

Prevalence of Asymptomatic Bacteriuria in Antenatal Women with Preterm Labor at an Egyptian Tertiary Center

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Abstract: Background and objective: Urinary tract is second only to the respiratory tract in acquiring microbial infection, especially in females. It is more common in pregnant than in non-pregnant women^{1,2}. Studies from different parts of the world have showed that urinary tract infection (UTI) during pregnancy leads to low birth weight babies, increased perinatal mortality and premature births along with acute and chronic sequelae in mothers³. This study was conducted to explore the relation of asymptomatic bacteriuria in Egyptian females to preterm labor and different aspects of UTI during pregnancy. Patients and Methods: This was a cross sectional study that was done at Ain Shams University Maternity Hospital. The study included 1830 antenatal women, over a 3-year period, between January 2007 and December 2009. Out of these patients; 780 patients had premature uterine contractions while 1050 antenatal women with no history of premature uterine contractions. Results: Prevalence of asymptomatic bacteriuria (ASB) in those with premature uterine contractions and others with no history of uterine contractions were 23.5% and 16.9% respectively. A highly significant association between ASB of the mothers and preterm labor was noted. Conclusion & recommendations: The results of this study suggested that patients with asymptomatic bacteriuria were more prone to develop preterm delivery than that of the healthy mothers (without bacteriuria). The unwanted sufferings of the pregnant mothers and their offspring could easily be prevented by early screening and treatment of asymptomatic bacteriuria in pregnancy which must be considered as an essential part of antenatal care in order to reduce the morbidities associated with preterm labor.

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1. Introduction

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 pyelonephritis⁴. Urinary tract infection is the common of all bacterial infections, affecting human beings throughout their life span especially in women⁵. 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 women⁶. Symptomatic bacteriuria is an iceberg of total bacteriuria. Pregnancy is a provocation for the asymptomatic to become symptomatic⁷. About 10% of those with asymptomatic bacteriuria develop symptomatic bacteriuria during pregnancy⁸. 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 non-pregnant women⁹. Asymptomatic bacteriuria is

especially important in pregnancy because 30-40% of untreated pregnant women with asymptomatic bacteriuria develop acute pyelonephritis at the late pregnancy^{10,11}. 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^{10,12}. 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 term¹³. Thus, any mechanical changes associated with estrogen do not appear to be responsible for asymptomatic bacteriuria in pregnancy. Kass¹⁴ reported that severe uterine contractions occur within moments after endotoxin injection in an animal model, thus linking bacteriuria with early delivery. Furthermore, Apitz¹⁵

reported that endotoxin causes a generalized Shwartzman reaction in the pregnant rabbit. Zahl and Bjercknes¹⁶ used the same substance to induce decidual - placental hemorrhage in the female mouse. Also, as gestation lengthens, the uterus was shown to be progressively more susceptible to endotoxin, and some, but not all, rabbit wombs primed with estrogen and progesterone exhibited uterine hyperirritability. Conversely, the uterus of the nonpregnant rabbit did not react at all. Thus, gestation somehow sensitizes the uterus to these powerful oxytocics, and, when the situation is complicated by bacteriuria due to gram-negative organisms, the endotoxins elaborated by the organisms causing infection could theoretically precipitate preterm labor.

The present study was undertaken to estimate the prevalence of asymptomatic bacteriuria as a causative agent in cases of preterm labor and because asymptomatic bacteriuria in pregnancy remains prevalent and preventable, a review of this important subject is relevant at this time.

2. Patients and Methods:

Material for the present study consisted of 780 urine samples (cases group) obtained from pregnant women attending as outpatients & inpatients admitted at Obstetric department of Ain Shams University Maternity Hospital, during the years 2007 to 2009 with history of premature uterine contractions and 1050 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 pregnancy, 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 presence 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 10⁵ 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 per plate. 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 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.

Statistical Analysis: Analysis of data was done by using SPSS (statistical program for social science 12) as follows:

- Description of quantitative variables as mean and SD and range.
- Description of qualitative variables as number and %.
- Unpaired t-test was used to compare two groups as regard a quantitative variable.
- Chi-Square test was used to compare qualitative variables between groups.
- P value > 0.05 insignificant, P<0.05 significant (*) & P<0.01 highly significant (**)

3. Results

This study was carried out in Ain Shams University Maternity Hospital on 1830 antenatal mothers. They were divided into two groups; group I (cases group) were 780 patients with history of preterm labor and group II (control group) were 1050 pregnant females with no history of preterm labor. They were compared as regards the mean age and parity with no significant difference between the two groups (table 1).

The incidence of asymptomatic bacteriuria (ASB) in group I (cases) was 23.5% while the incidence of in group II (control group) was 16.9% with highly significant difference between the two groups. As regards the prevalence of positive urine cultures in the two groups the incidences were 95.1% (175) and 81.9% (145) in group I and II respectively with highly significant difference between the two groups (table 2).

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

variable	Cases group (n = 780)	Control group (n = 1050)	t- value	P- value
Age (years)	22.1 ± 1.1	21.6 ± 1.3	0.8	0.43
Parity	2.8 ± 1.1	2.9 ± 2.1	1.23	0.22

Values are expressed as means ± standard deviation or number and percentage.
No significant difference between the two groups in all variables (P value > 0.05)

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

Variable	Cases group (n = 780)	Control group (n = 1050)	Chi- square	Odds ratio	Relative risk	P- value
ASB*	184 (23.5%)	177 (16.9%)	12.811	1.523	1.399	< 0.001
Positive cultures	175 (95.1%)	145 (81.9%)	15.585	4.291	1.161	< 0.001

*ASB: asymptomatic bacteriuria

Highly significant difference between the two groups in all variables (P value < 0.001)

Out of the 1.830 pregnant mothers screened in this study, 361 (19.7%) had asymptomatic bacteriuria. The commonest organism causing

bacteriuria was *Escherichia coli*. The prevalence of different types of causative organism in both groups of bacteriuria was more or less the same (Table 3).

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

Causative organisms	Percentage in cases	Percentage in control
<i>E coli</i>	56	61
<i>Candida albicans</i>	10	8
Group B streptococci	9	11
Staphylococci	8	9
<i>Klebsiella</i>	10	9
<i>Proteus</i>	5	2

The sensitivity pattern of the isolated organisms revealed that all were highly sensitive to ceftriaxone and moderately sensitive to cephalixin,

erythromycin, nitrofurantoin, amoxicillin-clavulanic acid ranging 24 to 72%. (Table 4)

Table 4 Shows the sensitivity of different organisms to different antibiotics

	<i>E. coli</i>	Group B streptococci	Staphylococci	<i>Klebsiella</i>	<i>Proteus</i>
Cephalexin	52.3	68.6	63.8	44.6	72.4
Erythromycin	37.3	24.8	44.5	35.9	49.8
Nitrofurantoin	55.1	44.2	56.5	27.5	34.4
amoxicillin-clavulanic acid	61.7	67.1	41.8	39.7	51.1
Ceftriaxone	87.2	78.8	79.7	66.9	75.1

4. Discussion

Asymptomatic bacteriuria (ASB) occurs in 2-10% of all pregnancies¹⁷. The majority of the most recent studies^{17,24}, including observational studies

from developing countries found the prevalence of asymptomatic bacteriuria in pregnant women ranged between 4-10%. This range during pregnancy was reported to be as high as 78.7% in a population from

Nigeria. This variation in studies can be attributed to several factors such as the geographical variation, socio-economic status, ethnicity of the subjects, setting of the study (primary care, community based, or hospitals), and the variation in the screening tests (urine dipstick, microscopy, and culture). Race-specific rates show significant variation, as well as there is variation within same race living in different geographical areas or with socio-economic status. Thus, it is important to evaluate the prevalence of ASB in a specific population. This study reported that the prevalence of ASB among pregnant women attending prenatal visits in a tertiary center in Cairo was 23.5% in patients with premature uterine contractions and 16.9% in control patients (95% CI, Chi Square 12.811, Odds Ratio 1.523, relative risk 1.399, P value < 0.001) with highly significant differences between the two groups. The reported prevalences of ASB were 30%, 4.8%, 9.9% and 3.3-6.1% among pregnant women in Yemen¹⁹, United Arab Emirates (UAE)¹⁸, Qatar²⁴ and Iran²⁵ respectively.

Our findings regarding perinatal complications in patients with ASB confirm the conclusion of Hazhir et al. 2007²² who showed significant bacteriuria in preterm group and term group of 36% and 12% respectively. There are many studies^{10, 14-16} that link so many pregnancy complications like hypertensive disorders in pregnancy, low birth weight, premature with asymptomatic bacteriuria. The results of the present study also agree with these findings. The association between asymptomatic bacteriuria and pregnancy complication especially prematurity is out of question, it is now an established fact⁷⁻⁹. But the mechanism is not well defined to the researchers. Several investigators have observed a high incidence of pyelonephritis in bacteriuric pregnant mothers²⁶. It is convincing that the effect of urinary tract infection on premature labor could be indirectly mediated by antenatal maternal hypertension. It is also plausible that urinary tract infection affects premature labor directly, through the development of amnionitis. It has been previously suggested that bacterial infection of the amniotic fluid is a risk factor for premature delivery^{17, 18}. Another hypothesis contends that bacterial enzymes such as collagenase may weaken the fetal membranes and predispose them to premature rupture¹⁹.

E. coli has been identified as the most common pathogen isolated among the pregnant women in this study, which was consistent with the majority of the reported studies in literature^{13-19,22-24,27,28}. However, *E. coli* formed 56% of the isolated organisms in the cases group, and 61% in the control group which is lower than what have been reported in

countries such as Turkey 2005 (77%)¹⁷, UAE 2005 (66.7%)¹⁸, Iran 2009 (70%)²⁵ and in Pakistan 2006 (78.6%)²⁰. Moreover, higher than in Nigeria 2006 (11.1%)²¹ and Qatar 2009 (31%)²⁴. *E. coli* is the most common microorganism in the vaginal and rectal area. Because of the anatomical and the functional changes that occur during pregnancy, the risk of acquiring UTI from *E. coli* is high¹⁴. It is consistent with the findings of Rahman et al. (1990)³⁰ and Ahmed et al. (1996)³¹. The findings of the study showed that staphylococcus Saphrophyticus, which was formerly believed to be normal commensal, was recognized as a pathogen accounting overall 8% of bacteriuria in this community.

The presence of *Candida albicans* in this present study is 10 and 8% in the cases and control groups respectively and is higher than other studies^{14,27}, Nigeria, 2006²¹ (7.9%) and Malaysia,1997²⁷ (2 out of 32 cultures; 6.25%). The physiological alterations during pregnancy that affects immunity and high prevalence of diabetes, including gestational diabetes, among our population may account for this high prevalence of *C. albicans*. Group B streptococcus (GBS), which is occasionally isolated in urine (10%)²⁹ had a prevalence of 9% in this study. GBS bacteriuria may be associated with preterm rupture of membranes, premature delivery, and early onset neonatal sepsis. Thus, all pregnant women with these bacteria during gestation should receive treatment at the time of diagnosis, as well as intrapartum antibiotic prophylaxis^{2,32}. The result in our study is less than those reported from Malaysia (17.2%)²⁷ and less than 25.5% reported by Amadi et al. from Nigeria²⁶.

Like other studies^{10, 13} the findings of the study also indicate that ceftriaxone is highly effective to the urinary pathogens. Rahman et al.³⁰ in 1990 in their study observed that urinary pathogens at very high percentage ranging 75 to 100% were sensitive to cephalixin, 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 wide spread and indiscriminate use of the drugs.

In a meta-analysis performed by Romero et al.³³, only selective studies were evaluated. For studies to qualify for the analysis, the definitions of asymptomatic bacteriuria had to be clearly specified, the numerical data for the outcome variables had to be reported individually, and, in studies using the randomized clinical trial design, a control group was required in the treatment trials. Because of a failure to satisfy these requirements, 12 of 31 studies were

excluded from analysis; eight of the 19 qualified studies were randomized clinical trials. Most of the acceptable studies required that two clean-catch urine specimens contain at least 10^5 organisms/ mL to be considered to represent true infection, as opposed to contamination. When data were pooled in the meta-analysis, bacteriuric mothers were found to have a 54% higher risk of giving birth to a low-birth-weight infant and twice the risk of giving birth to a preterm infant than did nonbacteriuric mothers. Furthermore, a meta-analysis including only randomized clinical trials showed that antibiotic treatment of bacteriuric mothers significantly reduced the risk of low birth weight (relative risk = 0.56; 95% confidence interval = 0.43-0.73). Thus, maternal bacteriuria is a risk factor for premature delivery that can be reduced by treatment with appropriate antibiotics.

5. Conclusion:

In conclusion, the result of this study found that the prevalence of ASB among pregnant women with preterm labor in a tertiary center in Cairo, Egypt was high (23.5%), and the predominant organism of *E. coli* was 56%. A large scale national study that includes primary health care centers should be conducted to determine the actual prevalence of ASB in the obstetric population in Egypt, and to identify the group that is vulnerable for developing a UTI. If low prevalence is confirmed at the national level and vulnerable groups are identified, it is more cost effective to recommend selective rather than universal screening for ASB in pregnancy. To the best of author knowledge this the only recent paper reporting prevalence of ASB among pregnant women in Cairo, persistent asymptomatic bacteriuria in pregnancy causes different types of serious complications like pyelonephritis, hypertensive disorders, low birth weight, premature labor, anemia etc, which are the leading causes of high maternal and infant morbidity

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