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A cross sectional study on prevalence of asymptomatic bacteriuria in type 2 diabetes mellitus

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Abstract: *Background:* Diabetes Mellitus (DM) is an important health problem with increasing incidence nowadays. Asymptomatic bacteriuria (ASB) and its prevalence in diabetes and risk factors associated with it were analysed in this study. *Aims and Objectives:* The study aims to find the association of ASB with patient age, duration of diabetes, glucosuria, and plasma glucose levels. *Materials and Methods:* It were an observational cross-sectional study conducted in Shifaa hospital, among 150 type 2 DM patients over a period of 12 months. The investigations done were RBS, HbA1c, urine routine and urine culture. Data were entered into Microsoft excel sheet and was analysed. *Results:* The prevalence of ASB among type 2 DM was found to be 23.3%. The most common organism isolated in this study was Escherichia coli (62.9%), Klebsiella pneumoniae and Proteus mirabilis (11.4%). Association of ASB with female sex, duration of diabetes, bacteriuria, pyuria and glucosuria found to have significant association among Diabetics. Where as poor glycemic control, age, proteinuria, BMI does not found to have any significant association with ASB in diabetics. *Conclusions:* Overall prevalence of ASB among diabetics was around 23.3%. 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 was an important risk factor for the development of ASB. The risk of ASB is also significantly increased in those with glucosuria.

Keywords: Asymptomatic Bacteriuria, Diabetes Mellitus, Urinary Tract Infection.

Introduction

DM refers to a group of metabolic disorders that share the common feature of hyperglycaemia [1-2]. Although the prevalence of both types of DM is increasing worldwide, that of type 2 DM is rising much rapidly and is becoming a serious health problem in developing countries especially in India [3-7]. Individuals with DM have a greater frequency and severity of infections compared with non-diabetic patients [8-10]. Many people with DM have dysfunctional bladder, which allow the stasis of urine for long time, leading to bacterial growth. Apart from impaired host defence system, high level of glucose concentration in urine also serve as a culture medium for pathogenic organisms [11]. These UTI can be symptomatic or asymptomatic [12]. ASB can be one of the leading forerunners to UTI.

ASB is the presence of bacteria in urine in the absence of clinical symptoms or signs of urinary tract infection[1]. The microbiological criteria is bacteria more than 10^5 CFU/ml of urine [1, 13]. Urinary tract being the prevalent site of infection, serious complications such as emphysematous cystitis, pyelonephritis, renal or perinephric abscess, bacteraemia and renal papillary necrosis occur more commonly in DM [14-15].

It has been demonstrated that women with both DM and ASB have lower urinary cytokine and leucocyte concentrations than women without DM but with ASB [16]. This is associated with an immune systemic imbalance in certain patients with recurrent ASB and subsequently UTI. The reason for this predisposition is not well defined.

The major risk factor associated with ASB varies with age, duration of diabetes and complications like proteinuria, pyuria, glucosuria etc [14]. Several studies clearly demonstrated that most diabetic patients with urinary tract infection finally ends up in subclinical pyelonephritis [17].

So, it is essential to document the prevalence of ASB in DM. And also, the association of other risk factors in developing ASB in DM. It is important that the most common organisms and their sensitivity pattern to be identified. This will form the basis for studies to formulate management plans for the prevention of complications of ASB such as pyelonephritis. The present study aims to find out the prevalence of ASB in type 2 DM and its association on certain factors such as age, sex, duration of diabetes, glucosuria and pyuria.

Material and Methods

Study setting: The study was conducted in Department of General Medicine in Shifaa Hospital, Bangalore.

Study duration: The study was conducted for a period of 12 months from March 2020 to March 2021.

Study design: An Observational Cross-sectional study.

Study population: The study was conducted on both out-patients and in patients with Type 2 DM in Department of General Medicine.

Inclusion criteria:

a) Patients diagnosed with type 2 DM and came to our hospital with ailments other than urinary tract infection.
b) Patients diagnosed with type 2 diabetes aged more than 30 years and less than 60 years.

Exclusion criteria:

a) Those with symptoms of UTI
b) Those with known urinary tract abnormalities
c) Those individuals who had received antimicrobial drugs during the previous 2 weeks prior to giving urinary sample.
d) Recent urinary tract instrumentation including catheterization.

Methods:

a) History and examination of patients included in the study were taken according to study proforma.
b) For urine analysis and urine culture and sensitivity, clean catch midstream urine sample was collected after explaining the procedure and was sent to lab within 2 hours.
c) In case of in-patient's urine sample was collected at the time of admission after explaining the procedure and consent.
d) Blood was collected for measuring plasma blood glucose and HbA1c.

Statistical method: Qualitative data was summarized by frequency and percentage. Quantitative data was summarized by descriptive statistics such as mean and standard deviation. The prevalence was reported with its 95% confidence interval. The association of ASB with other risk factors and demographic factors were done by t-test/ANOVA and Chi-square test of independence. P-Value of < 0.05 was considered as statistically significant.

Sample size: As per the study of Singhal S et al 2015, [18] the prevalence of ASB among type 2 diabetes was reported as 28%. With 10% precision and 95% confidence interval the required sample size was 80. The following formula was used to derive the sample size.

$$n = \frac{(1.96)^2 \times p(1-p)}{d^2}$$

Where d was the precision (=0.10) and p was the prevalence (=0.28). To improve the power of study, the sample size was increased to 150.

Data management and data analysis plan: A structured questionnaire was developed in the form of a case report that included the fields for all necessary parameters. Data was entered into MS Excel data sheet and analysed using R version 4.0.1 software. Further an excel data base was constructed and questionnaire was entered. The numbers were assigned to each of the categories of qualitative parameters and was entered the same in the data base to minimize entry error. Description

of those numeric categories was also entered on a separate excel sheet adjacent to main data.

Ethics: Study was conducted after obtaining ethical committee clearance from Santhosh hospital, Bangalore. Participants were explained about the study and informed written consent was taken.

Results

There were 150 type 2 DM patients in this study.

Demographic characteristics: Majority of study population were in the age group of 51-55 years and 56-60 years with a percentage of 28% and 29.3% respectively. Among 150 participants 100 were female and remaining 50 were male, in percentage 66.7% and 33.3% respectively [Table 1].

Quantitative variables: In my study population majority has had the condition for 1-5 years followed by 6-10 years, with a mean of 6.29 ± 4 years and a median of 6. In my study majority of type 2 DM patients were over weight. 39.3% having normal BMI and 15.3 % having obesity class I and 1.3% with obesity class II [Table 2].

Distribution of study population based on HbA1c levels: In majority of study population the HbA1c levels were above 6.5%, indicating poor control of diabetes with a mean HbA1c level of 8.88 ±2.09 and a median of 8.6.[Table 2]

Qualitative variables:

Prevalence of ASB in type 2 DM: Out of 150 patients, 35 people had positive urine culture. That means the prevalence of ASB was around 23.3 % among type 2 DM patients of my study. This is statistically significant as the p value is < 0.001 by fischers exact test (Fig-1) [Table 1].

ASB – Microorganisms isolated: The figure 15 shows the microorganisms isolated from urine culture of the study population. Out of 35 culture positive patients, the most common organism isolated was Escherchia coli (n = 22, 62.9%) [Table 1].

E.coli was found to be the most predominant organism in diabetic patients with ASB (62.9%) , followed by Klebsiella pneumoniae (n = 4 , 11.4%) and Proteus mirabilis (n = 4 , 11.4 %) followed by Enterococcus species (n = 2 , 5.7 %) followed by Citrobacter koseri (n = 1 , 2.9%), Coagulase negative Staphylococcus (n = 1 , 2.9%) and Candida albicans (n = 1 , 2.9%) (Fig-2).

According to our study, there was a significant association in diabetic patients between ASB and female sex, glycosuria, bacteriuria, and pyuria. However, there did not appear to be any notable association of ASB with poor glycemic control and proteinuria [Table 3].

Fig-1: Pie diagram showing distribution of type 2 DM based on urine culture

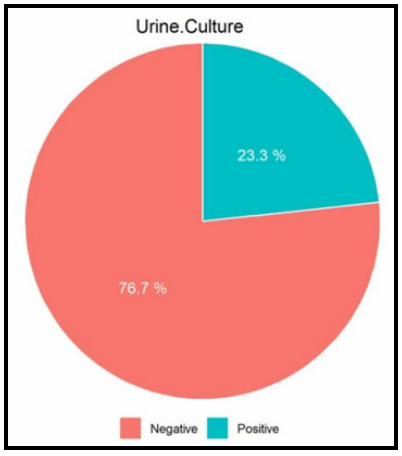

Fig-2: Bar diagram showing various organisms isolated

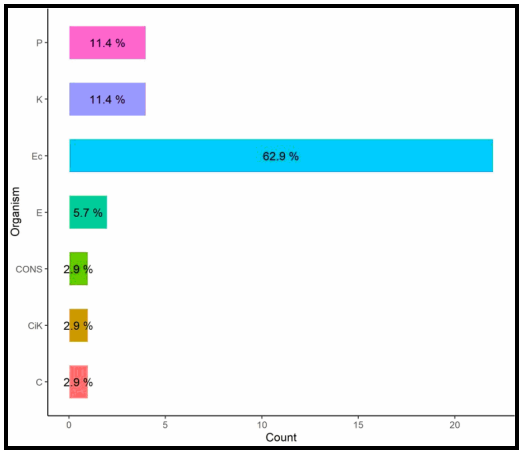

Table-1: Summary of qualitative variables based on frequency and percentage				
Sl no.	**Variables**	**Levels**	**Frequency**	**Percentage**
1	Sex	Females	100	66.67
		Males	50	33.33
2	Previous sugar levels	Elevated	80	53.33
		Normal	70	46.67
3	Urine protein	No	110	73.33
		< 30 mg/dl	31	20.67
		30 – 100 mg/dl	9	6
4	Urine sugar	Trace / no	71	47.33
		Low – moderate	32	21.33
		High	47	31.33
5	Urine bacteria	Absent	115	76.67
		Present	35	23.33
6	Urine culture	Positive	35	23.33
		Negative	115	76.67
7	Organism	E coli	22	62.86
		Proteus mirabilis	4	11.43
		Citrobacter koseri	1	2.86
		Candida albicans	1	2.86
		Klebsiella	4	11.43
		CONS	1	2.86
		Enterobacter	2	5.71

Association of different variables with ASB:

Table-2: Summary of association of quantitative variables with ASB								
Sl no	**Variable**	**Urine culture**	**Frequency (n)**	**Mean**	**SD**	**Test.Stat**	**P.value**	**P.value. NP**
1	Age	Negative	115	50.5478	6.4089	0.55	0.584	0.377
		Positive	35	51.2571	6.7403			
2	Duration of DM	Negative	115	5.7739	3.7698	2.75	0.008	0.007
		Positive	35	8.0	4.3114			
3	BMI	Negative	115	25.7748	4.0316	0.95	0.346	0.324
		Positive	35	26.4057	3.24			
4	RBS	Negative	115	232.356	85.2269	2.2	0.032	0.007
		Positive	35	269.6859	88.6668			
5	HbA1c	Negative	115	8.7513	2.1564	1.55	0.127	0.065
		Positive	35	9.32	1.8238			
6	Urine pus cells	Negative	115	3.0609	1.9229	7.61	< 0.001	< 0.001
		Positive	35	10.9143	6.0116			

Table-3: Summary of association of qualitative variables with ASB									
Sl no	variables	Levels	Culture negative		Culture positive		Chi square	P value	P value fisch
			n	%	N	%			
1	Sex	F	69	60	31	88.6	8.613	0.003	0.002
		M	46	40	4	11.4			
2	Previous sugar	Normal	58	50.4	12	34.3	2.2	0.138	0.122
		Elevated	57	49.6	23	65.7			
3	Urine protein	Nothing	85	73.9	25	71.4	0.536	0.765	0.743
		< 30 mg/dl	24	20.9	7	20			
		30 -100 mg / dl	6	5.2	3	8.6			
4	Urine sugar	Trace / nothing	62	53.9	9	25.7	9.248	0.01	0.008
		Low – moderate	23	20	9	25.7			
		High	30	26.1	17	48.6			
5	Urine bacteria	Present	4	3.5	31	88.6	103.908	<0.001	<0.001
		Absent	111	96.5	4	11.4			

Discussion

The present study was an observational cross sectional study conducted in Department of General Medicine in Shifaa hospital, Bangalore over a period of 12 months. This study was conducted among 150 type 2 diabetes patients after obtaining informed consent and those who satisfied the inclusion and exclusion criteria. This study aims to find out the prevalence of ASB in type 2 diabetes patients and its association with certain variables like age, duration of diabetes, glucosuria and plasma glucose level. And also to find the common organism causing ASB among type 2 DM.

In this study it was found that, the prevalence of ASB among type 2 DM patients was 23.3% [Figure 1]. The P value calculated was < 0.001, so confirms the high prevalence of ASB among type 2 DM. This was supported by various other studies. Study by Maisnam I and its associates [19] in 2019, found prevalence of ASB around 21.25% among 80 type 2 DM patients. A study to determine prevalence of ASB among type 2 DM by Kaur S and its associates [2], also found to have a prevalence of around 21%. Similar observation were noted in other studies, such as studies by Singhal S and its associates (28.2%) [18], Bissong M [20] and its associates (38.3%) and Vishwanath S and its associates (21%) [21].

So majority of the studies, both Indian and out of India concluded the high prevalence of ASB among type 2 DM. The studies by Gurjar D and its colleagues [8] and Kalpana Devi Venkatesan and her associates [22] also concluded the high prevalence of ASB among type 2 DM, which was around 34.4% and 32% respectively. This variation in percentage of ASB has been attributed to factors such as geographical variation, ethnicity of subjects and variations in screening.

The most common micro organism isolated in our study was E.coli (62.9%), followed by Klebsiella pneumoniae (11.4%) and Proteus mirabilis (11.4%), followed by Enterococcus species (5.7%), which was followed by Citrobacter koseri (2.9%), CONS (2.9%) and Candida albicans (2.9%) [Figure 2]. E.coli as the most common organism was obtained in the studies by Kaur S and its associates in 2019[2], Gurjar D and its associates [8], Kalpana Devi Venkateshan and her colleagues [22], and Papazafiropoulou and its associates [23].

A study by AS Reddy et al [14] also concluded E.coli as the most common organism isolated in diabetic women. Even though majority of the studies shown E.coli as the most common organism, there were some exceptions. Klebsiella was the most common

organism isolated in male population in the study by Maisnam I and its associates [19] and E.coli among female population in their study.

A change in etiologic spectrum was observed with Staphylococcus species in a study by Bissong M and its associates [20]. Whereas in the study by Vishwanath S and his colleagues [21] shown Enterococcus (50%) as most common orgnaism, followed by Staphyloccus saprophyticus (25%) and E.coli (25%). On analysing various studies we observed that E.coli as the most common organism isolated, which supports our study. The reason for predominant organism as E.coli is that, it can bind to Glycoconjugate receptor of Epithelial cells of human urinary tract, and initiate infection itself.

The study group ages ranges from 35 to 60 years with mean age of 50.71. The mean age distribuition among ASB positive and negative groups were almost same, with a p value of 0.584 which is statistically not significant [Table 2]. Only few studies showed significant association of increasing age with ASB. Those were, studies by Singhal S and its associates [18] and by Reddy AS and its associates [14]. The most of the studies did not find any significant association of age with ASB, as observed in this study. Next compared the association of gender with ASB. In this study we observed female sex predominates in both ASB positive and negative group. Out of 35 urine culture positive diabetic patients 88.6% were females, with a P value of 0.003. This study concluded a significant association of ASB among females [Table3].

This was supported by various other studies by Singhal S and its associates in 2015[18], Maisnam I and its associates in 2019[19] and also by Gurjar D and its colleagues in 2015 [8]. Association of duration of diabetes with ASB was the another important variable studied. In this study it was found to have a significant association with ASB [Table2].

Studies by Gurjar D and its associates in Jaipur [8], Singhal S and its associates [18] in India and AS Reddy and its associates [14] among diabetic women along sea coast also found to have an increased duration of diabetes as a significant risk factor for ASB. Even though some studies by Boroumand MA and Geerlings SE [10-11] has show association of ASB with BMI, this study did not find any significant association between BMI and ASB [Table 2]. One study which supported our finding was study conducted by Papazafiropoulou A in 2010 [23]. Their study also did not found any significant association between ASB and BMI.

On comparing recent RBS levels, Hba1c, previous sugar levels we found recent RBS levels had significant association with ASB in diabetes. But HbA1c levels and previous sugar levels had no significant association with ASB, with a mean RBS level of 269.68 and mean HbA1c level of 9.32 [Table 2].

Previous sugar levels were classified into two groups, whether elevated or normal levels. We found majority of the persons with ASB had elevated previous sugar levels. But on comparing previous sugar levels in diabetics without ASB and those with ASB, it was found that both groups were statistically same. So poor glycemic control has no significant association with ASB among diabetes.

This finding was supported by certain studies, such as study by Maisnam I and its associates [19] also found no significant association between ASB and poor glycemic control. This finding was against as in certain studies [2, 8, 18, 23] were they shown a significant association of poor glycemic control and ASB. This difference may be due to difference in study groups, ethnicity of the study group, study area and laboratory parameters.

Next we compared proteinuria, pyuria, glucosuria and bacteriuria with urine culture. We found significant association of bacteriuria, pyuria and glucosuria among diabetics with ASB [Table 3]. This was supported by studies by AS Reddy [14], Gurjral D [8]. These studies by them also found significant association between proteinuria and ASB. But our study did not found any significant association between proteinuria and ASB. Despite evidence, these differences may be due to the characteristics of study population such as in duration of diabetes, glycemic control etc.

Conclusion

ASB was a common finding in type 2 diabetic patients especially women have more prevalence than men. The prevalence of ASB among type 2 DM was around 23.3% in this study. The most common organism isolated in this study was Escherichia coli. There was no statistically significant association between age and body mass index with ASB in diabetics.

Significant association of ASB was noted with longer duration of DM and higher recent RBS values. There was no significant association between high HbA1c levels and previous elevated sugar levels. Highly significant association was found between presence of pyuria and bacteriuria with ASB. ASB was significantly associated with glucosuria in diabetic individuals but not with proteinuria.

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