WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.074
Volume 8, Issue 4, 131-142. Research Article ISSN 2277– 7105

# PREVALENCE OF ASYMPTOMATIC BACTERIURIA IN ANTENATAL WOMEN WITH PRETERM LABOR

**Batol Tami Homdy* and Nidaa Shakir Abdullah**

Ministry of Health - Baghdad Medical office - Al-Karkh, Al Karama Educational Hospital, Baghdad, Iraq.

Article Received on
21 Jan. 2019,

Revised on 11 Feb. 2019,
Accepted on 04 March 2019

DOI: 10.20959/wjpr20194-14447

***Corresponding Author**
**Batol Tami Homdy**
Ministry of Health - Baghdad Medical office - Al-Karkh, Al Karama Educational Hospital, Baghdad, Iraq.

## ABSTRACT

In conclusion, the present study showed a high occurrence of ASB in pregnant women. It also demonstrated that if the disease was detected late in pregnancy it might lead to various maternal and neonatal complications like PET, PTL, PPROM, IUGR and LBW despite treatment of infection. All the sequelae of ASB during pregnancy could be reduced by antimicrobial treatment early in pregnancy. Hence, screening and treatment of ASB need to be incorporated as routine antenatal care for an integrated approach to safe motherhood and newborn health.

**KEYWORDS:** Asymptomatic Bacteriuria, Antenatal Women.

## INTRODUCTION

Urinary tract infections are a common health problem among women compared with men due to a short urethra, vaginal proximity, and facilitated entry of pathogens by sexual activity[1].

Pregnant women are more susceptible to symptomatic and asymptomatic urinary tract infection due to their anatomical and physiological status and increased sex hormones during pregnancy. Asymptomatic bacteriuria refers to the presence of more than 100,000 colony-forming units (CFU) of a type of pathogen per mL of urine in two successive samples from the middle of the urine flow or a catheterized specimen.

About 30% of untreated women with asymptomatic bacteriuria are prone to pyelonephritis during pregnancy, where the systemic febrile infections of the mother, including pyelonephritis, are associated with preterm labor and low birth weight.

Asymptomatic bacteriuria in pregnancy may lead to hypertension, preeclampsia, intra uterine growth restriction, low birth weight, postpartum endometritis, septicemia, and maternal death[2]. With early screening during pregnancy, a relatively high prevalence of urinary tract infection, especially asymptomatic bacteriuria, can be prevented due to its significant complications[3]. A golden standard for screening asymptomatic bacteriuria from urine specimens is during 12-16 weeks of gestation age of the pregnancy. The results of several studies have shown that preterm labor in pregnant women with asymptomatic bacteriuria is higher than other 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 and appropriate treatment of ABU has become a standard of obstetrical care[6]. Urinary Tract Infections (UTI) is the microbial invasion and subsequent multiplication on part or entire urinary tract.

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[9]. 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. 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. About 10% 0f those with asymptomatic bacteriuria develop symptomatic bacteriuria during pregnancy. 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.[11]

Asymptomatic bacteriuria is especially important in pregnancy because 30-40% of untreated pregnant women with asymptomatic bacteriuria develop acute pyelonephritis at late pregnancy[12]. 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.[13] 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.[14]

**Patients and Methods**

Material for the present study consisted of 200 urine samples (cases group) obtained from pregnant women attending as outpatients & inpatients admitted at Obstetric department of alkhark Hospital, with a history of premature uterine contractions and 200 urine samples (control group) obtained from pregnant patients with no history of preterm labor.

**Inclusion criteria**

Age ranging between 20 – 40 years, any parity, gestational age less than 37 weeks, singleton, no history of rupture of membrane (ROM), no history of preterm labor in previous pregnancies.

**Exclusion criteria**

Well known cases of uterine malformations, multiple pregnancies, history of ROM, history of previous preterm labor.

Data were collected on a predesigned proforma and patients were instructed to collect only mid stream sample of urine into sterile bottles. These were transported within half an hour to the laboratory and processed without delay. Specimens were subjected to cultures by the standard loop technique on blood agar, MacConkey's agar and nutrient agar.

Specimens were processed by screening methods namely a (counting of pus cells in the uncentrifuged urine using slide micrometry method:

a - value of 10 cells/cumm or more corresponds to pyuria and signifies the presene of UTI.

b- Gram staining of the urine smear by Jensen's modification (presence of at least one organism per oil immersion field was taken to correlate with significant bacteriuria of more than 10 cfu/cumm, discarding as negative after examining at least 20 fields.

c- Triphenyl Tetrazolium Chloride (TTC) Test; and

d- Catalase Test. All the specimens that yielded positive results by any one of the above four screening methods were subjected to culture by the pour plate method. Colonies were counted from plates which showed between 50 and 400 colonies perplate. Colonies were counted on a colony counter.

The specimens were classified into significant with counts being those equal to or more than 105 cfu/mL. The significant bacterial isolates were identified by standard procedures and subjected to antibiotic susceptibility by the disc diffusion method. Patients yielding a positive

culture for a second time by the same organism were advised antibiotic treatment. Cultures were repeated after a three-day course to make sure that the infection was controlled.

**The statistical** heterogeneity was explored using the chi-square (Chi2) test at 10% significant level. In addition, the heterogeneity across the results of the included studies was quantified by I2 statistic, and the between study variance was estimated using tau-square (Tau2) statistic. The statistical software Stata 11 (Stata Corp, College Station, TX, USA) was used for data analysis. Meta-analysis was conducted to obtain the overall prevalence of asymptomatic bacteriuria in pregnant women. The extracted data were analyzed and the results were reported using a random-effects model 19 with a 95% confidence interval (CI).

## RESULTS

**Table (1): shows the clinical characteristics of the patients under the study.**

| Variable | Cases group | Control Group | T test | P value |
|---|---|---|---|---|
| Age (years) | 23.4 ± 1.2 | 24.6 ± 1.5 | 1,0 | 0,865 |
| Parity | 2.2 ± 1.1 | 2.3 ± 1.1 | | |

**Table 2: Comparison between the two groups in the incidence of ASB and the prevalence of positive urine.**

| | Cases group | Control group | Chi-square | Odds ratio | Relative risk | P value |
|---|---|---|---|---|---|---|
| ASB | 186 | 178 | 12.345 | 1.433 | 1.2 | 0,0000 |
| Positive cultures | 173 | 147 | 15.52 | 3.231 | 1.211 | |

**Table 3: comparison of the prevalence of causative agents of bacteriuria in the two groups.**

| Causative organisms | Percentage in cases | Percentage in control |
|---|---|---|
| E coli | | |
| Candida albicans | | |
| Group B streptococci | | |
| Staphylococci | | |
| Klebsiella | | |
| Proteu | | |

The results of this meta-analysis showed 13% of pregnant women in Iraq had ASB. Our results indicated the difference in the prevalence of ASB according to the date of study conduction in Iraq was not considerable. Prevalence in recent studies (13%) was slightly

lower than older studies (14%). In addition, the prevalence of ASB in southern regions was lower than the northern regions.

However, the difference was not substantial (11vs.13%). According to the results of this meta-analysis, the prevalence of ASB among pregnant women is considerable in Iraq. Some factors such as increase of age, sexual activity, history of urinary tract infection before pregnancy, socio economic status, several pregnancies and lack of personal hygiene increase the risk of ASB in pregnancy.[15] There is a strong association between ASB and low birth weight in pregnant women.[16]

In addition, ASB has other complications such as premature delivery[17]. Therefore, a proportion of low birth weight and premature delivery may be attributed to ASB among pregnant women in Iraq. However, it seems that the design of studies, in order to determine the attributable fraction of ASB, is necessary to study complications of pregnant women in Iraq. The antibiotics resistance to some antibiotics such as ampicillin, cotrimoxazole amoxicillin, oxacilin and nitrofurantoin is high in Iraq[18]. On the other hand, a recently completed trial in the Netherlands has questioned the screen and treat approach to ASB in pregnant women. They reported no increased risk of preterm birth in women with ASB. They also observed that while untreated or placebo treated women with asymptomatic bacteriuria had a 3.9-fold higher risk of pyelonephritis compared to asymptomatic bacteriuria negative women, the overall risk of pyelonephritis was low: ASB positive women developed pyelonephritis in five [24%] of 208 cases, compared with 24 [06%] of 4035 ASB negative. This is significant for Iraq due to the high rates of antibiotic resistance but also because of the possible adverse effects of antibiotics on the neonate[19].

Prevalence of ASB in pregnant women in Asian countries such as Pakistan, Bangladesh, and India was reported to be 6–10.2%[20]. Prevalence of ASB in these mentioned studies was lower than our meta-analysis. However, the comparison between the results of our metaanalysis with cross-sectional studies may not be correct because the prevalence of ASB in the different regions of each country varies. In addition, the prevalence of ASB in Iraq varies from 4–29%.[21]

There was considerable heterogeneity (large I2 and a small p-value of the Chi2 test) among the results of included studies. Included studies were conducted in different regions of Iraq. This difference may be a source of heterogeneity. However, the interpretation of a Chi2 test

for heterogeneity should be taken with caution as the Chi2 test has limited capability when the sample size is small. On the other hand, the effectiveness of this test is high in identifying a small heterogeneity that might not be practically important[22]. In subgroups, based on the date of study conduction, geographical regions, and quality of included studies, the heterogeneity was high. Nonetheless, if the results of the meta-analysis are to be used as a guide for health decision-making, the meta-analysis of the heterogeneous results of studies is possible[23]. The Prevalence of Asymptomatic Bacteriuria in Pregnant

There were some limitations to this meta-analysis. First, the type of detected bacteria in eight studies was unknown. Therefore, we cannot determine the prevalent bacteria in pregnant women with ASB. A second limitation is the quality of included studies as only one study (5%) had high quality and 35% of them had low quality. This may increase the possibility of information bias[24].

Several authors have reported an increasing rise of asymptomatic bacteriuria with age and parity like Patrick Met al in their study. Most (96.5%) of the patients in the present study belonged to the low socioeconomic group as is true with most of the other studies e.g. Whalley et al.8 However, Gulfareen et al did not find any association of socio-economic status with bacteriuria. Preterm births in the current study were 18.2 % in asymptomatic bacteriuria patients. Meta-analysis of exposure to antenatal UTI has a relative risk of 1.5 and 2 for association with low birth and prematurity respectively.

This was confirmed by Robert Mittendorf et al10 by a Meta-analysis Low birth weight was seen in 15.2% of the present study. Romero et al11 proved that there was a strong association between untreated urinary tract infection and low birth weight. The incidence of gestational HTN and preeclampsia were 9.1% and 6.1% respectively in this study. Abayad et al12 found that asymptomatic bacteriuria was associated with hypertension and preeclampsia. In his study 10% of women with bacteriuria and 8.9% women without bacteriuria developed gestational hypertension. However, there is no compelling evidence of an association of asymptomatic bacteriuria with hypertension in pregnancy or of long-term renal damage associated with asymptomatic bacteriuria of pregnancy in the antibiotic era.[25]

The pregnant women who had the previous history of UTI were approximately three times more likely to develop asymptomatic bacteriuria compared to those who had no history of UTI, in this study. Various studies[26] showed that the history of UTI is considered as the

strongest predictor of asymptomatic bacteriuria. The study found that nitrofurantoin is effective for most of the isolates in the study (87.9%).

The prevalence of resistance by urinary isolates to nitrofurantoin and gentamicin was 0%-2% as proved by Gupta et al. He stated that nitrofurantoin is relatively safe in pregnancy and is effective in most UTI, except that it can cause haemolysis in a glucose 6 phosphate deficiency baby, if used near term. So, first trimester urine culture remains the screening test of choice as advocated by Nicotle et al[27] and American academy of family physician and several others.

The ideal time for it to be done was considered between 12-16 weeks of gestation.

## CONCLUSIONS

Urinary tract infections are the most common bacterial infections during pregnancy. The incidence of UTI varies, and one of the major risk factors in developing UTI is asymptomatic bacteriuria. The urinary tract is second only to the respiratory tract in acquiring the microbial infection, especially in females. 90% of pregnant women develop urethral dilatation which starts at about 6th week and peaks at about 22-24 weeks and remains so till delivery.

Increased bladder volume and decreased bladder & urethral tone contribute to increased urinary stasis and ureterovesical reflux. This accounts for 70% of asymptomatic UTI among unscreened pregnant women.

Different determinants of virulence such as the presence of adhesions, stasis produced by the gravid uterus etc play a role in the causation of UTI.1

The term asymptomatic bacteriuria is used when a bacterial count of the same species>105 /ml in a midstream clean catch urine on two occasions is detected without symptoms of UTI. Delzell JE et al[28] defined asymptomatic bacteriuria as persistent, actively multiplying bacteria of more than or equal to 100,000 colony forming unit per ml of urine without any symptoms of urinary tract infection, which include lower abdominal pain, burning micturition, fever, dysuria, frequency, urgency, supra pubic discomfort, offensive smelling urine, strangury, urge incontinence and nocturia[29].

The apparent reduction in immunity of pregnant women appears to encourage the growth of both commensal and non-commensal microorganisms. The female urethra is relatively short

and is anatomically proximal to the vagina which is colonised with organisms from GIT. Bacteria originate from the large bowel and colonize the urinary tract transperineally. The most common organism colonised is E coli. Others include Proteus, Klebsiella, coagulase negative staphylococci and pseudomonas[30].

Normal physiological changes predispose the woman to a higher risk for pyelonephritis which can lead to complications like premature delivery, infants with low birth weight, IUGR, anaemia, thrombocytopenia, deranged liver function test and renal function test. Hence it is important to treat the infected group as 40% of asymptomatic bacteriuria develops symptomatic UTI.

There is good evidence of any type of urinary tract infection and sudden unexpected infant death. Relapse and reinfections are also common in pregnancy. Relapse is the occurrence of infection by the same strain of organism within six weeks of initial infection whereas reinfection is the recurrence of bacteria with a different strain of bacteria after successful eradication of initial infection. Approximately 15% of patients will have a recurrence during pregnancy necessitating repeat culture. Screening for asymptomatic bacteriuria in pregnant women has been shown to be cost effective when compared with treating UTI and pyelonephritis without screening. The various screening techniques used to detect bacteriuria include urine analysis, leukocyte esterase activity, a nitrite test and urine cultures. A midstream urine culture is still considered the best diagnostic test. The American College of Obstetrics and Gynaecology advocates routine screening for bacteriuria with a urine culture at the first prenatal visit and during the third trimester.

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