

Original Research Article

Asymptomatic bacteriuria and its associated factors in type II diabetes mellitus

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ABSTRACT

Background: With the dawn of modern era the diabetes epidemic has spread over continents affecting the developed and the developing nations alike. Asymptomatic bacteriuria which is quite prevalent in the diabetic population is associated with increased diabetic complications and thereby increased morbidity. Thus, the aim of this study was to assess the proportion of cases with asymptomatic bacteriuria (ASB) among type II diabetes mellitus patients as compared to non-diabetic healthy controls and studying the factors associated with ASB.

Methods: 93 eligible type II diabetes mellitus cases without genitourinary symptoms or abnormalities along with 93 non-diabetic healthy controls were recruited. Mid-stream urine was collected after taking informed consent and each sample tested using the dipstick, microscopy and culture techniques. Isolates were identified using standard biochemical tests.

Results: Prevalence of ASB in our study was found to be 34.4% among cases of type II diabetes mellitus while it was 6.45% among non-diabetic healthy controls. Amongst the diabetics with ASB 71.9 % were females and 28.13 % were males. *E. Coli* was isolated in 21 subjects among diabetic cases (22.58%) and in 5 subjects among non-diabetic healthy controls (5.38%). Fasting blood sugar (FBS) in diabetic cases group was 151.08 ± 48.16 and in control group was found to be 98.57 ± 25.95 ($p < 0.001$). Mean duration of patients with DM who had ASB (32) was 8.46 ± 4.14 years and those who were culture negative was 4.59 ± 4.2 years ($p < 0.05$). 24 subjects (75%) out of 32 diabetic ASB cases had glycosuria compared to 27 subjects (44.26%) out of 61 culture negative cases ($p < 0.05$). 9 out of 32 (28.13%) diabetic ASB subjects had proteinuria compared to 4 out of 61 (6.56%) culture negative cases ($p < 0.05$).

Conclusions: Overall prevalence of ASB was significantly more in diabetic population as compared to non-diabetic healthy controls (34.4% vs 6.45%). Females have an increased likelihood of developing ASB as compared to males. *E. Coli* was the most common pathogen isolated in ASB cases. Longer duration of diabetes and poor glycemic control are independent predictors for the development of ASB. The risk of ASB is also significantly increased in those with glycosuria and proteinuria.

Keywords: Asymptomatic bacteriuria, Diabetes

INTRODUCTION

Diabetes mellitus and its complications have great socioeconomic and health implications on human society.¹ Type II diabetes mellitus which is a complex endocrine and metabolic disorder is characterized by the interaction of several genetic and environmental factors

resulting in a heterogeneous and progressive disorder with variable degrees of insulin resistance and pancreatic β -cell dysfunction.² The magnitude of the diabetic epidemic can be judged by its global prevalence estimated at around 194 million people and with the prevalence of diabetes in India alone expected to increase

from 31.7 million in 2000 to 79.4 million in 2030 it is already a force to reckon with.^{3,4}

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-void midstream urine sample from an individual without symptoms of a urinary tract infection (UTI) like dysuria, frequency, urgency, strangury, abdominal distention or fever⁵. The urinary tract is usually sterile. Diabetes mellitus patients are at an increased risk of infection and urinary tract infections are thus commonly encountered in clinical practice. The prevalence of asymptomatic bacteriuria is about 3 times higher in diabetic women (ranging from 15% to 30%) than in nondiabetic women (less than 10%).⁵⁻⁷

Over the past decade or so there has been a steep rise in the incidence of diabetes mellitus (DM) throughout the world and more so in the developing countries with scarce resources where they pose a major clinical challenge both from diagnosis and management point of view. It has a long term effect on the incidence of ASB and it has been reported to be around four times higher in diabetics compared to nondiabetic patients.⁸ The exact reasons for this trend remain unclear, however a few studies have shown that the reason could be the presence of static pools of urine due to dysfunctional bladders contracting poorly, which serves a favourable media for bacterial growth while others suggest that hyperglycemic urine promotes rapid bacterial growth and colonization.⁹ Also, local secretion of cytokines and increased adherence of uropathogens to uroepithelial cells have been proposed to account for the greater prevalence of bacteriuria in diabetics.^{5,10}

Hence, this study was designed to assess the proportion of cases with asymptomatic bacteriuria (ASB) among type II diabetes mellitus patients as compared to non-diabetic healthy controls and studying the factors associated with ASB.

METHODS

This hospital based observational, descriptive, comparative analysis was carried out as a cross sectional prospective study recruiting 93 type II diabetes mellitus cases and same no. of non-diabetic healthy controls. The screening of patients was done by applying inclusion and exclusion criterion and the selected groups were subsequently evaluated for ASB and factors associated with it.

Inclusion criterion

- 18-75 years of age,
- Type 2 diabetes documented as per ADA criterion,
- Presented in the Department of Internal Medicine as indoor and outdoor patients at S.M.S. Hospital, Jaipur.

- Willing to be a part of the study.

Exclusion criterion

- Pregnancy,
- Recent hospitalization or surgery (within the past 4 months),
- Known urinary tract abnormalities (including cystopathy),
- Recent urinary tract instrumentation (in last 6 weeks),
- Symptoms of UTI (presence of dysuria, frequency, urgency, stranguria, abdominal discomfort or fever).

Statistical analysis

Statistical analysis was performed with the SPSS, trial version 20 for Windows statistical software package (SPSS Inc., Chicago, USA). The categorical data was presented as numbers (percent) and was compared among groups using Chi square test. Groups were compared for demographic data presented as mean and standard deviation and were compared using students t-test. Multivariate logistic regression was used for finding the significant independent predictors for ASB. Probability P value <0.05 was considered statistically significant.

RESULTS

A total of 93 subjects were studied in both the case (diabetics) and control (healthy non-diabetics) groups. The youngest patient was aged 29 years, while the oldest patient was aged 75. The mean age of the study group was 51.37±10.41 years, which was 52.04±9.24 years for cases, and 50.70 ± 11.48 years for the control group. On comparing the two groups, no significant difference was observed. Out of 93 cases, 48 (51.61%) were females and 45 (48.3%) were males. The highest proportion of type 2 diabetics in females 15 (31.25%) were in age group 40-49 years, followed by 14 (29.17%) in 50-59 years, 11 (22.92%) in 60-69 years, 5 (10.42%) in age group 30-39 years, and only 3 (6.25%) cases above 70 years were enrolled. There were no subjects among females below the age of 30 years. Among the male subjects, the highest proportion 21 (46.67%) subjects were observed in age group 50-59 years and no cases were seen above 70 years of age. Mean Fasting blood sugar (FBS) in cases group was 151.08 ± 48.16 and in control group was found to be 98.57 ± 25.95. A statistically significantly higher mean FBS was observed in cases as compared to controls (p <0.001). Urine culture was positive in 32 (34.41%) subjects out of 93 diabetic patients (cases) compared to 6 (6.45%) subjects out of 93 non-diabetic healthy controls. This association was found to be highly significant with p < 0.05. The most common organism isolated was E. Coli in 21 (22.58%) subjects among cases and in 5 (5.38%) subjects among healthy control group. Other organisms found among cases were, 4 (4.30%) subjects with Coagulase Negative Staphylococcus; 2 (2.15%) subjects each with Coagulase Positive Staphylococcus and

Enterococcus and a single (1.08%) subject with Enterobacter, Proteus vulgaris and Pseudomonas. Among the healthy controls a single (1.08%) subject grew Coagulase Negative Staphylococcus in their urine culture.

Out of 32 diabetes cases with ASB, 23 (71.9%) were females. The highest prevalence was found in 50-59 years age group, wherein the prevalence among female and male subjects was found to be equal with 5 cases each. The next highest prevalence was seen in the 40-49 years age group, wherein, the majority (77.78%) were females. Similarly, in the 30-39 years age group, 83.33% of subjects were females compared to 16.67% males. The most frequent age group in females for ASB was the 40-49 years group, while the most common age group in males for ASB was the 50-59 years age group. A greater proportion of subjects with ASB were females (71.88%) compared to males (28.13%). This association was found to be statistically significant with $p < 0.05$. Among the 93 cases, 32 (34.4%) were culture positive (ASB), and out of the 32 ASB cases 75% cases were due to gram negative microorganisms and 25% due to gram positive microorganisms. E. coli was found to be the most common organism constituting 87.5% of all gram-negative organism and 65.6% of total ASB cases. E. coli was most frequently grown in both females and males. It was higher in females (29.16%) compared to males (15.5%). Coagulase Negative Staphylococcus (8.33%), Coagulase Positive Staphylococcus (4.17%) and Enterococcus (4.17%) were grown only in the urine samples of female subjects. Proteus vulgaris (2.22%) and Pseudomonas (2.22%) were observed only in male subjects. The proportion of cases sterile after 48 hours of incubation were 75.56% in males as compared to 56.25% in females. This association was found to be statistically significant with $p < 0.05$. Similarly, 24 subjects (75%) out of 32 ASB cases showed glycosuria compared to 27 subjects (44.26%) out of 61 culture negative cases who did not. This association was found to be statistically significant with $p < 0.05$.

On comparing the association of proteinuria with ASB, 9 out of 32 (28.13%) ASB subjects had proteinuria as compared to 4 out of 61 culture negative cases (6.56%). This was found to be statistically significant with $p < 0.05$. The mean fasting blood sugar (FBS) of 93 diabetic patients was 151.08 ± 48 . The mean FBS of diabetic patients with ASB (32) was 178.75 ± 40 compared to those who were culture negative who had a mean FBS of 136.56 ± 45 . Association of FBS and ASB was found to be statistically significant with $p < 0.05$. Mean duration of patients with DM who had ASB (32) was 8.46 ± 4.14 years and those who were culture negative was 4.59 ± 4.2 years. Association of duration of Diabetes and ASB was found to be statistically significant with $p < 0.05$.

A logistic regression analysis was done to predict the occurrence of ASB for patients using age, sex, FBS and duration of diabetes as predictors. A test of full model

was statistically significant indicating that the predictors as asset reliably distinguish between ASB occurring or not. (Chi square 29.68, df 5, $p < 0.001$). Nagelkerke R^2 of 0.371 indicates fair relationship between predictors and grouping. Prediction success overall was 74.2% (With specificity of 84.2% and sensitivity 58%). The Wald criteria demonstrated that FBS and duration of diabetes ($p < 0.05$ S) made a significant contribution to prediction. For one-unit change in the significant predictors, the log odds of occurrence of ASB were 1.015 (for fasting blood sugar) and 1.244 times (for duration of DM).

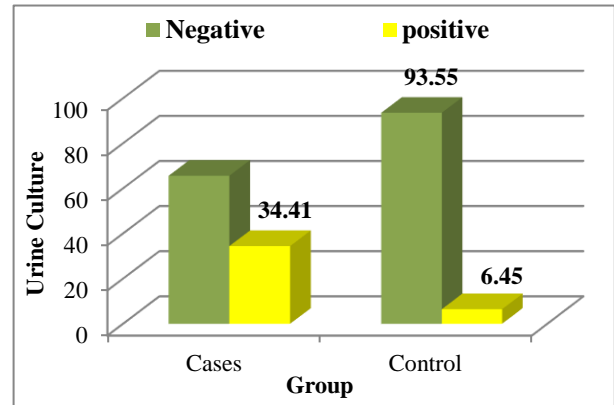


Figure 1: Association of groups with urine culture outcome.

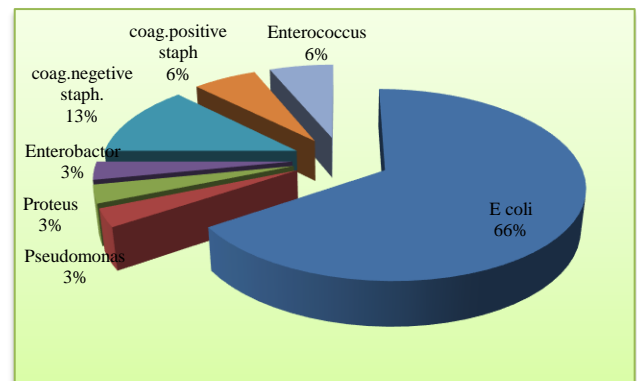


Figure 2: Distribution of microorganisms grown on urine culture

DISCUSSION

This study was undertaken to find out the prevalence of asymptomatic bacteriuria (ASB) in Type II diabetes mellitus (DM) patients and its associated variables.

In our study among the 93 cases, 32 subjects (34.41%) were found to have ASB compared to 6 subjects (6.45%) among the control group who had ASB.¹¹ These results are in accordance with the study conducted by Lakhan Singh et al in which they had observed ASB in 36.15% of urine samples in diabetic population. Janifer J et al in their study observed the prevalence to be 42.8%. Similarly, Ophori EA et al found it to be 36% while

Sunnesh Reddy et al found prevalence of ASB to be 26.6%.^{12,13} The likes of Alebiosu et al have even reported much lower ASB prevalence values between 5.8-19% but Assel MT et al in their study suggested that these variations in prevalence of ASB might be attributed to factors such as geographical variations, ethnicity of the subjects and variation in the screening test.^{14,15}

E. coli was the most common pathogen isolated among patients with ASB in this study constituting 65.6% of the total ASB cases. This is in contrast to the report of Alebiosu et al where *K. pneumoniae* was the most commonly isolated form.¹⁴ However, the result is consistent with the majority of reports where *E. coli* has been reported to be the major pathogen in ASB (59.6% in the study by Lakhan Singh et al, 71% in the study by J. Janifer et al, 57% in the study by Ophori EA et al and 55% by Zamnazard et al).^{10-12,16} Other organisms, like *Staphylococcus* and *Enterococcus* were also found in significant proportion. In our study *Staphylococcus* was grown in 18.75% ASB cases, *Enterococcus* in 6.25% and *Enterobacter*, *Proteus* and *Pseudomonas* each in 3.12% of ASB cases. Zamnazard et al in their study described the proportion as being 20% for *Staphylococcus*, 15% for *Enterococcus*, and 10% for *Klebsiella*.¹⁶

The prevalence of ASB might be influenced by the various patient related factors like age, sex, duration of diabetes, glycemic control and urinary findings of glycosuria and proteinuria.

Meiland R et al and Greelings SE et al in their study considered age as a well-known risk factor for ASB in type II diabetes patients.^{17,18} In our study, urine culture was positive in 32 out of 93 cases. Out of 32 asymptomatic bacteriuric diabetes cases (ASB), 23 (71.9%) were females. The highest prevalence among all ASB cases was found to be in 50-59 years age group, wherein the prevalence among female and male subjects, were found to be equal, with 5 cases each. The most frequent age group for females for ASB was the 40-49 years group, while the most common age group for males for ASB was the 50-59 years age group. Ophori E. A. et al in their study stated the most common age group in females as 35-39 years and in males as 45-49 years.¹³ In our study it was observed that majority of ASB cases were females, out of 32 ASB diabetes cases, 23 subjects (71.9%) were females as compared to male 9 (28.13%). This association was found to be statistically significant.

When we compared the outcome of urine culture with duration of diabetes, we observed a direct relationship which was statistically significant. In agreement to our results, Sunnesh Reddy et al and Nicolle LE et al in their study had also showed that patients with long standing diabetes mellitus had increased risk of ASB; however, Ishay et al in their study did not find any association between these two.^{13,19,20}

Collee JG et al in their study stated uncontrolled blood sugar level as an important risk factor for ASB in diabetic patient.²¹ The high prevalence of ASB among diabetics in our study may be due to uncontrolled blood sugar level. In our study there was a significant correlation between FBS and ASB ($p=0.001$). Jha BK et al in their study had also showed that all the cases of ASB were detected in patients with $FBS > 140$ mg/dl.²² Jenifer S et al stated that poor glycemic control was significantly associated with UTI among subjects with diabetes.¹¹ However Schmitt JK et al did not find any such association with ASB, which was in contrast to other studies.²³ This may be due to, shift in the plasma glucose levels, which is related to dietary intake, physical activity and drugs (oral hypoglycemic agents or insulin). Hyperglycemia leads to increase in the renal threshold which causes glycosuria. Renal threshold to glucose is variable in different individuals and also in the same individual at different times.

Zhanel et al, Schmitt JK et al and Qster HR et al in their study stated that proteinuria and glycosuria were major risk factors among the diabetics for ASB.^{5,23,24} In our study too the association between glycosuria and ASB was found to be statistically significant with $p < 0.05$. Sunnesh Reddy et al and Turan H et al also proposed glycosuria as a risk factor in patients of type 2 diabetes mellitus, however our study showed higher correlation with glycosuria compared to these studies.^{13,15}

Athanasia P et al and Matteucci E et al suggested proteinuria as a risk factor for ASB.^{26,27} In our study also ASB had a statistically significant association with proteinuria with $p < 0.05$.²⁰ also showed that macro-albuminuria was an independent and significant risk factor for ASB in type 2 Diabetes Mellitus women which was reiterated by our study as well

CONCLUSION

Overall prevalence of ASB was significantly more in diabetic population as compared to non-diabetic healthy controls. Females have an increased likelihood of developing ASB as compared to males. Most common age group for ASB in females was 40-49 years and in males was 50-59 years. *E. Coli* was the most common pathogen isolated in ASB cases. Longer duration of diabetes and poor glycemic control are independent predictors for the development of ASB. The risk of ASB is also significantly increased in those with glycosuria and proteinuria.

REFERENCES

1. Watson RR, Dokken B. Glucose Intake and Utilization in Pre-diabetes and Diabetes: Implications for Cardiovascular Disease. 1st ed. Elsevier;2014.
2. Siddiqui AA, Siddiqui SA, Ahmad S, Siddiqui S, Ahsan I, Sahu K. Diabetes: Mechanism,

- Pathophysiology and Management-A Review. *Int. J. Drug Dev. Res.* 2013;5(2):1-23.
3. Vishwanath S, Sarda R, D'Souza A, Mukhopadhyay C. Asymptomatic bacteriuria among patients with diabetes mellitus at a tertiary care center. *Nation J Lab Medic.* 2013;2(3):16-9.
 4. Pozzilli P, Leslie RD. Infections and diabetes: mechanisms and prospects for prevention. *Diabet Med.* 1994;11:935-41.
 5. Zhanel GG, Nicolle LE, Harding GKM, Manitoba Diabetic urinary infection study group. Prevalence of asymptomatic bacteriuria and associated host factors in women with diabetes mellitus. *Clin. Infect. Dis.* 1995;21:316-322.
 6. Joshi N, Caputo GM, Weitekamp MR et al. Infections in patients with diabetes mellitus. *NEng J Med* 1999;341:1906-12
 7. Hoepelman AI, Meiland R, Geerlings SE. Pathogenesis and management of bacterial urinary tract infections in adult patients with diabetes mellitus. *Inter J Antimicro Agents.* 2003;22:35-43.
 8. Pozzilli P, Leslie RD. Infections and diabetes: mechanisms and prospects for prevention. *Diabet Med* 1994; 11: 935-41.
 9. Joshi N, Caputo GM, Weitekamp MR et al. Infections in patients with diabetes mellitus. *NEng J Med* 1999;341:1906-12.
 10. Singh L, Murthy R, Singh H, Nigam P: Asymptomatic Bacteriuria In Patients With Type-2 Diabetes Mellitus
 11. Janifer J, Geethalakshmi S, Styavani K, Vishwanath V. Prevalence of lower urinary tract infection in South Indian type 2 diabetic subjects *Ind J Nep* 2016;20(2):120.
 12. EA Ophori, P. Imade and E. J. Johnny, prevalence of asymptomatic bacteriuria (ASB) in patient. *J Bac Res.* 2010;2(2):14-7.
 13. Reddy SA, Kale D, Venkat K, Reddy RM, Kandati J, Sreenivasa Rao P. Prevalence of ASB and its antibiotic sensitivity in type two diabetic women. *aaaa Inter J Res Med Sci.* 2013;1(4):487-495.
 14. Alebiosu CO, Osinubei OA, Olajubu FA. Significant asymptomatic bacteriuria among Nigeria type 2 diabetics. *J. Nat. Med. Assoc.* 2003;95(5):344-8.
 15. Assel MT, AI-Meer FM, AI-Kuwari MG, Ismail MF (2009). Prevalence and predictor of asymptomatic bacteriuria among pregnant women attending Primary health care in Qatar Middle East. *J. Fam. Med.* 2009;4:14-7.
 16. Zamanzad B and Moezzi M. Prevalence of Asymptomatic. *J Res Health Sci,* 2006;6(2):14-20.
 17. Meiland R, Greeling SE, Hoes AW, Hoepelman IM Asymptomatic bacteriuria management choices in different patient groups. *Ned Tigd Schr Geneesk.* 2002;146(14):659-62.
 18. Geerlings SE. Consequences of asymptomatic bacteriuria in women with diabetes mellitus. *Arch Intern Med* 2001; 161(11):1421-7. 57
 19. Nicolle LE. Asymptomatic bacteriuria in diabetic women. *Diabetes Care.* 2000;23:722-3.
 20. Ishay A, Lavi I, Luboshitzky R. Prevalence and risk factors for asymptomatic bacteriuria in women with type 2 diabetes mellitus. *Diabet Med.* 2006;23:185-7.
 21. Collee JG, Duguid JP, Fraser AG, Marmion BP. Mackie and Mc Cartney practical medical microbiology: laboratory strategy in the diagnosis of infective syndromes. 13th ed. London (UK): Churchill Livingstone; 1989:601-7.
 22. Jha BK, Singh YI, Khanal LK et al. prevalence of asymptomatic bacteriuria (ASB) in elderly diabetic patient Chitwan, Khathmandu. *Med J.* 2009;7(2):157-61.
 23. Schmitt JK, Fowcett CJ, Gullickson G. Asymptomatic bacteriuria and hemoglobin A1C *Diabetes Care.* 1986;9:518-20.
 24. Qsterby HR. Bacteriuria in diabetic and nondiabetic out patients. *Acta Med Scand.* 1964;176:721-30.
 25. Turan H, Serefhanoglu K, Torun AN, Kulaksizoglu S, Kulaksizoglu M, Pamuk B, et al. Frequency, risk factors, and responsible pathogenic microorganisms of asymptomatic bacteriuria in patients with type 2 diabetes mellitus. *J Infect Dis.* 2008;61:236-8.
 26. Athanasia P, Daniil I, Sotiropoulos A, Petropoulou D, Konstantopoulou S, Peppas T, Pappas S. Urinary tract infection, uropathogens and antimicrobial resistance in diabetic and nondiabetic patients. *Diabetes Res Clin Pract.* 2009;85:e12-3.
 27. Matteucci E, Troilo A, Leonetti P, Giampietro O. Significant bacteriuria in outpatient diabetic and non-diabetic persons. *Diabet Med.* 2007;24:1455-9.

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