

ASYMPTOMATIC BACTERIURIA IN WOMEN WITH DIABETES MELLITUS

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Submitted: 23/12/2014; Accepted: 12/5/2015; Published: 1/12/2015



ABSTRACT

Background

Asymptomatic bacteriuria is a problem in women with diabetes mellitus and may lead to urinary tract infection. *Escherichia coli* remains the single most common bacteria isolated from asymptomatic bacteriuria in women.

Objectives

To determine the prevalence and antibiotics resistance profile of asymptomatic bacteriuria among women with diabetes mellitus, this is important for epidemiological study.

Methods

A total of 600 non-pregnant women with diabetes (type 1 and type 2), and 300 women without diabetes (control group) were screened for asymptomatic bacteriuria. All the women were free from any symptoms of urinary tract infection. Two separate clean catch midstream urine samples were collected, examined microscopically and cultured. Bacteria were isolated and identified using standard bacteriological methods. Antibiotic susceptibility testing was performed using standard disk-diffusion assays.

Results

Asymptomatic bacteriuria was detected in 15.67% of diabetic women (14.33% in type 1 and 17.00% in type 2), and 3.67% in non-diabetic women ($P < 0.001$). *Escherichia coli* (58.51%) was the most prevalent pathogen isolated in diabetic subjects. Most of the bacteria were resistant to Ceftriaxone (85.11%), Cefixime (73.40%), and Trimethoprim (73.40%).

Conclusion

Asymptomatic bacteriuria is not uncommon among diabetic women and might be added to the list of diabetic complications in these women.

Keywords: *Diabetes Mellitus, Bacteriuria, Asymptomatic, UTI, Antibiotics Resistance*

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INTRODUCTION

The prevalence of diabetes increases worldwide ^(1, 2), and its complications become more important ⁽³⁾. Diabetes mellitus is associated with increased risk for common infections ⁽⁴⁻⁷⁾, and is a strong predictor of mortality related to infection ⁽⁸⁾. The risk of developing infection in diabetic patients is high, and urinary tract is the most common site for infection ⁽⁹⁾. Furthermore, asymptomatic bacteriuria (ASB) is common and major problems in women with diabetes ⁽¹⁰⁾, and ASB has been identified as a risk factor for developing a urinary tract infection (UTI) especially in diabetic women ⁽¹¹⁾. The term ASB refers to the presence of two consecutive clear-voided urine specimens showing at least 10^5 colony forming units/ml of the same microorganisms, in a patient without UTI symptoms ^(10, 12, 13).

Diabetes leads to higher glucose concentration in urine that may serve as a culture medium for bacterial growth, when adding glucose to it enhances the growth of bacteria *in vitro*, the association has not been verified *in vivo* ^(3, 14, 15). It appears that the incidence of ASB is high in women with diabetes type 1, and type 2 ⁽¹⁶⁾, and glucosuria can be associated with ASB in diabetic women ⁽⁹⁾. Moreover, impaired immune response may play a role in the decreased ability of the patient's defend against bacterial proliferation ⁽¹⁷⁾.

Asymptomatic bacteriuria is common among diabetic than non-diabetic woman ⁽¹⁸⁾, and the prevalence of ASB ranges between 9.1-29.3% in diabetic women ⁽¹⁹⁾, which is tend to have persistent or recurrent ASB ⁽²⁰⁾. The clinical significance and management of ASB differs with different groups of patients ⁽²¹⁾. Guidelines published by the Infectious Disease Society of America (IDSA) recommended that there is no measurable benefit to provide antibiotic treatment of ASB in diabetic women ⁽²²⁾.

METHODS

The study population included 600 women with diabetes mellitus attended to Shahid Layla Qasim Diabetic Center in Erbil City. The medical official documentations were used to diagnose diabetes mellitus (type 1 or type 2). A randomly selected control group of 300 women without diabetes whom were visiting public health centers for eye problems. This study was conducted during the period from June 2012 to January 2014.

Asymptomatic bacteriuria is a microbiologic diagnosis determined with a urine specimen that has been

collected in a manner to minimize contamination and transported to the laboratory in a timely fashion to limit bacterial growth. Diagnosis of ASB in all women were conducted according to the IDSA guideline as two consecutive clean-catch voided urine specimens with isolation of the same bacterial species in quantitative counts of $\geq 10^5$ colony forming units/ml ^(22, 23).

Exclusion criteria were pregnancy, symptoms of UTI (including dysuria, hematuria, urgency, frequency, abdominal discomfort, or fever), known urinary tract abnormalities (e.g. neurogenic bladder), urinary tract instrumentation (within the past 4 months), recent hospitalization or surgery, women older than 65 years, serum creatinine level of more than 2.2 mg/dL, the use of antibiotics in the last 14 days.

Ethic committee and scientific committee of Nursing College, Hawler Medical University were approved the study protocol. An informed consent was obtained from all women. All information about women screened was kept confidential.

The urinary specimens were microscopically examined by standard method. The urinary specimens that contain significant crystals were excluded from the study.

Bacterial culture were performed by streaking one milliliter of urine with a calibrated loop on MacConkey agar (Oxoid, England) and 5% Blood agar plates (Oxoid, England). These agar plates were incubated at 37°C for 24 hours under aerobic condition. Bacterial colony counts of 10^5 /ml or more of pure bacteria isolates were considered as significant ASB ^(22, 24). Mixed growths of three different organisms were considered to be contaminated, and excluded from the study. Bacterial species were identified with standard laboratory techniques ⁽²⁵⁾.

The standardized Kirby-Bauer disc diffusion test was performed for all pathogenic bacteria ⁽²⁶⁾. The antibiotics disc were obtained from Bioanalyse Co., Ltd., (Turkey), the antibiotics disc used were Cephalexin (10 mcg), Cefixime (5 mcg), Ceftriaxone (30 mcg), Ciprofloxacin (5 mcg), Gentamicin (10 mcg), Nitrofurantoin (300 mcg), Tobramycin (10 mcg) and Trimethoprim (5 mcg).

Statistical package for social sciences (SPSS) 18.0 software were used to analyzed the results. Chi-square (X^2) test was used to compare categorical variables, in addition calculation of Odds Ratio (OR) and 95% Confidence Intervals (95% CI). P (predictive) value less

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than 0.05 were considered as a significant association between the variables tested.

RESULTS

Among 600 women with diabetes and 300 women without diabetes (control group), the prevalence of ASB was 15.67%, and 3.67%, respectively. The risk of ASB were approximately five-fold higher in diabetic women than the control group (OR: 4.881, 95% CI: 2.571- 9.266, P<0.001) (Table 1).

Table 2 shows that among 300 women with type 1 diabetes and 300 women with type 2 diabetes. The prevalence of ASB was 43 (14.33%) among women with type 1 diabetes and ASB was detected in 51 (17.00%) women with type 2 diabetes. Statistical analysis revealed that the difference between type 1 diabetes and type 2 diabetes were not significant.

Gram-negative bacteria were the commonest bacteria isolated (77.66%), which statistically (P<0.001) higher than Gram-positive bacteria (22.34%) (Table 3). Among

11 types of bacteria species isolated from ASB, the predominant bacterium was *Escherichia coli* (58.51%), followed by *Klebsiella pneumoniae* (8.51%), Group B Streptococcus (7.45%), *Staphylococcus saprophyticus* (5.32%), and *Staphylococcus aureus* (4.26%) (Table 4).

The antibiotics resistances profile of Gram-negative and Gram-positive bacteria are summarized in Table 5. High percentage of antibiotic resistance (85.11%) was shown in Ceftriaxone (97.26% in Gram-negative bacteria, and 42.86% in Gram-positive) followed by 73.4% in Cefixime (80.82% in Gram-negative and 47.62% in Gram-positive) and 73.4% in Trimethoprim (71.23% in Gram-negative, and 80.95% in Gram-positive). There are significant difference between Gram-negative and Gram-positive bacteria resistance to Cephalexin (P= 0.005) and Cefixime (P= 0.002) only. On other hand, there are no significant difference between the effect of antibiotics on Gram-negative and Gram-positive bacteria to others antibiotics.

Table 1. Compared asymptomatic bacteriuria in diabetic women with control group

Bacteriuria	Diabetic women		Non-diabetic women (control group)	
	No.	%	No.	%
Asymptomatic bacteriuria	94	15.67	11	3.67
Bacteriuria negative	506	84.33	289	96.33
Total	600		300	

OR: 4.881, 95% CI: 2.571- 9.266, P<0.001

Table 2. Type 1 and 2 diabetic's women with asymptomatic bacteriuria

Bacteriuria	Type 1 diabetics		Type 2 diabetics		Total	
	No.	%	No.	%	No.	%
Asymptomatic bacteriuria	43	14.33	51	17.00	94	15.67
Bacteriuria negative	257	85.67	249	83.00	506	84.33
Total	300		300		600	

Not significant different between diabetics type 1 and type 2 ($X^2 = 0.81$, P= 0.369)

Table 3. Gram-negative and positive bacteria isolate from asymptomatic bacteriuria in diabetic women

Bacteria	No.	%
Gram-negative	73	77.66
Gram-positive	21	22.34
Total	94	

High significant difference between Gram-negative and Gram-positive bacteria ($X^2= 15.58, P<0.001$)

Table 4. Bacterial isolate from asymptomatic bacteriuria among diabetic women

Bacteria	No.	%
<i>Escherichia coli</i>	55	58.51
<i>Klebsiella pneumoniae</i>	8	8.51
<i>Group B Streptococcus</i>	7	7.45
<i>Staphylococcus saprophyticus</i>	5	5.32
<i>Staphylococcus aureus</i>	4	4.26
<i>Staphylococcus epidermidis</i>	3	3.19
<i>Proteus spp</i>	3	3.19
<i>Pseudomonas spp</i>	3	3.19
<i>Citrobacter freundii</i>	3	3.19
<i>Enterococcus faecalis</i>	2	2.13
<i>Klebsiella oxytoca</i>	1	1.06
Total	94	

Table 5. Antibiotics resistant of 73 Gram-negative and 21 Gram-positive bacteria isolate from asymptomatic bacteriuria in diabetic women

Antibiotics	Gram-negative		Gram-positive		Statistical analysis		Total	
	No.	%	No.	%	X²	P-value	No.	%
Cephalexin	30	41.1	16	76.19	8.04	0.005	46	48.94
Cefixime	59	80.82	10	47.62	9.21	0.002	69	73.40
Ceftriaxone	71	97.26	9	42.86	38.08	0.679	80	85.11
Ciprofloxacin	15	20.55	3	14.29	0.41	0.520	18	19.15
Gentamicin	18	24.66	4	19.05	0.29	0.593	22	23.40
Nitrofurantoin	11	15.07	5	23.81	0.88	0.348	16	17.02
Tobramycin	8	10.96	3	14.29	0.17	0.676	11	11.70
Trimethoprim	52	71.23	17	80.95	0.79	0.374	69	73.40

DISCUSSION

Several studies had been reported that a high prevalence of ASB among women with diabetes type 1 and type 2 than women without diabetes^(7, 27-31), which is in agreement with this study. The majority of investigators have reported approximately a three-fold higher prevalence of ASB among diabetic women than among non-diabetic women^(7, 10), and the increased prevalence of ASB among diabetic women maybe result from differences in the host responses between diabetic and non-diabetic women^(22, 32). On other hand, another study reported that the rate of ASB among women with diabetes is similar to non-diabetes women⁽³³⁾.

Asymptomatic bacteriuria was more common both in patients with type 1 diabetes and in type 2 diabetes than in non-diabetic⁽³⁾, which is in agreement with present study. However, another study found that the prevalence of ASB among women with type 1 diabetes was 21%, and 29% in type 2 diabetes⁽¹⁰⁾, that is higher than the present study.

Gram-negative bacteria are the most prevalent uropathogens⁽¹⁵⁾, that is in agreement with this study, and the increased frequency of Gram-negative bacteria may be attributed to increase the percentage of *Escherichia coli* isolated. It appears that the most common bacterium is usually *Escherichia coli*⁽³⁴⁾. In present study, *Escherichia coli* was predominant bacteria isolated from diabetic women with ASB, these findings were confirmed by other studies^(30, 31, 34), ASB might be result by normal flora around the urethra, vagina, and digestive tract, which is at the entrance to the urinary bladder.

The antibiotics resistance pattern varies from community to community, and from region to region. In our region, there are no guidelines and stewardship of antibiotics use to treat UTI and ASB among diabetic women, self-medication, overuse and misuse of antibiotics especially overuse of cephalosporin antibiotics to treat ASB among diabetic women, which may be the reason for increased the antibiotic resistance to Ceftriaxone, Cefixime and Trimethoprim in this study. In Southwest Cameroon, most bacteria responsible for ASB in diabetics were multiple antibiotic resistance⁽²⁴⁾. Furthermore, the emergence of antibiotic resistance is associated with the indiscriminate usage of antibiotics^(35, 36). Transmission of antibiotic resistant bacteria might leads to diabetic foot infection among poor hygiene women with ASB.

The prevalence of ASB in women with diabetes was higher than non-diabetic, and the bacterial isolated from ASB among women with diabetes is resistance to Ceftriaxone, Cefixime and Trimethoprim. This study provides important information on the prevalence and antibiotic resistance pattern of bacterial isolated from ASB among women with diabetes.

Acknowledgments

We thank the diabetic women for their participation, and staff of Shahid Layla Qasim Diabetic Center for cooperation.

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