Asymptomatic bacteriuria

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Abstract

Introduction: Asymptomatic bacteriuria (ASB) is a condition characterised by significant infection in urine. Its association with diabetes mellitus is strongly suggested. However, the exact prevalence has been controversial.

Objectives: The study was undertaken with the aim of evaluating the prevalence and aetiology of asymptomatic bacteriuria in diabetics as well as non-diabetics.

Materials and Methods: A total of 460 patients were included in the study with 230 diabetics and 230 non-diabetics. Midstream clean catch urine samples were collected alongwith parallel blood samples for estimating the glycosylated haemoglobin levels.

Results: Of the total 460 subjects, 78 (17.0%) had ASB with 56 in diabetics and 22 in non-diabetics, depicting a higher rate of ASB in diabetes mellitus. Majority of the patients who had ASB were aged more than 60 years, irrespective of whether in the diabetic or non-diabetic category. Also, there was a significant difference in the type of infective organism in urine from diabetic patients as compared to the non-diabetic patients.

Conclusion: A higher prevalence rate of ASB was observed in diabetic patients as compared to non-diabetics. Furthermore, the newer infecting organisms that are more common in patients with diabetes mellitus was highlighted in the study

Keywords: Asymptomatic bacteriuria, Urine, Diabetes, Glycosylated haemoglobin.

Introduction

The term asymptomatic bacteriuria (ASB) refers to the presence of high count of bacteria with a positive urine culture in an asymptomatic individual. Most patients who have asymptomatic bacteriuria do not present with any clinical presentation and do not get benefit with antibiotic therapy. Usually urinary pathway is sterile. It has been observed that in patients with diabetes the chances of getting infected is more as well as the nature of infection is detrimental. Besides, the rate of upper urinary tract involvement is much higher than in normal individuals. Urine which is otherwise sterile contains both specific as well as non-specific defence systems to protect from infections.

Diabetic patients have an increased susceptibility to develop urinary tract infections such as acute cystitis, emphysematous infections, renal and perinephric abscess, and Candida infections.

The aim of the present study was to estimate the prevalence of ASB in urine sample of diabetics as compared to non-diabetics. Also, to identify the common organism leading to ASB.

Material and Methods

A total of 460 patients were included in the present study. The cut-off level of glycosylated haemoglobin as 7.0 was considered.

Individuals serving as control were selected during Health check-up camps as part of the screening procedure. Individuals selected for inclusion in the study included – 18 years and above, presence or absence of diabetes mellitus. All patients who were pregnant, had any illness, features of UTI or have had undergone antibiotic therapy in the past one week were excluded from the study. Diabetic status was further confirmed using IDF standards i.e diabetes (FBS > 126mg/dl and or the use of oral hypoglycemic drugs). Ethical clearance was obtained from the Institutional Ethical committee. A questionnaire was prepared to collect the demographic and clinical data from all those included in the study and specimens were collected only from subjects that gave their consent for inclusion in the study.

The participants were asked to provide a "clean-catch" midstream urine specimen without contamination. They were advised on washing of hands prior to collection and separation of prepuce in males and labia in females. Urine samples were collected into sterile containers, placed in a cool box (4°C) and transported to the laboratory immediately. The samples were then stored in a refrigerator and analysed within 8 hours of collection. Each sample was separated into two parts under sterile conditions; one part for urinalysis and the other for culture. Wet preparation of centrifuged urine was observed using high power to look for any evidence of blood, WBC or other cells.

A calibrated 10µl wire loop was used to inoculate urine without centrifugation into MacConkey, CLED, blood and Sabouraud's agar culture plates and further incubated aerobically at 37°C for 24 hours.[1] Samples that showed growth of any microbe were discarded and not included in the study. Significant ASB was defined as urine culture of $>10^5$ cfu/ml in the absence of cystitis. [Alebiosu CO] Isolates were identified using standard biochemical techniques.[Wayne PA]

Antimicrobial susceptibility testing was done by the Kirby Bauer disk diffusion method using standard procedures according to NCCLS guidelines.[Wayne PA] The plates were incubated aerobically at 37°C for 18 hours after which the zones of inhibition were measured in milliliters and recorded.[Lyamuya EF, Bonadio M] Blood samples for FBS and PPBS (1½ hours after meal) were collected in fluoride vials for HbA_1C estimation blood sample was collected in EDTA. Data were analyzed using SPSS Version 17.0 to measure differences between variables. P-values <0.05 were considered statistically significant.

Results and Observations

A total of 460 patients were included in the present study. Of these 230 were diabetes and equal number of non-diabetics serving as control. Among diabetics 156 were males while 76 were females. Among the non-diabetics 100 were males and 130 females. (Table I). Table II shows the age and sex distribution of asymptomatic bacteriuria of the total 78 patients presenting with asymptomatic bacteriuria 56 were diabetics while 22 were non-diabetics of the total diabetic patients, 23 were moles (14.9%) and 33 females (43.4%) who presented with asymptomatic bacteriuria. While among non- diabetics there were 7 males (7.0%) and 15 females (11.5%). Patients with HbA1c levels below 7.0 included 17 diabetic males and 13 diabetic females and those with levels more than 7.0 included 6 diabetic males and 20 diabetic females (Table III).

The ASB rates in diabetic males was 23/156 (14.7%) and in diabetic females 33/76 (43.4%), while in non-diabetic males was 7/100 (7.0%) and in non-diabetic females was 15/130 (11.5%).

Majority of participants were in the age group of more than 60 years and above the overall prevalence of ASB in this study was 17.0%. There was a significant difference in the prevalence of ASB between diabetics and non-diabetics

The distribution of urine isolates among study participants is presented in Table IV. There was a significant difference in the type of species isolated from diabetics and non-diabetics. Majority of the patients had E. coli as the causative agent (50%), while candida formed a smaller percentage of cases.

Discussion

Urinary tract infections (UTI) are more common in individuals with diabetes mellitus. Females with diabetes are more likely to develop symptomatic UTI especially in those with ASB. Asymptomatic bacteriuria (ASB) is common in diabetics and predisposes these patients to more severe urinary tract infections (UTIs).

Pyelonephritis is a common and often severe complication of diabetes mellitus. The mechanism of pathogenesis for this association is not fully known, however, it is suggested that high glucose concentration in urine may favour the growth of pathogenic microorganisms.

Asymptomatic bacteriuria (ASB) is defined as the presence of at least 105 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)7, like dysuria, frequency, urgency, strangury, abdominal distention or fever.[1,2]

Several studies have documented the association of ASB with diabetes; however, reports on the prevalence rate are different. Majority of the studies have reported the prevalence to be higher in individuals with diabetes than in those without diabetes.[3-5] However, other studies reported a non-significant difference in the prevalence of ASB between females with diabetes and non-diabetes.[6]

The most frequently isolated uropathogens in various studies include Escherichia coli, Klebsiella pneumoniae, Streptococcus agalactiae, Enterococcus faecalis, coagulase negative Staphylococcus and Streptococcus pyogenes.[1-3] Although E. coli is known to be the most common uropathogen, other microorganisms are emerging with predominance in cases of ASB.

Report from previous study noted a changing pattern of ASB with Klebsiella sp accounting for the majority of asymptomatic bacteriuria among diabetic individuals.[1] Another recent study in Nigeria reported Staphylococcus aureus to be the most common uropathogen isolated from patients with ASB in both diabetics and non-diabetics.[7] Antibiotic resistance of uro-pathogens is increasingly being reported with high occurrence of multiple drug resistant strains.[1,3,8] Some recent studies have reported high resistance to commonly used antibiotics.

Similarly, ASB is common among diabetic patients and may lead to life-threatening complications if not properly managed.[9] ASB has been identified as a risk factor for acquiring symptomatic UTIs especially in females with diabetes.UTIs are more severe in diabetic patients involving life-threatening complications such as emphysematous pyelonephritis and renal papillary necrosis.[9] Despite the importance of bacteriuria in diabetics; there is paucity of information on the relationship between UTI and diabetes.

The present study revealed an overall prevalence of ASB of 24.3% in diabetics and 9.6% in non-diabetics This result is different with that of earlier reports which recorded prevalence of 36.2 % in diabetics[8] and 18.5 % in non-diabetics.[3] On the contrary, the prevalence of ASB in this study is similar to studies across the globe which recorded 5.3 – 26% rates in diabetics and 3.5–15% in non-diabetics.[1,2,10-12] Consequently, of prevalence of ASB remains debatable. This difference in the rate can be attributed to variations in sample size, geographical location, culture or screening methods.[13] In the present study, ASB was significantly higher in

diabetics than non-diabetics (p = 0.038). This is in concurrence with majority of the earlier reports.[5,7] The prevalent microorganisms in the present study was E. coli. This is consistent to that of previous studies where E. coli was the predominant bacteria.[3,5,6,9] The rising prevalence of Staphylococus species in ASB may be due to the fact that these organisms are mostly normal skin flora and can be introduced in the urinary tract during sexual intercourse.[7,14,15] The high prevalence of coagulase negative staphylococcus could also be have to improper use of antibiotics that may result in the proliferation of highly resistant bacteria such as CNS.[16] High rate of Candida sp has also been reported especially in diabetic individuals and could be due to the presence of excess glucose their urine which may result in the proliferation of Candida species.[17]

The high prevalence of ASB and the multiple resistances of most isolates is a major concern that requires prompt action. Consequently, there is the need to enhance sensitization against antibiotic abuse so as to curb the spread of multi resistant uropathogens. Emphysematous cystitis, pyelonephritis, renal and perinephric abscess, bacteraemia, and renal papillary necrosis are more commonly seen in diabetic individuals. Infections also cause considerable morbidity and mortality in those patients. They may result in the precipitation of metabolic derangements. The prevalence of ASB is about 3 times higher in diabetic women than in non-diabetic women.[18]

The non-specific defence mechanisms of urinary tract include normal commensal flora, flushing effect of voiding, bladder glycocalyx, Tamm-Horsfall glycoprotein, endotoxin induced shedding of bladder epithelial cells, phagocytosis and presence of Immunoglobulins especially secretory IgA and circulating IgG and IgM antibodies. Diabetes mellitus causes several abnormalities of the host defense system that might result in a higher risk of certain infections, including UTI. Possible underlying mechanisms include: Reduced function of neutrophils, increased adherence of uro-pathogens to bladder epithelial cells, In diabetics due to sweetness in the urine it serves as a rich culture media for the growth of microorganisms and, Neuropathic bladder leading to delayed bladder emptying.[3,5,8]

The prevalence of ASB might be influenced by the various patient related factors.[19] Keane et al found a correlation between duration of the diabetes mellitus and the presence of ASB in type 1 and 2 diabetic patients. **[20]** Longer duration of diabetes mellitus increased the chances of developing ASB. High levels of glucose in the urine of persons with diabetes mellitus might create a culture medium for pathogenic microorganisms.

Many authors have analysed the possible impact of metabolic control, as proven by glycosylated haemoglobin levels on the prevalence of bacteriuria. While Geerlings et al,[9] Boroumand et al,[21] Ishay et al[6] did not find a significant relation, Bonadio et al[3] and Kelestirnur et al[22] argued that a high glycosylated haemoglobin level may be a risk factor for ASB. Another risk factor for ASB in type 2 diabetic patients is at least one episode of UTI during the past one year. It has been proposed that the colonisation of uropathogens in the urinary tract of diabetics after episodes of UTI and also local secretion of cytokines, can lead to the prolonged release of bacteria from urinary tract which may cause bacteriuria.

Some studies have demonstrated a higher rate of ASB in females who had recent sexual intercourse, or are using diaphragm,[14] or condoms pre-coated with spermicide jelly.[15] However, it has been reported by some authors that recent sexual intercourse was not a risk factor and also there was no difference in the rates of UTI using different contraceptive methods.[23]

Advanced age has been proposed as a risk factor for ASB in patients with type 2 diabetes mellitus.[9] Microalbuminuria and renal dysfunction has not demonstrated any correlation with ASB in recent studies. Few previous authors have reported that declining renal functions may lead to ASB in diabetics.[3,9]

Conclusion

The present study showed a high prevalence of ASB of 24.14% in diabetes mellitus patients against 20.01% in non-diabetics. In addition, it reiterates the clinical significance of CNS and *Candida* species in UTI.

References

1. Alebiosu CO, Osinupebi OA, Olajubu FA. Significant asymptomatic bacteriuria among Nigerian type 2 diabetics. J Natl Med Assoc. 2003;95:344–51.
2. Lyamuya EF, Moyo SJ, Komba EV, Haule M. Prevalence, antimicrobial resistance and associated risk factors for bacteriuria in diabetic women in Dar es Salaam, Tanzania. Afr J Microbiol Res. 2011;5(6):683–9.
3. Bonadio M, Costarelli S, Morelli G, Tartaglia T. The influence of diabetes mellitus on the spectrum of uropathogens and the antimicrobial resistance in elderly adult patients with urinary tract infection. BMC Infectious Diseases. 2006;6(54):1–7.
4. Manhal FS, Gauad SA. Asymptomatic bacteriuria in pregnant and diabetic women. Al-Kindy Col Med J. 2011;7(1):39–46.
5. Zamanzad B, Moiezzi M. Prevalence of asymptomatic bacteriuria and associated host factors in women with diabetes type 2. J Res Health Sci. 2006;6(1):14–20.
6. Ishay A, Lavi I, Luboshitzky R. Prevalence and risk factors for asymptomatic bacteriuria in women with Type 2 diabetes mellitus. Diabet Med. 2006;23:185–8.
7. Omoregie R, Erebor JO, Ahonkhai I, Isibor JO, Ogofere H. Observed changes in the prevalence of uropathogens in Benin City, Nigeria. NZJ Med Lab Science. 2008; 62:29–31.
8. Ophori EA, Imade P, Johnny EJ. Asymptomatic bacteriuria in patients with diabetes. J Bacteriol Research. 2010;2(2):14–7.

9. Geerlings SE, Stolk RP M, Camps MJL, Netten PM, Hoekstra JB, Bouter PK, et al. Asymptomatic bacteriuria may be considered a complication in women with diabetes. Diabetes Care. 2000;23:744–9.
10. Hamdan HZ, Ziad AHM, Ali SK, Adam I. Epidemiology of urinary tract infections and antibiotics sensitivity among pregnant women at Khartoum North Hospital. Annals Clin Microbiol Antimicrob. 2011;10(2).
11. Odetoyin WB, Aboderin AO, Ikem RT, Kolawole BA, Oyelese AO. Asymptomatic bacteriuria in patients with diabetes mellitus in Ile-Ife, South-West, Nigeria. East Afr Med J. 2008;85:18–23.
12. Wogu MD, Ogbebor NE. Prevalence of asymptomatic bacteriuria in secondary school students in Benin City. Afr Res Rev. 2011;5(4):145–51.
13. Assel MT, Al-Meer FM, Al-Kuwari MG, Ismail MF. Prevalence and predictor of asymptomatic bacteriuria among pregnant women attending Primary health care in Qatar Middle East. J Fam Med. 2009;4:14–7.
14. Strom BL, Collins M, West SL et al. Sexual activity, contraceptive use, and other risk factors for symptomatic and asymptomatic bacteriuria. Ann Intern Med 1987;107:816-23.
15. Fihn SD, Boyko EJ, Chen CL *et al*: Use of spermicide coated condoms and other risk factors for urinary tract infection caused by *Staphylococcus saprophyticus*. Arch Intern Med 1998;158:281-7.
16. Kloos WE, Bannerman TL. Update on the clinical significance of coagulase-negative Staphylococci. Clin Microbiol Rev. 1994;7(1):117–40.
17. Al-Attas SA, Amro SO. Candidal colonization, strain diversity and antifungal susceptibility among adult diabetic patients. Annals of Saudi Medicine. 2010;30(2):101–8.
18. Meiland R. Asymptomatic bacteriuria management choices in different patient groups. Ned Tigdschr Geneeskd 2002;146(14):659-62.
19. Vejlsgaard R. Studies on urinary infection in diabetics. II. Significant bacteriuria in relation to long-term diabetic manifestations. Acta Med Scand 1966;179:183-8.
20. Keane EM, Boyko EJ, Barth Reller L, Hamman RF. Prevalence of asymptomatic bacteriuria in subjects with NIDDM in San Luis Valley of Colorado. Diabetes Care 1988;11:708-12.
21. Boroumand MA, Sam L, Abbasi SH, Salarifar M, Kassaian E, Forghani S. Asymptomatic bacteriuria in type 2 Iranian diabetic women: a cross sectional study. BMC Women's Health 2006;6:4.
22. Zhanel GG, Harding GK, Nicolle Lii. Asymptomatic bacteriuria in patients with diabetes mellitus. Rev Infect Dis 1991;13:150-4.
23. Wahl PW, Savage PJ, Psaty BM, Orchard TJ, Robbins JA, Tracy RP: Diabetes in older adults: comparison of 1997 American Diabetes Association classification of diabetes mellitus with 1985 WHO classification. Lancet 352:1012–5,1998