Study on Asymptomatic Bacteriuria in Diabetic Patients

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ABSTRACT

Introduction: The incidence of diabetes mellitus is escalating remarkably. Diabetes mellitus has a number of long term effects on the genitourinary system. Asymptomatic bacteriuria (ASB) is a common problem in diabetic patients and is associated with increased risk of septicemia and pyelonephritis if untreated. This study was carried out to determine the prevalence of asymptomatic bacteriuria in diabetic patients and the susceptibility pattern of the pathogens isolated.

Material and methods: One hundred type -2 diabetics (50 males and 50 females) without genitourinary symptoms or abnormalities were included in the study. Midstream urine samples were collected from the study participants after getting informed consent. Urine samples were processed and examined for the various pathogens using the standard microbiological procedures. The spectrum of uropathogens causing asymptomatic bacteriuria and their antibiotic susceptibility profile was noted.

Results: Among the 100 diabetic patients, 32 (32%) had asymptomatic bacteriuria of which 20 (62.5%) were females and 12 (37.5%) were males. *Escherichia coli* (37.5%) was the most prevalent organism followed by *Klebsiella pneumoniae* (18.7%), *Enterococcus faecalis* (15.6%), *Staphylococcus aureus* (9.4%), *Pseudomonas sp* (6.3%), *Proteus sp* (6.3%), *Coagulase Negative Staphylococcus*(3.1%), and *Candida sp* (3.1%).The antibiotic susceptibility testing revealed that most of the isolated organisms were resistant to nalidixic acid, ampicillin, ciprofloxacin and cefotaxime.

Conclusion: The overall prevalence of ASB in the diabetic patients was 32%. Female sex was found to be a significant risk factor in developing asymptomatic bacteriuria. *E.coli* was the most prevalent organism. Therefore close monitoring of diabetic status and regular screening for ASB in diabetics would help resolve ASB related complications in diabetes. Further studies substantiating the efficacy of antimicrobial therapy in preventing complications secondary to asymptomatic bacteriuria in diabetic patients is needed.

Keywords: Asymptomatic bacteriuria, Bacteriuria, *Escherichia coli*, Diabetes

INTRODUCTION

Diabetes mellitus has become a major health challenge worldwide. In India alone, the prevalence of diabetes is expected to increase from 31.7 million in 2000 to 79.4 million in 2030.[1] Diabetes mellitus has a number of long term effects on the genitourinary system. This effect predisposes to bacterial Urinary Tract Infection (UTI).[2,3] It is also a predisposing factor for significant asymptomatic bacteriuria (ASB). Presence of ASB in patients with Type 2 diabetes is a predictor of subsequent development of a symptomatic UTI. Untreated asymptomatic bacteriuria predisposes the individual to recurrent UTI which can cause renal disease (pyelonephritis and gram negative septicemia). UTI is one of the most important cause of morbidity in diabetic patients.[4] The mechanism of pathogenesis for this association between diabetes mellitus and urinary tract infections is not completely clear. However, it is suspected that the high glucose concentration in the urine of these patients may favour the growth of uropathogens.[5]

Asymptomatic bacteriuria (ASB) is defined as the presence of at least 10^5 colony forming units (CFU) per ml of 1 or 2 bacterial species in clean-voided midstream urine sample from an individual without symptoms of a urinary tract infection (UTI), like dysuria, frequency, urgency, strangury, abdominal distention or fever.[6] The prevalence of asymptomatic bacteriuria in diabetic patients varies from 9-27% in various studies. Studies have also reported that diabetic patients with asymptomatic bacteriuia tend to have more symptomatic urinary tract infections than those without it. A meta analysis by Renko et al has also reported that on a long term follow up the diabetic individuals with asymptomatic bacteriuria had significantly lower GFR than those without it.[7,8] Hence there is a need for studying the impact of ASB in patients with diabetes mellitus. Therefore the present study was conducted to determine the prevalence of asymptomatic bacteriuria in patients with type 2 diabetes mellitus and the antibiotic sensitivity pattern of the isolates.

MATERIAL AND METHODS

The present cross sectional study on asymptomatic bacteriuria in diabetic patients was carried out at the Department of General Medicine and Department of Microbiology of A.C.S Medical College and Hospital from January 2016 to April 2016.To be included in the study, they had to conform to the WHO criteria for diagnosis of Diabetes.[9] After getting informed consent, 100 (first 50 males and first 50 females) diabetic patients presenting to the hospital with ailments other than urinary tract infection were included in the study. Pregnant female, patients with history of urogenital symptoms, prior bladder catheterisation and instrumentation or surgery of the urogenital tract or individuals who have received antimicrobial drugs or non- steroidal inflammatory drugs or immunosuppressors in the last 14 days were excluded from the study. Clinical details including duration of diabetes mellitus, drug therapy, clinical symptomatology especially urinary complaints were recorded. Fasting blood sugar and 2 hour postprandial blood sugar were estimated.

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Clean catch midstream urine samples were collected in sterile wide mouthed container and the samples were processed using standard microbiological procedures. The specimens were inoculated on to Cystine Lactose Electrolyte Deficient agar, by standard loop method for semi quantitative culture and incubated at 37°C for 24 hours. After 24 hours of incubation, the plates were examined. Cultures with colony count $\geq 10^5$ were considered as significant bacteriuria. In those cases with significant bacteriuria, the pathogens isolated were gram stained and characterized as per the standard microbiological procedures.[10] Asymptomatic bacteriuria (ASB) was defined as the presence of at least 10^5 colony-forming units (CFU) per ml of 1 or 2 bacterial species in clean-voided midstream urine sample from an individual without symptoms of UTI. Antibiotic susceptibility testing of the isolated strains was done by Kirby – Bauer's disc diffusion method following Clinical Laboratory Standards Institute (CLSI) guidelines.[11]

RESULTS

A total of 100 type-2 diabetic patients were selected for the study which included 50 males and 50 females. Out of the 100 patients in the study group, 32 (32%) were found to have asymptomatic bacteriuria. Among these 32 patients, 20 (62.5%) were females and 12 (37.5%) males. In the present study, occurrence of asymptomatic bacteriuria among female diabetic patients was 40% as opposed to 24% in males. Majority of the patients were within the age group of 45-49 years. The age and gender distribution of diabetic patients with asymptomatic bacteriuria is shown in Table-1.

Age (years)	Males with ASB (%)	Females with ASB (%)	Total (%)
35-39	2 (16.7%)	-	02 (6.2%)
40-44	-	3 (15%)	03 (9.4%)
45-49	5 (41.6%)	6 (30%)	11 (34.4%)
50-54	1 (8.3%)	4 (20%)	05 (15.6%)
55-59	2 (16.7%)	4 (20%)	06 (18.8%)
60	2 (16.7%)	3 (15%)	05 (15.6%)
Total	12 (37.5%)	20 (62.5%)	32 (100%)

Table-1: Age and gender wise distribution of diabetics with asymptomatic bacteriuria

Table-2 shows the microorganisms isolated from the urine specimens of the study population. Among the organisms isolated, Gram negative bacilli 22 (68.8%) were the predominant organisms followed by Gram positive cocci 9 (28.1%) and *Candida albicans* 1(3.1%).

Urine isolates	Number (%)
Escherichia coli	12 (37.5%)
Klebsiella sp	6 (18.7%)
Enterococcus sp	5 (15.6%)
Staphylococcus aureus	3 (9.4%)
Pseudomonas sp	2 (6.3%)
Proteus sp	2 (6.3%)
CONS	1 (3.1%)
Candida albicans	1 (3.1%)
Total	32 (100%)

Table-2: Distribution of urine isolates among diabetics with asymptomatic bacteriuria

E. coli were found to be the most prevalent isolate in diabetic patients with asymptomatic bacteriuria (37.5%) followed by *Klebsiella pneumoniae* (18.7%), *Enterococcus faecalis* (15.6%), *Staphylococcus aureus* (9.4%), *Pseudomonas sp* (6.3%), *Proteus sp* (6.3%), *Coagulase Negative Staphylococcus* (3.1%), and *Candida sp* (3.1%).

The resistance pattern of the gram negative and gram positive isolates against different antimicrobial agents is shown in Table 3 and 4 respectively. The antibiotic susceptibility pattern of gram negative organisms revealed that most of the isolates showed high level resistance to nalidixic acid (72.7%) and ampicillin (63.6%) whereas moderate level resistance against ciprofloxacin (59.1%) and cefotaxime (59.1%)and low level resistance to amikacin (22.7%), gentamycin (27.3%), nitrofurantoin (31.8%) and norfloxacin (31.8%). *E.coli,* the most prevalent organism in this study, showed 100% susceptibility to nitrofurantoin and maximum resistance to nalidixic acid (75%) followed by ciprofloxacin (66.6%), cefotaxime (58.3%) and ampicillin (41.6%).

Among the gram positive organisms, highest percentage of resistance was seen to erythromycin, ciprofloxacin followed by ampicillin.

DISCUSSION

Asymptomatic bacteriuria is common among diabetic patients and may lead to serious complications if not properly managed.[12] The important clinical concerns of ASB in diabetic individuals are its contribution to morbidity, either the short term risk of developing a symptomatic urinary tract infection followed by its complications or by the long term risks of developing serious diabetic complications like nephropathy.[1] ASB has

Organism	No.	AMP 10 mcg	AK 10 mcg	G 10mcg	CIP 5 mcg	NIT 300mcg	NA 30mcg	NX	CTX 30 mcg
Escherichia coli	12	5 (41.6%)	2 (8.3%)	2 (16.6%)	8 (66.6%)	0	9 (75%)	3 (25%)	7 (58.3%)
Klebsiella pneumonia	6	6 (100%)	1 (16.6%)	2 (33.3%)	3 (50%)	3 (50%)	5 (83.3%)	2 (33.3%)	4 (60%)
Proteus mirabilis	2	2 (100%)	1 (50%)	1 (50%)	1 (50%)	2 (100%)	1 (50%)	1 (50%)	1 (50%)
Pseudomonas sp	2	1 (50%)	1 (50%)	1 (50%)	1 (50%)	2 (100%)	1 (50%)	1 (50%)	1 (50%)
Total	22	14 (63.6%)	5 (22.7%)	6 (27.3%)	13 (59.1%)	7 (31.8%)	16 (72.7%)	7 (31.8%)	13 (59.1%)

AMP - Ampicillin, AK - Amikacin, G - Gentamycin, CIP - Ciprofloxacin, CTX - Cefotaxime, NIT – Nitrofurantoin, NA - Nalidixic acid

Table-3: Antibiotic resistance pattern of gram negative isolates

Organism	No	AMP 10 mcg	AK 10 mcg	G 10mcg / HL-G*-120mcg	CIP 5 mcg	NIT 300mcg	E 15 mcg	VA 30 mcg	LZ 15mcg
Enterococcus sp	5	3 (60%)	1 (20%)	1* (20%)	4 (80%)	1 (20%)	4 (80%)	0	0
Coagulase Negative Staphylococcus	1	0	0	0	0	0	0	0	0
Staphylococcus aureus	3	1 (33.3%)	0	1 (33.3%)	1 (33.3%)	0	2 (66.7%)	0	0
Total	9	4 (44.4%)	1 (11.1%)	2 (22.2%)	5 (55.5%)	1 (11.1%)	6 (66.6%)	0	0
AMP - Ampicillin, AK - Amikacin, G - Gentamycin, HLG - High level gentamycin, CIP - Ciprofloxacin, AMC-Amoxyclav, E - Erythromycin, VA - Vancomycin, LZ - Linezolid									

Table-4: Antibiotic resistance pattern of gram positive isolates

been identified as a risk factor for acquiring symptomatic UTI especially in diabetic women.[12]

In the present study, the prevalence of asymptomatic bacteriuria among the diabetics was 32% which is in agreement with the earlier reports which recorded the prevalence of 38.3% by Bissong et al, 2013[12] and 36.15% by Ophori et al, 2010.[3] However other studies have reported a higher prevalence of 42% (Hari et al, 2013)[5], 47.2% (Njunda et al, 2012)[13] and 50.84% (Sharma V et al, 2012) respectively.[14] Some studies have even reported a lower prevalence rate of 12% (Girish Babu et al., 2013)[3], 16% (Odetoyin et al., 2008)[15], 21% (Baqai et al., 2003)[16] and 26% (Alebiosu et al., 2003)[17] when compared to the present study report. The variations in percentage of ASB have been attributed to factors such as geographical variations, ethnicity of the subjects and variation in the screening (Assel et al., 2009).[18] The higher susceptibility of diabetic patients to bacterial infection is not clearly explained; however factors such as bladder dysfunction due to autonomic nerve dysfunction and defective polymorphonuclear leucocyte functions (opsonization, chemotaxis, phagocytosis and killing) are potential contributing factors.[14]

Occurrence of ASB is higher in females than males in the present study which is in concordance with the previous studies.[4,12,13] Highest percentage of ASB cases were in the age group of 45 -50 which is a similar finding by Arun Hari *et al* (2013).[4] *E. coli* was the most common pathogen isolated in this study (40.6%).This is consistent with the majority of the reports where *E. coli* has been reported to be the major pathogen in diabetic patients with asymptomatic bacteriuria.[13,14,19] The reason for predominant *E. coli* isolation is that it can bind to the glycoconjugate receptor of the epithelial cells of human urinary tract so that it can initiate infection itself. However the current study result showing *E.coli* predominance is in contrast to the study done by Alebiosu et al (2003)[17] where *Klebsiella pneumoniae* was the most common isolate followed by *E. coli*.

Other uropathogens isolated in the present study were *Klebsiella pneumoniae* (18.7%) *Enterococcus faecalis* (15.6%), *Staphylococcus aureus* (9.4%), *Pseudomonas sp* (6.3%), *Proteus sp* (6.3%), *Coagulase Negative Staphylococcus*(3.1%), and *Candida sp*(3.1%) which is in accordance with numerous other studies.[3,13,14]

The antibiotic susceptibility of the isolates in this study showed that most of them were resistant to nalidixic acid, ciprofloxacin, cefotaxime and ampicillin which is similar to the previous study report.[19] Majority of the isolates in the present study were resistant to ampicillin which is relatively a cheaper drug and ciprofloxacin also showed moderate activity against our study isolates, which is a routinely prescribed drug for UTI in OPD clinics.

E.coli, the most prevalent pathogen in the present study, was sensitive to nitrofurantoin, amikacin and gentamicin. Nitrofurantoin showed strong activity against *E. coli,* thus indicating that the drug is still a useful urinary antibiotic in our environment. The sensitivity of *E. coli* in this study is in agreement with previous study report.[19] In this study, among the gram positive isolates, Enterococcus sp was the most common organisms and it showed susceptibility against vancomycin, linezolid, amikacin and gentamicin. But it is advocated that vancomycin and linezolid should be kept as reserve and can only be used as last line antibiotics. Hence our study suggests that amikacin, gentamicin, nitrofurantoin and norfloxacin can be considered as ideal first line drugs of choice for treating ASB in diabetics. However, keeping various attributes in mind such as emerging drug resistance, varying drug susceptibility pattern in different geographical areas and changing prevalence of uropathogens in ASB cases, antibiotic therapy should be formulated based on the antibiotic susceptibility results obtained from microbiology laboratory. Further studies substantiating the efficacy of antimicrobial therapy in preventing complications secondary to asymptomatic bacteriuria in diabetic patients is needed.

CONCLUSION

The prevalence of ASB in the study population was 32% which is of major public health concern. Females are at more risk of developing ASB with *E. coli* being the predominant uropathogen. The high level of resistance to routinely used antibiotics in clinical settings is of great concern. Close monitoring of diabetic status, regular screening for ASB in diabetics and judicial use of antibiotics would help resolve ASB related complications in diabetes.

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