ORIGINAL RESEARCH ARTICLE

Prevalence of asymptomatic bacteriuria among Thai diabetic pregnant women

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Abstract

Diabetic pregnant women are susceptible to urinary tract infection, which can result in preterm labor and a low birth weight of the neonate. This was a prospective observational study. In total, 110 diabetic pregnant women between 12–20 weeks of gestation were recruited. Asymptomatic bacteriuria (ASB) was diagnosed when the urinalysis presented a white blood cell (WBC) count ≥ 5 WBCs per high power field (HPF). Urine culture was later performed. Most of the diabetic pregnant women were classified as GDM A1. The prevalence of ASB was 7.2% (8/110 cases). *Klebsiella aerogenes* was found in only one case from urine culture. ASB was commonly found in the pregnant women with a high BMI, with statistical significance. The prevalence of ASB in the diabetic pregnant women was 7.2%. Urinalysis should be considered for diabetic pregnant women with a high body mass index. *(Afr J Reprod Health 2021; 25[5]: 133-139).*

Keywords: Asymptomatic bacteriuria, diabetic, pregnant women

Résumé

Les femmes enceintes diabétiques sont sensibles aux infections des voies urinaires, ce qui peut entraîner un travail prématuré et un faible poids à la naissance du nouveau-né. Il s'agissait d'une étude observationnelle prospective. Au total, 110 femmes enceintes diabétiques entre 12 et 20 semaines de gestation ont été recrutées. Une bactériurie asymptomatique (ASB) a été diagnostiquée lorsque l'analyse d'urine a présenté un nombre de globules blancs (WBC) ≥ 5 WBC par champ à fort grossissement (HPF). Une culture d'urine a ensuite été réalisée. La plupart des femmes enceintes diabétiques ont été classées comme DG A1. La prévalence de l'ASB était de 7,2 % (8/110 cas). Klebsiella aerogenes a été trouvée dans un seul cas à partir d'une culture d'urine. L'ASB a été fréquemment trouvé chez les femmes enceintes avec un IMC élevé, avec une signification statistique. La prévalence de l'ASB chez les femmes enceintes diabétiques était de 7,2 %. L'analyse d'urine doit être envisagée pour les femmes enceintes diabétiques ayant un indice de masse corporelle élevé. *(Afr J Reprod Health 2021; 25[5]: 133-139).*

Mots-clés: Bactériurie asymptomatique, diabétique, femmes enceintes

Introduction

Asymptomatic bacteriuria (ASB) can be found in about 2–7% of pregnant women. The prevalence is highest in the first trimester and decreases in the second and third trimesters of pregnancy[1]. A recent study from Taiwan reported that the prevalence of ASB during the first trimester was 21.3% and was related to complications during pregnancy[2]. Relevant factors for ASB during pregnancy include a previous history of urinary tract infections, diabetes mellitus, and multiple pregnancy. ASB during pregnancy can cause symptomatic acute pyelonephritis, preterm labor, hypertensive disorder in mothers postpartum, anemia, and a low birth weight of the fetus[3-5].

Diabetic pregnant woman are susceptible to urinary tract infection. A previous study from Siriraj Hospital reported that the prevalence of ASB in pregnant women without diabetes was 2.3%, without a significant difference between the first, second, and third trimesters[6]. That study concluded

that it was not worth performing urinalysis for all pregnant women. However, the prevalence of ASB in pregnant patients with diabetes is reported to be higher than in women without diabetes mellitus[7]. Urinary tract is the common infection site of diabetic pregnant women due to the increased urine glucose excretion[8]. Urinary tract infection during pregnancy relates to maternal and neonatal complications[9]. Diabetic pregnant women with ASB may have an increased risk of preterm labor, hypertensive disorder, anemia, and other adverse pregnancy outcomes[3-5]. Consequently, there is a question about whether urinalysis should be performed for diabetic pregnant women as part of routine screening or not.

Since Siriraj Hospital does not currently do routine urinalysis for diabetic pregnant women at its antenatal clinic, the researchers wanted to study the prevalence of ASB in diabetic pregnant women to collect baseline information at the Department of Obstetrics and Gynecology, Siriraj Hospital, with an aim to improve the prenatal care of diabetic pregnant women.

Methods

This was a prospective observational study that was approved by the Ethics Committee of the Siriraj Institutional Review Board, Si252/2019. The Thai Clinical Trials Registry number was TCTR20190503003. During the study period of November 2019–July 2020, 110 diabetic pregnant women attended the Antenatal Clinic, Faculty of Medicine, Siriraj Hospital, Mahidol University, and were recruited to take part in the study. The sample size of diabetic pregnant women needed was based on an expected 95% sensitivity of the study tool and a 0.03% prevalence of ASB in diabetic pregnant women reported in a previous study[10]. As stated before, in total, 110 diabetic pregnant women (with an allowance for a 10% loss) were recruited.

The inclusion criteria were: pregnant patients ≥ 18 years old, with a gestational age between 12–20 weeks of gestation, and without any symptom of urinary tract infection. All the participants gave their written informed consent before the study began. The patients who had received antibiotic therapy one month prior to antenatal care, had prior sexual intercourse 1-2 days before urinalysis and had abnormal vaginal discharge were excluded from the study. The process for the diagnosis of diabetes mellitus during pregnancy is described as following. If the 50 grams–1 hour screening test for gestational diabetes was positive (≥ 140 mg/dl), 100 grams oral glucose tolerance test (OGTT) for the diagnosis of gestational diabetes were performed. The patients who were diagnosed with gestational diabetes mellitus (GDM) classified as GDM A1, GDM A2, and overt DM were included in the study. Patients with GDM A1 were diagnosed when 2/4 numbers in their OGTT were abnormal. GDM A2 was diagnosed when the patient was treated with insulin. Overt DM was diagnosed when the disease was diagnosed before getting pregnant or when the blood sugar result in the 50 grams–1 hour test was ≥200 mg/dL.

Demographic data, including baseline characteristic data, family history, obstetrics history, and underlying disease, were obtained from all the recruited patients. Urinalysis was performed under the guidance of how to collect clean voided-midstream urine. Urine analysis is done by technician of the central laboratory at Mahidol University, Siriraj Hospital. The machine was set by Sysmex Corporation (HQ: Kobe, Japan; President and CEO: Hisashi Ietsugu) and Roche (SIX: RO, ROG; OTCQX: RHHBY). ASB was diagnosed when the urinalysis results presented a white blood cell (WBC) count ≥ 5 WBCs per high power field. Urine culture was performed in the ASB diabetic pregnant women. Amoxycillin (500 mg) 3 times/day × 5 days or nitrofurantoin (100 mg) 2 times/day × 5 days (in penicillin-resistant women) was given to the pregnant women with ASB. The patients were informed of their urine culture result one week later.

Statistical analysis

Demographic data were summarized using descriptive statistics. Continuous data are presented as the mean ± standard deviation, and categorical data are presented as the number and percentage. The Mann–Whitney U test was used to analyze the continuous data. The chi-square test was used to compare the categorical data. A p-value less than 0.05 was considered statistically significant. All the statistical analysis was performed using PASW Statistics (SPSS) 18.0 (SPSS Inc., Chicago, IL, USA).

Table 1: Demographic data, baseline laboratory blood test results and underlying diseases of the diabetic pregnant women included in the study

Demographic data	**Negative (n = 102/110)**	**Positive (n = 8/110)**	**p-value#**
Age (years)	33.4 ± 5.1	35.6 ± 5.1	0.219
Weight (kilograms)	68.8 ± 15.3	83.2 ± 11.4	0.006*
Height (centimeters)	158.8 ± 6.2	160.1 ± 6.9	0.608
Body mass index (kilogram/meter^2)	27.2 ± 5.8	32.7 ± 5.7	0.015*
Occupation			0.748
Housewife	24 (23.5%)	1 (12.5%)	
Laborer	54 (53.0%)	4 (50.0%)	
Merchant	11 (10.8%)	2 (25.0%)	
Government	6 (5.9%)	1 (12.5%)	
State enterprise employees	3 (2.9%)	0 (0.0%)	
Personal business	4 (3.9%)	0 (0.0%)	
Income (Thai Baht)			0.570
5,000−10,000	10 (9.8%)	0 (0.0%)	
>10,000−20,000	42 (41.2%)	3 (37.5%)	
>20,000−50,000	42 (41.2%)	5 (62.5%)	
>50,000	8 (7.8%)	0 (0.0%)	
Gravida (G)			0.724
1	29 (28.4%)	2 (25.0%)	
2	36 (35.3%)	4 (50.0%)	
3	26 (25.5%)	2 (25.0%)	
4	11 (10.8%)	0 (0.0%)	
Parity (P)			1.000
0	48 (47.1%)	4 (50.0%)	
1	36 (35.3%)	3 (37.5%)	
2	18 (17.6%)	1 (12.5%)	
Abortion (A)			0.899
0	64 (62.7%)	5 (62.5%)	
1	30 (29.4%)	3 (37.5%)	
2	7 (6.9%)	0 (0.0%)	
3	1 (1.0%)	0 (0.0%)	
Gestational age (GA) (weeks)	17.5 ± 6.3	17.6 ± 7.6	0.899
*VDRL	110	0 (0.0%)	1.000
**Anti-HIV	110	0 (0.0%)	1.000
Hepatitis B carriers	2 (2.0%)	0 (0.0%)	1.000
Hematocrit	37.2 ± 3.9	38.4 ± 4.4	0.454
Thalassemia			0.709
No	58 (56.9%)	6 (75.0%)	
Hemoglobin E trait	23 (22.5%)	2 (25.0%)	
Alpha thalassemia 1 trait	9 (8.8%)	0 (0.0%)	
Hemoglobin E Homozygote	6 (5.9%)	0 (0.0%)	
Others (***Alpha thal 2 trait, Beta thal trait, Hb H disease, Hb CS trait)	6 (5.9%)	0 (0.0%)	
Type of gestational diabetes (GDM)			0.555
GDM A1	69 (67.6%)	4 (50.0%)	
GDM A2	12 (11.8%)	2 (25.0%)	
Overt DM	21 (20.6%)	2 (25.0%)	
Underlying disease			0.676
No	89 (87.3%)	7 (87.5%)	
Heart disease	4 (3.9%)	0 (0.0%)	

Chronic hypertension	4 (3.9%)	1 (12.5%)
Others (gestational hypertension, systemic lupus erythrematosus, idiopathic thrombocytopenic purpura , thyroid disease, depression)	5 (4.9%)	0 (0.0%)

[#]Mann–Whitney U test for continuous data, Fisher's exact or chi-square test for categorical data
*VDRL: venereal disease research laboratory test
**Anti-HIV: human immunodeficiency virus
***Alpha thal: Alpha thalassemia, Beta thal: Beta thalassemia, Hb H: Hemoglobin H, Hb CS: Hemoglobin constant spring

Results

Almost all the demographic data along with the laboratory blood test results and underlying diseases were not different between both groups of positive and negative ASB diabetic pregnant women, except for their weight and body mass index (BMI) (Table 1). ASB was commonly found in the pregnant women with a high BMI, with statistical significance (Table 1). Most of the diabetic pregnant women were GDM A1 (66.4%; 73/110 cases). The prevalence of ASB (WBC count $\geq$ 5 cells/HPF from urinalysis) was 7.2% (8/110 cases) (Table 2). The pathogen *Klebsiella aerogenes* was found in only one case from urine culture (Table 2). Details of the diabetic pregnant women with a positive ASB result are presented in Table 3. The positive urine culture of *Klebsiella aerogenes* was found in pregnant women with GDM A1 and a WBC count $\geq$ 5–10 cells/HPF from the urinalysis (Table 3).

Table 2: Type of diabetes mellitus in pregnant women and the urinalysis and urine culture results

Data	**Mean of the data (n = 110)**
Type GDM*	
GDM A1	73 (66.4%)
GDM A2	14 (12.7%)
Overt DM	23 (20.9%)
Urinalysis result	
WBC** < 5 cells/HPF*** (negative)	102 (92.8%)
WBC $\geq$ 5 cells/HPF (positive)	8 (7.2%)
WBC 5- < 10 cells/HPF (positive)	3 (2.7%)
WBC $\geq$ 10 cells/HPF (positive)	5 (4.5%)
Urine culture result	
Klebsiella aerogenes [WBC 5- < 10 cells/HPF (positive)]	1 case
No growth	7 cases

* GDM, gestational diabetes; ** WBC, white blood cell; *** HPF, high power field

Discussion

Our study revealed a prevalence of ASB from urinalysis (WBC count $\geq$ 5 per high power field) of 8/110 cases (7.2%) and a positive result for pathogens in 1/8 cases (*Klebsiella aerogenes* with a WBC count from urinalysis of 5–10 cells per high power field). From previous studies, it was found that the most common pathogens in diabetic women with ASB were *E. coli* 70%[11], followed by *Klebsiella* 3% and *Enterobacter* species 3%, Proteus 2%, and gram-positive organisms, such as group B Streptococcus 10%[11].

Only 25% of asymptomatic bacteriuria (ASB) found in the second to third trimester[12]. Diabetes mellitus is one of many risk factors associated with ASB during pregnancy[13] and is related to a number of adverse pregnancy outcomes, including preterm labor and a low birth weight[14,15]. ASB in diabetic pregnant can be related to an adverse outcome of pregnancy and to the neonate[5,15]; therefore, routine urinalysis should be considered during ante-natal care. Pregnant women with ASB may progress to urinary tract infection in 20–35% of cases[14]. Therefore, the treatment of ASB during pregnancy is beneficial. However, the previous study at Siriraj Hospital reported that it was not worth performing urinalysis for all pregnant women due to the low prevalence of ASB[6], and therefore we selected only diabetic pregnant women as our target in the present study.

Asymptomatic bacteriuria refers to the detection of bacteria in a urine culture, but where pregnant women do not have symptoms that are compatible with urinary tract infection. According to the Infectious Diseases Society of America guidelines, screening should be performed for all pregnant women during the first trimester[1] or during 12–16 weeks gestation through urine culture[12].

Table 3: Detailed of the pregnant women with ASB included in the study

Case number	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
Age (year)	26	37	42	40	38	36	35	31
Weight (kilograms)	89.0	75.3	62.0	102.0	84.8	82.3	83.0	87.0
Height (centimeter)	153	163	165	160	170	150	155	165
Body mass index (kilogram/metre^2)	38.0	28.3	22.8	39.8	29.3	36.6	34.6	32.0
Occupation	Laborer	Laborer	Laborer	Laborer	Merchant	Housewife	Merchant	Government
Income	>20,000–50,000	>10,000–20,000	>10,000–20,000	>20,000–50,000	>20,000–50,000	>20,000–50,000	>20,000–50,000	>10,000–20,000
Gravida	1	2	2	2	3	1	3	2
Parity	0	0	1	0	2	0	1	1
Abortion	0	1	0	1	0	0	1	0
Gestational age (week)	12	23	9	18	12	17	33	17
HBsAg	neg	neg	neg	neg	Neg	neg	Neg	neg
VDRL	neg	neg	neg	neg	neg	neg	Neg	neg
Anti HIV	neg	neg	neg	neg	neg	neg	Neg	neg
Hematocrit	36.4	42.2	37.3	39.4	31.1	44.1	34.6	42.1
Thalassemia	No	No	No	No	Hb E trait	No	Hb E trait	No
Type of gestational diabetes (GDM)	GDM A1	Overt DM	GDM A1	GDM A2	GDM A2	GDM A1	Overt DM	GDM A1
Underlying disease	No	No	DLP	No	No	No	No	No
Urinalysis (white blood cell count)	>10	>10	>10	>10	>10	5-10	5-10	5-10
Urine culture	NG	NG	NG	NG	NG	*Klebsiella aerogenes*	NG	NG

Urine culture tests are considered the gold standard in screening for asymptomatic bacteriuria in pregnant women with high risk factors, including recurrent urinary tract infection, a previous history of preterm birth, and diabetes mellitus[13]. The diagnosis of ASB is based on urine culture according to the isolation of a bacterial infection in quantitative counts of $\geq 10^5$ colony-forming units (cfu)/mL[11].

However, urine culture is not performed for all pregnant women due to its high cost and high labor-consumption needed for the test. Regular urinalysis is a standardized diagnostic test to exclude bacteriuria. Urine culture is not mainly part of the diagnosis test for ASB but may be necessary for symptomatic urinary tract infection[16]. If the urinalysis result is positive, a diagnostic urine culture for pathogen and antimicrobial susceptibility testing is done. Specimens with a cut-off $\geq$ 5 and $\geq$ 10 WBCs/HPF have 91% and 92% negative predictive values, respectively[17,18]. The strength of this study is the usage of a common diagnostic test, which allowed retrieving the result in a shorter time than from urine culture, which generally takes several days. Therefore, proper treatment could proceed more rapidly without waiting for the results from pathogen and antimicrobial susceptibility testing. Overtreatment can prevent symptomatic bacteriuria and an adverse outcome of ASB in advance.

The limitation of the study was the small numbers of diabetic pregnant women included in the study. A larger study may confirm the necessity of urinalysis in high-risk diabetic pregnant women in clinical practice. However, the accepted definition of ASB is actually obtaining a positive

urine culture in a patient without symptoms of urinary tract infection. The more conventional way of diagnosing ASB is to subject all women to a urine culture which is difficult to apply in routine practice. Perhaps, this would explain why only one positive urine culture was obtained. The next larger study may achieve more accurate result. The very small number of positive urine cultures may not allow any associations or risk factors for ASB to be defined or studied.

Conclusion

The prevalence of ASB in diabetic pregnant women was 7.2% in our study. Urinalysis in those pregnant women should be considered, especially in women with a high BMI. The early detection and prompt treatment of ASB may prevent the risk of preterm delivery and low-birth-weight neonates.

Conflicts of interest

The authors have each completed the International Committee of Medical Journal Editors Form for Uniform Disclosure of Potential Conflicts of Interest. All the authors declare they have nothing to disclose. All the procedures performed in studies involving human participants were carried out in accordance with the ethical standards of the institutional research committee (Si 252/2019) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

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Contribution of authors

Saifon Chawanpaiboon contributed to the conception and design, acquisition, analysis and interpretation of the data, drafting and critically revising the manuscript, and approval of the final version submitted for publication. Tirawan Buayaem contributed to the recruitment of the patients, revising the manuscript, and approval of the final version submitted for publication. Supavade Sodsee contributed to the recruitment of the patients and approval of the final version submitted for publication. Vitaya Titapant contributed to the revising of the manuscript and approval of the final version submitted for publication. Julaporn Pooliam contributed to the analysis and interpretation of the data, critically revising the manuscript, and approval of the final version submitted for publication.

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