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PREVALENCE OF ASYMPTOMATIC BACTERIURIA IN PREGNANCY

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ABSTRACT

Asymptomatic bacteriuria is a common infection. Pregnant women with asymptomatic bacteriuria are at an increased risk for adverse maternal and fetal outcomes which could be prevented by antimicrobial therapy. Screening for asymptomatic bacteriuria is a standard of obstetrical care and is included in most antenatal guidelines. There is good evidence that treatment of asymptomatic bacteriuria will decrease the incidence of pyelonephritis. All pregnant women should be screened for asymptomatic bacteriuria, and there are no new data that would indicate otherwise. Antibiotic treatment of asymptomatic bacteriuria is associated with a decrease in the incidence of preterm delivery or low birth weight, but the methodological quality of the studies means any conclusion about the strength of this association needs to be drawn cautiously. A better understanding of the mechanism by which the treatment of asymptomatic bacteriuria could prevent preterm delivery is needed.

KEYWORDS: Asymptomatic bacteriuria, pregnancy.

INTRODUCTION

Asymptomatic bacteriuria (ASB) is defined as the presence of bacteria in urine without having signs and symptoms. This condition affects all groups, but women, particularly pregnant women, are more susceptible than men because of a short urethra and easy contamination of the track with fecal flora Asymptomatic bacteriuria (ASB) is defined as two consecutive voided urine specimens or one properly collected specimen of urine from pregnant women any signs and symptoms of urinary tract infection with isolation of the same bacterial strain in quantitative counts of 10^5 CFU/mL.[1]

ASB during pregnancy relates to the physiologic and anatomic changes in the urinary tract. The prevalence of ABS in pregnant women is estimated to be approximately 1.9–15%.[2] Pregnant women with ASB are at an increased risk for severe outcomes so that without antibiotic therapy, approximately 30% of pregnant women affected by symptomatic bacteriuria may have complications such as preterm delivery and low birth weight infants. In addition, the risk of developing pyelonephritis during pregnancy is approximately 20–30 fold higher than that in women without bacteriuria. Treatment of asymptomatic bacteriuria during pregnancy decreases the risk of subsequent complications.[3]

Therefore, screening of pregnant women is necessary for early diagnosis and treatment of ASB and subsequent prevention of its complications. Until now, several studies estimated the prevalence of asymptomatic bacteriuria among pregnant women in different regions. However, there is controversy in the results of the conducted studies. The aim of this meta-analysis was to estimate the overall prevalence of asymptomatic bacteriuria among Iraqi pregnant women.[4]

Asymptomatic bacteriuria in pregnancy is defined as the presence of ≥ 1,00,000 organisms per milliliter (ml) of urine taken from a clean catch mid-stream urine specimen with no symptoms referable to the genito-urinary tract However ASB often is the primary cause of complications such as pyelonephritis, preterm labor, low birth weight fetus, maternal Sepsis, anemia, and prenatal death.[5]

Treatment of ASB has been shown to reduce the rate of pyelonephritis in the later part of pregnancy and therefore regular screening for appropriate treatment of ABU has become a standard of obstetrical care. Urinary Tract Infections (UTI) is the microbial invasion and subsequent multiplication on part or entire urinary tract.[6]

Pregnancy causes numerous changes in the physiology of a woman's system. Various anatomic and physiological changes which include dilatation of the renal pelvis and ureters in as early as the eighth week of pregnancy.[7] and displacement of the bladder itself superiorly and anteriorly are responsible for ASB. Also, smooth muscle relaxation induced by progesterone may also play a role. As a consequence of smooth muscle relaxation peristalsis of the ureters is decreased, bladder capacity is increased which in turn lead to urinary stasis.[8]

Henceforth, screening and treatment of ASB prerequisite to being incorporated as routine antenatal care for an integrated approach to safe motherhood and newborn health. Bacteriuria occurs commonly in pregnancy, typically during early pregnancy. Without treatment, as many as 30 to 40 percents of pregnant women with asymptomatic bacteriuria will develop symptomatic urinary tract infection (UTI). The smooth muscle relaxation and subsequent ureteral dilatation that occurs in pregnancy are thought to facilitate the ascent of bacteria from the bladder to the kidney, accounting for the greater risk of pyelonephritis. Additionally, untreated bacteriuria may be associated with an increased risk of preterm birth, low birth weight, and perinatal mortality.[9]

Background

Urinary tract infection (UTI) is one of the most common diseases encountered in clinical practice today. Urinary tract infection is not only common but the range of clinical effects varies from asymptomatic bacteriuria to acute pyelonephritis.[10] Urinary tract infection is common of all bacterial infections, affecting human beings throughout their life span especially in women.[11] Nearly 50% of all women develop symptoms of urinary tract infection at some stage during their life. The urinary tract undergoes profound physiological and anatomical changes during pregnancy facilitating the development of bacteriuria both symptomatic and asymptomatic in women. Symptomatic bacteriuria is an iceberg of total bacteriuria. Pregnancy is a provocation for the asymptomatic to become symptomatic.[12] About 10% 0f those with asymptomatic bacteriuria develop symptomatic bacteriuria during pregnancy.[13] Symptomatic bacteriuria poses no problems because it is easy in diagnosis and treatment due to its overt symptoms but asymptomatic bacteriuria is difficult to diagnose and it is more common in pregnant women than nonpregnant women 9. Asymptomatic bacteriuria is especially important in pregnancy because 30-40% of untreated pregnant women with asymptomatic bacteriuria develop acute pyelonephritis at late pregnancy.[14]

Also, there is evidence that when there is no symptom, untreated bacteriuria in pregnancy may lead to less favorable pregnancy outcomes and complications like preterm delivery, low birth weight, pre-eclampsia and anemia of pregnancy. Prematurity is one of the leading causes of perinatal mortality. Uterine contractions may be induced by cytokines and prostaglandins, which are released by microorganisms.[15]

Very little is known about possible biological mechanisms of preterm labor in women with asymptomatic bacteriuria, but a few studies on this subject have been published. However,

despite the fact that the synthesis of both estrogen and progesterone is known to increase throughout pregnancy, the incidence of bacteriuria does not increase as the pregnancy approaches term. Thus, any mechanical changes associated with estrogen do not appear to be responsible for asymptomatic bacteriuria in pregnancy. Kass reported that severe uterine contractions occur within moments after endotoxin injection in an animal model, thus linking bacteriuria with early delivery.[16]

Asymptomatic bacteriuria defines as true bacteriuria in the absence of symptoms of acute urinary tract infection (UTI), complicates 2–10% of pregnancies. During pregnancy, asymptomatic bacteriuria is not considered benign, because pregnancy induces stasis and accordingly increases the risk for pyelonephritis.[17]

Controversy exists regarding the association between asymptomatic bacteriuria during pregnancy and adverse perinatal outcome, including preterm deliveries and low-birthweight (LBW). However, a meta-analysis of cohort studies showed that untreated asymptomatic bacteriuria during pregnancy significantly increased rates of LBW and preterm delivery.[18] Moreover, analysis of randomized clinical trials showed that antibiotic treatment significantly reduced the risk of LBW (relative risk RR ¼ 0.56; 95% confidence interval CI 0.43, 0.73).[19]

Accordingly, screening for and treatment of asymptomatic bacteriuria during pregnancy has become a standard of care.[20]

The present population-based study was aimed to test the association between asymptomatic bacteriuria during pregnancy, among patients in whom antibiotic treatment was recommended, and perinatal outcomes. Our study was also aimed to characterize common bacteria and risk factors associated with asymptomatic bacteriuria during pregnancy.

Profound physiologic and anatomic changes in the urinary tract during pregnancy contribute to the increased risk for infection. Asymptomatic bacteriuria (ASB) is defined as a pure culture of at least 105 organisms/ml of urine in the absence of symptoms1. It is the most common bacterial infection requiring medical treatment in pregnancy. A prevalence of 2 -10 percent has been reported.[21]

The relationship between asymptomatic bacteriuria in pregnancy with symptomatic urinary-tract infections and adverse pregnancy outcomes was first suggested by Kass in 1959, with the publication of his original randomized placebo-controlled trial showing that treatment of

bacteriuric pregnant women prevented pyelonephritis and avoided up to 20% of preterm deliveries.1 Other studies quickly followed, and it became generally accepted that detecting asymptomatic bacteriuria in pregnancy was important and that symptomatic urinary-tract infection could be prevented with treatment. Screening for asymptomatic bacteriuria became standard obstetric care, and most antenatal guidelines today include routine screening for asymptomatic bacteriuria.[22]

Bacteriuria is the presence of bacteria in the urine. Bacteriuria is said to be significant in the presence of 105 colony forming units (CFU)/mL. One issue with bacteriuria is that it does not always present with symptoms. Occult infection occurs in approximately 2e7% of pregnancies, and 30e40% of cases develop acute pyelonephritis later into their pregnancy.[23]

Additionally, there are associations between maternal pregnancy complications and pyelonephritis, including hypertension, preeclampsia, anemia, amnionitis, and endometritis.[24] Pyelonephritis can lead to renal scarring, hypertension and renal failure in the long term.4 In pregnancy, pyelonephritis increases the risk of preterm labor and delivery, which results in premature delivery and low birth weight (LBW) with high perinatal morbidity and mortality.[25]

Another study showed that asymptomatic bacteriuria (ASB) is independently associated with preterm delivery, hypertensive disorders, recurrent abortions, intrauterine growth restriction (IUGR), polyhydramnios and oligohydramnios, premature rupturing of membranes, and labor induction.[26]

Many screening tests are available for the diagnosis of bacteriuria. An ideal test requires only limited technical expertise, is cheap and has high accuracy, enabling a quick diagnosis in high-risk patients. Although urine cultures are expensive, require laboratory expertise and take 24-48 hours for results to become available, quantitative culture remains the gold standard for diagnosis of urinary tract infection in pregnancy because it has high sensitivity and negative predictive value in this population, and the performance of rapid urine screening tests in pregnancy is poor.[27] The biochemical reagent strip test (dipstick test) operates by detection of a leucocyte esterase (LE) and a nitrate reductase (NR) activity. These tests have poor negative predictive values to detect bacteriuria in asymptomatic persons.[28] Disparities in urine collection and analysis, and patient selection may influence the presence of microorganisms which can be detected by the dipstick, as well as the presence of substances

that may give false results.[29] The dipstick test for NR had its highest accuracy and lowest sensitivity in pregnant women.[30]

The sensitivity of the urine dipstick test for leukocyte-esterase was slightly higher than for the dipstick test for NR, while the specificity was slightly lower[31], and combining the results of both parts of the dipstick tests should logically increase sensitivity. Though the presence of nitrite is highly specific for bacteria, several uropathogens do not reduce nitrate to nitrite, and therefore its utility is restricted to Enterobacteriaceae which reduce nitrate to nitrite and give a positive test result.[32]

This study focuses on the prevalence of ASB in pregnant women attending the antenatal clinic of the University of Port Harcourt Teaching Hospital, identification of the uropathogens involved and their antimicrobial sensitivity patterns, and to evaluate the diagnostic efficacy of urinalysis in screening for ASB among pregnant women.[33]

SIGNIFICANCE OF BACTERIURIA IN PREGNANCY

There is good evidence that screening for and treatment of asymptomatic bacteriuria will decrease the incidence of pyelonephritis. Combining data from more than 20 of the early descriptive studies from the 1960s, Whalley showed that symptomatic urinary-tract infections occurred in 30% of patients if asymptomatic bacteriuria was untreated, compared with 1.8% of non-bacteriuric controls.[34] Cohort studies have confirmed that the incidence of pyelonephritis is low with routine prenatal screening for asymptomatic bacteriuria compared to historical control groups.[35]

In the most recent prospective longitudinal study over a 2-year period from 2000 to 2001, the incidence of hospitalization for acute pyelonephritis was 1.4%, less than the 3–4% rate reported in the early 1970s before screening for asymptomatic bacteriuria became routine.[36] A meta-analysis of 13 randomized or quasi-randomized controlled trials of antibiotic treatment versus no treatment for pregnant women with asymptomatic bacteriuria found that treatment substantially decreased the risk of the development of pyelonephritis (odds ratio (OR) 0.24, 95% confidence interval (CI) 0.19, 0.32).[37] The methodological quality of the studies included was, however, weak, and no study adequately addressed selection bias. In less than half of the studies was the control group given a placebo, and performance and detection biases were not satisfactorily handled. The results, however, were highly consistent among studies, and the reduction in the incidence of pyelonephritis was dramatic. It was

estimated that the number of women needed to treat to prevent one episode of pyelonephritis was seven (CI 6, 9) and treatment of asymptomatic bacteriuria would lead to approximately a 75% reduction in pyelonephritis. Although an association between asymptomatic bacteriuria and preterm delivery has been consistently shown, the interpretation of this finding remains controversial compared with the widely accepted relationship between asymptomatic bacteriuria and pyelonephritis. Findings from the Cardiff Birth Survey, which prospectively studied 25,844 births, reported that asymptomatic bacteriuria, adjusted for demographic and social factors, was not associated with preterm delivery (OR 1.2, 95% CI 0.9, 1.5).[38]

METHODS

This study included 300 pregnant women who attended the antenatal clinic at the Department of Obstetrics and Gynaecology in al dark hospital. Specimens were processed at the Central Laboratory of Microbiology.

The samples were collected from asymptomatic pregnant females with a gestation period of 28 weeks or less. Prior to sample collection, socio-demographic and clinical data were collected by face-to-face administration of structured questionnaires. Pregnant women with a history of UTI symptoms (e.g., dysuria, frequency, and urgency, etc), pregnancy-induced diabetes mellitus/hypertension, a history of antibiotic therapy taken within two weeks prior to the study, pyrexia of unknown origin and known congenital anomalies of the urinary tract were excluded from this study.

RESULTS AND DISCUSSION

The result of this study found that the prevalence of ASB among pregnant women with preterm labor in Iraq was high (32.1%).

Table 1: Causative agents of bacteriuria in rural pregnant mothers.

	N
Escherichia coli	**169**
Staphylococcus and Saprophytic	**98**
Klebsiella	**11**
Proteus	**22**

Table 2: Comparison of the proportions of adverse outcomes among the asymptomatic bacteriuric and healthy mothers during pregnancy.

Adverse outcome	Asymptomatic bacteriuric Mothers N	Healthy Mothers	P value
Symptomatic bacteriuria	**33,6**	**4,6**	**0,001**
Hypertensive disorders in pregnancy (HDP)a	**13,6**	**7,6**	**0,020**
Premature delivery	**31,3**	**13,8**	**0,0034**
Premature delivery	**17,7**	**11,2**	**0,08**

Asymptomatic bacteriuria (ASB) in pregnant women is an important causative factor of premature birth, low birth weight, postpartum UTIs and higher fetal mortality rates. Women with bacteriuria have a 20e50-fold increased risk of developing pyelonephritis compared to women who do not have bacteriuria.[39] Women who have positive urine cultures should be treated based on the antimicrobial sensitivity patterns of the bacteria isolated from their samples to prevent maternal and fetal morbidities.

In this study, the prevalence of asymptomatic bacteriuria was 23.34%, which was similar to that observed by a study in Chitwan, Nepal conducted by Neupane et al., (26%) and that observed by a study in Cameroon conducted by Mokube M.N. et al. (23.5%).[40]

These varying results may have been due to differences in the areas being studied, in the social habits of the communities being studied and in the socio-economic statuses, standards of personal hygiene and education levels of the patients being studied. The current study that the 21e30-year-old age group had the highest prevalence of infection (64.04%), followed by the 31e40-year-old age group (22.71%) and these results were similar to those of a study conducted in India by Sujatha R. et al.[41] Alghalibi et al.,[42] reported a higher prevalence of UTIs in pregnant women who were 21e25 years of age and Turpin et al.,[43] reported a higher prevalence of ASB in pregnant women who were 35e39 years of age. Advanced maternal age (of above 35years) was reported as a risk factor for asymptomatic bacteriuria.19 The observed trend of bacteriuria in pregnant women in this study and other studies showed that the 21e 40-year-old age group is a high-risk group for the development of UTIs during pregnancy.

The bacteria which are responsible for asymptomatic bacteriuria are of fecal origin and colonize the periurethral area. The predominant bacterial isolates observed in this study were

E. coli (61.51%), followed by K. pneumonia (17.03%) and P. aeruginosa (7.57%). The predominance of E. coli was reported previously by Chandel et al.[44] I made et al.,1 and Sujatha R. et al.,[45] K. pneumonia was found to be the second most prevalent pathogen in this study, and this result is in agreement with those of studies recently conducted, However, Muharram S. H. et al reported a higher incidence of K. pneumonia than was observed in this study.[46]

Asymptomatic bacteriuria is generally defined as true bacteriuria in the absence of symptoms of acute urinary tract infection, although many women found to have asymptomatic bacteriuria may report experiencing occasional episodes of dysuria, urgency, and frequency retrospectively.[47] A semi-quantitative urine culture increases the probability of differentiating contamination from true bacteriuria.

Urinary tract infections are remarkably common in women. Some 20% of women in the age range 20-65 years suffer from at least one attack per year, 50% develop a urinary tract infection within their lifetime.[48] Not surprisingly infections of the urinary tract are the most common bacterial infections encountered during pregnancy. These can be both symptomatic and asymptomatic. Ten percent of pregnant women attended in an antenatal clinic had symptomatic urinary tract infections4. In another study by Khatun et al.[49], it was found that 30% of clinically healthy pregnant women had asymptomatic bacteriuria. Findings of the present community-based study indicate that the bacteriuria in pregnancy both symptomatic and asymptomatic is also a major health problem in rural Rajshahi. Observed from this study that E. Coli was the commonest pathogen responsible for bacteriuria. It is consistent with the findings of Rahman et al.[50] and Ahmed et al.[51] The findings of the study show that staphylococcus Saphrophyticus, which was formerly believed to be normal commensal, was recognized as the second most common pathogen accounting overall 19.5% of bacteriuria in this rural community. It corresponds with the findings of Ahmed et al.[52] Like the other studies 10, 13, the findings of the study also indicate that ciprofloxacin is highly effective to the urinary pathogens. It may be due to less use of Ciprofloxacin in the rural community since it is comparatively a newer introduction and also costly.

Rahman et al.[53] in their study observed that urinary pathogens at very high percentage ranging 75 to 100% were sensitive to cephalexin, nitrofurantoin and nalidixic and ranging from 50 to 100% were sensitive to co-trimoxazole in non-diabetic patients. The findings of

this study did not consistent with the findings of Rahman et al. This fact 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. There are many studies[54] that link so many pregnancy complications like hypertensive disorders in pregnancy, 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.[55] The results of the present study also agree with these findings. The association between asymptomatic bacteriuria and pregnancy complication especially prematurity is out of the question, it is now established the fact.[56]

But the mechanism is not well defined to the researchers. Several investigators have observed a high incidence of pyelonephritis in bacteriuric pregnant mothers.[57] It is convincing that the effect of urinary tract infection on premature labor could be indirectly mediated by antenatal maternal HDP. It is also plausible that urinary tract infection affects premature labor directly, through the development of communities. It has been previously suggested that bacterial infection of the amniotic fluid is a risk factor for premature delivery.[58] Another hypothesis contends that bacterial enzymes such as collagenase may weaken the fetal membranes and predispose them to premature rupture.[59] The results of the present study support the first one because the association between asymptomatic bacteriuria and premature labor became insignificant when the mothers with HDP and their pairs were excluded from the analysis.[60]

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