



International Journal of Medical Research & Health Sciences

www.ijmrhs.com

Volume 4 Issue 2

Coden: IJMRHS

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ISSN: 2319-5886

Received: 31st Jan 2015Revised: 10th Feb 2015Accepted: 9th Mar 2015

Research article

PATTERN OF ANTIMICROBIAL USE FOR URINARY TRACT INFECTION DURING PREGNANCY IN A TERTIARY CARE TEACHING HOSPITAL

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ABSTRACT

Background: Urinary Tract Infection (UTI) may be classified as lower (cystitis and asymptomatic bacteriuria) or upper urinary tract infections (pyelonephritis). The recommended antibiotics for use in pregnancy for management of ASB include amoxicillin, oral cephalosporins and nitrofurantoin; and for the treatment of lower UTI during pregnancy include penicillins, oral cephalosporins. Data from the antibiotic usage study in UTI during pregnancy will help in establishing a proper antibiotic utilisation guideline and promotes rational prescribing of medicines. **Aim:** To study the antimicrobial prescription practices for urinary tract infection during pregnancy. **Materials & Methods:** The study was conducted in the Department of Pharmacology and Department of Obstetrics & Gynaecology, Himalayan Institute of Medical Sciences (HIMS), Dehradun, over a period of 12 months. This was an observational cross sectional study done in 45 pregnant women with or without symptoms of UTI. **Results:** 29.4% of the pregnant women with symptomatic UTI were culture positive while all were culture positive who had asymptomatic UTI. Cephalosporins were most frequently prescribed followed by nitrofurantoin. **Conclusion:** Urine culture should be performed as a screening and diagnostic tool for UTI during pregnancy. Various classes of antimicrobials were being prescribed for UTI during pregnancy.

Keywords: Antimicrobials, Urinary Tract Infection, Pregnancy

INTRODUCTION

Urinary Tract Infection (UTI) is caused by pathogenic invasion of the urinary tract which leads to inflammatory response of the urothelium ^[1]. Organisms causing bacteriuria are similar in both pregnant and non pregnant women, with *Escherichia coli* [*E. coli*] being the most common pathogen ^[2]. UTI may be classified as lower [cystitis and asymptomatic bacteriuria] or upper urinary tract infections (pyelonephritis). Pregnancy enhances the progression from asymptomatic to symptomatic bacteriuria (abdominal pain, urinary frequency, urgency, fever, loin tenderness) which could lead to pyelonephritis and adverse maternal and fetal

outcomes ^[3]. Early screening of asymptomatic bacteriuria (ASB) in pregnant women should be done ^[4]. Quantitative urine culture is the gold standard for the diagnosis of bacteriuria ^[5]. The recommended antibiotics for use in pregnancy for management of ASB include amoxicillin, oral cephalosporins and nitrofurantoin (50-100mg four times daily or 100mg twice daily for 3 days) ^[6]. Recommended antibiotics for the treatment of lower UTI during pregnancy include the Food & Drug Administration (FDA) category B antimicrobials including penicillins (amoxicillin 500mg three times daily for 3 days or ampicillin 250mg four times daily for 3 days), oral

cephalosporins (250mg four times daily for 3 days). Upper UTI during pregnancy should be treated preferably with parenteral cephalosporins, penicillins with beta lactamase inhibitors or monobactams [7]. The antibiotic chosen should have a good maternal & foetal safety profile, excellent efficacy and low resistance rates in a given population [8]. Antibiotics are usually given empirically before the laboratory results of urine culture are available. To ensure appropriate therapy, current knowledge of the organism that causes UTI and their antibiotic susceptibility pattern is mandatory [9]. Data from the antibiotic usage study in UTI during pregnancy will help in establishing a proper antibiotic utilisation guideline and promotes rational prescribing of medicines. Hence this study was carried out to study the pattern of use of antimicrobials for UTI during pregnancy.

MATERIAL AND METHODS

Ethics clearance: Ethical clearance was obtained from the Ethics Committee prior to initiation of study. Written informed consent was obtained from each subject prior to sample collection.

Study design: This was an observational cross sectional study

Sample size: 45 pregnant women (20-40 years).

Study place & period: The study was conducted in the Department of Pharmacology and Department of Obstetrics & Gynaecology, Himalayan Institute of Medical Sciences (HIMS), Dehradun, over a period of 12 months from November 2012 till October 2013.

Inclusion criteria: Pregnant women with or without symptoms of UTI were recruited in the study irrespective of their age, race, parity, gravida and trimester.

Exclusion criteria:

- Those on antimicrobial therapy for any pre-existing infection
- Previous history of UTI, pyelonephritis, obstructive uropathy, chronic renal disease
- Urine bag collected specimens
- Specimens submitted in leaking or dirty unsterile container
- Specimens revealing growth of more than two types of bacteria on culture

Relevant information reviewing socio demographic details, medical history, obstetrical and gynaecological history, UTI signs and symptoms and

drug history were taken on case reporting form. Pregnant women were started on empirical antimicrobial treatment which was modified later according to the susceptibility pattern of the urine culture report. Fresh midstream urine was collected aseptically in sterile wide mouth capped disposable universal container on the same day of enrolment. Urine samples were labelled and immediately the sample was processed for microbiology and parasitology with the help of expert microbiologist. Urine culture was done to study the distribution of pathogens. The isolated organisms from culture plates were identified by standard laboratory techniques. Antimicrobial susceptibility testing was done by Kirby Bauer disc diffusion method as recommended by Clinical Laboratory Standards Institute (CLSI) M2-A9 [10]. Women were followed up weekly for one month to look for symptomatic cure, recurrence due to inadequate therapy or resistance. Repeat urine culture was done on the last follow up to confirm bacteriological cure. Data was analysed using Microsoft (MS) Excel & Statistical Package for Social Sciences (SPSS) version 22. Graphical representation of the data was done in terms of figures using MS Excel 2007. Data was presented in descriptive statistics using percentage and proportions.

RESULTS

A total of 45 pregnant women were included in the study and followed up weekly till one month. Table 1 show that out of 45 pregnant women, maximum women were found in 20-25 age group. Overall mean of age was 25.04 ± 3.29 years. Figure 1 show that out of 45 pregnant women, maximum were symptomatic. Of the asymptomatic women, all were culture positive while of the symptomatic women only 29.4% were culture positive. Table 2 shows that of the 19 cases, Gram negative bacteria were isolated in 52.3% and Gram positive in 38.1% of the culture isolates. E. coli was the predominant organism among the gram negatives and CONS (Coagulase Negative Staphylococci) among the gram positives. Yeast was also present in 9.6% cases. Table 3 shows that cephalosporins were the most commonly used class of antimicrobials 41.7% followed by nitrofurantoin 29.2%. Figure 2 show that Nitrofurantoin was the most commonly prescribed antimicrobial followed by Cefuroxime axetil. All these antimicrobials were

prescribed empirically while Linezolid and Fluconazole were prescribed after the culture report showed resistance to the initial antibiotic being prescribed.

Table 1: Age wise distribution of pregnant women (n=45)

Age Group [years]	Number	Percentage [%]
20 – 25	29	64.5
26 – 30	15	33.3
> 30	1	2.2

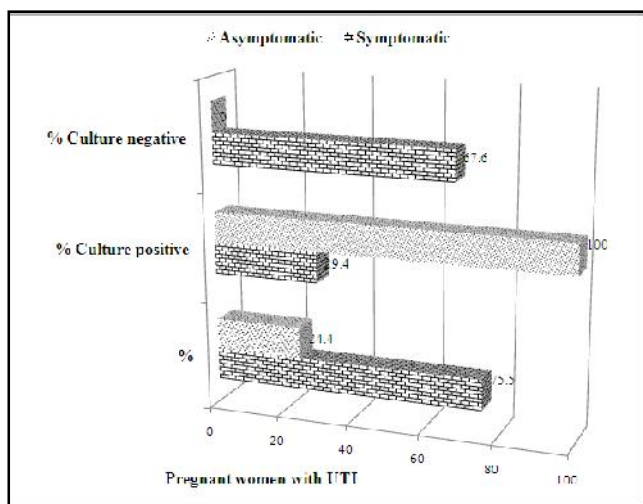


Fig 1: Clinical presentation of UTI in pregnant women (n=45)

Table 2: Distribution of culture isolates in pregnant women with UTI (n=21)

Organism	Gram stain	Number	%
E.coli	GNB	8	38.2
Klebsiella oxytoca	GNB	1	4.7
Proteus vulgaris	GNB	1	4.7
Enterobacter aerogenes	GNB	1	4.7
CONS	GPC	5	23.8
Staph aureus	GPC	2	9.6
Enterococcus faecalis	GPC	1	4.7
Yeast		2	9.6

GNB – Gram Negative Bacilli; GPC – Gram Positive Cocci

Table 3: Distribution of class of antimicrobials in pregnant women with UTI (n=45)

Class of Antimicrobials	Number	%
Penicillin-beta lactamase inhibitor	7	14.5
Cephalosporins 2 nd generation	20	41.7
3 rd generation	14	29.2
Cephalosporin-beta lactamase inhibitor	6	12.5
Nitrofurantoin	5	10.4
Miscellaneous	14	29.2
	2	4.2

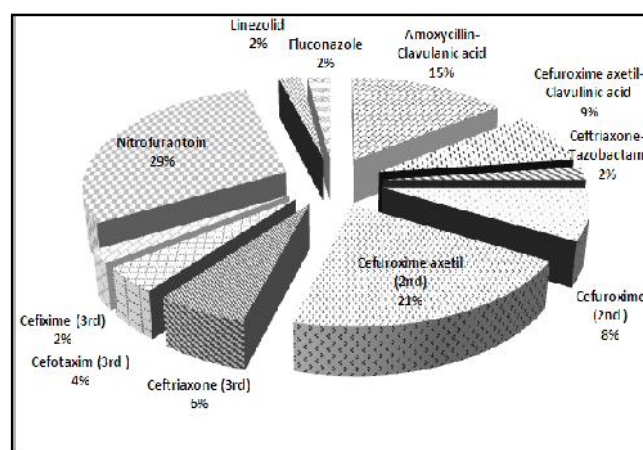


Fig 2: Distribution of various antimicrobials in pregnant women with UTI (n=45)

DISCUSSION

Pregnancy is a unique state with profound anatomic and physiologic urinary tract changes that facilitate the development of symptomatic UTI. UTI itself is no threat to the pregnant women or the foetus, but it may progressively spread to the bladder and kidneys causing cystitis and pyelonephritis respectively as well as prematurity, low birth weight, foetal growth retardation, still birth, mental retardation, developmental delay and increased perinatal mortality in the foetus. It is clear that ASB is a major risk factor for developing symptomatic UTI. Screening of ASB in pregnancy has become a standard of obstetric care. All women should be screened at the first antenatal visit preferably in the first trimester for the presence of bacteriuria with urine culture. Prompt treatment is needed to prevent the serious life threatening condition and morbidity due to UTI. It has been recommended that after patients have completed their treatment course, a repeat culture should be done to document successful eradication of bacteriuria. The aim of the treatment is to maintain sterile urine throughout pregnancy without causing toxicity to the mother or foetus [11]. The present study was conducted to study the pattern of antimicrobial usage for UTI during pregnancy. In the current study maximum numbers of women were in age group 20-25 years. Similarly Okonko and Ijandipe et al; and Olsen and Hinderaker et al also showed that maximum number of women were in the age group 15-24 years [12]. The higher prevalence of UTI in younger age group may be attributed to various factors like lack of personal hygiene and

health awareness, low education status and early age of marriage in developing countries. Majority of the pregnant women had ASB which is higher than that reported by Sabharwal^[13]. Higher prevalence of UTI may be attributed to various factors such as low socioeconomic status, illiteracy, poor housing and drainage system. Furthermore, HIMS acts a tertiary care referral hospital in a rural setting where more serious high risk pregnancies, symptomatic patients with bad obstetric history are referred from nearby nursing homes and private practitioners. Early screening of all pregnant women is therefore recommended because timely intervention with the appropriate antibiotics can prevent drastic consequences. Prevalence of symptomatic bacteriuria in the present study was 29.4% which was similarly seen by Rizvi and Khan et al 25.2%^[14]. Gram negative bacterial isolates on culture were more prevalent than gram positive bacterial isolates. Similar pattern has been observed in all other studies. *E. coli* was the most common gram negative pathogen isolated which is in accordance with all other studies. More prevalence of *E. coli* could be due to the fact that urinary stasis is common in pregnancy and since most *E. coli* strains prefer that environment, they cause UTI. Among the gram positive cocci, CONS was isolated more frequently which matches with many other studies. In few cases yeast was also isolated in the present study. They are less common organisms causing UTI. In the present study all pregnant women were screened by urine culture and were started on empirical therapy initially which was modified later according to susceptibility pattern. Linezolid and Fluconazole were prescribed as definitive therapy after the culture report of antibiotic susceptibility pattern showed resistance to the initial antimicrobial prescribed. The study of prescribing pattern is a component of medical audit, which seeks monitoring, evaluation in the prescribing practices of prescribers to achieve rational medical care. Various classes of antimicrobials were prescribed for UTI during pregnancy in the present study. Cephalosporins were most frequently prescribed followed by Nitrofurantoin. Nitrofurantoin has minimal side effects and can be safely used for the treatment of uncomplicated cystitis and ASB even during pregnancy^[8]. Cephalosporins are recommended for initiating therapy for pyelonephritis^[15] and they were the most commonly used antimicrobials in the

present study. Widespread empiric use of antibiotics, while convenient, potentially contributes to development of antimicrobial resistance. Although irrational and unnecessary use of drugs in India has been documented before, to the best of our knowledge there are no other studies from India where antibiotic use in pregnant women has been addressed. It is likely that our findings reflect the reality in many other developing countries. Encouraging guideline based treatment is an important aspect of changing prescribing behaviour, a goal of antibiotic stewardship. The main limitation of the study was short duration and small number of pregnant women with UTI. Future studies are recommended with a large sample size and conducted over a longer period of time to establish a trend in antibiotic prescription. The present study has highlighted the need to raise awareness of UTIs during pregnancy and to expand services for prevention and treatment of UTI in pregnant women.

CONCLUSION

It is concluded from the present study that there was a high prevalence of ASB among pregnant women. It is therefore imperative that early screening of bacteriuria in pregnancy must be considered as a part of routine antenatal care. Urine culture should be performed as screening and diagnostic tool of UTI in pregnancy. *Escherichia coli* was the most common isolated organism followed by CONS. All pregnant women with UTI should be treated. Cephalosporins were the most commonly prescribed antimicrobials followed by Nitrofurantoin. Periodic and continuous follow up is mandatory to reduce the consequences of ASB and symptomatic UTI.

ACKNOWLEDGEMENT

We sincerely thank all the subjects who gave consent and participated in the present study.

Conflict of Interest: Nil

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