

## OUTCOMES OF ASYMPTOMATIC BACTERIURIA IN PATIENTS WITH DIABETES MELLITUS IN A YEAR-LONG FOLLOW UP STUDY

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### ABSTRACT

#### BACKGROUND

Diabetes mellitus is a major public health problem worldwide today. It affects the genitourinary system. It predisposes patients to a variety of urinary tract infections and has long term effects on patient health. Asymptomatic bacteriuria (ASB) in diabetic patients, its effects on renal function, microalbuminuria, hypertension are not clearly defined. This study was carried out to determine the prevalence of asymptomatic bacteriuria, its clinical and microbiological outcomes in Indian diabetic patients.

#### METHODS

Two hundred and fifty type -2 diabetics (100 males and 150 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 examined and processed for the culture using the standard microbiological procedures. The spectrum of uropathogens causing asymptomatic bacteriuria was noted. Follow up after one year was done to evaluate clinical and microbiological outcomes.

#### RESULTS

Among the 250 diabetic patients, 43 (17.2%) had asymptomatic bacteriuria of which 31 (72.1%) were females and 12 (27.9%) were males. *Escherichia coli* (37.2%) was the most prevalent organism followed by *Klebsiella* (13.9%), *Enterococcus faecalis* (9.3%), *Pseudomonas aeruginosa* (6.9%), *Staphylococcus aureus* (6.9%), *Candida* species (6.9%), *Proteus* species (4.7%) and *Coagulase Negative Staphylococcus* (4.7%). On follow up it was found that incidence of symptomatic UTI in the study duration was 10 (23.26%) in the group with ASB and 39 (18.84%) in patients not having ASB at baseline. Prevalence of hypertension was also similar at the end of one year in both the groups. eGFR, prevalence of microalbuminuria and macroalbuminuria was also similar in both the groups at one year of follow up.

#### CONCLUSIONS

The overall prevalence of ASB in the diabetic patients was 17.2%. It was more common in females. Post-menopausal females have higher prevalence of ASB. *E. coli* was the most prevalent organism. Risk of symptomatic UTI appears to be comparable to general diabetic population. Hypertension, renal function and microalbuminuria do not appear to be affected by presence of ASB.

**HOW TO CITE THIS ARTICLE:** Singh A, Godara S, Jeswani JA. Outcomes of asymptomatic bacteriuria in patients with diabetes mellitus in a yearlong follow up study. *J. Evid. Based Med. Healthc.* 2019; 6(19), 1437-1442. DOI: 10.18410/jebmh/2019/293

#### BACKGROUND

Diabetes mellitus is a major public health problem worldwide. There is a rapid increase in the number of patients with Diabetes in India with more than 62 million diabetic individuals in India.<sup>1,2</sup> According to Wild et al. the prevalence of diabetes is going to increase two fold worldwide from 171 million in 2000 to 366 million in 2030,

*Financial or Other, Competing Interest: None.*  
*Submission 03-05-2019, Peer Review 05-05-2019,*  
*Acceptance 11-05-2019, Published 13-05-2019.*

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*DOI: 10.18410/jebmh/2019/293*



with India becoming the Diabetes capital of the world.<sup>3</sup> Diabetes mellitus has a range of effects on various organ systems including genitourinary system which predisposes patients with diabetes to a variety of urinary tract infections.<sup>4</sup> Diabetes is also considered to increase risk of having asymptomatic bacteriuria (ASB). Asymptomatic bacteriuria (ASB) is defined as having significant bacteriuria without symptoms attributable to urinary tract like burning micturition, frequent micturition, urinary incontinence, urgency, painful micturition, suprapubic pain, flank pain or fever.<sup>5</sup> The urinary tract is usually sterile. Urinary tract infections constitute a cause of significant morbidity and mortality in patients with diabetes mellitus.<sup>6</sup> There are various factors contributing to increased risk of UTI in diabetic patients like impairments in the immune system, poor metabolic control, and autonomic neuropathy leading to poor bladder functioning.<sup>7-12</sup> Another factor which contributes to increased morbidity in diabetic patients is more common progression of urinary tract infections to

involve upper urinary tract compared to general population.<sup>13</sup> Upper urinary tract infections in diabetes can present in a variety of pattern like pyelonephritis, emphysematous pyelonephritis, xanthogranulomatous pyelonephritis, renal abscess, perinephric abscess, and papillary necrosis.<sup>14,15</sup> Infections cause considerable morbidity and mortality in patients with diabetes mellitus and urinary tracts infections are among the most common infections seen in diabetes. Studies have reported varying prevalence of ASB in diabetic patients, with estimates ranging from 8%–26%.<sup>10</sup> ASB is more prevalent in women, due to a short urethra and shorter distance between rectum and vulva.<sup>6</sup> Effect of ASB on renal function, microalbuminuria, and its effect in causation of hypertension is not clearly defined.<sup>16</sup> There is little information available regarding natural history and outcome of ASB in diabetes in North western India. In an era where drug resistance is emerging as major global challenge it is important to define outcomes of ASB and better define need of antibiotics in their management.

## METHODS

Present follow up study on asymptomatic bacteriuria in type 2 diabetic patients was conducted in Mahatma Gandhi hospital Jaipur from March 2016 to February 2018. Patients for the study were recruited from Medicine and Endocrinology outpatient department of the hospital. Patients were recruited from April 2016 to December 2016. Patients aged more than 18 years with Type 2 Diabetes Mellitus (diagnosed by treating physician based on WHO definition of Diabetes Mellitus) were eligible to participate. They were included if they had two positive urine culture in females (more than  $10^5$  cfu/ml of urine in a midstream clean catch sample with the same organism within a duration of 2 weeks) or one positive culture in males (more than  $10^5$  cfu/ml of urine in a midstream clean catch sample), done as per definition and had no symptoms related to urinary tract.

## Exclusion Criteria

Patients having pregnancy or planning pregnancy, lower urinary tract anomalies, prior urogenital problems requiring instrumentation, surgery or per urethral/supra pubic catheterization, recent hospitalization (within last 90 days), using antimicrobial drugs like anti tuberculosis drugs or on immunosuppressant were excluded from the study.

## Data Collection

Detailed clinical history with emphasis on symptoms pertaining to Diabetes, microvascular and macrovascular complications of Diabetes Mellitus and lower urinary tract was taken, general and systemic physical examination and relevant laboratory work up (Haemoglobin, glycated haemoglobin levels, serum creatinine, urine complete examination, urinary microalbuminuria, urinary proteinuria and urine culture and sensitivity) was done.

Mid-stream urine sample was 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.

At one year of follow up again detailed clinical history and examination was done for all patients. Laboratory work up was done (Haemoglobin, glycated haemoglobin levels, serum creatinine, urine complete examination, urinary microalbuminuria, urinary proteinuria) for all the patients. Urine culture was done for patients having ASB at enrolment.

## Definitions

### 1. Asymptomatic Bacteriuria

- The definition of ASB in mid-stream clean catch urinary sample is growth of equal to or more than 100, 000 colony-forming units (CFU)/mL of urine without signs or symptoms attributable to urinary tract infection. In women, it is preferable to take two urinary samples within a period of 2 weeks.<sup>17</sup>

### 2. Diabetes Mellitus

- Criteria used for the diagnosis of diabetes as recommended by American Diabetes Association. Presence of any one of the following.
- Glycated haemoglobin level equal to or more than 6.5%(48 mmol/mmol).
- Fasting plasma glucose levels equal to or more than 126 mg/dl (7.0 mmol/l).
- 2-h plasma glucose levels equal to or more than 200 mg/dl (11.1 mmol/l) during an OGTT.
- In a patients having symptoms of hyperglycaemia, random plasma glucose equal to or more than 200 mg/dl (11.1 mmol/l).

### 3. Microalbuminuria

Microalbuminuria is defined as levels of albumin ranging from 30 to 300 mg in a 24-h urine collection. It can also be diagnosed on spot urine sample with excretion rate of albumin in the urine in the range of 30-299 mg/g creatinine.<sup>13</sup>

## RESULTS

A total of 275 patients of type 2 diabetes mellitus with female to male in ratio of 2: 1 were selected and screened, of these 250 patients completed one year follow up and provided sufficient information to be included in the study. Of the included patients, 150 were females and 100 were males. Out of the selected 250 patients 43(17.2%) were found to have asymptomatic bacteriuria at baseline. Among these 43 patients, 31 (72.1%) were females and 12 (27.9%) males. In the present study, prevalence of asymptomatic bacteriuria among female diabetic patients was 20.6% as opposed to 12% in males. Prevalence of ASB was 24.14% in post-menopausal females compared to 18.48% in pre-menopausal females. The age and gender distribution as well as baseline important characteristics of study population are shown in Table-1. Patients with or without ASB were

comparable in baseline characteristics including age, BMI, hypertension, renal function, complications of diabetes and control of diabetes as shown in Table 1.

Table-2 shows the microorganisms isolated from the urine specimens of the study population at baseline. Among the organisms isolated, Gram negative bacilli 31(72.1%) were the predominant organisms followed by Gram positive cocci 9 (20.9%) and Candida albicans 3(6.9%). E. coli was found to be the most prevalent isolate in diabetic patients with asymptomatic bacteriuria (37.2%) followed by Klebsiella pneumoniae (13.9%), Enterococcus faecalis (9.3%), Staphylococcus aureus (6.9%), and Candida species (6.9%).

On follow up it was found that incidence of symptomatic UTI in the study duration was comparable in both groups, 10(23.26%) in the group with ASB and 39(18.84%) in patients not having ASB. Prevalence of hypertension was also similar at the end of one year in both the groups. eGFR, prevalence of microalbuminuria and macroalbuminuria was also similar in both the groups at one year of follow up.

Out of 43 patients with ASB at beginning 15 patients received antibiotics for various reasons (10 for symptomatic UTI, 3 for upper respiratory tract infection and 2 for fever) within one year. Of these 15 patients 6(40%) patients were found to have persistent bacteriuria at one year follow up. Among 28 patients who were not exposed to antibiotics during the study period 19(67.8%) continued to have bacteriuria. Overall 25(58.14%) patients out of 43 patients had persistent ASB at the end of study period.

Variable	Total Patients N=250	Asymptomatic Bacteriuria N=43	Non Bacteriuric Patients N=207	p Value
Age (years)	54.6±9.4	56.3±6.9	53.7±11.2	0.34
M:F	1.5: 1	4.4: 1	1.25: 1	<0.01
Females	150 (60%)	31 (72.1%)	119 (57.48%)	<0.01
Pre-menopausal	92 (36.8%)	17 (39.5%)	75 (36.2%)	<0.01
Post-menopausal	58 (23.2%)	14 (32.6%)	44 (21.2%)	<0.01
Males	100 (40%)	12 (27.9%)	88 (42.5%)	<0.01
BMI (kg/m <sup>2</sup> )	24.6±2.6	23.9±3.2	25.4±1.9	0.23
Hypertension	96 (38.4%)	18 (41.86%)	78 (37.68%)	0.51
EGFR (ml/min./1.73 m <sup>2</sup> )	96.1±12.5	98.3±18.7	95.4±10.8	0.49
HbA1c	8.6±1.4	8.2±1.1	8.6±1.5	0.84
Autonomic Neuropathy	56 (22.4%)	11 (25.6%)	45 (21.7%)	0.62
Micro-	38	7	31	0.76

albuminuria	(15.2%)	(16.3%)	(14.9%)	
Macro-albuminuria	16 (6.4%)	3 (6.9%)	13 (6.3%)	0.57
Macrovascular complications	72 (28.8%)	11 (25.6%)	61 (29.5%)	0.95

**Table 1. Baseline Characteristics**

**Abbreviations:** BMI- Body Mass Index (Calculated as weight in kilograms divided by height in meters squared); DM,- Diabetes Mellitus; eGFR- Estimated Glomerular Filtration Rate; HbA1c- Glycated Haemoglobin; UTI- Urinary Tract Infection.

Organism	Prevalence
Escherichia coli	16 (37.2%)
Klebsiella pneumoniae	6 (13.9%)
Enterococcus sp.	4 (9.3%)
Pseudomonas aeruginosa	3 (6.9%)
Staph aureus	3 (6.9%)
Candida sp.	3 (6.9%)
Coagulase negative staphylococci	2 (4.7%)
Proteus sp.	2 (4.7%)
Other Gram-negative bacteria	4 (9.3%)

**Table 2. Urine Isolates Among Diabetic Patients with ASB**

**Abbreviations:** ASB- Asymptomatic Bacteriuria; Staph- Staphylococcus; sp- Species.

Outcome	Asymptomatic Bacteriuria N=43	Non Bacteriuric Patients N=207	p Value
Symptomatic UTI	10 (23.26%)	39 (18.84%)	0.07
Hypertension	16 (37.3%)	75 (36.2%)	0.39
eGFR (ml/minute/1.73m <sup>2</sup> )	94.7±13.2	96.5±11.6	0.42
HbA1c	8.4±1.2	8.2±1.4	0.57
Microalbuminuria	7 (16.28%)	30 (14.49%)	0.31
Macroalbuminuria	3 (6.98%)	14 (6.76%)	0.24

**Table 3. Outcomes at One Year of Follow up**

**Abbreviations:** eGFR- Estimated Glomerular Filtration Rate; HbA1c- Glycated Haemoglobin; UTI- Urinary Tract Infection.

Variable	Outcome
Persistent bacteriuria at 1 year (n=43)	25 (58.14%)
Persistent bacteriuria at 1 year, without antibiotic exposure (n=28)	19 (67.8%)
Persistent bacteriuria at 1 year, with antibiotic exposure (n=15)	6 (40%)
Symptomatic UTI	10 (23.25%)
<b>Table 4. Outcomes at One Year in Diabetic Patients with ASB at Enrolment</b>	
<b>Abbreviations: ASB-</b> Asymptomatic Bacteriuria.	

## DISCUSSION

Diabetic patients are predisposed to a variety of infections and urinary tract is one of the most commonly involved.<sup>18</sup> Asymptomatic bacteriuria is more commonly found in diabetic patients compared to general population.<sup>19</sup> In a meta-analysis done by Renko M et al showed that the prevalence of ASB was three times higher in patients with diabetes.<sup>13</sup> Urinary infections also hold special significance as they are more likely to get complicated in diabetic patients leading to significant morbidity.

In our study we found that ASB is more common in females as compared to males. Previously done studies also found similarly higher prevalence of ASB in females compared to males. A study done by Venkatesan et al, found a prevalence of ASB of 40% among females as opposed to 24% in males.<sup>20</sup> Similarly study done by Bissong M E A et al, showed a prevalence of ASB in 34% of females compared to 7% in males in their study group.<sup>21</sup>

Earlier studies have shown a prevalence of 8 to 26% in female diabetic patients. In this study prevalence of ASB was 17.2% in study group, 20.6% in female patients and 12% in male patients which is in agreement with results shown by earlier studies. Girish Babu et al. showed a prevalence of 12% in their study.<sup>22</sup> While a metaanalysis involving studies with total 3539 patients showed a prevalence of 12.2%.<sup>13</sup> Slightly higher prevalence was reported by Venkatesan et al, with ASB present in 32% of their study population.<sup>20</sup> Similarly Bissong et al., showed a prevalence of 38.3% in their study group.<sup>221</sup>

We also noted that among female patients ASB is more common in post-menopausal compared to pre-menopausal. Similar trend is also seen in general population as well as diabetic patients and is probably due to atrophic changes of the vaginal mucosa and urethra in the postmenopausal period and changes of the vaginal flora.<sup>23,24,25</sup> Epidemiologic studies have shown that 15% to 20% of 65-70 year-old women have bacteriuria, compared with 20% to 50% of women >80 years old. Inyang-Etoh et al., reported a prevalence of bacteriuria in 20% of post-menopausal patients which was significantly higher than in premenopausal females in whom bacteriuria was seen in only 14% of patients.<sup>26</sup>

Gram negative bacteria were the most common cause of ASB in this study group, E.coli being most common among them. This finding is in concordance with findings of earlier

studies which have shown E.coli as the most common cause of ASB or symptomatic UTI gram negative organisms in general population and diabetic population. 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. In a study Bharti A et al, showed Escherichia coli (E. coli) as the most common organism causing ASB.<sup>27</sup> Venkatesan et al. also observed that E. coli (37.5%) was the most prevalent organism isolated from urine cultures in their study. In contrast to these studies few have shown other organisms being more common. Bissong et al, in their study found Coagulase-negative staphylococci were the predominant organisms (36.3%) isolated.<sup>13</sup> Klebsiella pneumonia (seen in 42.4%) was the most common organism isolated in the study done by Alebiosu et al.<sup>28</sup> The other commonly isolated organisms included Klebsiella pneumoniae (13.9%), Enterococcus faecalis (9.3%), Staphylococcus aureus (6.9%), and Candida spp. (6.9%) which is in concordance with findings of various studies.

Incidence of symptomatic UTI was similar in both the groups at one year of follow up. Other studies have also shown equal incidence of symptomatic UTI in diabetic patients with or without ASB. A study involving follow up of 3 years of group of diabetic patients with ASB did not found any beneficial effects of antibiotic treatment.<sup>29</sup> Geerlings SE et al, followed up 636 diabetic patients for 18 months and found a higher incidence of symptomatic UTI in patients with type 2 diabetes mellitus and ASB compared to those without ASB at baseline.<sup>24</sup> Although study by Ribera M.C. et al had shown increased incidence of symptomatic UTI in diabetic patients with ASB (69.2%) compared to those not having ASB(9.8%).<sup>30</sup> Metanalysis done by Koves B et al found that for most people, treatment was not beneficial and may be harmful.<sup>31</sup>

We also found that presence of ASB does not affect renal function, rate of renal function decline, presence of microalbuminuria or hypertension. Microalbuminuria and renal dysfunction has not demonstrated any correlation with ASB in recent studies.<sup>32,33</sup> Study by Meiland R et al included 644 female patients with diabetes mellitus with ASB did not found an increased risk for development of hypertension or worsening of renal function at 6 years of follow up.<sup>16</sup> A population-based screening study in Sweden done by Bengtsson C et al enrolled women with ASB were treated for bacteriuria at time of initial diagnosis. At 2 years of follow-up after treatment of bacteriuria it recurred in 52%.<sup>34</sup> These women were further followed up and evaluated at 15<sup>35</sup> and 28<sup>36</sup> years follow-up, an increased frequency of bacteriuria was found in women with initial ASB, incidence of kidney disease and hypertension was not increased in patients with ASB at recruitment.

We found that most patients who had ASB at enrolment continued to have bacteriuria even at follow up of one year. Similarly follow up studies have also shown persistent bacteriuria in diabetic females initially detected to have ASB.<sup>35</sup> Study conducted by Nicolle, L.E. et al found the prevalence of bacteriuria to be 50% in diabetic female

patients at about 9 months of follow up and this persisted throughout their 3 years of follow-up.<sup>37</sup>

## CONCLUSIONS

Asymptomatic bacteriuria is common in diabetic patients and it is more common in females. Post-menopausal females have higher prevalence of ASB. Risk of symptomatic UTI appears to be comparable to general diabetic population. Gram negative organisms are most common causative organism of ASB, E.coli being most common. Hypertension, renal function and microalbuminuria do not appear to be affected by presence of ASB.

## REFERENCES

- [1] Joshi SR, Parikh RM. India--diabetes capital of the world: now heading towards hypertension. *J Assoc Physicians India* 2007;55:323-324.
- [2] Kumar A, Goel MK, Jain RB, et al. India towards diabetes control: key issues. *Australas Med J* 2013;6(10):524-531.
- [3] Wild S, Roglic G, Green A, et al. Global prevalence of diabetes--estimates for the year 2000 and projections for 2030. *Diabetes Care* 2004;27(5):1047-1053.
- [4] Ophori EA, Imade P, Johnny EJ. Asymptomatic bacteriuria in patients with type-2 diabetes mellitus. *Journal of Bacteriology Research* 2010;2(2):14-17.
- [5] Joshi N, Caputo GM, Weitekamp MR, et al. Infections in patients with diabetes mellitus. *N Engl J Med* 1999;341(25):1906-1912.
- [6] Nitzan O, Elias M, Chazan B, et al. Urinary tract infections in patients with type 2 diabetes mellitus: review of prevalence, diagnosis, and management. *Diabetes, Metab Syndr Obes* 2015;8:129-136.
- [7] Delamaire M, Maugendre D, Moreno M, et al. Impaired leucocyte functions in diabetic patients. *Diabet Med* 1997;14(1):29-34.
- [8] Valerius NH, Eff C, Hansen NE, et al. Neutrophil and lymphocyte function in patients with diabetes mellitus. *Acta Med Scand* 1982;211(6):463-467.
- [9] Geerlings SE, Stolk RP, Camps MJ, et al. Asymptomatic bacteriuria can be considered a diabetic complication in women with diabetes mellitus. *Adv Exp Med Biol* 2000;485:309-314.
- [10] Fünfstück R, Nicolle LE, Hanefeld M, et al. Urinary tract infection in patients with diabetes mellitus. *Clin Nephrol* 2012;77(1):40-48.
- [11] Truzzi JC, Almeida FM, Nunes EC, et al. Residual urinary volume and urinary tract infection--when are they linked? *J Urol* 2008;180(1):182-185.
- [12] Hosking DJ, Bennett T, Hampton JR. Diabetic autonomic neuropathy. *Diabetes* 1978;27(10):1043-1055.
- [13] Renko M, Tapanainen P, Tossavainen P, et al. Meta-analysis of the significance of asymptomatic bacteriuria in diabetes. *Diabetes Care* 2011;34(1):230-235.
- [14] Kofteridis DP, Papadimitraki E, Mantadakis E, et al. Effect of diabetes mellitus on the clinical and microbiological features of hospitalized elderly patients with acute pyelonephritis. *J Am Geriatr Soc* 2009;57(11):2125-2128.
- [15] Mnif MF, Kamoun M, Kacem FH, et al. Complicated urinary tract infections associated with diabetes mellitus: pathogenesis, diagnosis and management. *Indian J Endocrinol Metab* 2013;17(3):442-445.
- [16] Meiland R, Geerlings SE, Stolk RP, et al. Asymptomatic bacteriuria in women with diabetes mellitus: effect on renal function after 6 years of follow-up. *Arch Intern Med* 2006;166(20):2222-2227.
- [17] Nicolle LE, Bradley S, Colgan R, et al. Infectious Diseases Society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults. *Clin Infect Dis* 2005;40(5):643-654.
- [18] Patterson JE, Andriole VT. Bacterial urinary tract infections in diabetes. *Infect Dis Clin North Am* 1995;9(1):25-51.
- [19] Harding GK, Zhanel GG, Nicolle LE, et al. Antimicrobial treatment in diabetic women with asymptomatic bacteriuria. *N Engl J Med* 2003;348(10):957-958.
- [20] Venkatesan KD, Chander S, Loganathan K, et al. Study on asymptomatic bacteriuria in diabetic patients. *International Journal of Contemporary Medical Research* 2017;4(2):480-483.
- [21] Bissong ME, Fon PN, Tabe-Besong FO, et al. Asymptomatic bacteriuria in diabetes mellitus patients in Southwest Cameroon. *Afr Health Sci* 2013;13(3):661-666.
- [22] Girishbabu RJ, Prakash R, Prashanth HV, et al. Asymptomatic bacteriuria in patients with diabetes mellitus. *National Journal of Laboratory Medicine* 2013;2(2):11-13.
- [23] Geerlings SE, Stolk RP, Camps MJ, et al. Consequences of asymptomatic bacteriuria in women with diabetes mellitus. *Arch Intern Med* 2001;161(11):1421-1427.
- [24] Jackson SL, Boyko EJ, Scholes D, et al. Predictors of urinary tract infection after menopause: a prospective study. *Am J Med* 2004;117(12):903-911.
- [25] Kasyan G, Berketova TY, Rogozin AK, et al. Asymptomatic bacteriuria in postmenopausal women with diabetes mellitus. *Cent Eur J Urol* 2013;66(3):320-326.
- [26] Inyang-Etoh PC, Akpan AU, Usanga VU, et al. Asymptomatic bacteriuria amongst menopausal women in Calabar, Nigeria. *Asian Journal of Medical Sciences* 2018;9(4):51-56.
- [27] Bharti A, Chawla SPS, Kumar S, et al. Asymptomatic bacteriuria among the patients of type 2 diabetes mellitus. *J Family Med Prim Care* 2019;8(2):539-543.
- [28] Alebiosu CO, Osinupebi OA, Olajubu FA. Significant asymptomatic bacteriuria among Nigerian type 2 diabetics. *J Nat Med Assoc* 2003;95(5):344-349.
- [29] Harding GK, Zhanel GG, Nicolle LE, et al. Antimicrobial treatment in diabetic women with asymptomatic bacteriuria. *N Engl J Med* 2002;347(20):1576-1583.
- [30] Ribera MC, Pascual R, Orozco D. et al. Incidence and risk factors associated with urinary tract infection in diabetic patients with and without asymptomatic

- bacteriuria. *Eur J Clin Microbiol Infect Dis* 2006;25(6):389-393.
- [31] Köves B, Cai T, Veeratterapillay R, et al. Benefits and harms of treatment of asymptomatic bacteriuria: a systematic review and meta-analysis by the European association of urology urological infection guidelines panel. *Eur Urol* 2017;72(6):865-868.
- [32] Geerlings SE, Stolk RR, Camps MJ, et al. Asymptomatic bacteriuria may be considered a complication in women with diabetes. *Diabetes Mellitus Women Asymptomatic Bacteriuria Utrecht Study Group. Diabetes Care* 2000;23(6):744-749.
- [33] Bonadio M, Boldrini E, Forotti G, et al. Asymptomatic bacteriuria in women with diabetes: influence of metabolic control. *Clin Infect Dis* 2004;38(6):e41-e45.
- [34] Bengtsson C, Bengtsson U, Lincoln K. Bacteriuria in a population sample of women. Prevalence, characteristics, results of treatment, and prognosis. *Arch Med Scand* 1980;208(6):417-423.
- [35] Tencer J. Asymptomatic bacteriuria--a long term study. *Scand J Urol Nephrol* 1988;22(1):31-34.
- [36] Bengtsson C, Bengtsson U, Bjorkelund C, et al. Bacteriuria in a population sample of women: 24-year follow-up study. Results from the prospective population based study of women in Gothenburg, Sweden. *Scand J Urol Nephrol* 1998;32(4):284-289.
- [37] Nicolle LE, Zhanel GG, Harding GKM. Microbiological outcomes in women with diabetes and untreated asymptomatic bacteriuria. *World J Urol* 2006;24(1):61-65.