Microbiological and Antimicrobial Susceptibility Pattern of Asymptomatic Bacteriuria in Pregnant Women Attending SQUH

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Abstract

Objectives: The research aims to study the microbiology and antimicrobial resistance in asymptomatic bacteriuria among Omani pregnant women who received care at SQUH.

Method: A retrospective study included 196 Omani pregnant women with asymptomatic bacteriuria who received care at SQUH from 2010- 2019. Data was obtained from patients' electronic medical including demographics, clinical details, the isolated organism, antimicrobial susceptibility results, and the prescribed antibiotics and it was analyzed using SPSS program.

Results: *56%* of asymptomatic bacteriuria (ASB) was detected during the 3rd trimester. *Klebsiella pneumoniae* was the most frequently isolated organism (32% of the cases) followed by *Escherichia coli* (29%). 10.2% of the isolates were extended spectrum beta-lactamase (ESBL) producing organisms. The overall microbiological susceptibility pattern showed that organisms have high susceptibility rate to Nitrofurantoin reaching up 82% followed to a lesser extent by Cefuroxime and Augmentin. Susceptibly of *E. coli and klebsiella* pneumoniae to Cefuroxime was 74% and 71% respectively. Only 52% of all isolated ESBL-producing organisms were susceptible to Nitrofurantoin.

Conclusion: *Klebsiella pneumoniae* and *Escherichia coli* were the most frequently isolated bacteria in ASB representing almost 60% of total isolates. High prevalence of ESBL-producing organisms reaching up to 10.2% of the total isolates was observed. Cefuroxime is an appropriate empirical antibacterial therapy for ASB and UTI in pregnant woman .Nitrofurantoin should be considered for an empirical antibiotic therapy in the settings of high prevalence of ESBL-producing organisms.

Keywords: Keywords: Asymptomatic bacteriuria (ASB), bacteria, empirical antibiotics, pregnancy.

Introduction

Asymptomatic bacteriuria (ASB) is defined as presence of bacteria in the urine in the absence of urinary symptoms. It is a common during pregnancy where screening and prompt treatment are required once identified. The estimated prevalence of ASB in pregnancy is around 2-10%.[1,2]

During pregnancy women are at increased risk of symptomatic UTI including pyelonephritis than non-pregnant woman due to physiological and hormonal changes that occur during pregnancy.[3] The estimated risk of symptomatic UTI and pyelonephritis in untreated ASB ranges between 20-40%.[4-7] ASB may also increase the risk of pre-term delivery and intrauterine growth retardation.[4,8,9] Thus, screening all pregnant women for ASB is the standard of care and it is recommended worldwide. The introduction of the screening program was found to reduce risk of pyelonephritis and other related complications during pregnancy.[5]

Different oral antibiotics options have been recommended for empirical therapy for ASB including amoxicillin, co-amoxiclav, co-trimoxazole, and ciprofloxacin. However, in view of emerging antimicrobial resistance, Nitrofurantoin is recommended by some guidelines as the standard empirical therapy.[10] Understanding the microbiology and antimicrobial resistance of the causative bacteria in our settings will help to guide appropriate empirical antibacterial therapy in pregnant women with ASB or urinary tract infection.

Methods

This retrospective cross-sectional study conducted included all pregnant women with asymptomatic bacteriuria seen at Sultan Qaboos University Hospital during the period from January 2010 to December 2019. Detailed clinical data and patient's demographics as well as antimicrobial susceptibility of the causative pathogens were obtained from patients' electronic medical record (TRACKCARE). Data was analyzed using SPSS program version 20. Mean, 95% Confidence interval and standard deviation was calculated to describe continuous variables while chi-square test was used to describe categorical variables.

Results

A total of 196 pregnant women aged 19-44 years were included in in the study with a mean age of 29 years. The gravidity of studies group ranged between 1and14 (mean 3.3) and parity between 0 and9 (mean 1.68). 56% (109/196) of the pregnant women had the asymptomatic bacteriuria in the 3rd trimester. Diabetes mellitus and gestational diabetes (GDM) are reported in 21% of women with ASB. GDM was found in 15.8% of the studied cohort [Table 1].

Table 1: frequency of ASB across the different pregnancy trimester.

	Frequency	**Percent %**
First trimester	28	14.3
Second trimester	58	29.6
Third trimester	110	56.1
Total	196	100.0

In regards to the microbiologic pattern, *Klebsiella pneumoniae* was the most frequently isolated organism followed by *Escherichia coli* representing 32% and 29% of all isolates respectively. The two organisms represent around two thirds of total number of isolates together. 10.2% of the isolates were extended spectrum beta-lactamase (ESBL) producing organisms. Other bacterial species including *Staphylococcus aureus* and *group B streptococcus* were isolated in a small number of patients Table 2.

Table 2: Frequency of commonest organisms isolated in ASB,

Isolated bacteria	**Frequency**	**Percent%**
Escherichia coli	58	29.6
Klebsiella pneumoniae	63	32.1
Enterococcus faecalis	22	11.2
ESBL species	21	10.2
Group B Streptococcus	15	7.2
Others	17	9.7
Total	196	100.0

In this study, cefuroxime followed by co-amoxiclav were the most frequently empirically prescribed antibiotics and 33.8% of the patient did not receive any antibiotics for ASB likely due to delayed follow up of urine culture results. However, most of pregnant women with ASB had a follow up urine culture and targeted antibacterial therapy for any growth as per local treatment protocol. The overall microbiological susceptibility pattern show high susceptibility rate to Nitrofurantoin reaching up to 82.8% followed to a lesser extent by cefuroxime and co-amoxiclav. Susceptibly of *E. coli and klebsiella pneumoniae* to Cefuroxime was 74% and 71% respectively in comparison with other oral options including ampicillin, ciprofloxacin and co-trimoxazole. Among oral antibiotics tested in our study, Nitrofurantoin showed susceptibility of 52% in all isolated ESBL-producing organisms [Table 3].

Table 3: Antimicrobial susceptibility of bacteria causing ASB in pregnant women.

	Antibiotic susceptibility					
Organism	**Co-Amoxiclav n (%)**	**Cefuroxime n (%)**	**Ampicillin n (%)**	**Nitrofuranation n (%)**	**Ciprofloxacin n (%)**	**Trimethoprime/ Sulfamethoxazole n (%)**
Escherichia coli	37 (63.8)	43 (74.1)	26 (44.8)	48 (82.8)	19 (32.8)	32 (55.2)
Klebsiella pneumoniae	46 (73.0)	45 (71.4)	3 (4.8)	28 (44.4)	21 (33.3)	43 (68.3)
Enterococus fecalis	7 (33.3)	3 (14.3)	19 (90.5)	14 (66.7)	5 (23.8)	3 (14.3)
group B streptpcoccus	5 (35.7)	3(21.4)	7 (50)	4(28.5)	2 (14.2)	3 (21.3)
ESBL species	6 (28.5)	5 (23.8)	1 (4)	11 (52)	7 (33)	10 (47.6)

Discussion

There was a significant difference in prevalence of asymptomatic bacteriuria with regards to trimester as previous studies showed increased prevalence of in the first trimester.[11,12] In comparison to these studies, our study showed high prevalence of ASB in the third trimester reaching up to 56% of cases. This is likely related to complexity of cases seen at the tertiary care hospital late in pregnancy where screening for ASB is done routinely. Majority of pregnant women get their urine culture screened early in pregnancy at the local health center.

Patients with Diabetes mellitus have 3-5-fold increased risk of ASB in comparison with general population.[13] In this study, diabetes mellitus and gestational diabetes mellitus were reported in around 25% pregnant women with ASB and poses a major risk factor for developing ASB during pregnancy.

Klebsiella pneumoniae followed by *Escherichia coli* (*E. coli*) were the most prevalent organisms in our study population, in comparison to results of previous studies conducted in different parts of the world where *E. coli* was the predominant organism.[2,9,14] *E. coli* represented 89%, 70%, 66.9% of total isolates in KSA, Iran and UAE respectively[11.] On contrary Klebsiella species were infrequently and less than <1% of total isolates in some regions in the world such as UK and KSA.[10,15]

The rise of antimicrobial resistance is a global threat and increasing incidence of urinary tract infections causes by antibiotic resistance pathogens including extended spectrum beta lactamase producing organisms (ESBL) is concerning. In this study, 10% of total isolates causing ASB were ESBL producing organisms which is lower than what has been reported in some other countries. In Iraq, the estimated prevalence is around 23%.[16] High prevalence of ESBL producing organisms as a cause of UTI or ASB has been reported in Africa and India with an estimated prevalence of 45% and 33% respectively.[17] Europe and South America have the lowest rates with an incidence rate of 4% and 3% respectively.[18]

This study revealed that nitrofurantoin, cefuroxime and co-amoxiclav sustained a good susceptibility level against the most isolated urinary pathogens. High percentage of *E. coli and Klebsiella pneumonia*e species. High resistance rate of *E.coli* to Amoxicillin has been reported in some parts of the world and hence it is recommended against its use as an empirical therapy.[19,20] Data from the UK show an increasing resistant rate of pathogens causing UTI to most of the oral antibiotics including amoxicillin, co-trimoxazole, co-amoxiclav and ciprofloxacin.[10] In the view of global increase antimicrobial resistance and high prevalence of ESBL producing organisms, Nitrofurantoin is considered as

a preferred choice for empirical treatment of UTI in pregnancy and it is recommended by multiple guidelines.[10,21] However, Nitrofurantoin should be avoided in late 3rd trimester due to risk of G6PD induced hemolytic anemia in both mother and fetus near term.[22,23]

This study showed reduced subspecialty of the isolates to ciprofloxacin which is not recommended during pregnancy and due to increased risk of congenital malformation (FDA risk category C). Despite Cotrimoxazole showed a better susceptibility but it is also not recommended during early pregnancy due to risk of congenital malformation and near term due to risk of hemolytic anemia and kernicterus.[24]

There was significant proportion of pregnant women who were not prescribed any antibiotics due to lack of a close outpatient follow up and delayed knowledge of the results of urine cultures until the follow up appointment. This emphasizes the importance of the close follow up of urine culture results in pregnant women to avoid complications including urinary tract infections. The effectiveness of anti-microbial therapy in the clearance asymptomatic bacteriuria has been reported in multiple studies, A Cochrane study compared treatment with antibiotic to placebo or no treatment, concluded 75% reduction in risk of pyelonephritis with treatment.[25]

With regards to the asymptomatic bacteriuria related complications, there was no significant complication reported in the study except of one case of acute pyelonephritis and IUGR in another case.

Conclusion

This study shows that 21% of pregnant woman with asymptomatic bacteriuria had diabetes mellitus or gestational diabetes mellitus as major risk factors. *Klebsiella pneumoniae* and *Escherichia coli* were the most frequently isolated bacteria representing almost 60% of total isolates. There was a high prevalence of ESBL-producing organisms representing 10.2% of the total isolates. Based on these results, Cefuroxime is an appropriate empirical antibacterial therapy for ASB and UTI in pregnancy woman for which 70% of *Klebsiella pneumoniae* and *Escherichia coli* were susceptible Nitrofurantoin should be considered as an empirical antibiotic therapy in the settings of high prevalence of ESBL-producing organisms.

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References

1. Celen S, Oruç AS, Karayalçin R, Saygan S, Unlü S, Polat B, et al. Asymptomatic bacteriuria and antibacterial susceptibility patterns in an obstetric population. ISRN Obstet Gynecol 2011;2011:721872.

2. Sibiani S, Arabia S. Asymptomatic Bacteriuria in Pregnant Women in Jeddah, Western Region of Saudi Arabia: Call for Assessment. Magalat Game'at al-Malik Abdul Aziz Al-U'lum al-Tibyat 2010;17:29-42.

3. Beydoun SN. Morphologic changes in the renal tract in pregnancy. Clin Obstet Gynecol 1985 Jun;28(2):249-256.

4. Andrews WW, Cox SM, Gilstrap LC. Urinary tract infections in pregnancy. Int Urogynecol J Pelvic Floor Dysfunct 1990;1:155-163.

5. Patterson TF, Andriole VT. Bacteriuria in pregnancy. Infect Dis Clin North Am 1987 Dec;1(4):807-822.

6. Masinde A, Gumodoka B, Kilonzo A, Mshana SE. Prevalence of urinary tract infection among pregnant women at Bugando Medical Centre, Mwanza, Tanzania. Tanzan J Health Res 2009 Jul;11(3):154-159.

7. Scan guideline. Lower UTI in Pregnancy, https://viewer. microguide.global/SCAN/SCAN#content,d6d0a7e5-a215- 436f-a296-72675a7d2ae6. last update October 2019

8. Emamghorashi F, Mahmoodi N, Tagarod Z, Heydari ST. Maternal urinary tract infection as a risk factor for neonatal urinary tract infection. Iran J Kidney Dis 2012 May;6(3):178-180.

9. Awoke N, Tekalign T, Teshome M, Lolaso T, Dendir G, Obsa MS. Bacterial Profile and asymptomatic bacteriuria among pregnant women in Africa: A systematic review and meta analysis. EClinicalMedicine 2021 Jun;37:100952.

10. Cotton E, Geraghty R, Umranikar S, Saeed K, Somani B. Prevalence of asymptomatic bacteriuria among pregnant women and changes in antibiotic resistance: a 6-year retrospective study. J Clin Urol 2022;0(0).

11. Zumla A. Mandell, Douglas, and Bennett's principles and practice of infectious diseases. Lancet Infect Dis 2010 May;10(5):303-304.

12. Wingert A, Pillay J, Sebastianski M, Gates M, Featherstone R, Shave K, et al. Asymptomatic bacteriuria in pregnancy: systematic reviews of screening and treatment effectiveness and patient preferences. BMJ Open 2019 Mar;9(3):e021347.

13. Jeffrey L. Ecker, Camille E Powe. Pregestational (preexisting) diabetes mellitus: Obstetric issues and management from: https://www.uptodate.com/contents/pregestational-preexisting-diabetes-mellitus-obstetric-issues-and-management- accessed June/23.

14. Abdullah AA, Al-Moslih MI. Prevalence of asymptomatic bacteriuria in pregnant women in Sharjah, United Arab Emirates. East Mediterr Health J 2005;11(5-6):1045-1052.

15. Abduljabbar H, Moumena RA, Mosli HA, Khan AS, Warda A. Urinary tract infection in pregnancy. Ann Saudi Med 1991 May;11(3):322-324.

16. Alkhudhairy M, Alshammari M, Extended spectrum β-lactamase-producing Escherichia coli isolated from pregnant women with asymptomatic UTI in Iraq. EurAsian Journal of Biosciences. AugDec2019.

17. Demilie T, Beyene G, Melaku S, Tsegaye W. Urinary bacterial profile and antibiotic susceptibility pattern among pregnant women in north west ethiopia. Ethiop J Health Sci 2012 Jul;22(2):121-128.

18. Mansouri F, Sheibani H, Javedani Masroor M, Afsharian M. Extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae and urinary tract infections in pregnant/postpartum women: A systematic review and meta-analysis. Int J Clin Pract 2019 Sep 18:e13422.

19. Tadesse S, Kahsay T, Adhanom G, Kahsu G, Legese H, G/Wahid A, et al. Prevalence, antimicrobial susceptibility profile and predictors of asymptomatic bacteriuria among pregnant women in Adigrat General Hospital, Northern Ethiopia. BMC Res Notes 2018 Oct;11(1):740.

20. Abdel-Aziz Elzayat M, Barnett-Vanes A, Dabour MF, Cheng F. Prevalence of undiagnosed asymptomatic bacteriuria and associated risk factors during pregnancy: a cross-sectional study at two tertiary centres in Cairo, Egypt. BMJ Open 2017 Mar;7(3):e013198.

21. Emami A, Javanmardi F, Pirbonyeh N. Antibiotic resistant profile of asymptomatic bacteriuria in pregnant women: a systematic review and meta-analysis. Expert Rev Anti Infect Ther 2020 Aug;18(8):807-815.

22. Cimolai N, Cimolai T. Nitrofurantoin and pregnancy. CMAJ 2007 Jun;176(13):1860-1861.

23. Nordeng H, Lupattelli A, Romøren M, Koren G. Neonatal outcomes after gestational exposure to nitrofurantoin. Obstet Gynecol 2013 Feb;121(2 Pt 1):306-313.

24. https://www.fda.gov/drugs/bioterrorism-and-drug-preparedness/ciprofloxacin-use-pregnant-and-lactating-women#:~:text=Non%2Dcontrolled%20prospective%20observational%20data,the%20first%20trimester%20was%204.7%25.

25. Smaill F. Asymptomatic bacteriuria in pregnancy. Best Pract Res Clin Obstet Gynaecol 2007 Jun;21(3):439-450.