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Prevalence of Silent Bacteriuria among Diabetic Patients in Khan Younis Governorate

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Abstract

Diabetes mellitus (DM) is a syndrome characterized by hyperglycemia. There is evidence that diabetics are more prone to urinary tract infection. This study aimed to investigate the prevalence of silent bacteriuria in diabetic patients in Khanyounis Governorate. This study is conducted on 100 DM patients and 100 healthy individual, aged 25-65 years old. The selected DM patients were non-immunocompromised, not on steroid therapy, not under antibiotic treatment and without structural abnormalities in their urinary tract. Demographic characteristics of the study population and clinical information and UTI situation of DM patients were collected by interview questionnaire. The percentage of population who had positive bacterial culture results was 23.0% of DM patients vs. 17.0% of the controls group. *E. coli* was the most common organism that causing asymptomatic bacteriuria in diabetic (9.0%) followed by *S.epidymidus* (5.0%) followed by *Klebsiella* and *S.saprophyticus* with the same percentage (3.0%) followed by *Pseudomonas* and *Proteus* with percentages (2.0% and 1.0%) respectively. On the other hand, *E. coli* was the most common organism that causing asymptomatic bacteriuria in controls group (2.0%), followed by *Citrobacter*, *Proteus* and *S.epidymidus* with the same percentage (1.0%). Moreover, there was a statistically correlation between bacterial culture results of diabetic patients and the duration of diabetes (P=0.006). Urinary tract bacteria pathogens were isolated more in diabetics than in controls. *E.coli* is the predominant organism that causing asymptomatic bacteriuria in diabetics and controls group. The prevalence of asymptomatic bacteriuria among DM patients is directly proportional with diabetes duration.

Keywords:

Diabetes mellitus,
Silent Bacteriuria,
Khanyounis Governorate.

1. Introduction:

Diabetes mellitus (DM) is a metabolic disorder characterized by hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both (Arneson and Brickell, 2007). The two major forms of diabetes mellitus are type 1

diabetes mellitus (T1DM) resulting from autoimmune destructions of β cells lead to lack or severe reduction in insulin secretion and type 2 diabetes mellitus (T2DM) resulting from both relative deficiency of insulin and insulin resistance (Cohen, 2006).

According to the 1998 World Health Organization (WHO) criteria, DM was defined as fasting glucose concentration of at least 6.1 mmol/l (110 mg/dl) or a two-hours postprandial glucose concentration of at least 10.0 mmol/l (180 gm/dl) (Nicolle, 2000). DM results in several abnormalities of the host defense system that might increase the risk of certain infections. Infection in diabetic patients is the most serious complication which continues to be a big health problem all over the world. Diabetic foot ulcer was the major cause of infection followed by pulmonary tuberculosis, Urinary tract infection (UTI), pneumonia and skin and subcutaneous infections. There is a view that urinary tract infection is more common in diabetic patients but remain in debate because of varying study designs (Douri, 2008).

Changes in host defense mechanisms, the presence of diabetic cystopathy and of microvascular disease in the kidneys may play a role in the higher incidence of UTI in diabetic patients (Patil et al., 2012). Asymptomatic bacteriuria, or asymptomatic urinary infection, is bacteria present in urine in the absence of clinical signs or symptoms of urinary infection in the host. The microbiologic definition is usually greater than or equal to 10^5 colony-forming units per milliliter of the same organism or organisms in two consecutive urine specimens (Nicolle, 2003). Bacteria isolated from the urine of patients with asymptomatic bacteriuria usually originate as colonizing flora of the gut, vagina, or periurethral area (Nicolle, 2003). Untreated asymptomatic bacteriuria predisposes the individual to recurrent UTI, which cause considerable morbidity if complicated and can also cause severe renal disease. According to the most literature reviews; *E.coli* is the most common organism that causing asymptomatic bacteriuria in both diabetics and non-diabetics (Douri, 2008; Patil et al., 2012; Chukwuocha et al., 2012). In diabetics, mortality due to bacteriuria is variable. Some reports have found it to be higher than non-diabetics, while others had reported similar mortality in both (Akbar, 2000). To the best of our knowledge, to date no study has been reported to investigate the prevalence of silent bacteriuria in DM patients in Gaza strip. However, this study aimed to investigate the prevalence of silent bacteriuria in DM patients as compared to control in Khanyounis governorate.

2. Materials and Methods:

2.1 Study Population, Sample Size and Sampling:

The study sample was consisted of 100 DM patients and 100 control from Khanyounis Governorate, aged between 25-65 years. The study subjects were taken from Shuhadaa Khanyounis clinic, Loyal Hand Society and Alshorog Society. Convenience sampling technique was used to select the study DM patients who are attending to the clinics. All diabetic patients selected were non-immunocompromised, not on steroid therapy, not under antibiotic treatment, and without structural abnormalities in urinary tract or any other anatomical abnormalities predisposing them to infection.

2.2 Questionnaire interview:

The volunteers were interviewed face to face and the questionnaire. It was filled by researcher's team. The questionnaire was consisted of three parts: demographic characteristics of the study population, Clinical information about DM patients and clinical information about UTI situation among DM patients.

2.3 Urine sampling processing:

Patients and controls were asked to collect 20 ml of midstream urine in a sterile cup. Urine was cultured on Blood agar, MacConkey agar and Nutrient agar (NA) then incubated for 24 hours at 37°C. Only cultures showing more than 10⁵ colony-forming units per milliliter on NA was considered as infection, and undergoes further studies. Bacteria was identified by traditional microbiological test, including, Gram stain and biochemical tests.

2.4 Microbe identification:

1. Growth on MacConkey Agar means bacteria is gram negative, this was confirmed by Gram stain (Crystal violet stain, Safranin, Decolorizer, Iodine stain), then biochemical tests were performed (IMViC, Triple Sugar Iron Agar (TSIA), Motility test, Urease).
2. Growth on Blood Agar means bacteria is gram positive, this was confirmed by Gram stain, then biochemical tests were performed;
Biochemical tests:
 - a) Catalase distinguish between *staphylococcus* and *streptococcus*.
 - b) Coagulase distinguish between *S.aureus* and other staphylococcus.
 - c) Novobiocin sensitivity test distinguish between *S.epidymidus* and *S.saprophyticus*.

2.5 Blood sampling and biochemical analysis:

Under aseptic technique, about 4 ml of fasting (8-12hours) venous blood sample were collected from each subject in two tubes the first was a plain tube and the other one was an EDTA tubes. Samples in plain tube were allowed to clot and the serum was centrifuged at room temperature at 4000 round/minute for 10 minutes. Serum was used to determine FBS for both groups using Glucose GOD FS Diasys kit & Samples in EDTA tubes were used to determine HbA1C for diabetic group using STANBIO kit in the laboratory of University College of Science and Technology.

2.6 Data analysis:

Data obtained were analyzed using Statistical Package of Social Sciences (SPSS) system (version 18.0). Descriptive statistics, Chi-Square Test and Correlation Test were applied. A significant result means that the P-value for the hypothesis test is less than 0.05. The confidence intervals (CI) was reported as 95%.

3. Results:

3.1 Demographic characteristics of the study population:

The finding showed that the mean \pm standard deviation (SD) of age among the diabetic group was 53.4 \pm 10.1 years whereas, the mean \pm SD of age was 42.9 \pm 9.2 among control group. In addition, the males in diabetic group represented 42.0%, while the males in control groups represent 37.0%; whereas the females in diabetic group represent 58.0% while the females in control group represent 63.0%.

3.2 Clinical information about diabetic patients:

Table 1 Clinical information about diabetic patients in the study

Variables	% of DM Patients
Antibiotic administration	
No	100.0%
Steroid therapy administration	
No	100.0%
Diabetes mellitus type	
T1DM	10.0%
T2DM	90.0%
Diabetes mellitus duration	
Less than 5 years	39.0%
5 years or more	61.0%
Type of hypoglycemic drugs	

No treatment	4.0%
Insulin injection	18.0%
Tablet	78.0%
Following diet to control diabetes	
No	40.0%
Yes	60.0%
Mean of the FBS within last three months	
Up to 120 mg/dl	16.0%
121 up to 180 mg/dl	49.0%
More than 180 mg/dl	35.0%
Total	100.0%

As shown in Table 1, all of DM patients did not take any antibiotic or steroid therapy. Moreover, T1DM patients represented 10.0%, while the T2DM represent 90.0%. In addition, 39.0% of DM patients their disease duration was less than 5 years, whereas 61% of them have diabetes for 5 years or more. Furthermore, the percentage of DM patients who take oral hypoglycemic drugs was 78.0%, whereas 18.0% of them used insulin injection as hypoglycemic drugs. Further to the above, 60.0% of the DM patients were going on diet. Also according to the table above, 16% of DM patients had FBS up to 120 mg/dl, whereas 49% of them had FBS in between 121 up to 180 mg/dl, while 35 % of them had FBS more than 180 mg/dl (Table 1).

Table 2 Clinical information about UTI situation among diabetic patients

Variables	% of DM Patients
Having previous UTI	
No	80.0%
Yes	20.0%
Result of urine analysis which was conducted within the last three months	
No test was performed	96.0%
Crystals	2.0%
Infection	2.0%
Having calculi	
No	98.0%
Yes	2.0%
Having catheter within the last three months	
No	98.0%
Yes	2.0%
Total	100.0%

As shown in Table 2, 80% of diabetic patients did not have previous UTI, whereas 20% of them had previous UTI. Moreover, the percentage of DM patients who did not perform urine analysis within the last three months were 96%, whereas 2% of them had an infection after performing urine analysis within the last three months

(Table 2). The table above also indicates that 98% of diabetic patients did not have calculi, whereas 2% of them had calculi (Table 2). Furthermore, Diabetic patients who had catheter within the last three month represented 2%, whereas the percentage of patients who had not catheter within the last three months was 98.8% (Table 2).

3.3 Bacterial culture results:

The percentage of the study population who had positive bacterial culture results was 23.0% of DM patients Vs. 17.0% of the controls group. *E. coli* was the most common organism that causing asymptomatic bacteriuria in diabetic patients (9.0%) followed by *S.epidyrmidus* (5.0%) followed by *Klebsiella* and *S.saprophyticus* with the same percentage (3.0%) followed by *Pseudomonas* and *Proteus* with percentages (2.0% and 1.0%) respectively. On the other hand, *E. coli* was the most common organism that causing

asymptomatic bacteriuria in controls group (2.0%), followed by *Citrobacter*, *Proteus* and *S.epidyrmidus* with the same percentage (1.0%).

3.4 Correlation of bacterial culture results with independents variables of the study:

After using of Pearson Correlation Test, there was a statistically significant correlation between the bacterial culture results of the cases and the duration of diabetes (P=0.006). Moreover, there was a statistically significant correlation between the FBS levels of the cases and the mean of the FBS within the last three months (P=0.012). In addition, there was a statistically significant correlation between the type of diabetes of the cases and the type of hypoglycemic drugs (P=0.000). On the other hand, there was no statistically significant correlation among the study cases with respect to any one of each other mentioned independent variables (P≥0.05) (Table 3).

Table 3 Correlation of bacterial culture results with independent variables of the study

Variables	Bacterial culture results	HbA1c levels	FBS levels	Duration of diabetes	Type of diabetes	Type of hypoglycemic drugs	Mean of the FBS within the last three months	History of UTI within the last three months
Bacterial culture results								
Pearson Correlation	1	-.068-	.057	-.273-	.169	-.092-	.055	-.037-
P.value		.503	.570	.006	.093	.362	.585	.713
HbA1c levels								
Pearson Correlation	-.068-	1	.068	.043	-.095-	.023	.124	.016
P.value	.503		.501	.674	.347	.822	.219	.873
FBS levels								
Pearson Correlation	.057	.068	1	.101	-.036-	.076	.250	-.118-
P.value	.570	.501		.317	.725	.455	.012	.243
Mean of the FBS within the last three months								
Pearson Correlation	.055	.124	.250	.012	-.053-	-.030-	1	.007
P.value	.585	.219	.012	.904	.599	.771		.943
Type of diabetes								
Pearson Correlation	.169	-.095-	-.036-	-.130-	1	.409	-.053-	.000
P.value	.093	.347	.725	.198		.000	.599	1.000
Type of hypoglycemic drugs								
Pearson Correlation	-.092-	.023	.076	.073	.409	1	-.030-	-.134-
P.value	.362	.822	.455	.470	.000		.771	.183
Duration of diabetes								
Pearson Correlation	-.273-	.043	.101	1	-.130-	.073	.012	-.010-
P.value	.006	.674	.317		.198	.470	.904	.919
History of UTI within the last three months								
Pearson Correlation	-.037-	.016	-.118-	-.010-	.000	-.134-	.007	1
P.value	.713	.873	.243	.919	1.000	.183	.943	
Number of Cases	100	100	100	100	100	100	100	100

Correlation is significant at the 0.05 level.

4. Discussion:

Urinary tract bacteria pathogens were isolated more in diabetics than in control in the present study. This agrees with the findings of Horcajada et al. (1999) that the incidence of bacteriuria is higher in diabetics; and with that of Geerlings (2008) that diabetics are more prone to UTIs. This is because diabetes affects many systems that protects against infection in general, and against UTI specifically (Goswami et al., 2001). Poor circulation in diabetes reduces the ability of infection-fighting white blood cells to get where they are needed, and even when they do, they are less able to ingest the offending bacteria and kill them than normal white blood cells. It may also be due to bladder dysfunction caused by diabetic neuropathy which allows urine to remain in static pools for long periods of time, providing luxurious ponds for bacteria to grow in (Acharya and Jadav, 1980).

The results of the present findings found that *E. coli* is the most common organism that causing asymptomatic bacteriuria in diabetics group (9.0%) and controls group (2.0%). However, according to Chi-Square Test, there was no statistically difference among the study population with respect to bacterial culture results ($P=0.224$). The result of the present study was in agreement with finding of other study conducted by Douri (2008) in Jordan to assess the prevalence of significant asymptomatic bacteriuria in DM patients and controls, where they reported that *E. coli* is the most common organism that causing asymptomatic bacteriuria in both diabetics (12.0%) and non-diabetics (2.0%) (Douri, 2008). Similar results were reported by the majority of the other studies, where they showed that *E. coli* was the most prevalent microorganism responsible for positive urine culture among DM patients infected with asymptomatic bacteriuria (Al-Dulaimi et al., 2010; Baloch et al., 2011; Patil et al., 2012; Chukwuocha et al., 2012).

Bacteria isolated from the urine of patients with asymptomatic bacteriuria usually originate as colonizing flora of the gut, vagina, or periurethral area (Nicolle, 2003). *E. coli* urinary strains from patients with asymptomatic bacteriuria display a lower frequency of genetic markers or phenotypic expression of potential virulence factors compared with strains isolated from acute uncomplicated urinary infection or acute non obstructive pyelonephritis (Geerlings, 2008; Nicolle, 2003).

Regarding the relationship of bacteriuria with duration of diabetes and glycemic control (as assessed by HbA1c levels); the present findings found that there was a statistically significant correlation between the asymptomatic bacteriuria among DM patients and the duration of diabetes ($P=0.006$), but there was no association with glycemic control ($P=0.503$). The findings of this study agrees with one study that showed diabetes duration and chronic complications including cystopathy appear to be more important risk factors than current glycemic control, but further evidence is needed (Reimr, 2004).

In addition, Patil et al. (2012) found that the rate of incidence of UTI increased with increasing duration of diabetes. Moreover, in other study; women with positive cultures had a longer duration of DM than those with negative cultures (Mendoza et al., 2003). One report suggested that the presence of asymptomatic bacteriuria is most strongly correlated with variables consistent with duration of diabetes, rather than of diabetes itself (Nicolle, 2001). Geerlings (2008) reported that longer duration of DM was a risk factor for asymptomatic bacteriuria in women with type 1 DM. Therefore, a longer duration of DM, with presence of complications, seemingly increases the risk of asymptomatic bacteriuria in type 1 diabetic women. There are few clinical studies addressing the impact of baseline glycemic level on subsequent UTI risk had conflicting results. Two case-control studies did not find significantly more UTI among diabetic patients with a baseline HbA1c level over or under 8.0% and respectively. Three 90% cohort studies reported no major differences in relative risk estimates for UTI according to glycemic control (Thomsen, 2004).

5. Conclusions:

UTI pathogens were isolated more in diabetics than in controls. *E. coli* is the predominant organism that causing asymptomatic bacteriuria in diabetics and controls group. The prevalence of asymptomatic bacteriuria among DM patients is directly proportional with diabetes duration, but there were no association with glycemic control, FBS levels, type of diabetes, type of hypoglycemic drugs, mean of the FBS within the last three months, and history of UTI within the last three months. In addition to routine biochemical test of DM patients, periodical urine culture should be performed to detect bacteriuria that may cause symptomless UTI.

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معدل انتشار البكتيريا المسببة لالتهابات المسالك البولية عديمة الأعراض في البول بين مرضى السكري في محافظة خان يونس

كلمات مفتاحية:

مرض السكري،
البكتيريا البولية عديمة الأعراض،
محافظة خان يونس.

داء السكري هو متلازمة تتميز بارتفاع السكر في الدم، تنتج عن انعدام أو انخفاض نسبي في إفراز أو عمل الأنسولين. السكري ومضاعفاته يمثلان مشكلة صحية كبيرة. كما أن هناك أدلة على أن مرضى السكري أكثر عرضة لعدوى المسالك البولية. وتهدف هذه الدراسة إلى اكتشاف معدل انتشار البكتيريا البولية الصامتة في مرضى السكري بالمقارنة مع الناس الطبيعيين في محافظة خان يونس.

اعتمد تصميم هذه الدراسة على مقارنة حالات مرضية بمجموعة ضابطة، نفذت في محافظة خان يونس على 100 مريض سكري و100 فرد سليم كمجموعة ضابطة، جميع المتطوعين في الدراسة كانت تتراوح أعمارهم بين 25-65 عام. مرضى السكري اللذين تم اختيارهم لا يعانون من نقص في المناعة كما أنهم لا يتناولون علاجات الستيرويد ولا أي مضادات حيوية وبدون تشوهات هيكلية في المسالك البولية. تم جمع الخصائص الديموغرافية لجميع المتطوعين، بالإضافة إلى معلومات عن الحالة الصحية ووضع التهابات المسالك البولية لمرضى السكري بواسطة الاستبيانات. البيانات التي تم جمعها، ونتائج التحليل البيوكيميائية ونتائج المزارع البكتيرية تم تحليلها بواسطة برنامج الحزمة الإحصائية للعلوم الإنسانية (SPSS) الإصدار 18. وجدت الدراسة أنه لا يوجد علاقة بين مرضى السكر والأشخاص في المجموعة الضابطة حسب نتائج المزرعة حيث أن نسبة المرضى الذين أظهروا نتائج إيجابية في المزارع البكتيرية كانت 23.0% مقابل 17.0% لدى المجموعة الضابطة. كما سجلت الدراسة أيضاً أن ال *E.coli* هي البكتيريا الأكثر شيوعاً في تسبب التهابات المسالك البولية عديمة الأعراض بين مرضى السكري (9.0%)، يليها ال *S.epidymidis* (0,5%)، يليها ال *Klebsiella* وال *S.saprophyticus* بنفس النسب (3.0%)، يليهما ال *Pseudomonas* وال *Proteus* (2.0% و 1.0%) على التوالي. من ناحية أخرى، كانت ال *E.coli* هي البكتيريا الأكثر شيوعاً في تسبب التهابات المسالك البولية عديمة الأعراض عند المجموعة الضابطة (2.0%) يليها كل من بكتيريا ال *Citrobacter* وال *Proteus* وال *S.epidymidis* بنفس النسب (1.0%). علاوة على ذلك أظهرت النتائج وجود علاقة ذات دلالة إحصائية بين النتائج المزرعية للبكتيريا بين مرضى السكري ومدة المرض لديهم (P = 0.006). معدل انتشار البكتيريا المسببة لالتهابات المسالك البولية عديمة الأعراض يزداد بين مرضى السكري مقارنة بالأناس الأصحاء. ال *E.coli* هي البكتيريا الأكثر شيوعاً في تسبب التهابات المسالك البولية عديمة الأعراض لدى مرضى السكري والأناس الأصحاء، انتشار البكتيريا البولية عديمة الأعراض بين مرضى السكري يتناسب طردياً مع مدة المرض لديهم.