

## **RESEARCH ARTICLE**

#### ASYMPTOMATIC BACTERIURIA AMONG TYPE 2 DIABETES MELLITUS PATIENTS IN PRIMARY CARE CENTRE IN SAUDI ARABIA.

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Manuscript Info	Abstract
Manuscript History	<b>Background:</b> The present study aimed to measure the prevalence of
Received: 19 March 2017 Final Accepted: 22 April 2017 Published: May 2017	ASB among type 2 diabetes mellitus (12DM) patients and to determine the demographic and clinical factors that may contribute to its development. Methods: A cross sectional study was conducted in the Chronic
<i>Key words:-</i> Asymptomatic bacteriuria; diabetes mellitus; Saudi Arabia.	<ul> <li>Diseases Center at primary care from 21 February to 24 March 2016. Patients with T2DM with any symptoms of urinary tract infection (UTI) were participated. Midstream urine Specimen (MSU) was collected and tested for infection and culture /sensitivity of ASB.</li> <li><b>Results:</b> A total of 406 patients (203 males and 203 females) with T2DM was included in the present study. Twenty two patients (5.6%) had a significant bacteriuria. The female participants had a significantly more bacteriuria compared to male participants (4 male versus 18 females). There was no statistically significant correlation between age, HbA1c, duration of diabetes, and body mass index (BMI). Logistic regression showed that there is each year increase in age, and one unit increase in HbA1c level among males compared with females.</li> <li><b>Conclusions:</b> The relatively low prevalence of ASB was found in patients with T2DM. There are no significant association between ASB and other factors.</li> </ul>
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#### Background:-

Asymptomatic bacteriuria (ASB) is a common problem in diabetic patients and it is associated with risk of septicemia and pyelonephritis if left untreated<sup>1,2</sup>. Type 2 diabetes mellitus (T2DM) has been associated with urinary tract infections<sup>3,4</sup>. The mechanism of pathogenesis for this link is not fully clear, yet, it's thought that a high glucose concentration in urine may favor the development of pathogenic microorganisms<sup>5</sup>. ASB is a type of urinary tract infection (UTI) described as the existence of large amounts (>105 cfu/ml) of bacteria in urine without symptoms of a UTI<sup>6,7</sup>. Significant considerable amount of bacteriuria utilize around 105 organisms per millimeter of a fresh "clean catch" urine specimen in any patient<sup>8</sup>. It shows active infection of the urinary tract<sup>9</sup>.

Kass was the first person to identify the significance of ASB<sup>10</sup>. He discovered that about 6 to 7% of pregnant women have ASB and nearly half of this developed pyelonephritis. ASB is also significant in the elderly and people who are

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known to be at high risk for frequent symptomatic infection like diabetics, patients with cystic- renal diseases, patients with a history of urethral catheterization and anatomic or neurologic urinary abnormalities<sup>11</sup>. Neglected ASB predisposes the patient to frequent UTI, which contribute to a significant morbidity if complicated and can also cause severe renal disease<sup>11</sup>. Morbidity and mortality from UTI at all ages remains significant<sup>12</sup>. The risk of developing an infection in diabetic patients is a high and urinary tract is the most common site for infection<sup>13,14</sup>.

Several studies were done regarding the prevalence of ASB among T2DM patients. In one study that included 124 T2DM patients with 55 males and 69 females, thirty-three patients (26.6%) had significant bacteriuria (9 males and 24 females). In this study ASB was more common among diabetic women with significant correlation with the duration of the diabetes and the age of the patients<sup>15,16</sup>. Another study included 1000 patients with T2DM, a significant ASB was found in 120 patients (70 females and 50 males ) with females being affected more than males<sup>17</sup>, this was comparable to previous reports in many countries including Italy, Scandinavia, Netherlands, and South Africa<sup>14,18-21</sup>. In other studies, the prevalence of ASB among T2DM was found to be 10.9%, 11.3% and 7.9 respectively<sup>11,21,22</sup>. Most of the studies showed higher prevalence of ASB in diabetic women compared to diabetic men<sup>3,4,15,16</sup>.

The highest prevalence of ASB in female was explained by the shortness of the female urethra, urethral opening near the anus and vagina, biologic changes due to menopause in females compared with males is due to prostate enlargement and neurogenic bladder in men<sup>23</sup>. The microorganisms causing ASB in persons with diabetes mellitus are similar to those causing bacteriuria in non-diabetic individuals<sup>16,20,24</sup>. In most previous studies, E coli was the most prevalent microorganism (59.1%) recovered from the urine cultures of the participants with high sensitivity to nitrofurantoin. In a few studies, the reported microorganisms were different. For example Kelebsiella was the most common organism in the Alebiosu study, but also highly sensitive to nitrofurantoin<sup>15,16</sup>.

Although ASB is a major issue in diabetics, there is minimal information on the existence of ASB among diabetic patients in the Arab countries. Therefore, a question is raised about the prevalence of ASB among diabetic in Saudi Arabia. The present study aimed to measure the prevalence of ASB among T2DM and to determine the demographic and clinical characteristic factors that may contribute to its development in the chronic diseases clinics of Wazarat Health center in Saudi Arabia.

## **Materials and Methods:-**

#### Setting:-

This study was conducted in the chronic diseases clinic at Al Wazarat Health Center in Riyadh, Saudi Arabia. The Chronic Disease Center (CDC) has six daily regular clinics, which receive around one hundred and twenty patients per day. It has a multidisciplinary team consisting of a Physician, 2 Clinical Pharmacists, 4 Diabetic Educators, aHealth Educator, Dietician, Psychologist, and aSocial worker.

#### Study Design:-

A cross sectional study was conducted in the Chronic Diseases Center at Wazarat Heath Center, Riyadh, Saudi Arabia.

#### Participants:-

All patients with T2DM (male and female) attending the chronic diseases clinics during the study period from 21 February to 24 March, 2016 were participated. Patients with type 1 DM, pregnant women, symptomatic UTI (dysuria, frequency and urgency. etc), patients with urinary catheter or Foley bag catheter, and history of antibiotic therapy in the previous two weeks were excluded from the study. Ethical approval for this study was obtained from the ethical committee of Prince Sultan Military Medical City (PSMMC). Approval from Wazarat/CDC was also obtained. A patient consent form was given to the patients for their agreement to participate in the study. All data were treated confidentially and was kept in a secured area.

#### Procedure:-

This study was conducted from 21 February to 24 March, 2016 in the male and female waiting areas health in the chronic diseases clinic at Al Wazarat Health Center during working hours (8:00 AM - 4:00 PM) from Sunday to Thursday. Patients were asked during their routine visits, whether they complained of any of urinary tract infection symptoms or not. Those who complained of any symptoms were excluded. In addition, any patient who had any of the exclusion criteria was also excluded. An informed consent was obtained from each patient who participated in

this study. A Midstream urine specimen (MSU) was collected from the eligible patients after they were given a clear instruction about how to collect clear catch mid-stream urine. The collected urine samples were sent to the laboratory for culture and sensitivity with the patient name and medical number. In addition to the MSU, other variables were collected from the patient's records which were available in the health center. The result of the MSU was retrieved from the computer and written in the data collection form below with other information obtained from the patients' record.

#### Statistical Analysis:-

The statistical analysis was done using the SPSS version 23. The analysis consisted of descriptive statistics for the patients' demographic and clinical characteristics. Furthermore, the urine test results were also described. Fisher's exact test was carried out to investigate the correlation between gender and the test results. Logistic regression was employed to investigate the relationship between the demographic and clinical characteristics with urine test results. A level of significant was p<0.05 for all the tests.

#### **Results:-**

A total of 406 patients with T2DM were included in the study (203 males and 203 females); only 10 specimens of urine in women were missing. They didn't give a sample to the laboratory. The demographic and clinical characteristics of the study were described in Table 1.

A total of 22 out of 406 (5.6%) patients with T2DM had ASB as seen in table 2. The mean age in this study was (56.3 $\pm$ 10.4 years). The means of HbA1c, duration of Diabetes (in years), and body mass index [BMI (kg/m<sup>2</sup>)] were 7.8 $\pm$ 1.2.9, 11.8 $\pm$ 7.6, and 33 $\pm$ 5.9, respectively.

There was a fivefold significant bacteriuria in female compared to male. There was no statistically significant correlation between age (P < 0.140), HbA1c (P < 0.730), duration of diabetes (P < 0.663), and BMI (P < 0.488) with ASB as shown in Table 3 and 4.

E coli was the most common organism causing the ASB in this study (46%). The second and third most common organism were Kelebsiella and Fecalis (13%, 9%), respectively, as shown in figure 1. Most of the organisms were sensitive to nitrofurantoin (68%); the second and third most sensitive antibiotics were SXT and ciprofloxacin (50%, 32%), respectively as shown in figure 2.

Table 5 shows the relationship between the urine test and the other variable using logistic regression. The variables were considered individually as reported in the descriptive part of the analysis. Table 5 shows that for each year increase in age, and one unit increase in HbA1c level among males, the odds ratio for the urine test to be positive increased by 2% while this was not the case factors related to females. **Table 1:-** Participant's characteristics (n=406).

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Characteristics	Mean $\pm$ SD
Age	$56.3 \pm 10.3$
HbA1c	$7.8 \pm 1.2$
Duration of Diabetes (Years)	$11.8 \pm 7.6$
Body mass index [BMI (Kg/m <sup>2</sup> )]	33.0 ± 5.9

Table 2:-Urine Culture and Sensitivity test. (n=396).

Test Result	Frequency	Percentage
Positive	22	5.6
Negative	374	94.4
Total	396	100.0

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	Urine	e Test		
Gender	Positive	Negative	P-value	Odds Ratio
Male	4	199	0.002	Reference group
Female	18	175		5.1 (1.7, 15.4)
Total	22	374		

<b>Table 4:-</b> The correlation between the urine test's results and the	ne continuous exploratory	y variables
Variable	Correlation*	P-value
Age	0.08	0.140
HbA1c	-0.02	0.730
Duration of Diabetes	0.02	0.663
BMI†	-0.04	0.488
*Point-Biserial correlation; †BMI: Body	Mass Index	

Table 4:-	The	correlation	between	the	urine	test's	results	and	the	continuous	exploratory	variables
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Table 5:- Logistic Regression for the relationship between the urine test's result and the demographic and clinical characteristics of the patients

Variable	Coefficient	P-value	OR (95% Confidence interval of OR)			
Constant	-2.27	< 0.001	-			
Male	-2.41	0.009	0.09 (0.01, 0.23)			
Age*Male*HbA1c	0.02	0.021	1.02 (1.01, 1.02)			
OR: Odds Ratio; $*R$ -squared = 0.12						



Figure 1:- Percentage of organism causing the ASB.



Figure 2:- Percentage of antibiotics sensitivity.

## **Discussion:-**

Significant asymptomatic bacteriuria is an important cause of pyelonephritis and gram negative septicemia among certain predisposed individuals, such as diabetics. A lot of studies showed that there is a high incidence of asymptomatic bacteriuria among diabetic patients and independent factors that might have an effect on the prevalence of ASB. Although ASB is a major issue among diabetics, there is scarcity in the studies regarding ASB in Saudi Arabia.

In the present study, the prevalence of ASB is 5.6%, which is lower compared to a study by Kayima et al.<sup>11</sup> done at the University of Nairobi, Kenya, which showed a prevalence of 11.1%. Similarly, Alebiosu et al.<sup>15</sup> and Makuyana et al.<sup>16</sup> reported a higher prevalence of 26.6%. In addition, a prospective study conducted by Chaudhuri et al.<sup>17</sup> in India has even shown a much higher prevalence of 58.3% and 41.7% in females and males, respectively. There is no clear cause to explain the differences in prevalence in these studies. It might be due to the difference in sample size sampling techniques, the nature of cross sectional studies or religious background. In the Muslim culture, ablution is five times a day and usage of water instead of tissue paper might have contributed to the lower prevalence. Our study showed higher prevalence of ASB among females as is seen in all the previous studies<sup>11,15-17</sup>, this could be explained by the anatomical variation between both genders.

In the present study, there was no correlation between ASB and other independent factors such as age, diabetes, duration of diabetes, HbA1c, neuropathy, etc. This is similar to the Iranian study which showed that age, duration of diabetes, HbA1c had no significant impact on ASB<sup>22</sup>. In contrast, the Nigerian study showed that ASB was related to the duration of diabetes and age<sup>15,16</sup>. In addition, the prospective study by Zhanel et al.<sup>20</sup> in the University of Chicago, Canada showed that ASB was related to women who have diabetes mellitus, longer duration of diabetes, neuropathy, and heart disease. Moreover, the study by Chaudhuri et al.<sup>17</sup> in India showed that ASB was related to HbA1C only. Furthermore, a case control study by Geerlings et al.<sup>3,4</sup> in the Netherlands showed that ASB was related to age, macro albuminuria, lower BMI and UTI during previous years.

In the present study, the E. Coli was the most prevalent microorganism recovered from urine cultures of the participants with high sensitivity to nitrofurantoin. All previous studies showed the same finding regarding the recovered organism and its sensitivity to nitrofurantoin, with exception of the Nigerian study, which showed Klebsiella as the most common organism<sup>15,16</sup>.

In the present study, there was a lack of matching of male and female participants in the sample which could influence the logistic regression result of the gender in relation to the disease. In addition, Albumin/Creatinine ratio was not measured in this study group. Furthermore, patients with renal impairment were not excluded. It would be interesting to investigate the prevalence of ASB among Muslim and non-Muslim diabetics to see whether there is a significant difference related to their micturition behavior. Further studies are warranted to assess the prevalence of asymptomatic bacteriuria in diabetic patients in other Saudi Arabia, population with proper design and matching between male and female to study the influence of gender in ASB and also to assess confounding factors that may affect the prevalence of significant ASB. In addition, long-term follow up should also be implemented for diabetic patients with ASB to detect any UTI development in the future.

#### **Conclusions:-**

In the present study, the relatively low prevalence of ASB was found compared with other studies. There are no significant association between ASB and other factors (duration of diabetes HbA1c, etc.). The results of the current study should be generalized to similar populations with caution. Further study in multicenter specialized clinics in primary care should be considered to examine this issue further.

#### Acknowledgements

The authors are thankful to the Deanship of Scientific Research, College of NursingResearch Center at King Saud University for funding this research

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