factor of similar pregnancy complications.[31] The results of the present study agree with these findings. The association between asymptomatic bacteriuria and prematurity is established,[8,9,54] but the mechanism is not well defined. Several investigators have observed a high incidence of pyelonephritis in bacteriuric pregnant mothers.[8,9] This study also found that asymptomatic bacteriuria was associated with lower maternal age. The prevalence of asymptomatic bacteriuria was reported to be as high as 21% in a study from Ibadan City, Nigeria,[10] and 86.6% in another study from Benin City, Nigeria.[18] Significant pyuria with bacteriuria was found only in 51% of patients in the current study. So the presence of significant pyuria should not be used as a screening test for asymptomatic bacteriuria in pregnancy.

Using this method for screening of asymptomatic bacteriuria would have obtained a false-negative rate of ~50%. This is consistent with the results of other studies. Two studies found that there was only 50% significant pyuria with positive cultures.[10,55] It is recommended that all

samples should be sent for culture because none of the rapid tests, including the screen for pyuria, are reliable for detecting asymptomatic bacteriuria in pregnant women.[10,55–57] Wadland and colleagues[58] showed that screening for asymptomatic bacteriuria is cost-saving unless the prevalence of asymptomatic bacteriuria falls below 2%, the risk of pyelonephritis with asymptomatic bacteriuria falls below 13%, or the efficacy of treatment in preventing pyelonephritis falls below 38%. Thus, in this region, this intervention remains cost-saving. Finally, in accordance with Stenqvist and colleagues,[59] the author chose 18 weeks' gestation as the optimal time to perform the screening culture in order to maximise the chances of detecting bacteriuria. However, in North America the current approach is to screen for asymptomatic bacteriuria at 12 weeks of gestation.[60]

In conclusion, screening for bacteriuria in pregnancy and proper treatment must be considered as an essential part of antenatal care in this community. A negative test for pyuria is not a reliable indicator of the absence of asymptomatic bacteriuria in pregnant women. Thus, all urine specimens, regardless of leucocyte count, should be sent for culture and sensitivity. Available studies are limited by inconsistencies in the definition of asymptomatic bacteriuria and maternal and perinatal outcomes, regional variation in the prevalence of group B *Streptococcus*, incomplete information on follow-up, and adjustment of risk factors. Therefore, ongoing surveillance and evaluation of outcomes in pregnancies complicated by GBS bacteriuria is required to optimise maternal and newborn care. □

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