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Glycemic Control and Urinary Tract Infection in Diabetes Mellitus: A Cross Sectional Study.

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Research Article

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ABSTRACT

Urinary tract infections (UTI) are a frequent occurrence in diabetic patients, with associated complications arising if not properly managed. The potential benefit of proper glycemic control has not been fully realized in most developing countries including Cameroon owing to the associated poverty and limited resources.This study was therefore aimed at determining the effect of glycemic control on UTI and also to determine the antibiotic susceptibility profile of the isolates associated with UTI in the study population.In a cross-sectional study, diabetic patients were recruited from diabetic centers in Limbe and Buea, and venous and midstream urine samples were collected. Venous blood was used to determine glycosylated hemoglobin by ion exchange resin method. Glycemic control was classified as Good control (HbA1c <7%), Fair control (7%<HbA1c<9%) and Poor control (HbA1c ≥9%). Midstream urine samples were cultured to determine the presence of UTI and susceptibility testing was performed on all isolates.219 diabetic patients successfully took part in the study among them, 98 (44.8%) had good glycemic control, 33 (15.1%) had fair glycemic control and 88 (40.2%) had poor glycemic control levels. Overall, the prevalence of UTI in the study population was 23.7%. 13 (13.3%) of the participants with good glycemic control, 9 (27.3%) of those with fair glycemic control and 30 (34.1%) with poor glycemic control had UTI. The incidence of UTI was observed to be associated with the level of glycemic control (P = 0.0005) and individuals with poor glycemic control were more at risk of having UTI than individuals with good glycemic control (RR = 2.57; 95% CI 1.43 – 4.6; P = 0.0009). The most sensitive drugs were Gentamicin and Nitrofurathion (antibiotic), and Amphotericin B and Nystatin (antifungal).A significant association was observed between the incidence of UTI and level of glycemic control and individuals with poor glycemic control were more likely to suffer from UTI than individuals with good glycemic control. Proper glycemic control is thus recommended for all diabetic patients in Cameroon to prevent UTI and its associated complications.

INTRODUCTION

Diabetes presents a serious public health problem worldwide with virtually every country on the planet reporting a rise in the number of patients [1]. This increase is seen more in Sub-Saharan Africa where a number of factors including the changing lifestyle of the population and rapid urbanization have been incriminated [2]. Africa has the highest diabetes-associated mortality [1], which makes proper management of the disease very crucial. But one of the major problems facing these patients is the onset of urinary tract infection (UTI). Diabetic patients have been shown to be 3 to 4 times more likely to suffer from UTI than their non-diabetic counterparts [3]. Diabetes is thought to lead to immunologic impairments which predispose these patients to UTI [4]. UTI in diabetes may result to

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severe complications ranging from dysuria (pain or burning sensation during urination), organ damage and sometimes even death due to complicated UTI (pyelonephritis).

In Cameroon, like in most countries in Sub-Saharan Africa, diabetes is also of public health importance with over 517, 000 (prevalence of 6.15%) persons living with the disease. An estimated 14,588 deaths associated with diabetes was recorded in the country in 2012 [1]. Although national control programmes have been put forth to improve on the management of diabetes, the full benefits of proper glycemic control on the onset of UTI has not been fully realized in the country partly due to the inadequate knowledge of the patients, poverty and limited resources.

This study was aimed at determining the effect of glycemic control on the incidence of UTI in a cross section of diabetic patients, and also to determine the antibiotic susceptibility profile of some of the antibiotics routinely used to treat UTI in the country.

MATERIALS AND METHODS

Ethics Statement

This study was approved by the Faculty of Health Science Institutional Review Board (FHS IR) of the University of Buea. All participants were required to sign an informed consent form which was duly explained to them. In cases where the participants could not read nor sign the informed consent form, their guardian or next of kin did on their behalf.

Study area

The study was carried out at the Buea and Limbe Regional hospital, which is found in Buea and Limbe respectively. Buea and Limbe are respectively the political and the economic capital of the Fako division, South West Region of Cameroon. These two towns constituted a favourable site for the study due to the newly created Diabetic and hypertensive Centers, which enable patients from all over the Region to converge for treatment and monitoring.

Study population

This cross sectional study was conducted from April to July 2013. The inclusion criteria were males and females of all ages with confirmed diabetes, and who have been enrolled in the diabetic clinic for at least 6 months. Participants were not to be on any antibiotic and antifungal therapy for at least 30days prior to the study. Exclusion criteria were diabetic patients on wheelchair, with severe psychiatric disorders, under urinary catheterization, chronic antibiotic or antifungal use, and refusal to give their informed consent.

Questionnaire

A questionnaire was administered to participants who consented to take part in the study. The questions were meant to determine demographic characteristics including age, sex, glycemic control method, and symptoms of UTI. The participants were guided on how to answer the questions by members of the study team.

Sample collection

5ml of blood was collected into EDTA tubes from all participants and stored at 2 – 8 °C for the determination of glycosylated haemoglobin.

Participants were instructed on how to collect clean-catch midstream urine samples into labeled sterile McCartney bottles for urinalysis and culture. Urine samples were stored in an ice pack flask prior to transportation to the laboratory. Precaution was taken to perform urine culture within 30 minutes from specimen collection.

Sample analysis

Culture and susceptibility test

Urine samples were inoculated on MacConkey agar, Blood agar, Sabouraud dextrose agar and cysteine lactose electrolyte deficient (CLED) media for culture using a calibrated loop to determine colony forming units. The spread plate inoculation technique was used to inoculate plates. The plates were incubated at 37ºC aerobically for 24hrs. Cultures with colony counts greater than 10^5 CFU/ml, for a single isolated uropathogen and colony counts of 10^4 CFU/ml for more than one isolated uropathogen coupled to at least one of the following symptoms arising from

the urinary tract, such as dysuria, increased frequency of urinary or flank pain, were considered urinary tract infection (UTI).

The organisms were identified using cultural morphology (form, margins, colour and Gram stain) and followed by biochemical identification using API 20E system. Antibiotic sensitivity test was performed by the disc diffusion (Kirby-Bauer) method using Mueller-Hinton agar for bacterial isolates and Sabouraud dextrose agar for fungal isolates. The antibiotics used included gentamicin, imipenem, amikacin, ciprofloxacin, ceftriaxone, ofloxacin, nitrofurathion, cephradine, amoxicillin and cefotaxime. Antifungals used included amphotericin B, nystatin, ketoconazole, itraconazole, miconazole, flucytosine and fluconazole. The sensitivity plates were incubated aerobically at 37°C for 24hrs, and the zone of inhibition were recorded. A zone of inhibition greater than 15mm was considered as sensitive, a zone between 13 and 15 as intermediate, and a zone less than 13mm as resistant.

Glycosylated haemoglobin determination

Glycosylated haemoglobin levels were determined using the ion exchange resin method. The results of glycemic control were categorised into three groups such as “Good control” (HbA1c <7%), “Fair control” (7 %< HbA1c <9%) and “Poor control” (HbA1c ≥ 9%) [5].

Statistical analysis

Statistical analysis was performed using MINITAB statistical software for Windows version 15.0. Analysis performed included the Chi-square test and the Risk ratio. Statistical significance was set at P≤ 0.05 to represent 95% of the population.

RESULTS

247 diabetic patients were eligible for the study of which 219 (88.7%) successfully took part in the study. Among them were 123 (56.16%) females and 96 (43.8%) males. The participants were between 20 and 75 years of age, with a mean age of 54 years (Table 1).

Table 1: Age and sex distribution of UTI in study population

Age group	Females		Males		Total	
	N	UTI n (%)	N	UTI n (%)	N	UTI n (%)
20 – 40	43	4 (9.3)	26	2 (7.7)	69	6 (8.7)
41 – 60	52	15 (28.9)	40	9 (22.5)	92	24 (26.1)
>60	28	10 (35.7)	30	12 (40)	58	22 (37.9)
Total	123	29 (23.6)	96	23 (24)	219	52 (23.7)

52 (23.7%) of the 219 participants had urinary tract infection (UTI) which was defined by the presence of a positive urine culture plus one of the following symptoms including dysuria, pyuria, increased urination frequency and/or painful urination. UTI was observed more in individuals above 60 years (Table 1). No significant difference was observed in the rate of infection between males and females (P = 1.0), as well as the age of the individual (P = 0.4243).

8 different microorganisms were isolated and identified from the participants with UTI. *Escherichia coli*was the most prevalent pathogen (53.9%), followed by *Staphylococcus aureus* (36.5%). *Pseudomonas aeruginosa* was the least isolated pathogen that was observed in only 3 (5.8%) of the participants (Table 2).

Table 2: Uropathogens isolated from the diabetes mellitus participants

Uropathogen	Number (%) of patients with pathogen
Escherichia coli	28 (53.9)
Staphylococcus aureus	19 (36.5)
Streptococcus pyogenes	10 (19.2)
Proteus mirabilis	9 (17.3)
Candida albicans	7 (13.5)
Enterococcus faecalis	6 (11.5)
Klebsiellapneumoniae	5 (9.6)
Pseudomonas aeruginosa	3 (5.8)

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Antimicrobial susceptibility pattern revealed that Nitrofurathion and Gentamicin (Fig. 1) were the most sensitive meanwhile Ciprofloxacin and Ceftriaxone were the most resistant antibiotics to treat UTI caused by bacteria in the study population. Antifungal susceptibility revealed Amphotericin B and Fluconazole as the most sensitive antifungals for the treatment of fungiuria due to *Candida species* in diabetic patients (Fig 2).

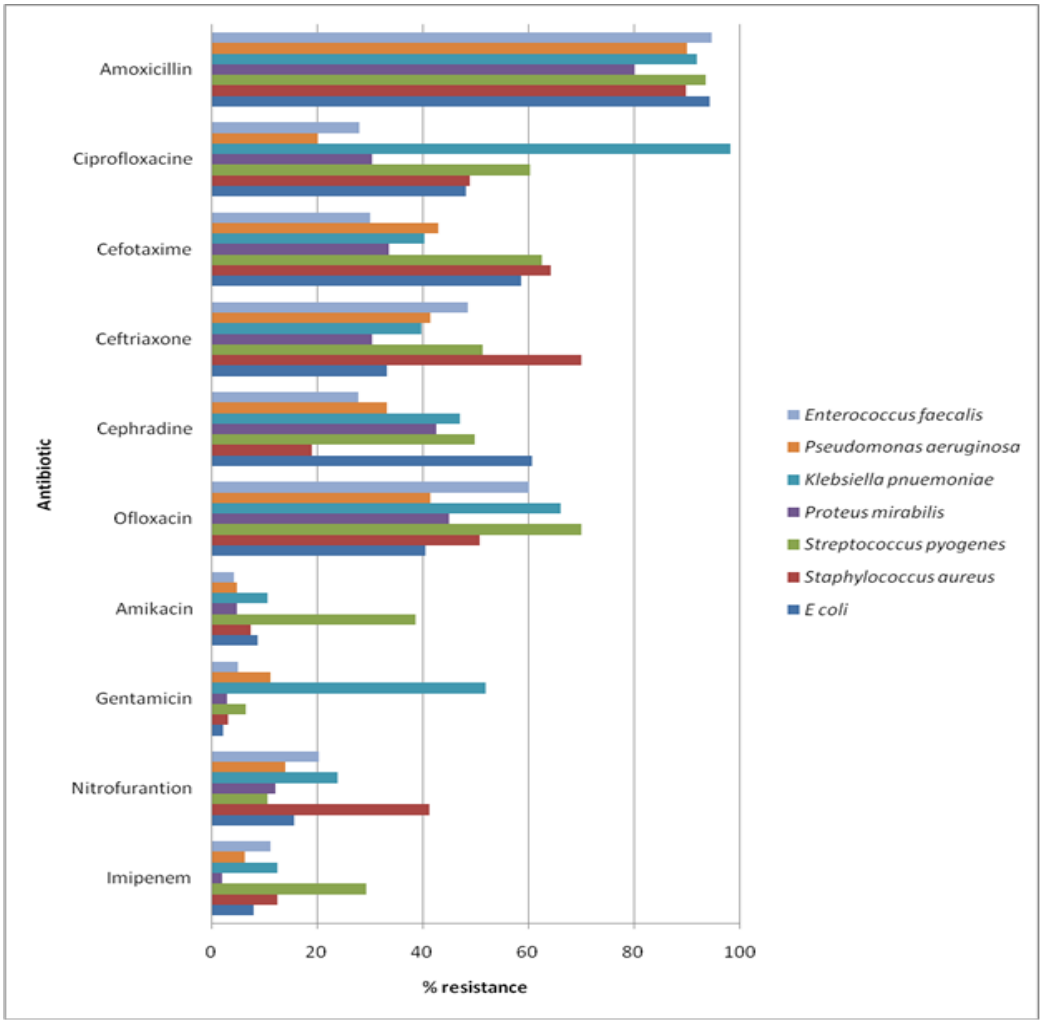

Figure 1: Susceptibility pattern of bacteria isolates to some common antibiotics

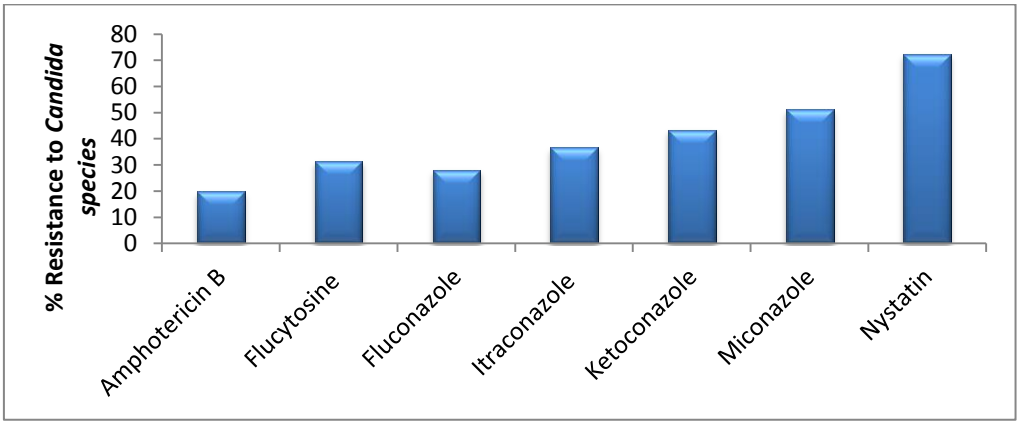

Figure 2: Antifungal susceptibility pattern

Among the 219 diabetic patients, 98 (44.8%) had good glycemic control, 33 (15%) had fair control and 88 (40.2%) had poor control. UTI was observed in 13 (13.3%) of the 98 participants with good glycemic control, 9 (27.3%) of 33 of participants with fair control, and 30 (34.1%) of 88 participants with poor control (Table 3). A significant association was observed between glycemic control and UTI (P = 0.0005), and the incidence of UTI was found to increase with decreasing levels of glycemic control from good to fair to poor (Fig 3). Individuals with poor

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glycemic control were more at risk of contracting UTI than individuals with good glycemic control (RR = 2.57, 95% CI = 1.43 – 4.61, P = 0.0009).

Table 3: Association between Glycemic control and UTIs

Glycemic control levels	Participants with UTIs n (%)	Participants without UTIs n (%)	Total
Good control HbA1c<7	13 (13.3)	85 (86.7)	98
Fair control 7<HbA1c<9	9 (27.3)	24 (72.7)	33
Poor control HbA1c≥9	30 (34.1)	58 (65.9)	88
Total	52	167	219

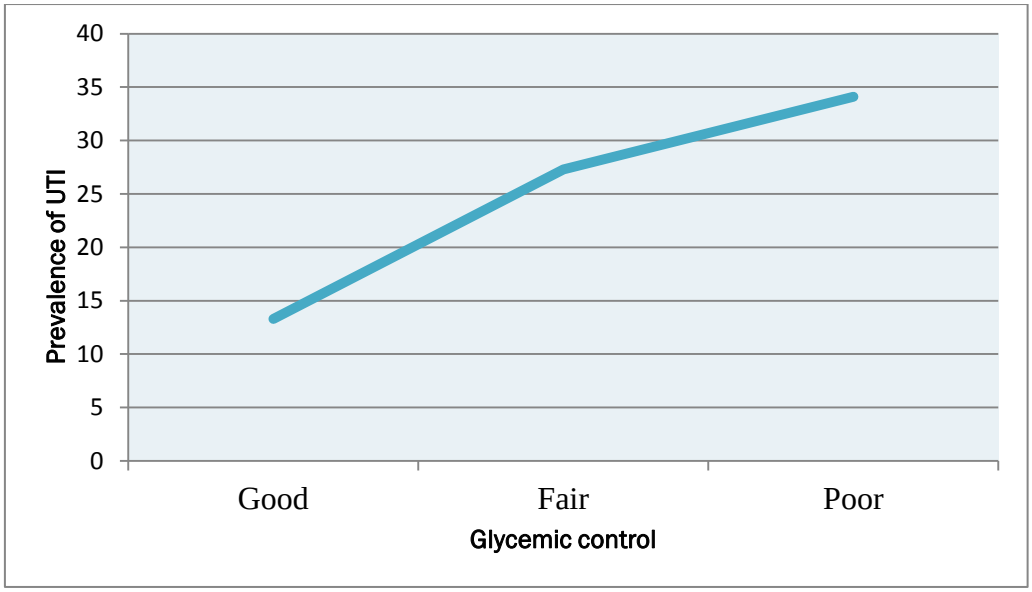

Figure 3: Graphical presentation of the association between glycemic control and UTI

DISCUSSION

In this study, UTIs was present in 52 (23.7%) of the 219 participants with diabetes mellitus. This result is lower compared to recent estimates of 36.15% reported in Nigeria [6] and 34.4% reported in Cameroon [7] but very high compared to the 9.3% reported in Ghana [8]. The variations in the prevalence of UTI have been attributed to factors such as geographical variations, ethnicity of the study participants and variation in screening test [9]. It was observed that age and sex did not influence the prevalence of UTI in this study (P = 0.4243).

In this study, a significant association was observed between the rate of UTI and glycemic control (P = 0.0005) and individuals with poor glycemic control were more likely to have UTI (RR = 2.57, P = 0.0004). This is an indication that a proper glycemic control is therefore important and should be advocated for to reduce the likelihood of contracting UTI which may lead to life threatening complications in diabetic patients in Cameroon. These findings are analogous to those of Bonadio*et al*. [10] and Tura*et al*. [11] who argued that glycemic control is a risk factor for UTIs in diabetes. But contrary to those of Geerling*et al*. [12], Boroumand*et al*. [13], and Ishay*et al*. [14] who did not find any significant relationship. There may be several explanations for these discrepancies in the observations. Firstly, control of glycaemia amongst the study participants was very poor, than would have been expected. This contributed to an increase in the occurrence and severity of urinary tract infections. Secondly, the mean age of the study participants (54years) was high meaning that most of the participants were old and hence would experience a decrease in anatomical, physiologic and immunologic functions that would otherwise promote the high incidence of UTIs.

The predominant uropathogen isolated was *Escherichia coli* which confirms similar studies by Tahir and Uddin[15] and Saleem and Daniel [16] that *Escherichia coli* is the most common cause of UTI in diabetic patients. This pathogen together with the other pathogens isolated exhibited some degree of resistance against all of antimicrobials used in this study. The most resistant ones were Ciprofloxacin (61.3%) and Ceftriaxone (70.1%) which are currently in use for the treatment of UTI in Cameroon. The antibiotics that showed less resistance were Gentamicin (11.3%) and Nitrofurathion (13.4%) and the most sensitive antifungals were Amphotericin B and Nystatin.

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CONCLUSION

A high prevalence of UTI was observed in diabetic patients in this study. The rate of the infection was not found to be dependent on the age and the sex of the individual. But a very significant association was found between UTI and level of glycemic control. Individuals with poor glycemic control were more likely to have UTI than individuals with good glycemic control. Therefore maintaining proper glycemic control will reduce the risk of UTI and its associated complications in diabetic patients. In the present of UTI, the most effective drugs were Gentamicin and Nitrofurathion (antibiotic), and Amphotericin B and Nystatin (antifungal).

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List of Abbreviations

UTI: urinary tract infection
RR: Relative Risk
EDTA: Ethylenediaminetetraacetic Acid
CLED: Cysteine Lactose Electrolyte Deficient Agar

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