

# Asymptomatic Bacteriuria among Women Attending the Antenatal Clinics in Jeddah, Western Region of Saudi Arabia

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## Abstract

This retrospective chart review was conducted to determine the proportion of pregnant women with asymptomatic bacteriuria who were followed up at the antenatal clinics of King Abdulaziz University Hospital, Jeddah between January 2007 and January 2012. Clinical and paraclinical data were recorded for 337 women in their last trimester of pregnancy. The prevalence of asymptomatic bacteriuria in the cohort was 31.26%. The most frequently isolated bacteria included *Escherichia coli* and *Klebsiella pneumoniae* in 30.39% and 10.78% of the cases, respectively. In most cases, the isolated bacteria were sensitive to ampicillin (11.57%), amoxicillin (10.38%), and amikacin (5.63%). Most bacteria were resistant to nitrofurantoin (21.06%), tetracycline (21.06%) and cefixime (20.77%). The most common prescribed medications included multivitamins (n = 40; 11.87%), vitamin B12 (n = 47; 13.95%), folic acid (n = 45; 13.35%), and antibiotics (n = 43; 12.75%). Overall, it is possible that pregnant women with asymptomatic bacteriuria are undertreated at our institution. Gaps in the management of these patients should be identified to improve patient care.

## Keywords

Antibiotherapy; Asymptomatic bacteriuria; Pregnancy; Third trimester

## Introduction

Asymptomatic bacteriuria (ASB) is the presence of pathogenic bacteria in the urine at clinically significant levels (> 100,000 colony forming units / mL of urine) in the absence of symptoms suggestive of urinary tract infection<sup>[1]</sup>. The reported prevalence of ASB ranges between 2 and 10% among pregnant women<sup>[2]</sup>. Although the prevalence is not higher in pregnant women, pregnancy augments the progression rate from asymptomatic to symptomatic

disease<sup>[3]</sup>. During pregnancy, certain factors favor the multiplication of bacteria in urine<sup>[4]</sup>. These include weakening of the immune system, which occurs as a result of physiological changes<sup>[5]</sup>, increased plasma volume due to a decrease in urine concentration and the development of glycosuria in approximately 70% of pregnant women<sup>[6]</sup>. Other factors, such as poor socioeconomic status, gestational age, pregnancy duration, and multiparity have been associated with an increase in the incidence of asymptomatic bacteriuria<sup>[7,8]</sup>. According to a previous report, advanced

maternal age might increase the risk for asymptomatic bacteriuria in pregnancy<sup>[7]</sup>; however, women  $\geq 35$  years are likely to have had several pregnancies, and multiparity itself increases the risk of asymptomatic bacteriuria<sup>[7]</sup>. Poor genital hygiene is another risk factor that might promote bacterial infection and/or increase chances of bacterial colonization and, consequently, contribute to asymptomatic bacteriuria<sup>[9]</sup>.

A 2002 systematic review concluded that (a) the diagnosis of urinary tract infection can be confirmed with a  $> 90\%$  probability in a patient who presents a combination of dysuria and frequency in the absence of vaginal discharge or irritation and (b) a urine dipstick test cannot decrease the post-test probability sufficiently to exclude urinary tract infection if a patient has  $\geq 1$  symptoms<sup>[10]</sup>. Nevertheless, urine culture has a value beyond confirming the diagnosis as it can additionally help clinicians direct treatment based on the results of tests for antimicrobial susceptibility.

Previous reports found that, in up to 40% of the cases, ASB can progress to pyelonephritis, and the risk of pre-eclampsia, premature birth and low birth weight are presumably increased<sup>[11-16]</sup>. It has been demonstrated that it can be more cost effective to screen for ASB in pregnant women than treating women with UTI or pyelonephritis<sup>[17]</sup>. The American College of Obstetrics and Gynecology advocates routine screening for bacteriuria with a urine culture at the first antenatal consultation and during the third trimester<sup>[18]</sup>. The US Preventive Services Task Force recommends screening for bacteriuria with urine culture at 12-16 weeks of gestation in order to identify 80% of women who will subsequently develop ASB<sup>[19]</sup>.

Antibiotic treatment is rarely indicated in ASB; however, it is recommended in pregnant women<sup>[20]</sup>. The choice of antibiotic depends on several criteria, including the patient's individual risk (allergy to an antibiotic agent), previous antibiotic treatment, pathogen spectrum and results of tests for antimicrobial susceptibility, efficacy of the antibiotic, effects on the resistance situation in the patient, as well as the presence of undesired drug effects<sup>[21]</sup>. A Cochrane Review of treatments for ASB during pregnancy reported that based on the results of susceptibility testing, a cephalosporin, sulfonamide or sulfonamide-containing combination, penicillin, or nitrofurantoin were appropriate regimens for the management of ASB<sup>[22]</sup>. Nevertheless, an increase in the rates of antibiotic resistance complicates the choice of

empiric regimens. In addition, antibiotic resistance is likely to become an increasing issue. Few surveys of antibiotic resistance in urinary isolates from women with ASB have been conducted, but findings from surveys of antibiotic susceptibility in pathogens that cause community-acquired uncomplicated urinary tract infections indicate substantial variability<sup>[22]</sup>. In one survey of European countries and Canada<sup>[23]</sup>, investigators found that resistance to ampicillin in *Escherichia coli* was on average 29.8% but was as high as 53.9% in Spain.

There is a dearth of more recent data on ASB, including its screening and management, among pregnant women in Jeddah. It is important to identify the prevalence of ASB among our patients and to determine whether patients are managed according to current recommendations in order to limit complications and poor pregnancy outcomes. This study determines the proportion of women with ASB who were treated at the antenatal clinics of King Abdulaziz University Hospital (KAUH), Jeddah.

## Methods

A retrospective chart review was conducted of pregnant women who were followed up at the antenatal clinics of KAUH, Jeddah between January 2007 and January 2012. King Abdulaziz University Hospital is a tertiary center, which has a capacity of 104 beds for academic specialties only. Approximately 1500 pregnant women are received every month at the antenatal clinics of the hospital.

A total of 337 women in the last trimester of pregnancy were included, after excluding pregnant women in the first and second trimesters as well as pregnant women with non-urollogic infections. Permission to conduct the study was sought from the relevant ethics research committee.

A data collection sheet was used to record demographic and clinical data from the electronic medical records of included cases. According to our departmental protocol, routine urine microscopy was performed during each antenatal visit. A urine culture was also performed (midstream urine sample) during the third trimester or when urine microscopy results were suggestive of bacteriuria. Patients who had a positive culture were offered antibiotic therapy tailored to sensitivity results. After the course of antibiotics was completed, urine culture was repeated in the next antenatal visit for follow up.

## Statistical Methods

The data were entered and analyzed using IBM SPSS Statistics for Windows, version 22 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to define the characteristics of the study variables. Results are expressed as proportions and means (standard deviation [SD]).

## Results

The mean (SD) age of the cohort was 29.87 (4.80) years (range, 15 and 46 years). The mean gravidity was 3.05 (1.60) and the mean parity was 21.96 (1.40). Other characteristics are as shown in Table 1.

As shown in Table 2, the range of medications prescribed during pregnancy was broad, with the most commonly prescribed being calcium (n = 106; 31.45%), followed by multivitamins (n = 40; 11.87%), vitamin B12 (n = 47; 13.95%), folic acid (n = 45; 13.35%), and antibiotics (n = 43; 12.75%). Urinary tract symptoms were reported by a very small proportion of the women, with the most common being burning sensation on micturition (3.56%) and dysuria (3.26%). Urgency was reported in less than one percent of the women (Table 3).

Urinary tract infection was documented in ten women (n = 10; 2.96%). Approximately 19.58% of the women had leukocytosis, while 2.67% of the cases had a positive urine nitrite test (Table 4). Bacteria were isolated from the urine of 102 women, representing

a prevalence rate of 31.26%. Of these, *Escherichia coli* (*E. coli*) and *Klebsiella pneumoniae* (*K. pneumoniae*) were isolated from the urine of 30.39% and 10.78% of the cases, respectively. The relative frequency of other isolated bacteria was as follows: beta-hemolytic streptococci (2.94%), Gram-negative bacilli (1.96%), mixed bacteria growth (1.96%), *Enterococcus faecalis* (1.96%), Gram-negative *Klebsiella* (0.98%), Gram-positive cocci (0.98%), Gram-negative bacilli (1.96%), and *Proteus* species (0.98%). A summary of the prevalence rates and frequency of ASB due to *E. coli* across different geographic locations is presented in Table 5.

Table 6 shows that in most cases, the isolated bacteria were sensitive to ampicillin (11.57%), amoxicillin (10.38%), and amikacin (5.63%). Most bacteria were resistant to nitrofurantoin (21.06%), tetracycline (21.06%) and cefixime (20.77%).

**Table 1.** Characteristics of the sample.

Variables	Frequency (Percent)*
<b>Age (years)</b>	
< 20	84 (24.93%)
20-34	134 (39.76%)
35-45	101 (29.97%)
> 45	18 (5.34%)
<b>Nationality</b>	
Saudi	265 (81.29%)
Non-Saudi	61 (18.41%)
<b>Occupation</b>	
Employed	1 (0.87%)
Unemployed	114 (99.13%)
<b>Gravidity</b>	
G1	155 (41.11%)
G2-G5	114 (33.82%)
> G5	68 (20.17%)
<b>Diabetes</b>	
Yes	17 (5.15%)
No	313 (94.65%)

\*The total is < 337 due to missing data.

**Table 2.** Frequency of medications taken by the women during pregnancy.

Variables	Frequency (Percent)
Antibiotics	43 (12.75%)
Albuterol Sulfate Inhalation for asthma	1 (0.30%)
Cefuroxime	1 (0.30%)
Vitamin D	15 (4.45%)
Folic acid	45 (13.35%)
Vitamin B12	47 (13.95%)
Multivitamin	40 (11.87%)
Calcium	106 (31.45%)
Omega-3 Polyunsaturated Fatty Acids	4 (1.18%)
Dexamethasone	1 (0.30%)
Dydrogesterone	5 (1.48%)
Ranitidine	2 (0.59%)
Dexpanthenol Cream	1 (0.30%)
Cefazolin	1 (0.30%)
Calcium Carbonate	1 (0.30%)
Lactulose	1 (0.30%)
Ferrous Sulfate	11 (3.26%)
Bath Salts	1 (0.30%)
Pantoprazole	1 (0.30%)
Folic Acid Injection	1 (0.30%)
Meclizine	1 (0.30%)
Domperidone	1 (0.30%)

**Table 3.** Frequency of urogenital tract symptoms.

Variables	Frequency (Percent)
Dysuria	11 (3.26%)
Frequency	8 (2.37%)
Burning Sensation on Micturition	12 (3.56%)
Urgency	1 (0.30%)
Vaginal Discharge	24 (7.12%)

## Discussion

**Table 4.** Proportion of positive findings on urine analysis, cytology and culture.

Variables	Frequency (Percent)
Hematuria	3 (0.89%)
Leukocytes	66 (19.58%)
Proteinuria	11 (3.26%)
Nitrites	9 (2.67%)
Glucose	12 (3.56%)
Epithelial cells	
Few	134 (39.76%)
Moderate	35 (10.38%)
<i>Klebsiella pneumoniae</i>	11 (10.78%)
Gram-positive Cocci	1 (0.98%)
Beta-hemolytic Streptococci	3 (2.94%)
Gram-negative Klebsiella	1 (0.98%)
Gram-positive Cocci	1 (0.98%)
Gram-negative Bacilli	2 (1.96%)
<i>Escherichia coli</i>	31 (30.39%)
Mixed Bacteria Growth	2 (1.96%)
<i>Enterococcus faecalis</i>	2 (1.96%)
Proteus Species	1 (0.98%)

This analysis shows that the prevalence of ASB among pregnant women in the third trimester is 31.26%. The prevalence of ASB in this cohort is low compared with the rate reported by Yousef and Al-Aali<sup>[24]</sup>, who found that the prevalence of ASB was 62% among women attending the antenatal clinic at Al-Hada Armed Forces Hospital, Taif, Saudi Arabia. These results are converse of those reported by other authors<sup>[25-27]</sup>, with one study reporting that the prevalence of ASB was 5.1% among pregnant women who were followed up at the antenatal clinics of Hafez Hospital, Shiraz, Iran<sup>[27]</sup>. In another study conducted at Buea District Hospital, Cameroon<sup>[25]</sup>, it was found that the prevalence rate of ASB among pregnant women was 23.5%.

A Cochrane review recommended that treatment schedules for ASB in pregnant women should be directed by urine culture and sensitivity testing<sup>[28]</sup>. In the current study, although bacteria were isolated from the urine of approximately 31.26% of the cohort and sensitivity testing was done for all cases with bacteriuria, only 12.75% of the women received antibiotics. This finding suggests the possibility that departmental protocols are not followed or are

**Table 5.** Summary of prevalence rates and frequency of asymptomatic bacteriuria due to *E. coli* in studies conducted both in Saudi Arabia and abroad.

Study Sample and Location	Prevalence (%)	<i>E. coli</i> (%)
<b>Gulf Region</b>		
Current study: Women in the last trimester of pregnancy attending antenatal clinics at King Abdulaziz University, Jeddah, Jeddah Province	31.26%	30.39%
Women attending their first antenatal clinic at King Abdulaziz University Hospital and Dr. Erfan and Bagedo Hospital, Jeddah, Western Province <sup>[17]</sup>	1.7%	53.0%
Pregnant Saudi women visiting the antenatal clinics of a university hospital in Al-Khobar <sup>[41]</sup>	10.5%	Not reported
Pregnant women visiting the antenatal clinics of a maternity hospital in Yemen <sup>[42]</sup>	30.0%	41.5%
Women attending antenatal clinics at primary health care centers in Qatar <sup>[43]</sup>	9.9%	31.0%
Women visiting the antenatal clinics of public health centers in Semnan, Iran <sup>[44]</sup>	3.3%	70.0%
Women attending antenatal clinics at the Primary Health Care Center of Maternal Child Health in Sharjah, United Arab Emirates <sup>[45]</sup>	4.8%	66.7%
<b>Asia</b>		
Pregnant women attending the Department of Obstetrics and Gynecology at Raja Isteri Pengiran Anak Saleha Hospital in Brunei Darussalam <sup>[46]</sup>	4.1%	1.18%
Pregnant women who reside in Bahawalpur, Pakistan <sup>[47]</sup>	9.9%	78.6%
Women in the second trimester of pregnancy living in the rural areas of Rajshahi District, Bangladesh <sup>[48]</sup>	12.0%	75.9%
Women attending their first antenatal clinic at the Department of Obstetrics and Gynecology of Universiti Kebangsaan Malaysia, Malaysia <sup>[49]</sup>	1.9%	40.0%
<b>Africa</b>		
Women attending antenatal clinics at Komfo Anokye Teaching Hospital in Ghana <sup>[50]</sup>	7.3%	37.0%
Women attending antenatal clinics at the Federal Teaching Hospital in Abakaliki, Nigeria <sup>[51]</sup>	24.7%	28.4%
Women followed up at the antenatal clinics of Buea Regional Hospital Annex and health centers at Mile 16 in Buea, Cameroon <sup>[25]</sup>	23.5%	33.0%
<b>Europe</b>		
Women aged ≥ 18 years with a singleton pregnancy (gestational age, 16 and 22 weeks) attending antenatal clinics at eight hospitals and five ultrasound centers in the Netherlands <sup>[52]</sup>	5.0%	71.0%

**Table 6.** Frequency and antimicrobial susceptibility of the isolated bacteria.

Antibiotic		Frequency (Percentage)
Amikacin	Yes	19 (5.63%)
	No	55 (16.32%)
Cefixime	Yes	2 (0.59%)
	No	70 (20.77%)
Nitrofurantoin	Yes	1 (0.30%)
	No	71 (21.06%)
Tetracycline	Yes	1 (0.30%)
	No	71 (21.06%)
Oxacillin	Yes	4 (1.86%)
	No	69 (20.47%)
Ciprofloxacin	Yes	14 (4.15%)
	No	58 (17.21%)
Ampicillin	Yes	39 (11.57%)
	No	32 (9.49%)
Amoxicillin	Yes	35 (10.38%)
	No	39 (11.57%)
Moxifloxacin	Yes	6 (1.78%)
	No	66 (19.58%)
Levofloxacin	Yes	3 (0.89%)
	No	69 (20.47%)
Cephalexin	Yes	6 (1.78%)
	No	67 (19.88%)
Cefotaxime	Yes	3 (0.89%)
	No	67 (19.88%)
Levofloxacin	Yes	14 (4.15%)
	No	56 (16.61%)
Clindamycin	Yes	1 (0.30%)
	No	69 (20.47%)
Erythromycin	Yes	2 (0.59%)
	No	68 (20.17%)
Fosfomycin	Yes	2 (0.59%)
	No	68 (20.17%)
Gentamycin	Yes	2 (0.59%)
	No	68 (20.17%)
Cefazolin	Yes	1 (0.30%)
	No	69 (20.47%)
Imipenem	Yes	5 (1.48%)
	No	65 (19.28%)
Tigecycline	Yes	1 (0.30%)
	No	69 (20.47%)
Ciprofloxacin	Yes	3 (0.89%)
	No	67 (19.88%)
Meropenem	Yes	8 (2.37%)
	No	62 (18.39%)
Other Penicillins	Yes	15 (4.45%)
	No	57 (16.91%)
Other Cephalosporins	Yes	3 (0.89%)
	No	72 (21.36%)

selectively implemented by physicians. Nevertheless, further studies should be conducted at our academic center to investigate the reasons behind the non-prescription of antibiotics to pregnant women with ASB.

The most frequently isolated bacteria in this study were *E. coli* (30.39%) and *K. pneumoniae* (10.78%). According to recent reports<sup>[29-35]</sup>, *E. coli* is the most common uropathogen in pregnant women, representing at least 80% of isolates<sup>[22]</sup>. Other organisms that are commonly isolated in the urine samples of pregnant women with ASB include other gram negative bacteria and group B streptococci. In one retrospective study conducted on 9698 pregnant women at King Abdulaziz University Hospital and a private clinic at Dr. Erfan and Bagedo Hospital, Jeddah<sup>[17]</sup>, *E. coli* was isolated from urine specimens in up to 53% of the sample. Contrary to our report, where *K. pneumoniae* was identified in 10.78% of the cases, the authors found *Klebsiella* species in 0.6% of the women in their sample. In another study conducted in a tertiary care teaching hospital in north India<sup>[36]</sup>, the authors identified *E. coli* and *K. pneumoniae* in 60.0% and 22.5% of pregnant women, respectively.

In this study, we found that the isolated bacteria were most sensitive to amoxicillin, ampicillin, and amikacin. While antibiotic susceptibility patterns vary between populations or hospitals, several authors found that gentamicin, amikacin and nitrofurantoin were effective against most isolates<sup>[33,35,36]</sup>. Gentamicin and amikacin have been demonstrated to be effective in treating ASB in pregnant women; however, these drugs should only be used when the benefit outweighs potential risk, as they are nephrotoxic<sup>[37]</sup>. Some investigators<sup>[22]</sup> recommend the use of a sulfonamide or sulfonamide-containing combination, a penicillin, cephalosporin or nitrofurantoin, based on the results of susceptibility testing as appropriate regimens for the management of ASB. Nevertheless, increasing antibiotic resistance complicates the choice of empiric regimens, and is it likely to become an increasing issue, not only among other Gulf countries, but also in Saudi Arabia<sup>[38]</sup>.

In the current study, bacterial isolates were in most cases resistant to nitrofurantoin (21.06%), tetracycline (21.06%) and cefixime (20.77%). Results from hospital-based studies conducted in Saudi Arabia showed that resistance rates among isolates of *K. pneumoniae* and *E. coli* to ciprofloxacin were 23% and 46%, respectively<sup>[39,40]</sup>. Studies that investigated antibiotic

resistance in urinary isolates from women with ASB in Saudi Arabia showed varying results<sup>[17,38]</sup>, with some investigators reporting that all the strains identified in their study were susceptible to all tested antibiotics, and resistance to ampicillin was only observed in some strains of *K. pneumoniae*. The emergence of antimicrobial resistance in Saudi Arabia and other Gulf countries might have occurred for several reasons, including easy access to broad spectrum antibiotics, such as third and fourth generation cephalosporins, quinolones and carbapenems in hospitals and clinics<sup>[38]</sup>. Most Gulf countries do not have antimicrobial stewardship programs, especially in the inpatient setting where broad spectrum antimicrobial agents are administered. In addition, many hospitals allow 2 or more bedded rooms. Consequently, there is poor isolation of infected and colonized patients with multi-drug resistant organisms. The lack of strong infection control programs, trained infectious disease specialists and clinical pharmacists in the field of infectious diseases has also been reported as one of the factors associated with increased antibiotic resistance. We did not, however, investigate the factors associated with increased antibiotic resistance in this study, as it was not one of our objectives.

This study has all the limitations inherent to retrospective studies, including increased susceptibility to bias in data selection and analysis. Although the findings of this study might indicate whether physicians at our institution are currently following the recommended guidelines to treat pregnant women with ASB, we cannot draw relevant conclusions from this analysis.

### Conclusion

A very small proportion of pregnant women with ASB are treated, indicating possible gaps in the management of these patients, who are at risk of developing a more severe infection. We believe that these findings may be used to identify gaps in management and consequently improve patient care. We therefore recommend that future studies should incorporate items such as the qualification of the treating physician as well as patient- and hospital-related characteristics in the design. In referral centers such as KAUH, programs can be integrated to allow for the restricted use of antimicrobial agents and to provide decision-assisted physician order so as to control the use of antibiotics.

### Conflict of Interest

The author has no conflict of interest.

### Disclosure

The author did not receive any type of commercial support either in forms of compensation or financial for this study. The author has no financial interest in any of the products or devices, or drugs mentioned in this article.

### Ethical Approval

Obtained.

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## البولية الجرثومية الأعراضية بين النساء اللاتي يرتددن علي عيادات ما قبل الولادة في جدة بالمنطقة الغربية من المملكة العربية السعودية

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**المستخلص.** هذا الرسم البياني الاسترجاعي أجري لتحديد نسبة النساء الحوامل اللواتي يعانين من البكتيريا الأعراضية واللواتي تمت متابعتهم في عيادات رعاية الحمل قبل الولادة في مستشفى جامعة الملك عبدالعزيز في جدة بين يناير ٢٠٠٧ ويناير ٢٠١٢. وسجلت البيانات السريرية والغير سريرية لـ ٣٣٧ امرأة في الأشهر الثلاثة الأخيرة من الحمل. ان انتشار البكتيريا الأعراضية في المجموعة كانت ٢٦,٣١%. وكانت البكتيريا المعزولة في معظم الأحيان تشمل الإشريكية القولونية، العصوية الرئوية في ٣٩,٣٠% و ٧٨,١٠% من الحالات على التوالي. في معظم الحالات، كانت البكتيريا المعزولة حساسة للأمبيسلين (٥٧,١١%)، أموكسيسيلين (٣٨,١٠%)، وأميكاسين (٦٣,٥%). وكانت معظم البكتيريا مقاومة للنتروفورانتوين (٦,٢١%)، التتراسيكلين (٠٦,٢١%) والسيفيكسيم (٧٧,٢٠%). وشملت الأدوية الموصوفة الأكثر شيوعا متعدد الفيتامينات (ن = ٤٠ و ٨٧,١١%)، وفيتامين ب ١٢ (ن = ٤٧ و ٩٥,١٣%)، حمض الفوليك (ن = ٤٥ و ٣٥,١٣%)، والمضادات الحيوية (ن = ٤٣؛ ٧٥,١٢%). عموما، من الممكن أن تكون النساء الحوامل المصابات بالبكتيريا الأعراضية تلقين رعاية اقل من المستوى المطلوب في مؤسستنا وينبغي تحديد الثغرات في إدارة هؤلاء المرضى لتحسين رعاية المرضى.