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Biochemical and bacteriological profile of urinary tract infections in diabetics and non-diabetics

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Abstract
Introduction: The aim of this study was to investigate if differences exist in the clinical and microbiological characteristics of UTI between diabetic and non-diabetic patients and to study the influence of diabetes mellitus on the spectrum of uropathogens and antimicrobial resistance pattern in patients with UTI.
Materials and Methods: The study included 152 diabetic (69 males and 83 females) and 113 non-diabetic patients (46 males and 67 females) with culture positive UTIs. Patients with negative urine culture (n= 42), those diagnosed and treated outside (n= 58), not willing to participate in the study (n= 9) or with an age < 20 years were excluded. The following data including age, sex, occupation and symptomatology were taken and clinical examination was done.
Results: There was no significant statistical difference in clinical symptoms between diabetic and non-diabetic subjects calculated by Chi-square test. Although fever was the most common presenting symptom, almost 28% of the patients (both diabetics and non-diabetics) did not present with any urinary symptoms as shown.
Conclusion: Achieving an HbA1c < 6.5 per cent appears to protect those diabetics who do not have other underlying predisposing factors for UTI. An HbA1c > 8.0 per cent in patients with diabetes mellitus increases the chance of developing UTI and its recurrence. *E. coli* is the most frequent pathogen responsible for UTI and recurrent UTI among both diabetics and non-diabetics followed by Klebsiella and Enterococcus.

Keywords: Biochemical parameter, diabetic, UTI

Introduction

The urinary tract is the most common site of infection in diabetic patients. Most of the urinary tract infections (UTIs) in diabetic patients are relatively asymptomatic, which can lead to severe kidney damage and renal failure. Bacteriuria is more common in diabetics than in non-diabetics due to a combination of host and local risk factors [1]. The incidence of UTIs depends upon diverse risk factors such as diabetes mellitus (DM), advanced age, urinary tract obstructions, immunosuppression, and neurological disorders [2]. It has been documented that DM is one of the widely known risk factor for developing UTI [3]. Numerous studies corroborated that patients with DM are quite vulnerable to the adverse effects of UTIs as compared to non-diabetics [4-6]. In diabetic patients, urinary tract is the primary site of infection which carries the risk of variable complications such as emphysematous cystitis, pyelonephritis, renal or perinephric abscess, bacteremia, and renal papillary necrosis [7]. The higher prevalence of UTI in diabetic patients was ascribed to the differences in host immunity between diabetic and non-diabetic patients, or to a dissimilarities among infecting etiological agents. Diabetes mellitus imposes a significant burden in developing countries including Ethiopia. For instance, epidemiological studies in Ethiopia evinced that the prevalence rate of UTI is increasing in diabetic patients [8, 9]. This rise in the prevalence has been surmised due to emerging antibiotic resistance among urogenital pathogenic bacteria. Albeit, the prevalence, etiological profile and antibiotic susceptibility pattern of bacterial uropathogens among general people of Arba Minch has been elucidated [10], A similar study pertained to diabetic patients is seldom being investigated. The aim of this study was to investigate if differences exist in the clinical and microbiological characteristics of UTI betwee n diabetic and non-diabetic patients and to study the influence of diabetes mellitus on the spectrum of uropathogens and antimicrobial resistance pattern in patients with UTI.

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Material and Methods

A total of 374 patients were screened, of which 265 patients were included in the study. The study included 152 diabetic (69 males and 83 females) and 113 non-diabetic patients (46 males and 67 females) with culture positive UTIs. Patients with negative urine culture (n= 42), those diagnosed and treated outside (n= 58), not willing to participate in the study (n= 9) or with an age < 20 years were excluded. The following data including age, sex, occupation and symptomatology were taken and clinical examination was done. All proven diabetics with fasting venous glucose > 126mg/dl and postprandial (2h) venous glucose > 200mg/dl were included in the study irrespective of reason for admission. The patients who were treated with antibiotics for UTIs within three months, and those who were too ill to respond to the questions were excluded from the study. In order to identify the risk factors, interviews of all the suspected cases of UTI was performed using a structured questionnaire. Prior to the interview, informed verbal consent from each study participants was obtained after lucidly briefing about the purpose of the study. Details on study participants' sociodemographic (age, education, occupation, marital status, drinking and smoking habit) and clinical characteristics (glucose level, previous history of UTI and other chronic diseases) were solicited. Patients with a history of diabetes and those who were on treatment for the same were also eligible for admission. Controls consisted of patients admitted in hospital with comparable age and sex with no history of diabetes and fasting blood sugar < 110mg/dl. Data were analyzed using the statistical software SPSS for Windows, version 17.0 (SPSS, Chicago, IL, USA). Nonparametric Mann-Whitney test was used to determine significance of difference in means between the UTI groups. Correlations between variables were calculated with Spearman's rank or relation test. $P < 0.05$ was considered to be statistically significant.

Results

The mean age among diabetic and non-diabetic patients was 60.2 ± 13.76 years and 53.47 ± 18.56 years. Duration of diabetes was less than one year in 24 (16%) patients, 1 to 10 years in 97 (64%) patients and greater than 10 years in 31 (20%) patients. Of 152 patients, 47% (72) of the diabetics were on oral hypoglycemic agents (OHA's) alone, 37% (56) were on insulin and 16% (24) were on both insulin and OHA treatment.

Table 1: Shows the clinical characteristics of the groups

Symptoms	DM	NON-DM	p-value
Fever	101 (66.4%)	79 (69.9%)	0.92
Dysuria	72 (47.3%)	52(46.1%)	0.81
Increased frequency	40 (26.3%)	37 (32.7%)	0.51
Abdominal pain	31 (20.3%)	31 (27.4%)	0.83
Vomiting	42 (27.6%)	22 (19.4%)	0.23
Haematuria	6 (3.9%)	3 (2.2%)	-
Pyuria	5 (3.2%)	2 (2.6%)	-
Incontinence	24 (15.7%)	13 (11.5%)	0.16
Retention	3 (1.9%)	4 (3.5%)	-

There was no significant statistical difference in clinical symptoms between diabetic and non-diabetic subjects calculated by Chi-square test. Although fever was the most common presenting symptom, almost 28% of the patients (both diabetics and non-diabetics) did not present with any

urinary symptoms as shown.

The prevalence of pyelonephritis is significantly higher ($p= 0.04$) in diabetics (9.4 per cent compared with non- diabetic patients 3.2 per cent (Table 2). The most common organism isolated being *E. coli* (Table 3).

Table 2: Pyelonephritis in diabetics

	DM (n=152)	NON-DM (n=113)
Asymptomatic bacteriuria	53	35
Pyelonephritis	15	3

Table 3: Microorganisms causing pyelonephritis

	DM	NON-DM
E. coli	8	2
Klebsiella	2	0
Enterococcus	2	0
Pseudomonas	1	1
Proteus	1	0
Candida	1	0

Among the complications, Acute Kidney Injury (AKI) was most common followed by recurrent UTI. Recurrent UTI was noted in 24 of 152 diabetics and 12 of 113 non-diabetic subjects. The prevalence of recurrent UTI was higher in diabetics (15.7%) compared to non-diabetics (10.6 per cent); however difference was not statistically significant. The most common uropathogen among these patients was *E. coli*. More than 50 per cent of patients with recurrent UTI had HbA1c ≥ 7.0 (poorly controlled DM).

Mean HbA1c in diabetics with recurrent UTI was 8.22 ± 2.76 (i.e. > 7.0). Renal papillary necrosis was observed in two cases of Candidial septicaemia. The micro-organisms isolated from the urine cultures are listed in Table 5. The most common organism isolated among both diabetics and non-diabetics was *E. coli*.

Table 4: Organisms isolated from urine cultures

Organisms	DM	NON-DM	p-value
E. coli	104	70	NS
Klebsiella	14	14	NS
Enterococcus	16	8	NS
Pseudomonas	2	13	<0.05
Acinetobacter	3	0	-
Citrobacter	2	2	-
Proteus	3	1	-
Coag. Negative Staph	2	4	-
Coag. Positive Staph	3	1	-
Candida	3	0	-

The micro-organisms isolated from the urine cultures are listed in Table 5. The most common organism isolated among both diabetics and non-diabetics was *E. coli*. Aminoglycosides showed a better sensitivity profile than cefoperazone-sulbactum in both diabetics and non-diabetics; however the number of patients were too small to draw any conclusions from the above mentioned observation. Enterococcus showed maximum susceptibility to linidazole, teicoplanin and vancomycin. Of the five patients with coagulase positive staphylococcus, two cases were MRSA isolates which were sensitive to vancomycin and linidazole.

Discussion

Bonadio M *et al.* (2006) also made a similar observation in

his study (73.7 years in diabetics vs 72.7 years in non-diabetic subjects) [11]. Bahl AL *et al*. (1970) found significant correlation between duration of diabetes and the prevalence of bacteriuria.12 The prevalence of bacteriuria increased 1.9 fold for every 10 years of diabetes duration. Fever was the most common symptom associated with UTI in both diabetics and non- diabetics. So, the presence of fever should prompt a look at the urinary tract as a possible source of infection. However; there was no significant difference in the clinical symptoms among both groups as shown in Table 1. In the present study, no significant difference was found in the prevalence of asymptomatic bacteriuria (ASB) in females (diabetics 0.6 per cent vs. non-diabetics 27.8 per cent) and males (diabetics 31.3 per cent vs. non-diabetics 32.7 per cent). This is in agreement with the study conducted by Bonadio M *et al*. (2006) (diabetic females 14.9 per cent vs. non-diabetic females 13.1 per cent) and (diabetic males 12.76 per cent vs non-diabetic males 11.4 per cent) [11]. However in the study conducted by Geerlings SE *et al*. (2000) the prevalence of asymptomatic bacteriuria was higher in diabetic women when compared to non-diabetic women (26 per cent in diabetic subjects and 6 per cent in controls) [13]. Despite the fact that a precise cause-effect relationship has not yet been established, multiple factors are suggested to be involved in the high occurrence of UTIs in diabetes patients. These include but are not limited to glucosuria [14], increased bacterial adherence to uroepithelial cells due to hyperglycemia [15], and neurogenic bladder [16]. In this context, Canagliflozin and Dapagliflozin, new antihyperglycemia molecules inhibiting renal glucose reabsorption and thus increasing glucosuria, were recently tested in clinical trials and were found to be associated with only a slight increase of UTI in T2D [17, 18]. This suggests that the contribution of glucosuria is limited in UTI and it does not explainits increased prevalence in diabetic patients. Nevertheless, there was a higher correlation between glucosuria and genital infection in Dapagliflozin-treated patients probably due to a greater effect of glucosuria in promoting the growth of fungal pathogens associated with genital infection as compared to bacterial pathogens typically associated with UTI [17]. In a new report, James and Hijaz have reviewed recent publications on lower urinary tract symptoms (LUTS) and UTI in diabetic women and have concluded that aging and obesity are significantly associated with worsened LUTS [19]. Glucosuria was also found to be associated with UTI and diabetic patients appeared to be at a higher risk for colonization with the virulent, extended-spectrum βlactamase-producing E. coli and Klebsiella species in UTI [19]. In our studied population, obesity might be considered as a cofounder in the correlation between glycemic control and UTI as obesity rates are about 50% in Kuwait [20]. Unfortunately, we do not dispose of this parameter in our subjects to further investigate this potential hypothesis.

Conclusion

Elevated HbA1c correlates with occurrence of UTI and the predisposition of the diabetic to UTI depends on the degree of glycaemic control over a period of weeks to months. Achieving an HbA1c < 6.5 per cent appears to protect those diabetics who do not have other underlying predisposing factors for UTI. An HbA1c
> 8.0 per cent in patients with diabetes mellitus increases the chance of developing UTI and its recurrence.

E. coli is the most frequent pathogen responsible for UTI and recurrent UTI among both diabetics and non- diabetics followed by Klebsiella and Enterococcus. The current study, however, has some limitations including the small number of diabetic patients with controlled glycemia analyzed and the lack of historical information on the non UTI diabetic patients to allow detailed comparison between diabetic patients with and without UTI in relation to glycemic control. However, despite these limitations, we provided ample evidence that the control of glycemia in diabetics might help in reducing the occurrence of UTI in these vulnerable patients, specifically in aged subjects. We have also shown clear difference in the correlation between the UTI and age which seems to be directly affected by glycemic control. These findings add further evidence to the importance of tighter glycemic control in reducing the occurrence of UTI and most probably improving the clinical outcomes.

References

1. Patterson JE, Andriole VT. Bacterial urinary tract infections in diabetes. Infect Dis Clin North Am. 1997;11(3):735-50.
2. Redder JD, Leth RA, Moller JK. Analysing risk factors for urinary tract infection based on automated monitoring of hospital-acquired infection. J Hosp Infect. 2016;92:397-400.
3. Geerlings S, Fonseca V, Castro-Diaz D, List J, Parikh S. Genital and uri-nary tract infections in diabetes: Impact of pharmacologically-induced glucosuria. Diabetes Res ClinPract. 2014;103:373-81.
4. Nitzan O, Elias M, Chazan B, Saliba W. Urinary tract infections in patients with type 2 diabetes mellitus: review of prevalence, diagnosis, and management. Diabetes Metab Syndr Obes. 2015;8:129-36.
5. Aswani SM, Chandrashekar UK, Shivashankara KN, Pruthvi BC. Clinical profile of urinary tract infections in diabetics and nondiabetics. Australas Med J 2014;7:29-34.
6. Casqueiro J, Casqueiro J, Alves C. Infections in patients with diabetes mellitus: A review of pathogenesis. Indian J Endocrinol Metab 2012;16(Suppl 1):S27-36.
7. Mnif MF, Kamoun M, Kacem FH, Bouaziz Z, Charfi N, Mnif F, *et al*. Complicated urinary tract infections associated with diabetes mellitus: Pathogenesis, diagnosis and management. Indian J Endocrinol Metab 2013;17:442-5.
8. Nigussie D, Amsalu A. Prevalence of uropathogen and their antibiotic resistance pattern among diabetic patients. Turk J Urol 2017;43:85-92.
9. Gebre MW. Diabetes mellitus and associated diseases from Ethiopian perspective: Systematic review. Ethiop J Health Dev2013;27:249-53.
10. Gezmu T, Regasa B, Manilal A, Mama M, Hailu T, Merdekios B. Prevalence, diversity and antimicrobial resistance of bacteria isolated from the UTI patients of Arba Minch province, Southern Ethiopia. Transl Biomed. 2016;7:3.
11. Bonadio M, Costarelli S, Morelli G, Tartaglia T. The influence of diabetes mellitus on the spectrum of uropathogens and the antimicrobial resistance in the elderly adult patients with urinary tract infection. BMC Infect Dis. 2006;6:54.

12. Bahl AL, Chugh RN, Sharma KB. Asymptomatic bacteremia in diabetics attending a diabetic clinic. Indian J Med Sci. 1970;24:1-6.

13. Geerlings SE, Stolk RP, Camps MJ, Netten PM, Hoekstra JB, Bouter KP, *et al*. Asymptomatic bacteriuria may be considered a complication in women with diabetes. Diabetes Mellitus Women Asymptomatic Bacteriuria Utrecht Study Group. Diabetes Care. 2000;23(6):744–9.

14. Geerlings SE, Stolk RP, Camps MJL, Netten PM, Collet TJ, Hoepelman AIM. "Risk factors for symptomatic urinary tract infection in women with diabetes," Diabetes Care. 2000;23(12):1737–1741.

15. Geerlings SE. "Urinary tract infections in patients with diabetes mellitus: epidemiology, athogenesis and treatment," International Journal of Antimicrobial Agents. 2008;31(supplement 1):54-57.

16. Sauerwein D. "Urinary tract infection in patients with neurogenic bladder dysfunction," International Journal of Antimicrobial Agents. 2002;19(6):592-597.

17. Johnsson KM, Ptaszynska A, Schmitz B, Sugg J, Parikh SJ, List JF. "Urinary tract infections in patients with diabetes treated with dapagliflozin," Journal of Diabetes and its Complications, 2013;27(5):473-478.

18. Nicolle LE, Capuano G, Fung A, Usiskin K. "Urinary tract infection in randomized phase III studies of canagliflozin, a sodium glucose co-transporter 2 inhibitor," Postgraduate Medicine. 2014;126(1):7–17.

19. James R, Hijaz A. "Lower urinary tract symptoms in women with diabetes mellitus: a current review," Current Urology Reports. 2014;15(10):440.

20. Al Rashdan I, Al Nesef Y. "Prevalence of overweight, obesity, and metabolic syndrome among adult Kuwaitis: results from community-based national survey," Angiology. 2010;61(1):42-48.