Prevalence of urinary tract infection and antibiotic sensitivity among pregnant women having prenatal check-up at a tertiary hospital in Manila*

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ABSTRACT

Objective: The objective of this study is to determine the prevalence and the most common causative agent of urinary tract infection (UTI) in pregnant women having prenatal check-up at a tertiary hospital, as well as the antibiotic sensitivity of these organisms to selected antimicrobials that are currently recommended for use in the treatment of UTI in pregnancy (specifically Nitrofurantoin, Amoxicillin, Cephalexin, Cefuroxime, Amoxicillin with Clavulanic acid). The results of this study will not only update the hospital's biogram, it will also aid the physicians in prescribing patients with the most cost-effective regimen.

Methodology: Patients seen at the outpatient department were included in the study starting May 2017 up to September 2017. Patients with previous antibiotic intake during the current pregnancy were excluded. A questionnaire containing demographic data, prenatal history, checklist for symptoms, and consent were provided for each patient. As per guidelines, urine gram stain and culture studies were requested during their prenatal visit. All urine specimen were sent to the same laboratory for microscopy and culture. Results were analyzed using SPSS v 23.0

Result: The prevalence of urinary tract infection in pregnant patients having prenatal care at a tertiary hospital in Manila was 15.6%. The most common isolates were still E. coli and Staphylococcus. Symptoms were not reflective of the presence of UTI and previous prenatal care did not affect the presence UTI. Analysis of sensitivity and resistance patterns of the isolated organisms showed increasing resistance to the commonly used antibiotics given to pregnant patients, especially Co-Amoxiclav. Cephalosporins, on the other hand, remain to have good sensitivity.

Conclusion: Urinary tract infection is prevalent among pregnant women having prenatal check up at a tertiary hospital. It is recommended that guidelines on the diagnosis of UTI in pregnancy be strictly followed so that management will be culture-guided, thus preventing the development of antibiotic resistance.

Keywords: antibiotic sensitivity, asymptomatic bacteriuria, urinary tract infection in pregnancy

INTRODUCTION

Urinary tract infections are second only to anemia as the most common complication in pregnancy. Anatomical and physiological changes occurring in pregnant women make them more susceptible to such infections and its complications. Maternal genitourinary tract infections have been significantly associated with adverse perinatal and maternal outcomes, including preterm birth, neonatal and puerperal sepsis, neonatal mortality, and even maternal mortality.[2] According to current guidelines, urine culture and sensitivity studies are preferred over urinalysis in the diagnosis of urinary tract infection in pregnancy.

A study done in a tertiary-care government hospital in Manila showed an over-all prevalence of asymptomatic bacteriuria (ASB) in pregnant patients of 1.9% based on 2 urine cultures and 4.3% in the absence of a second culture. The incidence of acute cystitis, on the other hand, was noted to be only 1.3%, and was more commonly diagnosed during the second trimester.[4]

International literature show that the most common uropathogens include *Escherichia coli, Klebsiella pneumonia, Proteus, Acinetobacter, Saprophyticus Staphylococcus, Streptococcus Group B and Pseudomonas aeruginosa. A local study done by Sescon et al revealed Escherichia coli to be the most common isolate (63%), followed by Klebsiella pneumoniae 12%, Enterococcus 12%, Staphyloccus saprophyticus 7%, Staphylococcus aureus 4%, and Klebsiella ozanae 2%.*

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Table 1. Pregnancy risk and Hale's Lactation risk categories for commonly prescribed antimicrobials in UTI

Category B, L1, L2	Category C, L3	Category D, L3
Nitrofurantoin Amoxicillin- clavulanate Cephalosporins	TMP-SMX (Avoid in 1st and 3rd trimester)	Aminoglycosides
Lactation Risk Category		
L1 – safest, controlled study = fails to demonstrate risk L2 – safer, limited number of women studied without risk L3 – moderately safe, no controlled study or controlled study shows minimal, non-life-threatening risk L4 – hazardous, positive evidence of risk, may be used if maternal life-threatening situation L5 – contraindicated, significant, and documented risk		
FDA Pregnancy Risk Categories		
Category A – well-controlled human study = no fetal risk in first trimester. No evidence of risk in 2nd , 3rd trimesters. Risk to fetus appears remote. Category B – animal studies do not demonstrate fetal risk, but no controlled study in humans OR animal studies show adverse effect but not demonstrated in human study. Category C – no controlled study in humans available. Animal studies reveal adverse fetal effects Category D – Positive evidence of human fetal risk. Use in pregnant woman occasionally acceptable despite risk. Category E – animal or human studies demonstrate fetal abnormality. Evidence of fetal risk based on human study. No indication in pregnancy.		

Adapted from: Fitzgerald MA. Urinary Tract Infection: Providing the Best Care. Available at http://www.medscape.com/viewprogram/1920, Accessed Feb 3, 2004.

During pregnancy, treatment should be initiated immediately to prevent complications that may also affect the fetus, such as low birth weight and preterm delivery. A 7-day course of antibiotic treatment is recommended for both asymptomatic bacteriuria and acute cystitis. The choices of antimicrobials are limited to those known to be safe for use in pregnancy (Table 1). These include Nitrofurantoin (not for those near term), cephalosporins, and penicillins. The choice of antibiotics is ideally culture-guided. In the absence of urine culture and sensitivity, therapy should target local susceptibility patterns of uropathogens. A repeat urine culture is advised after completion of antibiotics.

Currently, there has been note of increasing resistance to drugs commonly used to treat urinary tract infection in pregnancy. A study by Meher et al showed significantly high resistance by gram negative bacilli and gram positive cocci to the beta-lactam group of antimicrobials. Inappropriate antimicrobial use can lead to inadequate therapy and may contribute to further drug resistance.[3]

OBJECTIVES

This study generally aims to determine the prevalence of urinary tract infection in pregnant patients having prenatal check-up at a tertiary hospital in Manila.

Specific objectives include the determination of the various organisms and most common causative agent of urinary tract infection in pregnancy, determination of sensitivity pattern of these organisms, and confirmation if current recommendations and guidelines for the management of UTI in pregnancy are applicable to the results.

MATERIALS AND METHODS

The sample population included pregnant patients being seen at the outpatient department starting May 2017 up to September 2017, regardless of gestational age. Exclusion criteria include: history of antimicrobial treatment during the current pregnancy, history of intake of immunosuppressive drugs and presence of co-morbidities and chronic diseases that would make the patient susceptible to infections such as autoimmune disease and Diabetes Mellitus. The sample size was calculated using the formula for a normal distribution, with a 5% margin of error and 95% confidence level. The population size used was computed based on the average number of new patients seen at the outpatient department of the said hospital.

A standardized questionnaire was used to obtain basic demographic data, prenatal history, signs or symptoms of urinary tract infection, and consent. After the patient has given consent, urine culture and sensitivity studies were done for each patient after thorough instructions on how to obtain the specimen. All samples were sent to the same laboratory.

The prevalence of urinary tract infection among pregnant women, the most common causative agent and the antimicrobial sensitivity profiles were determined from these results.

Data was analyzed using SPSS version 23.0 for windows. Means and proportions of the socio-demographic and obstetrical characteristics were compared between growth negative and growth positive groups using student t and X2 tests, respectively, to check for homogeneity of the population. Probability value of <0.05 was considered statistically significant for all results.

Consent for participation in the study was obtained from each patient. Copies of the culture and sensitivity results were given to the patients for their prenatal check-up. When necessary, treatment for urinary tract infection was given based on culture sensitivity study results. The identity of all subjects remained confidential.

RESULTS

A total of 128 patients were enrolled in the study. 10 patients were excluded due to previous antibiotic intake during the present pregnancy and another 2 subjects were excluded for having Gestational Diabetes Mellitus. Only 45 (35%) of the enrolled subjects were able to submit urine samples for culture studies due to financial constraints. Out of the 45 subjects with urine culture studies, only 7 (15.6%) had significant growth.

Table 2 shows the demographic characteristic of the study population. Age ranged from 15 years old to 45 years old. More than half of the subjects (60%) were seen for the first time at the outpatient department. 5 patients had known co-morbidities. However, these were not considered significant as these do not affect the susceptibility of the patients to infections.

Table 2. Demographic Profile (N=45)

	Frequency	Percentage
Gravidity		
Primigravida	18	40%
Multigravida	27	60%
Parity		
Nullipara	18	40%
Primipara	9	20%
Multipara	18	40%
Term		
0	18	40%
1	9	20%
2 to 5	18	40%
TOTAL	45	100%

Four (9%) patients were seen during the first trimester, 15 were on their 2nd trimester of pregnancy and more than half (58%) were at the last trimester of pregnancy. Compared to the patients with positive growths, 5 were in the second trimester of pregnancy and only 1 was in the first trimester.

Only a fifth of patients (18) have had previous prenatal check-ups while 80% (27) had no previous prenatal check-ups at all. 2 (28%) of the patients with positive culture growths were seen for the first time with no history of previous prenatal check-ups (Table 3).

Most patients denied symptoms associated with urinary tract infection. Only 7 patients reported symptoms and 5 of them had negative growths. The most commonly reported symptom was frequency, followed by low back pain, as shown in Figure 1. Only 1 patient out of those with positive growth experienced symptoms, specifically hypogastric pain.

Figure 2 shows the distribution of the different causative agents and Table 4 shows the comparative sensitivity patterns of these organisms to the different antibiotics. Figure 3 shows the distribution of sensitivity to the different antimicrobials. Linezolid had the highest sensitivity (57%), followed by Ampicillin-Sulbactam (43%). Majority of the antimicrobials that had good sensitivity were cephalosporins. The more commonly used drugs in pregnancy (namely Cefuroxime, Ceftriaxone and Co-

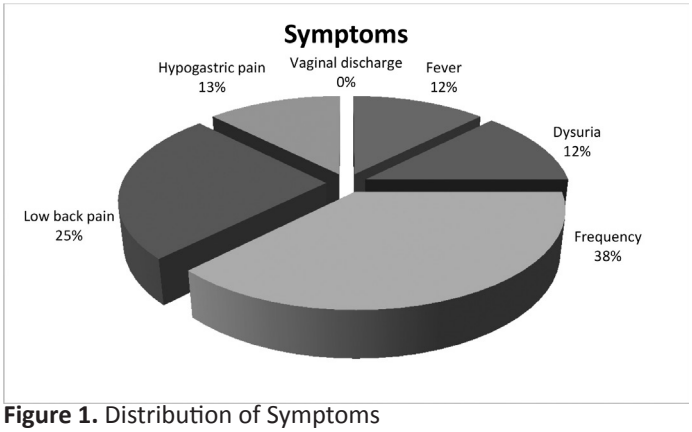

Figure 1. Distribution of Symptoms

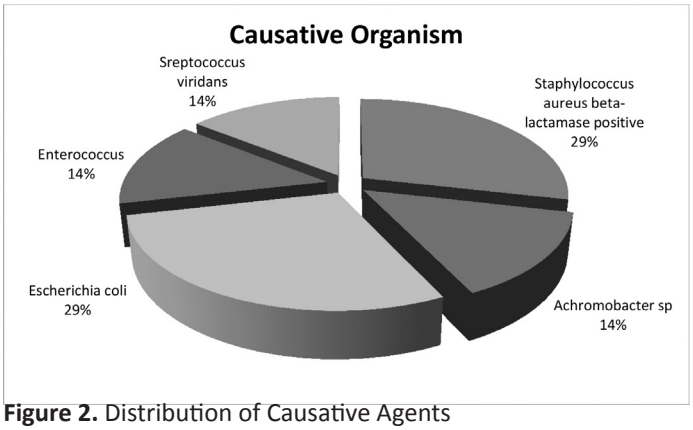

Figure 2. Distribution of Causative Agents

Table 3. Prenatal Check-up (N=45, N=7)

	Positive for growth				P value	Interpretation
	Frequency	Percentage	Frequency	Percentage		
PNCU						
New	27	60%	2	28%		
Follow-up	18	40%	5	72%		
Co-morbids						
Chronic HPN	1	2%	0	0%		
HPN	1	2%	0	0%		
PTB treated	1	2%	0	0%		
Thyroid disease	2	4%	1	14%		
With previous PNCU	36	80%	5	72%		
Without previous PNCU	9	20%	2	28%		
How many times?						
0	9	20%	2	28%		
1 to 2	10	22%	4	58%		
3 to 4	10	22%	1	14%	0.79	Not significant
5 to 6	5	11%	0	0%		
7 and above	2	4%	0	0%		
AOG						
1st tri	4	9%	1	14%		
2nd tri	15	33%	5	72%	0.031	Significant
3rd tri	26	58%	1	14%		
TOTAL	45	100%	7	100%		

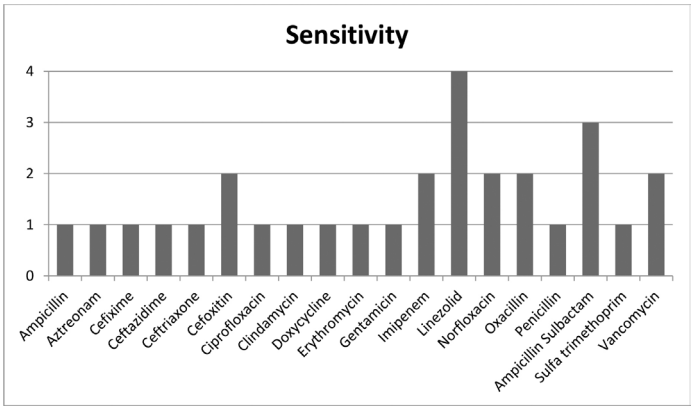

Figure 3. Distribution of Sensitivity to Antibiotics

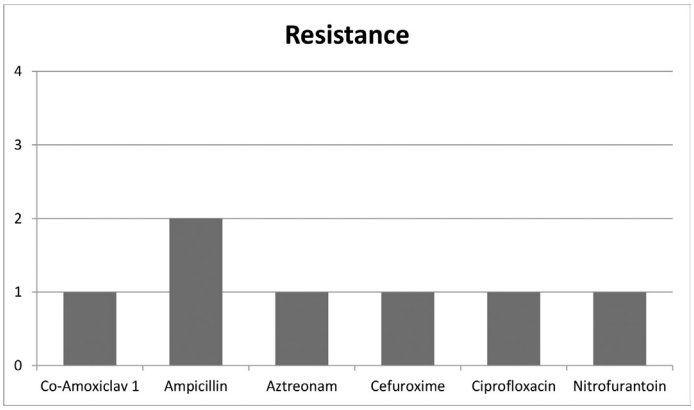

Figure 5. Distribution of Resistance to Antibiotics

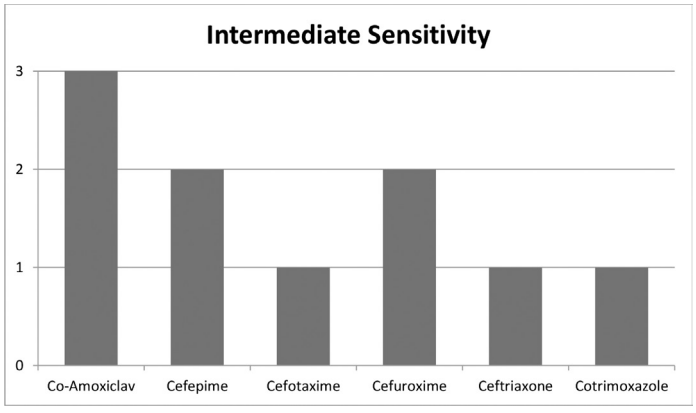

Figure 4. Distribution of Intermediate Sensitivity to Antibiotics

Amoxiclav) only had intermediate sensitivity (Figure 4). Resistance were noted for Co-Amoxiclav, Cefuroxime and Ampicillin (Figure 5).

The urine culture results of the other patients enrolled in the study will be followed-up on the subsequent prenatal visits.

DISCUSSION

According to the most recent local guidelines for urinary tract infection in pregnancy, asymptomatic bacteriuria (ASB) is defined "as the presence of > 100,000

Table 4. Sensitivity Pattern

	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage
Amikacin	0	0%	0	0%	0	0%
Co-Amoxiclav	0	0%	3	43%	1	14%
Amoxicillin	0	0%	0	0%	0	0%
Ampicillin	1	14%	0	0%	2	28%
Azithromycin	0	0%	0	0%	0	0%
Aztreonam	1	14%	0	0%	1	14%
Cefepime	0	0%	2	28%	0	0%
Cefixime	1	14%	0	0%	0	0%
Cefotaxime	0	0%	1	14%	0	0%
Cefazolin	0	0%	0	0%	0	0%
Ceftazidime	1	14%	0	0%	0	0%
Cefuroxime	0	0%	2	28%	1	14%
Ceftriaxone	1	14%	1	14%	0	0%
Cephalexin	0	0%	0	0%	0	0%
Cefoxitin	2	28%	0	0%	0	0%
Chloramphenicol	0	0%	0	0%	0	0%
Ciprofloxacin	1	14%	0	0%	1	14%
Clindamycin	1	14%	0	0%	0	0%
Dicarcyline with Clavulanic acid	0	0%	0	0%	0	0%
Doxycycline	1	14%	0	0%	0	0%
Erythromycin	1	14%	0	0%	0	0%
Furazolidone	0	0%	0	0%	0	0%
Gatifloxacin	0	0%	0	0%	0	0%
Gentamicin	1	14%	0	0%	0	0%
Imipenem	2	28%	0	0%	0	0%
Linezolid	4	57%	0	0%	0	0%
Meropenem	0	0%	0	0%	0	0%
Metronidazole	0	0%	0	0%	0	0%
Nalidixic acid	0	0%	0	0%	0	0%
Nitrofurantoin	0	0%	0	0%	1	14%
Norfloxacin	2	28%	0	0%	0	0%
Oxacillin	2	28%	0	0%	0	0%
Penicillin	1	14%	0	0%	2	28%
Piperacillin	0	0%	0	0%	0	0%
Streptomycin	0	0%	0	0%	0	0%
Ampi-sulbactam	3	43%	0	0%	1	14%
Sulfa trimethoprim	1	14%	1	14%	3	43%
Piperacillin tazobactam	0	0%	0	0%	0	0%
Tetracycline	0	0%	0	0%	0	0%
Ticarcylin with Clavulanic acid	0	0%	0	0%	0	0%
Tobramycin	0	0%	0	0%	0	0%
Trimethoprim	0	0%	0	0%	0	0%
Vancomycin	2	28%	0	0%	0	0%

cfu/ml of one or more uropathogens in two consecutive midstream urine specimens or one catheterized urine specimen, in the absence of symptoms attributable to a urinary tract infection". If obtaining a second urine culture is not feasible, only 1 urine culture is an acceptable alternative.[4] The purpose of a second urine culture for asymptomatic bacteriuria is to discriminate between true infection and contamination.

The diagnosis of acute cystitis, on the other hand, is clinical and may be characterized by symptoms such as urinary frequency, urgency, dysuria, costovertebral angle tenderness, and gross hematuria. Bacteriuria without fever may also be present.

Results of this study indicate that the presence or absence of symptoms (fever, frequency, dysuria, hypopgastric pain, etc.) is not reflective of the presence

of UTI. Figure 1 shows the distribution of symptoms as reported by the subjects. For the culture-positive group however, only 1 patient reported having symptoms (hypogastric pain). The most commonly reported symptoms were frequency and low back pain. This may be attributed to be caused by physiologic changes associated with pregnancy in general and not to the presence of urinary tract infection.

The physiological changes associated with pregnancy increases the likelihood of urinary tract infections (UTI) in pregnant women. If left untreated, ASB and acute cystitis can lead to acute pyelonephritis, as well as low birth weight infants and preterm delivery.

The most recent local study on ASB in pregnant patients was done by Sescon, et al. in 2003. The reported prevalence of ASB according to this study is 1.9% if 2 urine cultures were done and 4.3% if only 1 urine culture was obtained. Foreign studies report prevalence of ASB as high as 14.7% in pregnant women. Risk factors include anemia, history of UTI and presence of comorbids such as diabetes mellitus and preeclampsia.

In this study, the noted prevalence of urinary tract infection was computed to be 15.6%. This increase in prevalence could be due to the delay in health-seeking behavior and prenatal care of these patients. Previous prenatal check-up was also not a significant factor in the incidence of urinary tract infection in pregnancy, though it may be suggested that increasing the number of prenatal visits decreases the possibility of acquiring UTI because patients would have received more advice. The co-morbid conditions present in the study population are not considered significant factors to the predisposition of patients to UTI during pregnancy.

Comparison of the prevalence of UTI between the two groups in relation to age of gestation shows that UTI is noted to be more frequent during the second trimester.

The test of choice in screening for ASB is a clean catch midstream urine culture using standard media. Gram stain may be used as an alternative in the absence of culture studies. This is in accordance to the recommended diagnostics for prenatal work-up. Urinalysis alone is not recommended for screening due to its low sensitivity and specificity.

According to previous studies, *E.* coli remains to be the most common organism isolated, and antibiotics to which this organism is most sensitive and which are safe to give during pregnancy are recommended. Studies have reported increased resistance of *E.* coli to Ampicillin and Amoxicillin, as high as 20-40%. A study done by Meher et al in 2011, showed that Escherichia coli accounted for 41.9% of the urinary isolates. In the same study, coagulase negative species of Staphylococci were the most common pathogen, accounting for 6.4% of isolates among the gram-positive cocci. Significantly high resistance was shown by the gram negative bacilli as well as gram positive cocci to the β-lactam group of antimicrobials, flouroquinolones and aminoglycosides.

In this study, *E.* coli and Staphylococcus aureus β-lactamase positive were noted to be the most common isolates. This is comparable to results of previous studies.

Once asymptomatic bacteriuria or acute cystitis is diagnosed, a 7-day course of antibiotic treatment is recommended. Current recommendations suggest the following antimicrobials as safe for use in pregnancy: penicillins (Amoxicillin), Nitrofurantoin (not for those near term), cephalosporins (most commonly Cefalexin, Cefuroxime, or Co-Amoxiclav), and Co-trimoxazole (during the second trimester). Cotrimoxazole is recommended only during the second trimester because of the risk of kernicterus in the third trimester, while fluoroquinolones are relatively contraindicated due to the risk of teratogenicity. The choice of antibiotic should depend on the sensitivity of the cultured organism. Ideally, a repeat urine culture is done after completion of treatment. Table 3 shows the pregnancy risk and lactation risk of commonly prescribed antimicrobials in UTI.[4]

Table 4 shows the sensitivity pattern for those with positive growth on culture studies. The increased sensitivity to Linezolid and Ampicillin-Sulbactam could be attributed to the fact that these antimicrobials are not prescribed during pregnancy, hence decreasing the exposure of uropathogens to these antibiotics.

Majority of cephalosporins are noted to still have good sensitivity to uropathogens, although the more commonly used ones (Cefuroxime and Ceftriaxone) only have intermediate sensitivity. On the other hand, Co-Amoxiclav was noted to have both intermediate sensitivity and resistance to the isolated pathogens. It is a source of concern that included the list of antimicrobials with noted resistance (Figure 5) are antibiotics commonly prescribed for treatment of UTI in pregnancy, namely Ampicillin, Cefuroxime and Co-Amoxiclav.

The results of this study confirm that there is indeed increasing resistance of the most common causative agents of UTI in pregnant patients to the currently recommended antimicrobials safe for use in pregnancy. A reason for this may be due to the fact that the recommendations on the diagnosis of UTI using culture studies are not being strictly followed. It then follows that the management of urinary tract infection during pregnancy are not culture-guided. The exposure of uropathogens to a limited armamentarium is then increased, thereby causing antibiotic resistance.

CONCLUSION

The study shows that the prevalence of urinary tract infection in pregnant patients having prenatal care at a tertiary hospital in Manila was 15.6%. However, delay in consultation for prenatal care may be a reason. The most common isolates were still *E. coli* and *Staphylococcus.*

Symptoms are not specific and may be attributed to changes in pregnancy rather than the presence of infection. Previous prenatal care also does not affect the presence of UTI. Results of this study showed that the occurrence of UTI was more frequent during the second trimester.

Analysis of sensitivity and resistance patterns of the isolated organisms showed increasing resistance to the commonly used antibiotics given to pregnant patients. Cephalosporins remained to have good sensitivity, although Co-Amoxiclav seems to have decreasing sensitivity or increasing resistance.

It is therefore recommended that the current guidelines for diagnosis of urinary tract infection in pregnancy be strictly followed and that the management of these infections be culture-guided so as to prevent further resistance.

LIMITATIONS

The power of the study was limited by the small sample size, which was in turn limited by the financial capacity of the patients to request for culture studies despite subsidy provided by the investigator.

The diagnosis of urinary tract infection in pregnancy did not follow the recommendation of having 2 positive culture results. This would eliminate the presence of contaminants, which would make a more accurate diagnosis.

RECOMMENDATIONS

Screening for the presence of symptomatic or asymptomatic bacteriuria in pregnancy should be done regularly and specific guidelines for testing antimicrobial susceptibility should be strictly followed so that the appropriate drugs can be used for the treatment. Furthermore, given the limited drugs which are known to be safe for use in pregnancy, culture-guided treatment should be emphasized in order to prevent increase in antimicrobial resistance.

A larger sample size and longer duration of the research are recommended in order to strengthen the power of this study. More subsidy for the culture studies may also help in recruitment of more subjects.

The sensitivity pattern may be affected by or related to the hospital biogram. Comparison of the results to the hospital's biogram may strengthen the implications of the results. Inclusion of other health centers in the area may also help strengthen the results. ■

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