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Original Research Article

Asymptomatic Bacteriuria in Women with Type 2 Diabetes Mellitus

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Conflict of interest: Nil

Abstract:

Background: In this study, we wanted to find the association of asymptomatic bacteriuria with type 2 diabetes mellitus in women.

Methods: This was a hospital based case control study conducted among 100 female diabetic patients aged more than 40 years with type 2 diabetes mellitus attending Master Health Check-up OPD in Velammal Medical College and Hospital, Madurai, Tamil Nadu, from February 2015 to August 2015 after obtaining clearance from institutional ethics committee and written informed consent from the study participants.

Results: The mean FBS and mean PPBS levels and urine sugar and urine protien levels is significantly impaired and increased in patients with type 2 diabetes with asymptomatic bacteriuria which was found to be statistically significant. The increased incidence of positive urine culture in group type 2 diabetes compared to the control group was statistically significant.

Type 2 diabetic patients have 1.62 times significantly more risk of developing asymptomatic bacteriuria than patients in the control group. It was statistically significant.

Type 2 diabetic patients with urine sugar positivity have 3.04 times significantly more risk of developing asymptomatic bacteriuria than patients in the control group. It was statistically significant.

Type 2 diabetic patients with Urine Pus Cells > 4 cells/cu.mm have 4.29 times significantly more risk of developing asymptomatic bacteriuria than patients in the control group. It was statistically significant.

Conclusion: Escherichia coli was the most common cause of ABU in both diabetic and non-diabetic women in this study. Most of the isolated microorganisms in both diabetic and nondiabetic women were resistant to cotrimoxazole. All the isolated microorganisms in both the diabetic and nondiabetic groups were sensitive to norfloxacin.

Keywords: Asymptomatic Bacteriuria, Women, Type 2 Diabetes Mellitus.

Introduction

Asymptomatic bacteriuria" or asymptomatic urinary infection refers to a specific quantitative count of bacteria isolated in a properly collected urine specimen from an individual who does not have signs or symptoms suggestive of urinary tract infection.

For asymptomatic women, bacteriuria is defined as isolation of the same bacterial species in two consecutive voided urine specimens with quantitative counts of more than or equal to 10^5 CFU/ml. The prevalence of bacteriuria in diabetic women is 8%–14%. It usually correlates with duration of the disease and presence of other chronic complications, rather than with the parametesrs depicting glycemic control. *Escherichia coli* is the most common organism isolated from bacteriuric women. But the strains from asymptomatic patients have fewer virulence characteristics compared to those with symptomatic infection.

Other organisms of Enterobacteriaceae family such as *Klebsiella pneumoniae* and non Enterobacteriaceae family like coagulase-negative staphylococci, group B streptococci, *Enterococcus* species, and *Gardnerella vaginalis* are also responsible for bacteriuria.

Aims and Objectives

- To find the association of asymptomatic bacteriuria with type 2 diabetes mellitus in women.
- To describe the causative organisms of asymptomatic bacteriuria in diabetic women and non-diabetic women.

- To determine the antibiotic susceptibility of isolated organisms.

Methods

This was a hospital based case control study conducted among 100 female diabetic patients aged more than 40 years with type 2 diabetes mellitus attending Master Health Check-up OPD in Velammal Medical College and Hospital, Madurai, Tamil Nadu, from February 2015 to August 2015 after obtaining clearance from institutional ethics committee and written informed consent from the study participants.

Inclusion Criteria

- Age-matched
- Non diabetic
- Healthy women more than 40years of age with fasting blood sugar < 100mg/dl and post-prandial blood sugar<140mg/dl
- Attending Master Health Checkup OPD in GSH.

Exclusion Criteria

- Patients who have received antibiotics in the last 14 days.
- Patients who have had a Foley's catheter inserted within 2 months before enrolment of study.
- Pregnant patients.
- Patients with gynecological infections
- Patients with symptomatic urinary tract infection
- Patients who are taking diuretics.
- Patients with urinary tract abnormalities.
- Patients with urinary tract stones**.**

Statistical Methods

Descriptive statistics was done for all data and were reported in terms of mean values and percentages. Suitable statistical tests of comparison were done.

Continuous variables were analysed with the unpaired t test.0 Categorical variables were analysed with the Chi-Square Test and Fisher Exact Test. Statistical significance was taken as $P < 0.05$. The data was analysed using SPSS version 16 and Microsoft Excel 2007.

Results

Asymptomatic bacteriuria and duration of diabetes

Among patients with diabetes for more than 10 years 50% had asymptomatic bacteriuria compared to 15.4% of those with diabetes for less than one year.

Table 1:

Duration of Diabetes	**Total No. of Cases**	**ABU**	**Percentage**	
< 1 yr	13	2	15.4%	
2 - 5 yrs	20	2	10%	
6 - 10 yrs	13	3	23%	
>10 yrs	4	2	50%	
Total	50	9		
Fasting Blood Sugar	Cases	%	Control	%
≤ 100 mg/dl	3	6.00	34	68.00
101-150 mg/dl	29	58.00	16	32.00
151-200 mg/dl	12	24.00	0	0.00
> 200 mg/dl	6	12.00	0	0.00
Total	50	100	50	100
Fasting Blood Sugar	Cases		Control	
N	50		50	
Mean	147.98		92.50	
SD	49.08		10.83	
P value Unpaired t Test			0.0001	

FBS	Cases		Controls		P value Unpaired t Test
	ABU +	ABU -	ABU +	ABU -	0.0001
Mean Levels (mg/dl)	158.46	145.78	92.51	92.33	

In diabetics the mean fasting blood sugar is 145.78 mg/dl among ABU +ve patients and 148.46 mg/dl among ABU –ve patients. In control group, the mean fasting blood sugar is 148.46 mg/dl among ABU +ve patients and 92.51 mg/dl among ABU –ve patients The increased mean FBS in group type 2 diabetes

among ABU +ve compared to ABU –ve patients and controls is statistically significant as the p value is 0.0001as per unpaired t- test indicating a true difference among study groups. The mean FBS was meaningfully more in diabetic ABU+ve patients compared to ABU-ve patients by 12.68 mg/dl. The mean FBS was meaningfully more in diabetic ABU+ve patients compared to control group by 65.95 mg/dl. This significant difference of 1.09 times increase in mean FBS levels diabetics (ABU+ve Vs ABU-ve) and 1.71 times increase when compared to control group is true and has not occurred by chance. In this study we can safely conclude that the mean FBS levels is significantly impaired and increased in patients with type 2 diabetes with asymptomatic bacteriuria.

Table 2:

Fasting Blood Sugar		**Cases**	**ABU**	**Percentage**
≤ 100 mg/dl		3	1	33.3%
101-150 mg/dl		29	5	17.2%
151-200 mg/dl		12	1	8.3%
> 200 mg/dl		6	2	33.3%
Total		50	9	
Post Prandial Blood Sugar	Cases	%	Control	%
≤ 200 mg/dl	32	64.00	50	100.00
201-300 mg/dl	14	28.00	0	0.00
301-400 mg/dl	3	6.00	0	0.00
> 400 mg/dl	1	2.00	0	0.00
Total	50	100	50	100
Post Prandial Blood Sugar	Cases		Control	
N	50		50	
Mean	198.76		125.46	
SD	65.37		9.17	
P value Unpaired t Test			0.0001	
PPBS	Type 2 Diabetes	Controls	P value Unpaired t Test	
	ABU + / ABU -	ABU +	ABU -	0.0001

In diabetic patients the mean post prandial blood sugar is 209.44 mg/dl among ABU +ve patients and 196.41 mg/dl among ABU –ve patients. In control group, the mean fasting blood sugar is 127.67 mg/dl among ABU +ve patients and 125.32 mg/dl among ABU –ve patients The increased mean PPBS in diabetics with ABU +ve compared to ABU –ve patients and controls is statistically significant as the p value is 0.0001as per unpaired t- test indicating a true difference among study groups. The mean PPBS were meaningfully more in diabetic ABU+ve patients compared to ABU-ve patients by 13.03 mg/dl. The mean PPBS was meaningfully more in diabetics with ABU+ve compared to control group by 81.77 mg/dl.

This significant difference of 1.07 times increase in mean PPBS levels in group type 2 diabetes patients (ABU+ve Vs ABU-ve) and 1.64 times increase when compared to control group is true and has not occurred by chance. In this study we can safely conclude that the mean PPBS levels is significantly impaired and increased in patients with type 2 diabetes with asymptomatic bacteriuria.

Table 3:

Urine Sugar	**Cases**	**%**	**Control**		**%**
Nil	0	0.00	50		100.00
Trace	21	42.00	0		0.00
1+	15	30.00	0		0.00
2+	10	20.00	0		0.00
3+	4	8.00	0		0.00
Total	50	100	50		100
P value Fishers Exact Test			0.0001		
Urine Sugar	Cases		Controls		P value Fishers Exact Test
	ABU +	ABU -	ABU +	ABU -	0.0001
Urine Sugar Positivity	6/9	23/41	0	0	

Among diabetics, majority had trace urine sugar (n=21,42%). In control group majority showed nil urine sugar (n=50, 100%) The increased incidence of positive urine sugar in diabetic group compared

to the control group is statistically significant as the p value is 0.0001as per fishers exact test indicating a true difference among study groups. The urine sugar results were meaningfully more in diabetic group with ABU+ve compared to ABU-ve group by 10 percentage points. This significant difference of 1.18 times increase in diabetics with ABU+ve compared to ABU-ve group is true and has not occurred by chance. In this study we can safely conclude that urine sugar measurements is significantly impaired and increased in patients with type 2 diabetes with asymptomatic bacteriuria.

Table 4:

Urine protein	**Type 2 Diabetes**		**%**	**Control**	**%**
Nil	0		0.00	48	96.00
Trace	45		90.00	1	2.00
1+	2		4.00	1	2.00
2+	3		6.00	0	0.00
Total	50		100	50	100
P value Fishers Exact Test				0.0001	
Urine protein	Type 2 Diabetes		Controls		P value Fishers Exact Test
	ABU +	ABU -	ABU +	ABU -	0.0001
Urine Albumin Positivity	1/9	4/41	1/3	1/47	

In patients with type 2 diabetes, majority of the patients exhibited trace urine protein (n=45, 90%). In control group majority exhibited nil urine protein (n=48, 96%).

The increased incidence of positive urine protein in diabetic group compared to the control group is statistically significant as the p value is 0.0001as per fishers exact test indicating a true difference among study groups. The urine protein results were meaningfully more in group type 2 diabetes with ABU+ve compared to ABU-ve group by 2%.

This significant difference of 1.13 times increase in incidence in group type 2 diabetes with ABU+ve compared to ABU-ve group is true and has not occurred by chance. In this study we can safely conclude that urine protein measurements is significantly impaired and increased in patients with type 2 diabetes with asymptomatic bacteriuria.

Table 5:

Positive Urine Culture - 1st Sample	**Type 2 Diabetes**	**%**	**Control**	**%**
Positive	9	18.00	3	6.00
Negative	41	82.00	47	94.00
Total	50	100	50	100
P value Fishers Exact Test			0.0132	
Positive Urine Culture- 2nd Sample	Type 2 Diabetes	%	Control	%
Positive	9	18.00	3	6.00
Negative	41	82.00	47	94.00
Total	50	100	50	100
P value Fishers Exact Test			0.0132	

Among diabetic patients, many of them exhibited positive urine culture in the 1st and 2nd sample (n=9, 18%). In control group few exhibited positive urine culture (n=3, 6%) The increased incidence of positive urine culture in group type 2 diabetes compared to the control group is statistically significant as the p value is 0.0132as per fishers exact test indicating a true difference among study groups. The positive urine culture results were meaningfully more in diabetic group compared to control group by 12%. This significant difference of 3 times increase in incidence of positive urine culture test in diabetic group compared to control group is true and has not occurred by chance.

In this study we can safely conclude that asymptomatic bacteriuria is significantly increased in patients with type 2 diabetes.

Table 6:

Independent Variables	Dependent variable – ABU		
	Odds Ratio	**95% Confidence Interval**	**P value**
Age > 50 years	0.96	0.94-0.99	0.8225
Diabetic	1.62	0.56-3.84	0.0074
Duration of Diabetes > 5 years	5.36	0.48-59.92	0.2092
FBS > 150 mg/dl	1.10	0.86-1.41	0.4365
PPBS > 300 mg/dl	1.37	0.71-2.63	0.8649
Urine Sugar Positivity	3.04	1.33-6.95	0.0015
Macroalbuminuria	1.91	0.33-38.4	0.5819
Urine Pus Cells > 4 cells/cumm	4.29	1.12-16.52	0.0001

Type 2 diabetic patients have 1.62 times significantly more risk of developing asymptomatic bacteriuria than patients in the control group. It is statistically significant with a p-value of 0.0074.

Type 2 diabetic patients with urine sugar positivity have 3.04 times significantly more risk of developing asymptomatic bacteriuria than patients in the control group. It is statistically significant with a p-value of 0.0015.

Type 2 diabetic patients with Urine Pus Cells > 4 cells/cu.mm have 4.29 times significantly more risk of developing asymptomatic bacteriuria than patients in the control group. It is statistically significant with a p-value of 0.0001.

Discussion

The study confirms an increased prevalence of asymptomatic bacteriuria in diabetic women(18%) compared to non-diabetic women(6%). This is supported by various other studies. Study by Suzanne Geerlings & associates showed that the prevalence of asymptomatic bacteriuria was 26% in diabetic women compared to 6% in non-diabetic women.[1]

Study by Ruby Meiland et al on asymptomatic bacteriuria in diabetic women showed that the prevalence of asymptomatic bacteriuria in diabetic population including both type 1 and type 2 diabetes was 17%.[2]

The Infectious Disease Society of America claims that the prevalence of ABU in diabetic women varies from 9% to 27%, compared to 1% to 5% in non-diabetic healthy women, based on meta-analysis of various studies. In the meta-analysis of observational studies by Marjo Renko, they were able to show that the prevalence of ABU was three times higher in all patients with diabetes compared with control subjects.[3] a similar observation was also noted in the study by Mendoza et al.

Age

This study does not show increasing risk of ABU with increasing age. But the study by Geerlings & associates show that increasing age is an important risk factor for ABU in diabetic women. The Infectious Disease Society of America claims that the prevalence of ABU in elderly women in the community (age ≥70 years) is 10.8% to 16% compared to 1 to 5% in healthy non- diabetic premenopausal women.[4] Study by Meiland et al shows increasing prevalence of ABU with increasing age in the study group.

Duration of diabetes

This study shows that among patients with diabetes for more than 10 years 50% had culture positive urinary tract infection compared to 15.4% of those with diabetes for less than one year. But the statistical significance of duration of diabetes as a risk factor for ABU could not be proved.

Study by Suzanne Geerlings & associates show that the risk of ABU is more with increasing duration of diabetes. The IDSA claims that ABU better correlates with the duration of diabetes rather than the biochemical parameters of glycemic control. Marjo Renko showed in his meta-analysis of various observational studies that the mean duration of diabetes was longer in patients with ABU than in those without ABU.

Glycemic Control

Though this study shows that the mean FBS and PPBS are significantly impaired and increased in diabetic women with ABU, the relationship between ABU and glycemic control could not be fully established as correlation with HbA1c was not attempted. The IDSA claims that ABU does not correlate with the biochemical parameters of glycemic control based on various observational studies. Poor glycemic control has been shown to not correlate with the frequency of bacteriuria. Schmitt *et al*. found no relationship between HbA1c and bacteriuria in 752 type 2 DM patients. In another study by Rayfield, which compared HbA1c with ABU, the mean HbA1c was 11.5% in bacteriuric and 11.4% in non-bacteriuric diabetic women.5 Study by Mendoza et al. also showed no correlation between ABU and fasting blood sugar or HbA1c.[6]

Glycosuria

This study shows better correlation of culture positive bacteriuria with urine sugar than with blood sugar levels. Only 4.8% with trace sugar in urine had culture positivity whereas 40% with 2+ urine sugar showed culture growth. Study by Mohammed Ali Boroumand in Iranian women showed a significant relationship between ABU and glycosuria.[7] Similar results were also observed in a study conducted on Tanzanian women by Eligus F. Lyamuya et al. which showed that ABU was present in 16.6% of the diabetic individuals with glycosuria compared to 8% in diabetic individuals without glycosuria. But a study by Mikobiyol et al. shows no correlation between bacteriuria and glycosuria.[8]

Urine pus cells

This study shows that 88.9% diabetic patients with urine pus cells more than 4 had asymptomatic bacteriuria. Study by Boroumand et al inIranian women showed similar results of significant relationship of ABU with pyuria. The above observation is also supported by the study by Mikobiyol et al. which showed a positive correlation between pyuria and asymptomatic bacteriuria. The IDSA states that increased presence of pus cells in urine accompanies ABU in 32% of young healthy non-diabetic women, but upto 70 % in diabetic women.

Proteinuria

All the diabetic patients with ABU had associated proteinuria in this study. 88.89% was associated with trace proteins in urine. 11.11% had 1+ protein in urine. Study by Geerlings & associates show that macroalbuminuria is associated with increased risk of ABU. a study reports that the prevalence of bacteriuria in patients with diabetic nephropathy may be as high as 13%. Observations by Ruby Meiland et al. also state that ABU has a positive correlation with long standing complications of diabetes mellitus like microalbuminuria or macroalbuminuria.

Culture positivity

4 patients in the control group had a growth in both the first and second culture, out of which 3 were significant. All the 4 specimens grew Escherichia coli. In the diabetic group, 12 patients had growth in both the first and second culture of which 9 were significant. 4 cultures grew Escherichia coli, 2 cultures grew Klebsiella pneumonia and 3 cultures grew Pseudomonas aeruginosa. Escherichia coli was the most common organism isolated in both diabetic and non-diabetic women with ABU. It accounted for 100% of the growths in control group and 44.44% of the growths in the diabetic group. Klebsiella pneumonia accounted for 22.22% and pseudomonas aeruginosa accounted for 33.33% of the growths in diabetic women. Various studies have proven Escherichia coli to be the single most important organism responsible for bacteriuria. Leibovici et al showed in his study that Klebsiella pneumonia was responsible for 25% of the cases of ABU in diabetics which is similar to the observation in this study. But in the study by Meiland, Klebsiella pneumonia was isolated in only 6 % of the diabetic cases of ABU. Incidence of organisms other than Escherichia coli appears to be increased in diabetics with ABU compared to non-diabetics with ABU. Geerlings et al also noted a lower percentage of *E. coli* in women with diabetes versus women without the disease (42 vs. 78%). Lye et al. also showed that *E. coli* is the most common microorganism in UTIs in diabetic patients, but that *E. coli* occurs in significantly lesser proportion than in control subjects. According to the IDSA, pseudomonas commonly causes ABU in men and women with long term urological devices in place. But in this study, Pseudomonas was isolated from 33.33% of the cultures positive for ABU in diabetic women.

Antibiotic sensitivity

This study shows that in diabetics, 2 out of 4 E. coli strains(50%) isolated in urine were sensitive to cefotaxime, amikacin, gentamycin, ciprofloxacin and norfloxacin. One strain(25%) was sensitive only to amikacin gentamycin and norfloxacin and another(25%) was sensitive to cefotaxime, amikacin, gentamycin and norfloxacin. All the 4 strains were resistant to cotrimoxazole. This is in contrast to the observations in various study results, which consider cotrimoxazole to be the drug of choice in urinary infection. This is probably because of the extensive usage of cotrimoxazole as empirical therapy in various conditions leading to the development of resistance to this drug.

Of the two strains of Klebsiella pneumonia, one was sensitive to cefotaxime, amikacin, gentamycin, ciprofloxacin, norfloxacin and cotrimoxazole, while the other strain was sensitive only to amikacin and norfloxacin.

Of the three strains of Pseudomonas aeruginosa, two were sensitive to cefotaxime, amikacin, gentamycin, ciprofloxacin and norfloxacin, while the other strain was sensitive only to amikacin, gentamycin, ciprofloxacin and norfloxacin. Though various studies have shown that resistance to fluoroquinolones is an emerging threat, this study shows that most of the organisms isolated in both diabetic and non-diabetic population were sensitive to fluoroquinolones.

Aminoglycosides, amikacin and gentamycin also have good coverage against the isolated uropathogens in both the diabetic and non-diabetic population.

Conclusion

- Women with Type 2 diabetes mellitus have 1.62 times significantly more risk of developing

asymptomatic bacteriuria than patients in the control group.

- The prevalence of asymptomatic bacteriuria in type 2 diabetic group was 18%.
- The prevalence of asymptomatic bacteriuria in control group was 6%
- There was no statistical correlation between asymptomatic bacteriuria and duration of diabetes.
- No correlation between asymptomatic bacteriuria and glycemic control could be established.
- Asymptomatic bacteriuria was significantly associated with glycosuria in diabetic individuals.
- Asymptomatic bacteriuria was significantly associated with presence of more than 4 pus cells in urine in both diabetic and non-diabetic individuals.
- Escherichia coli was the most common cause of ABU in both diabetic and non-diabetic women in this study.
- Most of the isolated microorganisms in both diabetic and nondiabetic women were resistant to cotrimoxazole.
- All the isolated microorganisms in both the diabetic and nondiabetic groups were sensitive to norfloxacin.

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