Asymptomatic Bacteriuria in Pregnant and Diabetic Women

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ABSTRACT

Background: Asymptomatic bacteriuria (ASB) is defined as isolation of a specified quantitative count of bacteria in an appropriately collected urine specimen from an individual without symptoms or signs of urinary tract infection.

Aim of study: To evaluate the frequency of bacteriuria according to age, pregnancy, and type II diabetes mellitus in a sample of Iraqi women.

Patients and Methods: A total of 125 female individuals were involved. The study participants were classified into the following groups: non-pregnant women with type II diabetes mellitus, pregnant women with type II diabetes mellitus, pregnant women without type II diabetes mellitus, and apparently healthy non-pregnant women. Urine and blood specimens were tested to record positive urine culture, pyuria, and blood glucose according to standard microbiological and biochemical methods.

Results: Frequency of positive urine culture and pyuria in the total pregnant women was 7 (14%) and 15 (30%), respectively, whereas frequency of positive urine culture and pyuria in the total diabetic women was 8 (16%) and 23 (46%), respectively. The bacterial isolation rate in the studied groups was 13 (10%). *E-coli* recorded the highest isolation rate, 6(5%). There was no significant culture positive of urine specimens in the groups of diabetic non-pregnant, diabetic pregnant, and women with normal pregnancy (***P*-value**< 0.05**).** Pregnant women with culture positive urine and pyuria were more likely to have perinatal mortality. Sterile pyuria was detected in pregnant women aged 18-45, those in third trimester, and in multiparous pregnant women. There was significant positive urine culture and a highly significant pyuria in diabetic women with BMI > 25.

Conclusions: Asymptomatic bacteriuria is an independent risk factor for perinatal mortality. Sterile pyuria is a significant observation in pregnant and diabetic women; therefore it should bring more attention.

Recommendations Treatment of asymptomatic bacteriuria is appropriate for pregnant women but it is not recommended for diabetics. The study advised to perform urine culture as a part of the antenatal check-up for pregnant women.

Key Words: Asymptomatic bacteriuria, Pregnancy, Type II Diabetes.

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Introduction:

Urinary Tract infection (UTI) refers to both colonization of the urine and tissue invasion of any structure of the urinary tract [1]. Asymptomatic bacteriuria (ASB), in which urine culture reveals a significant growth of the pathogens, that is greater than 10^5 bacteria/ml, but without the patient showing symptom of UTI [2]. Bacteriuria occurs in two to seven percent of pregnancies particularly in multiparous women, a similar prevalence as in non-pregnant women. The organisms are also similar in species and virulence factor in pregnant and non-pregnant women. Thus the basic mechanism of entry of bacteria into urinary tract is likely to be the same for both groups [3]. Bacteriuria during pregnancy has a greater propensity to progress to pyelonephritis (up to 40 percent) than in non pregnant women [4]. Bacteriuria is also associated with an increased risk of preterm birth, low birth weight and perinatal mortality [5]. Treatment of Bacteriuria during pregnancy reduces the incidence of these complications [6], and lowers the long-term risk of sequelae following a symptomatic bacteriuria [7]. The Infectious Diseases Society of America (IDSA) guidelines for the diagnosis and treatment of a symptomatic bacteriuria in adults recommend screening and treatment for a positive culture in pregnancy [8].

Diabetes mellitus is a well recognized risk factor for occurrence of urinary tract infections [9]. Concern about a symptomatic bacteriuria in diabetic patients derives in part from three observations: there is a roughly five-fold greater propensity toward UTI in diabetic women [10]. A symptomatic Bacteriuria often precedes symptomatic UTI in type 2 diabetes, relative risk [RR] 1.65, 95% confidence interval [CI] 1.02 – 2.67 [11]. It was suggested that treatment of a symptomatic bacteriuria in diabetic women is not required. This recommendation was based upon multiple studies which have shown that antibiotic therapy is associated with no reduction in symptomatic infection and a high rate of recurrent bacteriuria once antibiotics are discontinued. In addition, persistent asymptomatic bacteriuria is not

associated with an adverse effect on rental function [12].

Data regarding association between bacteriuria and pregnancy and/or diabetes mellitus from Iraq are scarce, although substantial studies have been carried out for UTI investigation. This study was designed to determine the incidence of a symptomatic bacteriuria during pregnancy and diabetes mellitus in a population sample of Iraqi women in Baghdad city.

Methods:

The study participants were classified into the following groups:

1- Non-pregnant women with type II diabetes mellitus (n= 25)
2- Pregnant women with type II diabetes mellitus (n=25)
3- Pregnant women without type II diabetes mellitus (n=25).
4- Apparently healthy non-pregnant women aged 18-45 year (n=25).
5- Apparently healthy non-pregnant young women aged < 18 year (n=25)

All pregnant women consulting for their first antenatal check-up, who were willing to participate, were included in the study. Diabetes mellitus type II was defined by criteria of the American diabetes association and World Health Organization.

Exclusion criteria: Patients with currently symptomatic UTI, kidney transplantation, spinal cord injuries, urologic surgery, carcinoma, and those currently under antimicrobial therapy schedule were excluded.

A questionnaire form was designed including pregnancy trimester, age in years, parity, complications, body mass index (BMI), hospitalization, previous UTI, and current or recent antimicrobial therapy, either for pregnant or diabetic groups.

Location of study: This case-control study was carried out at the following locations during the period from June 2009 until October 2009:

1- National Diabetes Center, College of Medicine, Al-Mustansiriyah University.
2- Dept. of Gynecology in Al-Yarmook Teaching Hospital.

One hundred and twenty five clean-catch midstream (CCMS) urine specimens were aseptically collected from study females. In addition, fifty blood specimens were obtained from diabetic women to verify their disease status using conventional glucose testing. Urine specimens were tested to record positive urine culture, pyuria, according to standard microbiological methods[13]. Blood specimens were tested to record glucose elevation according to standard biochemical tests[14].

Statistical analysis was attempted to record any significant correlation among bacteriuria and some independent variables such as pregnancy and diabetes. Fisher's test is the best choice as it always gives the exact *P* value, while the chi-square test only calculates an approximate *P* value[15]. For all analysis, statistical significance was considered at highly significant level *P*-value of <0.01, significant level *P*-value of <0.05 and insignificant level *P*-value >0.05. All statistical analysis was done by using SPSS computer program version 16 and Excel application.

Results:

It was clearly demonstrated that frequency of positive urine culture and pyuria in the total pregnant women were 7 (14%) and 18 (36%), respectively. On the other hand, apparently healthy non-pregnant women recorded 3 (6%) positive urine culture and 7 (14%) pyuria.

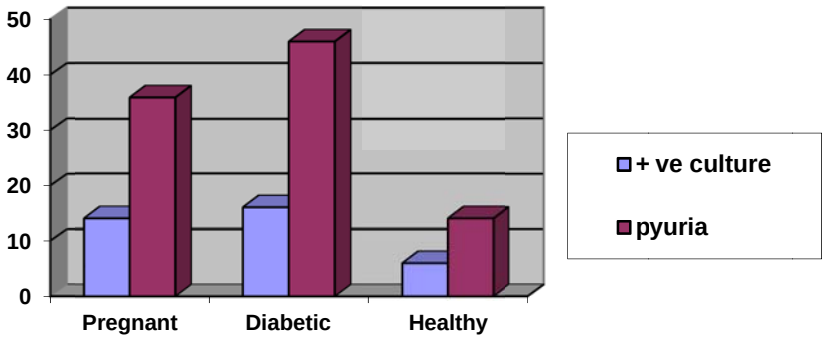

Fig.1 Positive culture of urine and pyuria in pregnant and diabetic women compared with healthy controls

Table (1) Frequency of asymptomatic bacteriuria in pregnant women (n=50) compared with non pregnant women (n=50)

Characteristic	Total number	Positive urine culture (%)	Pyuria (%)
1. Age in years			
• < 18 year	-	-	-
• 18-45 years	50	7(14%)	18 (36%)
• > 45 year	-	-	-
2. Pregnancy trimester			
• First trimester	14	2(4%)	5 (10%)
• Second trimester	14	2(4%)	6(12%)
• Third trimester	22	3(6%)	7(14%)
3. Parity			
• Uniparous	15	2 (4%)	3 (6%)
• Multiparous	35	5 (10%)	15(30%)
4. Complication during pregnancy			
• Preterm birth	-	-	-
• Low birth weight	-	-	-
• Perinatal mortality	3	2(4%)	2(4%)
• Abortion	13	3(6%)	6(12%)
• Hypertension	7	-	3(6%)
5. Previous UTI	12	1(2%)	2(4%)
Total pregnant women	50	7 (14%)	15 (30%)
Healthy non-pregnant women	50	3 (6%)	7 (14%)

Frequency of positive urine culture and pyuria in the total diabetic women were 8 (16%) and 23 (46%), respectively. Age group of 18-45 years recorded the highest positive urine culture and pyuria, 6 (12%) and 17 (34%), respectively, whereas age group of < 18 year did not record any positive results. The positive urine culture and pyuria were the highest in overweighed individuals (BMI > 25), 5 (10%) and 13 (26%), respectively. Patients with complicated diabetes recorded 1 (2%) and 2 (4%) positive urine culture and pyuria, respectively, whereas those with drug controlled D.M were 8 (16%) and 23 (46%), respectively as shown in Table (2).

Table (2) Frequency of asymptomatic bacteriuria in diabetic women (n=50) compared with healthy control women (n=50)

Characteristic	Total number	Positive urine culture (%)	Pyuria (%)
1. Age in years			
• < 18 year	-	-	-
• 18-45 years	32	6(12%)	17(34%)
• > 45 year	18	2(4%)	6(12%)
2. Body Mass Index			
• <20	12	1(2%)	4 (8%)
• 20-25	12	2(4%)	6(12%)
• > 25	18	5(10%)	13(26%)
3. Complicated diabetes	6	1(2%)	2(4%)
4. Drug controlled D.M	50	8(16%)	23(46%)
5. Hypertension	23	2(4%)	15(30%)
6. Kidney damage	2	-	2(4%)
7. Previous UTI	3	2(4%)	3(6%)
Total diabetic women	50	8 (16%)	23 (46%)
Healthy controls (non- diabetic) women	50	3 (6%)	7 (14%)

Frequency of microorganisms detected in urine specimens obtained from study group is shown in Table (3). The bacterial isolation rate in the studied groups was 13 (10%). It was clearly demonstrated that *E-coli* recorded the highest isolation rate in the studied groups, 6(5%), followed by Klebsiella spp. 3(2%) and *S. aureus*, 2(2%). The highest isolation rate of bacterial isolates was recorded in the group of pregnant women with diabetes mellitus, 5(20%). *Candida albicans* isolates were 3 (12%) recorded only in pregnant women with D.M.

Table (3) Frequency of microorganisms detected in urine specimens obtained from study group

Microorganism	G^1 % n=25	G^2 % n=25	G^3 % n=25	G^4 % n=50	Total n=125
E-coli	3(12%)	1(4%)	1(4%)	1 (4%)	6(5%)
Klebsiella spp.	-	2(8%)	-	1 (2%)	3(2%)
Proteus spp.	-	1(4%)	-	-	1(1%)
Coagulase –ve Staph	-	1(4%)	-	-	1(1%)
S. aureus	-	-	1(4%)	1 (2%)	2(2%)
Total	3(12%)	5(20%)	2(8%)	3 (6%)	13(10%)
Candida albicans	-	3(12%)	-	-	3 (2%)

G^1: Non pregnant with diabetes G^2: Pregnant with diabetes, G^3:Normal pregnancy, G^4: Healthy non – pregnant

Statistical evaluation of culture positive and pyuria in urine obtained from studied groups is shown in Table (4). It was clearly demonstrated that there was no significant culture positive of urine specimens in the groups of diabetic non-pregnant, diabetic pregnant, and women with normal pregnancy (***P*-value**< 0.05**).** However, highly significant pyuria was observed in the group of diabetic pregnant woman (***P*-value** > 0.001**).**

Table (4) Statistical evaluation of culture positive and pyuria in urine obtained from studied groups

Studied groups	Culture positive				Pyuria			
	OR	95% CI	*P*-value	X^2	OR	95% CI	*P*-value	X^2
Non-pregnant with D.M	2.136	0.39-11.4	< 0.05	0.393	2.89	0.90-9.21	< 0.05	7.594
Pregnant with D.M	3.916	0.8-17	< 0.05	2.116	9.21	2.9-28.5	> 0.001	13.898
Normal pregnant	1.362	0.2- 8.7	< 0.05	0.027	0.83	0.19- 3.5	< 0.05	0.020

OR: Odd Ratio, CI: Confidence Interval, X^2: Chi square value

Risk factors for asymptomatic bacteriuria in pregnant non-diabetic women are presented in Table (5). It was clearly demonstrated that pregnant women with culture positive urine and pyuria were more likely to have perinatal mortality (RR= 11.11, 95 % CI =2.85-43.20). In addition, aborted and hypertensive pregnant women were detected with a significant pyuria (RR=3.29, 95% CI= 1.33-8.31 and RR=3.06, 95%CI=1.02-9.17, respectively). Sterile pyuria was detected in pregnant women aged 18-45 (RR=2.57, 95 % CI =1.17-5.61), those in third trimester (RR=5.30, 95 % CI =1.51-18.62), and in multiparous pregnant women (RR= 3.06, 95 % CI=1.39-6.72).

Table (5) Risk factors for asymptomatic bacteriuria in pregnant non-diabetic women

Characteristic	Culture positive			Pyuria		
	RR	95% CI	*P*-value	RR	95% CI	*P*-value
1. Age in year						
• <18 year	-	-	-	-	-	-
• 18-45 year	2.3	0.63-8.51	0.31	2.57	1.17-5.61	0.019
• > 45 year	-	-	-	-	-	-
2.Pregnancy trimester						
• First trimester	2.38	0.44-12.88	0.299	2.55	0.95-6.81	0.114
• Second trimester	2.38	0.44-12.88	0.299	2.55	0.95-6.81	0.114
• Third trimester	2.27	0.49-10.38	0.361	5.30	1.51-18.62	0.007
3. Parity						
• Uniparous	2.22	0.40-12.08	0.32	1.42	0.42-4.85	0.68
• Multiparous	2.38	0.60-9.31	0.26	3.06	1.39-6.72	0.005
4. Complication						
• Preterm birth	-	-	-	-	-	-
• Low birth weight	-	-	-	-	-	-
• Perinatal mortality	11.11	2.85-43.20	0.02	11.11	2.85-43.20	0.02
• Abortion	3.84	0.87-16.88	0.09	3.29	1.33-8.31	0.019
• Hypertension	-	-	-	3.06	1.02-9.17	0.09

Risk factors for asymptomatic bacteriuria in diabetic non- pregnant women were presented in Table (6). It was shown that there was a highly significant pyuria in diabetic women aged 18 – 45 year, (RR=8.85, 95 % CI=2.81-27.80). In addition, there was a significant pyuria in overweighed women with 20-25 BMI, (RR=3.57, 95 % CI=1.46-8.69). There was significant positive urine culture and a highly significant pyuria in obese women with BMI > 25, (RR=4.62, 95 % CI=1.22-17.43) and (RR=5.15, 95 % CI of RR=2.45-10.85), respectively. Hypertensive diabetic patients were more likely to have pyuria in their urine specimens, (RR=4.65, 95% CI=2.20-9.85).

Table (6) Risk factors for asymptomatic bacteriuria in diabetic non- pregnant women

Characteristic	Culture positive			Pyuria		
	RR	95% CI	*P*-value	RR	95% CI	*P*-value
1- Age in years						
• < 18 year	-	-	-	-	-	-
• 18 – 45 year	3.12	0.84-11.61	0.14	8.85	2.81-27.80	0.0003
• > 45 year	1.85	0.33-10.19	0.60	2.38	0.92-6.14	0.08
2. Body Mass Index						
• < 20	1.38	0.15-12.20	1.00	2.38	0.82-6.83	0.199
• 20 – 25	2.77	0.52-14.82	0.24	3.57	1.46-8.69	0.01
• > 25	4.62	1.22-17.43	0.02	5.15	2.45-10.85	0.0001
3. Complicated D.M	2.77	0.34-22.65	0.37	2.38	0.63-8.94	0.24
4. Drug controlled D.M	12.12	3.81-38.48	0.19	3.28	1.55-6.95	0.0009
5. Hypertensive D.M	1.44	0.29-8.09	0.64	4.65	2.20-9.85	0.0001
6. Kidney damage	-	-	-	-	-	-

Discussion:

Frequency of bacteriuria in the pregnant study group

Our study demonstrated that the frequency of positive urine culture and pyuria in the total pregnant women were 7 (14%) and 18 (36%), respectively. On the other hand, apparently healthy non-pregnant women recorded 3 (6%) positive urine culture and 7 (14%) pyuria. Multiple studies showed that the prevalence of asymptomatic bacteriuria among healthy women increases with advancing age, from about 1 percent among schoolgirls to >20 percent among women over 80 years residing in the community. Pregnant and non-pregnant women have a similar prevalence (2 to 7 percent)[16]. A Turkish study revealed that the prevalence of ASB (n = 43) and symptomatic UTI (n = 19) were 10.6% and 4.7%, respectively[17]. A study dealt with asymptomatic bacteriuria among pregnant women in Shiraz, Iran recorded a prevalence of asymptomatic bacteriuria 5.1%, which was well within the reported range from the literature [18]. The result of our study differentiated between positive urine culture and pyuria. Some participants in our study showed what is called sterile pyuria, it is the presence of elevated numbers of white blood cells (>10/cubic mm) in a urine which appears sterile using standard culture techniques. Often found in female patients with symptoms of urinary tract infection and presence of pyuria but no bacterial growth can be cultured. However, these results may be misleading for various reasons:

- Standard laboratory culture conditions may not be optimal for growth of atypical organisms.
- Laboratory may not report significant growth either because it was not a single organism or recognized urinary pathogen.
- Less than 100,000 colony-forming units (cfu) per ml reported, e.g. may be urine was diluted by high fluid intake or organism may be slow growing. Studies have shown that approximately half of women presenting with symptoms and counts of 100-10,000 cfu/ml have genuine bladder infections.

Presence of pyuria increases significance of a low bacterial count. Cell count per high power field is inaccurate and use of counting chamber or similar gives more accurate results with 10 white cells/mm3 being diagnostic of infection[19].

Frequency of bacteriuria in diabetic study group

The result of this study demonstrated that the frequency of positive urine culture and pyuria in the total diabetic women were 8 (16%) and23 (46%), respectively. Apparently healthy women recorded 3 (6%) positive urine culture and 7 (14%) pyuria. Concern about asymptomatic bacteriuria in diabetic patients derives in part from three observations: There is a roughly five-fold greater propensity toward UTI in diabetic women [11]. Asymptomatic bacteriuria often precedes symptomatic UTI in type 2 diabetes (relative risk [RR] 1.65, 95 percent confidence interval [CI] 1.02-2.67). UTIs are likely to be more severe in diabetic than non-diabetic women [12]. The best estimate is an approximately three to fourfold increase in risk of bacteriuria in diabetic women (eg, 18 versus 6 percent, 26 versus 6 percent). Prevalence among diabetic women is 8 to 14 percent and is usually correlated with duration and presence of long term complications of diabetes, rather than with metabolic parameters of diabetes control [20]. It was shown from a previous study that the prevalence of ASB is increased in women with diabetes and might be added to the list of diabetic complication in those women[21]. On the other hand, it was previously demonstrated that treatment of asymptomatic bacteriuria in women with diabetes does not appear to reduce complications. Diabetes itself should not be an indication for screening or treatment of asymptomatic bacteriuria[22]. Another previous study showed a high prevalence of asymptomatic bacteriuria among diabetic women[23].

Bacterial isolates

The bacterial isolation rate in female groups of our study was 13 (10%), *E-coli* recorded the highest isolation rate, 6(5%), followed by Klebsiella spp. 3(2%) and *S. aureus*, 2(2%). This observation is in accordance with many studies. In a prospective study of the general obstetric population, it was demonstrated that *E. coli* accounted for approximately 70 percent of cases[24]. Other organisms responsible for infection included Klebsiella or Enterobacter (3 percent), Proteus (2 percent), and gram-positive organisms, including group B Streptococcus (10 percent). One of the previous studies revealed that the most common bacterium isolated was *Escherichia coli* (12; 40%); the others included group B Streptococcus (5; 15%), Klebsiella spp (5; 15%), Diphtheroids (2), and *Candida albicans* (2) [25].

Statistical evaluation of bacteriuria in studied groups

The present study demonstrated that there was no significant culture positive of urine specimens in the groups of diabetic non-pregnant, diabetic pregnant, and women with normal pregnancy (***P*-value**< 0.05**).** However, highly significant pyuria was observed in the group of diabetic pregnant woman (***P*-value** > 0.001**).** Other previously conducted studies revealed a higher rate of bacteriuria, either in pregnant or diabetic women. Bacteriuria during pregnancy has a greater propensity to progress to pyelonephritis (up to 40 percent) than in non pregnant women [5].

Risk factors of bacteriuria in pregnant group

This study showed that pregnant women with culture positive urine and pyuria were more likely to have perinatal mortality (RR= 11.11, 95 % CI =2.85-43.20). In addition, aborted and hypertensive pregnant women were detected with a significant pyuria (RR=3.29, 95% CI= 1.33-8.31 and RR=3.06, 95%CI=1.02-9.17, respectively). Other studies revealed approximately the same that bacteriuria is associated with an increased risk of preterm birth, low birth weight, and perinatal mortality[26]. A major study comparing normal and high-risk pregnant women reported 6.0% prevalence in healthy women; 12.2% rate in diabetic women and 18.7% in women with a previous history of urinary tract infection[27].

Risk factors of bacteriuria in diabetic group

Our study revealed that there was a highly significant pyuria in diabetic women aged 18 – 45 year, a significant pyuria in overweighed women, a significant positive urine culture and a highly significant pyuria in obese women. A prospective cohort study of 218 diabetic and 799 non-diabetic postmenopausal women examined risk factors for asymptomatic bacteriuria and UTI. Increased risk occurred mainly in women taking insulin (relative risk 3.7) and those with a longer diabetes duration (>10 years, relative risk 2.6) but not to glucose control[28]. A large cohort of diabetic women in the Netherlands was studied to determine the incidence of symptomatic UTIs. In women with type 2 diabetes (but not with type 1), the presence of asymptomatic bacteriuria at baseline increased the risk of subsequent symptomatic UTI in the 18 month follow-up period from 19 to 34 percent. The rate of asymptomatic bacteriuria in this population was approximately 28 percent. By contrast, incidence of asymptomatic UTI was 6 percent in women who were not diabetic but attended other clinics in the same institution. Even in this cohort of diabetic women, there were more symptomatic UTIs in the women who had negative baseline urine cultures than in those with positive ones. Thus, screening for later UTI risk would not be very cost effective even in this high-risk population[29].

Conclusions:

- There was no significant culture positive of urine specimens in the groups of diabetic non-pregnant, diabetic pregnant, and women with normal pregnancy (***P*-value**< 0.05**).**
- Highly significant pyuria was observed in the group of diabetic pregnant woman (***P*-value** > 0.001**).**
- Asymptomatic bacteriuria is an independent risk factor for perinatal mortality. Sterile pyuria is a significant observation in pregnant and diabetic women; therefore it should bring more attention.

Recommendations

- Treatment of asymptomatic bacteriuria is appropriate for pregnant women but it is not recommended for diabetics.
- The study advised to perform urine culture as a part of the pre-natal check-up for pregnant women.

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