

Prevalence of asymptomatic bacteriuria in pregnant women in Sharjah, United Arab Emirates

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معدل انتشار البيلة الجرثومية غير المصحوبة بأعراض لدى الحوامل في الشارقة بالإمارات العربية المتحدة

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الخلاصة: للتعرف على معدل انتشار البيلة الجرثومية غير المصحوبة بأعراض أثناء الحمل، أجرى الباحثان دراسة مسحية لـ 505 عينات من منتصف البيلة للحوامل من الشارقة، الإمارات العربية المتحدة، وذلك بتحليل البول وزرعه. وقد أظهرت مزارع البول نمواً كثيفاً (يبلغ 10^5 مستعمرة أو أكثر في كل ميلي لتر) لدى 4.8% من النماذج (24/505). وقد تم استفراد الإشريكيات القولونية في 16 نموذجاً من أصل 24 (66.7%). وكان للفحص المجهرى الحساسية العليا (67%)، أما النوعية العليا (99%) فكانت لاختبار غمسية dipstick النتريت التي أنصفت أيضاً بالقيمة التنبؤية الإيجابية العليا (57%). كما أظهرت اختبارات الحساسية للمضادات الحيوية على عينات المزارع الإيجابية حساسية مرتفعة لكل من الجنتاميسين، والأموكسي سيلين مع حمض الكلوفلينيك، والفوسفومييسين.

ABSTRACT To determine the prevalence of asymptomatic bacteriuria in pregnancy, midstream urine samples from 505 pregnant women in Sharjah, United Arab Emirates, were screened using urine culture and urinalysis. Urine cultures showed heavy growth ($\geq 10^5$ colony forming units/mL) in 4.8% (24/505) of the samples; 16/24 (66.7%) of these isolates were *Escherichia coli*. Microscopic examination had the highest sensitivity (67%), while nitrite dipstick testing showed the highest specificity and positive predictive value (99% and 57% respectively). Antibiotic sensitivity tests carried out on the positive culture samples showed high sensitivity to gentamicin, amoxicillin-clavulanic acid and fosfomycin.

Prévalence de la bactériurie asymptomatique chez les femmes enceintes à Sharjah (Émirats arabes unis)

RÉSUMÉ Afin de déterminer la prévalence de la bactériurie asymptomatique pendant la grossesse, on a analysé des prélèvements d'urine recueillis par la méthode du jet de milieu de miction chez 505 femmes enceintes à Sharjah (Émirats arabes unis) par mise en culture et examen des urines. Les cultures d'urine ont montré une forte croissance ($\geq 10^5$ unités formant colonie/mL) dans 4,8 % des échantillons (24/505) ; *Escherichia coli* a été isolée dans 16/24 (66,7 %) de ces derniers. L'examen microscopique avait la sensibilité la plus élevée (67 %), tandis que le test « nitrite » (bandelettes réactives) présentait la spécificité la plus élevée et la meilleure valeur prédictive positive (99 % et 57 % respectivement). L'étude de la sensibilité aux antibiotiques réalisée sur les échantillons de culture positifs a montré une forte sensibilité à la gentamycine, à l'amoxicilline-acide clavulanique et à la fosfomycine.

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Introduction

Asymptomatic bacteriuria is a major risk factor for the development of urinary tract infection (UTI) [1–3]. During pregnancy, many changes occur in the structure and function of the urinary tract that predispose pregnant women to upper UTI. Although there is a small risk of development of acute episodes of UTI in early pregnancy, there will be a substantial increase risk (to 30% to 60%) during the last trimester.

MacLean found that 6% of pregnant women had asymptomatic bacteriuria and this was associated with increased prematurity and perinatal mortality compared with healthy pregnant women [4]. In general, the prevalence of asymptomatic bacteriuria in pregnancy was found to be 2% to 7% [3,5]. Failure to treat bacteriuria during pregnancy increases the risk of development of acute pyelonephritis by 25% and may result in complications, such as preterm labour, transient renal failure, acute respiratory distress syndrome, sepsis, shock and haematological abnormalities [5–7]. Woman with untreated UTI during their third trimester of pregnancy are at-risk of delivering a child with mental retardation or developmental delay [8].

Diagnosis of UTI usually depends on different screening tests: urine microscopic examination, nitrite reductase, leukocyte esterase dipstick and urine culture. Urine dipstick tests have been evaluated by many researchers but their low sensitivity, high false negative (specificity) and poor positive predictive value makes them unreliable [9–15]. For such reasons urine culture remains the most reliable tool for the diagnosis of UTI. Urine culture has shown *Escherichia coli* to be the most common bacterial isolate of UTI during pregnancy [6,16]. *E. coli* serotyping is important in distinguishing the small number of strains that

cause disease since over 700 antigenic types of *E. coli* have been recognized based on O, H and k antigens [17]. *E. coli* serotype O5 was the most prevalent (29.3%) followed by O17 and O25 in patients with symptomatic UTI [18–21].

In Sharjah, United Arab Emirates (UAE), no data are yet available on the prevalence of asymptomatic bacteriuria during pregnancy. This study sought to investigate the prevalence of asymptomatic bacteriuria among pregnant women and to determine the most reliable diagnostic procedures, the most common types of bacteria and the most suitable antibiotics to use.

Methods

This study was approved by the University Research Centre, University of Sharjah, UAE and Sharjah Medical District. All participants signed a consent form.

Sample

The sample comprised 505 asymptomatic pregnant women visiting the primary health care centre (Maternal Child Health, Main Centre, Sharjah Medical District, Sharjah, UAE) between February 2001 and April 2002. The women's ages ranged from 15 to 41 years, with a mean age of 27.0 (standard deviation 4.9) years. None of the women had received antibiotics before screening.

Tests

Midstream urine (MSU) samples were collected from the women and each sample was divided into two parts. One part was used for general urine examinations. Direct microscopy for white blood cell (WBC) counts was considered positive if there were > 5 WBC per high-power field. Dipstick tests were made using Comber 10 reagent test strips (Analyticon, Germany) that have

panels to detect protein, blood and nitrite and leukocyte esterase in urine.

Urine cultures

The other urine sample was cultured on the following media: McConkey agar, eosin methylene blue agar, nutrient agars, blood agars and CLED (cystine-lactose-electrolyte-deficient) agar. The standard loop technique was used for colony counting (LP Italiana SpA, Milan, Italy). The urine culture was defined as positive if $\geq 10^5$ colony forming units (CFU) per mL of urine was found, regardless of the presence or absence of leukocytes [2]. Urine cultures with 10^3 – 10^4 CFU/mL were regarded as suspected infections, cultures with less than 10^3 CFU/mL were considered contaminated, while cultures with no growth of bacteria were said to be negative. From these criteria, the sensitivity, specificity and positive predictive values were calculated for each test.

Antibiotic sensitivity tests were carried out using the antibiotic sensitivity disc method with the following antibiotics: ampicillin, amoxicillin-clavulanic acid, nitrofurantoin, ciprofloxacin, nalidixic acid, trimethoprim, cephalixin, gentamicin, as well as fosfomycin, an antibiotic which has not been used or tested in the UAE.

Serotyping of *Escherichia coli*

Several kits (Mast Diagnostic, Amiens, France) were used to type the 16 *E. coli* strains isolated from cases of asymptomatic bacteriuria: O26, O86a, O111, O127a, O44, O119, O124, O112a, O28ac, O128, O20, O157, O55, O125, O126, O142, O114 and O18.

For comparison of serotypes from the community, the same kits were used to serotype another 16 *E. coli* isolates obtained from non-pregnant women with symptomatic community-acquired UTI.

Identification of bacteria was performed using a kit for API-20 (bioMérieux, Marcy-Etoile, France).

Results

Table 1 shows the prevalence of the asymptomatic bacteriuria of pregnant women (CFU $\geq 10^5$ /mL); 4.8% (24/505) of the screened urine samples were positive (CFU $\geq 10^5$ /mL), while 34.1% (172/505) were suspected infections.

Table 2 shows that urinalysis by microscopic examination was positive (> 5 WBC per high-power field) in 35.6% (180/505) of samples. However, the nitrite dipstick and esterase dipstick tests were positive in 1.4% (7/505) and 11.7% (59/505) of samples respectively.

Table 3 shows the sensitivity, specificity and positive predictive value for the leukocyte esterase dipstick, nitrite dipstick and microscopic urinalysis tests. Microscopic examination had the highest sensitivity (67%), while the nitrite dipstick showed the highest specificity and positive predictive value (99% and 57% respectively).

The most common bacteria isolated from the culture of the urine samples of

Table 1 Prevalence of asymptomatic bacteriuria in the urine of 505 pregnant women

| Bacteriuria | Colony forming units (No./mL) | No. of isolates | % |
|--------------|-------------------------------|-----------------|-------|
| Positive | 10^5 | 24 | 4.8 |
| Suspected | 10^4 – 10^3 | 172 | 34.1 |
| Contaminated | 10^2 | 19 | 3.8 |
| Negative | $< 10^2$ | 290 | 57.4 |
| Total | | 505 | 100.0 |

Table 2 Comparison of different tests used for diagnosis of urinary tract infection in the urine of 505 pregnant women

| Colony forming units (No./mL) | No. of isolates | Microscopic examination | | Nitrite dipstick | | Leukocyte esterase dipstick | |
|-------------------------------|-----------------|-------------------------|------|------------------|------|-----------------------------|------|
| | | No. +ve | % | No. +ve | % | No. +ve | % |
| 10 ⁵ | 24 | 16 | 66.7 | 4 | 16.7 | 4 | 16.7 |
| 10 ⁴ | 48 | 30 | 62.5 | 1 | 2.1 | 15 | 31.3 |
| 10 ³ | 124 | 56 | 45.2 | 2 | 1.6 | 25 | 20.2 |
| 10 ² | 19 | 7 | 36.8 | 0 | 0 | 1 | 5.3 |
| < 10 ² | 290 | 71 | 24.5 | 0 | 0 | 14 | 4.8 |
| Total | 505 | 180 | 35.6 | 7 | 1.4 | 59 | 11.7 |

the pregnant women with asymptomatic bacteriuria were *E. coli* in 66.7% of samples (16/24) (Table 4).

The different serotypes of *E. coli* isolated from the urine of asymptomatic bacteriuria of pregnant women and symptomatic bacteriuria isolated from the sample from women with community-acquired infection are shown in Table 5. The main *E. coli* serotype among the samples with asymptomatic bacteriuria was O112ac (25.0% of samples), while in symptomatic community-acquired bacteriuria the main serotype was O86a (31.3% of samples).

The pattern of antibiotic sensitivity of the 16 *E. coli* isolates is shown in Table 6. The results show that *E. coli* of asymptomatic bacteriuria of pregnancy were 100% (16/16) sensitive to gentamicin, ciprofloxacin and fosfomycin. The *E. coli* isolated from symptomatic bacteriuria showed 100% sensitivity to amoxicillin-clavulanic acid and fosfomycin. *E. coli* from both types of isolates were the least sensitivity to trimethoprim. The 8 non-*E. coli* isolates were also 100% sensitive to fosfomycin and amoxicillin-clavulanic acid.

Table 3 Accuracy of urine screening tests for asymptomatic bacteriuria in the urine of pregnant women

| Test | Sensitivity ^a | Specificity ^b | Positive predictive value ^c |
|-----------------------------|--------------------------|--------------------------|--|
| | % | % | % |
| Leukocyte esterase dipstick | 17 | 86 | 7 |
| Nitrite dipstick | 17 | 99 | 57 |
| Microscopic examination | 67 | 66 | 9 |

^aPercentage of patients with a positive culture who will have a positive test.

^bPercentage of patients with a negative culture who will have a negative test.

^cPercentage of patients with a positive test who have positive urine culture.

Table 4 Bacteria species isolated from the urine of pregnant women with asymptomatic bacteriuria

| Species | No. of isolates ^a | % |
|---|------------------------------|-------|
| <i>Escherichia coli</i> | 16 | 66.7 |
| <i>Staphylococcus epidermidis</i> (coagulase-negative staphylococcus) | 3 | 12.5 |
| <i>Staphylococcus aureus</i> | 2 | 8.3 |
| <i>Enterobacter saprophyticus</i> | 1 | 4.2 |
| <i>Enterococcus saprophyticus</i> | 1 | 4.2 |
| <i>Proteus mirabilis</i> | 1 | 4.2 |
| Total | 24 | 100.0 |

^aColony forming units $\geq 10^5$ /mL.Table 5 Serotypes of *E. coli* isolated from urine samples of women with asymptomatic and symptomatic bacteriuria

| Serotype | Asymptomatic bacteriuria ^a (n = 16) | | Symptomatic bacteriuria ^a (n = 16) | |
|----------|--|------|---|------|
| | No. | % | No. | % |
| O112ac | 4 | 25.0 | 3 | 18.8 |
| O125 | 3 | 18.8 | 1 | 6.3 |
| O26 | 2 | 12.5 | 1 | 6.3 |
| O20 | 1 | 6.3 | 1 | 6.3 |
| O142 | 1 | 6.3 | 1 | 6.3 |
| O119 | 1 | 6.3 | 1 | 6.3 |
| O28ac | 1 | 6.3 | 0 | 0 |
| O114 | 1 | 6.3 | 0 | 0 |
| O69 | 1 | 6.3 | 0 | 0 |
| O44 | 1 | 6.3 | 0 | 0 |
| O86a | 0 | 0 | 5 | 31.3 |
| O124 | 0 | 0 | 3 | 18.8 |
| O111 | 0 | 0 | 0 | 0 |
| O55 | 0 | 0 | 0 | 0 |
| O182 | 0 | 0 | 0 | 0 |

^aColony forming units $\geq 10^5$ /mL.

n = total number of samples.

Table 6 Antibiotic sensitivity pattern for *E. coli* isolated from urine samples of women with asymptomatic and symptomatic bacteriuria

| Antibiotic | <i>E. coli</i> antibiotic sensitivity | | | |
|-----------------------------|---------------------------------------|-------|----------------------------------|-------|
| | Asymptomatic bacteriuria (n = 16) | | Symptomatic bacteriuria (n = 16) | |
| | No. | % | No. | % |
| Fosfomycin | 16 | 100.0 | 16 | 100.0 |
| Gentamicin | 16 | 100.0 | 15 | 93.8 |
| Ciprofloxacin | 16 | 100.0 | 14 | 87.5 |
| Cephalexin | 13 | 81.3 | 13 | 81.3 |
| Amoxicillin-clavulanic acid | 13 | 81.3 | 16 | 100.0 |
| Nitrofurantoin | 11 | 68.8 | 12 | 75.0 |
| Nalidixic acid | 8 | 50.0 | 13 | 81.3 |
| Ampicillin | 8 | 50.0 | 10 | 62.5 |
| Trimethoprim | 6 | 37.5 | 10 | 62.5 |

n = total number of samples.

Discussion

The prevalence of asymptomatic bacteriuria of pregnant women in our study (4.8%) is similar to other reports (4% to 10%) [8,22]. This indicates that about 5% of pregnant women are at risk of development of acute episode of UTI during pregnancy if they are not properly treated. Suspected urine cultures with 10^3 – 10^4 CFU/mL (34.1% of our sample) need to be repeated at regular intervals during the course of pregnancy and the cases should be followed up or treated.

Comparing the urinalysis screening tests with the results of urine culture, which is the gold standard for the diagnosis and management of UTI, these tests were shown to be unreliable. The tests had low sensitivity, high false negative (specificity) and poor positive predictive value. Similar findings were reported by other authors [9,13–15].

Therefore, a urine culture should be routinely obtained from all pregnant women for screening during the first antenatal visit and repeated during the third trimester, because the urine of the treated patients may not remain sterile for the entire pregnancy.

The most common bacterial isolates from MSU samples of asymptomatic pregnant women were *E. coli* in 66.7%, followed by coagulase-negative staphylococci in 12.5%. Similar findings have been reported by other researchers [5,15]. *E. coli* is the most common microorganism in the vaginal and rectal area, and because of the anatomical and the functional changes that occur during pregnancy, the risk of acquiring UTI from *E. coli* is high [5].

The commonest *E. coli* serotypes were O112ac in the urine of pregnant women with asymptomatic bacteriuria and O86a in symptomatic bacteriuria. In India, Misra found that the commonest *E. coli* serotype in symptomatic UTI was O5 [18]. Other studies have found different *E. coli* serotypes in UTI (O1, O2, O4, O6, O18ac and O75) [18–21]. Geographical distribution and epidemiological factors may play a role in this variation [19]. Further studies are required to explore the relationship between different serotypes and virulence factors of *E. coli* causing UTI in different geographical regions by using tissue cultures and polymerase chain reaction analysis [18,23].

The antibiotic sensitivity patterns showed that most of the bacterial isolates were sensitive to gentamicin, ciprofloxacin, amoxicillin-clavulanic acid and fosfomicin. However, the data were insufficient to confirm the preference of a single dose or longer duration doses in treating asymptomatic bacteriuria in pregnant women.

Fosfomicin (Monurol) is a new antibiotic that can be taken as a single dose and has a good margin of safety during pregnancy [24]. Single-dose treatments have lower costs and better compliance than multiple doses, but need to be evaluated further [25]. Amoxicillin-clavulanic acid (Augmentin) is also considered safe for the treatment of pregnant women with urinary tract infection and is regarded as a good choice [26]. Trimethoprim-sulfamethoxazole was the least sensitive antibiotic in our study.

The choice of antibiotic should be based on urine culture, stage of gestation, maternal clinical data and the characteristics of the antibiotic [27]. However, aggressive antibiotic treatment may be necessary to reduce the risk of pyelonephritis in pregnancy [22,28]. All pregnant women with persistent bacteriuria or recurrent infection need follow-up cultures and a urological evaluation after delivery [17].

In conclusion, this study showed that 4.8% of the pregnant women examined had a positive urine culture without any symptoms of UTI. Hence, it is important that pregnant women are screened for asymptomatic bacteriuria at the first antenatal visit.

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