

An observational study on prescribing pattern of antimicrobials for urinary tract infection during pregnancy

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Abstract

Background: Urinary Tract Infection (UTI) refers to both microbial colonization of the urine and tissue invasion of the urinary tract. UTI may be classified as lower (cystitis and asymptomatic bacteriuria) or upper tract infections (pyelonephritis). The aim of antimicrobial therapy is to maintain sterile urine throughout pregnancy without causing toxicity to the mother or the foetus. The recommended anti biotics for use in pregnancy include amoxicillin, oral cephalosporins and nitrofurantoin and for the treatment of lower UTI during pregnancy include penicillin's, oral cephalosporins. Data from the anti-biotic usage study in UTI during pregnancy will help in establishing a proper anti biotic utilization guide line and will promote rational prescribing of medicines.

Aim & Objectives: To study the pattern of antimicrobial prescribing practices for urinary tract infection during pregnancy.

Materials & Methods: The study was conducted in the Department of Pharmacology and Department of Obstetrics & Gynaecology over a period of 12 months from 2012 - 2013. This was an observational cross-sectional study done in 45 pregnant subjects with or without symptoms of UTI.

Results: Cephalosporins were the most commonly prescribed antimicrobials followed by Nitrofurantoin. There were wide variations in dose, duration, route and frequency for which an antibiotic was being prescribed.

Conclusion: All pregnant women with UTI during pregnancy should be treated. Various classes of antimicrobials were prescribed for UTI during pregnancy with wide variations in dose, duration, route & frequency.

Keywords: Antimicrobials, Urinary Tract Infection, Pregnancy.

Introduction

Urinary Tract Infection (UTI) is caused by the pathogenic invasion of the urinary tract which leads to an inflammatory response of the urothelium.^[1]

UTI is a major health problem, it has been reported among 20% of the pregnant women and it is the most common cause of admission in obstetrical wards.^[2] Bacteria are most commonly responsible although yeast and viruses may also be involved.^[3]

UTI during pregnancy may manifest either as asymptomatic bacteriuria (ASB) or symptomatic UTI which includes acute cystitis or pyelonephritis.^[4]

Pregnancy enhances the progression from Asymp to Matic to symptomatic bacteriuria which could lead to pyelonephritis^[5] which in turn can further lead to acute respiratory distress, transient renal failure, sepsis and shock.^[6] Early screening of ASB in pregnant women should be done.^[7] The aim of the therapy is to maintain sterile urine throughout pregnancy without causing toxicity to the mother or foetus.^[8]

The recommended antibiotics for use in pregnancy for the management of ASB include amoxicillin, oral cephalosporins and nitrofurantoin (50-100mg four times daily or 100mg twice daily for 3 days).^[9]

Recommended antibiotics for the treatment of lower UTI during pregnancy include the Food & Drug Administration (FDA) category B anti-microbials including penicillin's (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).

Acute pyelonephritis (Upper UTI) during pregnancy should be treated preferably with parenteral

cephalosporins, Penicillin's with beta-lactamase inhibitors or monobactams.^[10] The anti-biotic chosen should have a good maternal & foetal safety profile, excellent efficacy and low resistance rates in a given population.^[11] Anti biotics 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 anti-biotic susceptibility pattern is mandatory.^[12] The duration of therapy has been a topic of debate, and treatment duration varies from a single dose to one week.^[13] Although therapy should be guided by antimicrobial susceptibilities, many short course regimens have been shown to be effective in eliminating bacteriuria of pregnancy. Short course therapy (either 3 days or 7 days) seems more effective than single dose therapy in eradicating bacteriuria in non-pregnant and pregnant women because the drugs are rapidly cleared from the urine and failures may occur with single dose therapy. Apart from the duration of therapy, appropriate follow up should be done to document the elimination of bacteriuria.^[14] Regardless of whether a conventional course or a shorter course is given, primary treatment failures and relapses and re-infections should be treated with a 7-day course of a different agent according to in vitro susceptibility. Patients with repeated episodes should be given long term low dose prophylactic therapy.^[15] The practice of prescribing anti-bacterial drugs for pregnant women with UTI varies in different countries. Apart from economic factors, the problem of selecting an antibacterial agent for treatment of UTI in pregnancy is the possible confusion between a well-established and well tolerated drug and of proven safety

to the foetus, and also a drug to which there is a low level of resistance.^[16]

Data from the antibiotic usage study in UTI during pregnancy will help in establishing a proper antibiotic utilization guideline and will promote rational prescribing of medicines. No similar study has been conducted in this set up previously. Hence this study was carried out to evaluate the anti-microbial prescription practices for UTI during pregnancy.

Materials & methods

The study was conducted in the Department of Pharmacology and Department of Obstetrics and Gynaecology over a period of 12 months from 2012-2013. Pregnant subjects with or without urinary symptoms were recruited. Written informed consent was obtained from each subject prior to sample collection. Ethical clearance was obtained from the Ethics Committee prior to initiation of study. This was an observational cross-sectional study done in 45 pregnant subjects.

Inclusion Criteria

- Pregnant women with or without symptoms of UTI.

Exclusion Criteria

- Those on anti-microbial 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. They 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 labeled and immediately sent to the Medical Microbiology and Parasitology Laboratory within an hour of collection. Urine samples were examined microscopically and cultured. Urine culture was done to study the distribution of pathogens. The isolated organisms from culture plates were identified by standard laboratory techniques.^[17] Antimicrobial susceptibility testing was done by Kirby Bauer disc diffusion method as recommended by Clinical Laboratory Standards Institute (CLSI) M2-A9.^[18]

The antibiotic panel for each group of isolates were selected according to the CLSI guidelines.^[19] The pattern of antimicrobial usage for treatment of UTI during pregnancy was determined in terms of dose, route, frequency and duration. Anti-biotic susceptibility of uropathogens was identified on the basis of culture report. Subjects 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. Data was analyzed 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. Quantitative variables were presented in terms of mean, standard deviation and percentages. Descriptive statistics were used to analyze qualitative variables.

Results

The present study was carried out in the Department of Pharmacology and the Department of Obstetrics and

Gynaecology over a period of 12 months from 2012-2013. A total of 45 pregnant subjects were included in the study and followed up weekly till one month. Table 1 shows that out of 45 pregnant subjects, maximum subjects were found in 20-25 age group. Overall mean of age was 25.04 ± 3.29 years. Figure 1 shows that Nitrofurantoin was the most commonly prescribed antimicrobial followed by Cefuroxime axetil.

Table 2 shows that there was a wide variation in dose, duration, route and frequency for which an antibiotic was being prescribed for pregnant subjects with UTI. Nitrofurantoin was prescribed 100mg orally for 5 days while Cefuroxime axetil was prescribed 500mg orally for 5 days in majority of the cases.

Amoxicillin-clavulanic acid was prescribed maximally at a dose of 1.2g through injectable route for 4 days.

Cephalosporins, nitrofurantoin and amoxicillin-clavulanic acid were prescribed twice daily in majority of the cases.

Discussion

Pregnancy is a unique state with profound anatomic and physiologic urinary tract changes that facilitate the development of symptomatic urinary tract infections. Screening for ASB in pregnancy has become a standard of obstetric care and most antenatal guidelines include routine screening for ASB which is reliably and inexpensively done with a culture. The present study was conducted to analyze the pattern of antimicrobial usage prescribed for UTI during pregnancy.

In the current study maximum numbers of women were in the age group 20-25 years. Similarly Okonkwo and Ijandipe et al; and Olsen and Hinder Aker et al also showed that maximum number of women were in the age group 15-24 years.^[20] 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. The study of prescribing pattern is a component of medical audit, which seeks monitoring, evaluation in the prescribing practices of prescribers to achieve rational and cost-effective medical care. Various classes of antimicrobials were prescribed for UTI during pregnancy in the present study.

Cephalosporins were most frequently prescribed 41.7% followed by Nitrofurantoin 29.2%. Nitrofurantoin and Cefuroxime remains the drug of choice among the orally administered antibiotics each followed by cefuroxime axetil. This is in accordance with the standard treatment guidelines^[21] which includes cephalosporins and nitrofurantoin as oral choice of drugs for ASB and cystitis.

Nitrofurantoin, which was commonly prescribed in our study, was given in the dose of 100mg orally in all subjects. There were wide variations in duration and frequency of administration. Similarly there were wide variations for cefuroxime axetil and amoxicillin-clavulanic acid in terms of dose, duration, route and frequency. Similar trend was also observed in a study conducted by Mathai and Thomas et al.^[8] Despite a consistent spectrum of causative organisms and treatment objectives, antimicrobial regimens for uncomplicated UTI, including drug selection and duration of therapy vary widely. The consequences of this could be severe and need to be investigated. Nitrofurantoin is a narrow spectrum antimicrobial with no systemic activity.^[22]

It has been used for more than five decades for the treatment of uncomplicated cystitis and it was found to remain active against most of the uropathogens. Oral

nitrofurantoin is a good antibiotic choice for treatment of pregnant women with ASB. Similar pattern was also observed in the current study.

Cephalosporins are recommended for initiating therapy for pyelonephritis [23] and they were the most commonly used antimicrobials in the present study.

Clinical trials comparing cephalosporins with combination of ampicillin and gentamicin show that the latter probably is more cost effective in curing UTI [24] although ampicillin and gentamicin were not used in the present study.

With concerns about increasing resistance being common, “antimicrobial stewardship” (using antibiotics in a way that helps limit development of resistance) must also be considered. There has been no systematic review of which antibiotic is best for the treatment of ASB. Although many review articles suggest antibiotic regimens for both symptomatic and ASB in pregnancy, increasing antibiotic resistance complicates empirical regimens. 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. Data from the present study document many deficiencies in the current practices of antimicrobial therapy for UTI during pregnancy. Possible reasons may be lack of adequate knowledge about drugs and non-availability or non-accessibility of guidelines for therapy. The main limitation of the study was short duration and small number of pregnant subjects 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 and susceptibility pattern. The limited number of pregnant women in our study did not provide a significant link between the previously described risk factors like socioeconomic status, parity, diabetes, sickle cell disease, anatomic or functional abnormalities of urinary tract and the development of ASB and symptomatic bacteriuria which may require investigation using a larger cohort of women selectively drawn from different risk groups.

Further studies to determine the risk factors for Indian women may be deemed necessary as risk factors varied vastly between different geographical settings.

This study has highlighted the need to raise awareness of UTIs and to expand services for prevention and treatment of UTI in pregnant women.

To do this effectively, however, it may be necessary to improve the quality of health care provided at the community level.

The present study paved a way for future research on pregnant women with UTI in large samples and for longer duration, establishment of antibiotic guidelines focusing more on the duration of the therapy, prescription auditing and antibiotic susceptibility studies.

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 |

Figure 1: Distribution of various antimicrobials in pregnant subjects with UTI (n=45)

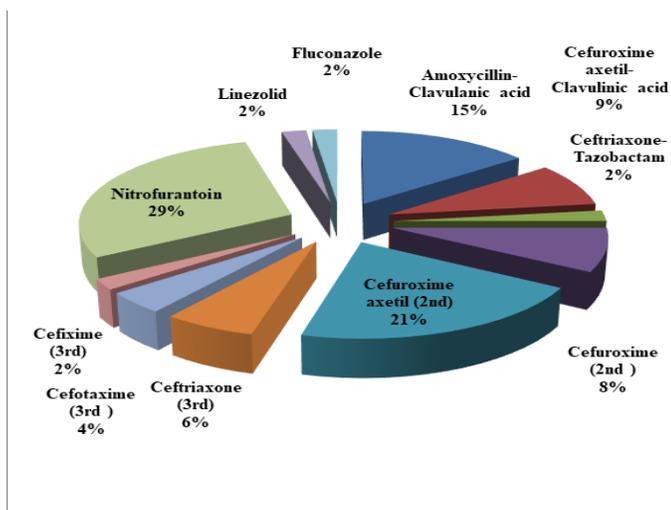


Table 2: Distribution of antimicrobials according to dose, duration and route in pregnant subjects (n=45)

| Antimicrobials (number of subjects prescribed) | Mean Dose (±SD) | Mean Duration (days) (±SD) | Mean frequency (±SD) | Oral | Injectable |
|--|-----------------|----------------------------|----------------------|------|------------|
| Amoxicillin-Clavulanic acid *# (7) | 268.5 (333.4) | 3.5 (0.9) | 2.3 (0.5) | 3 | 4 |
| Cefuroxime axetil-Clavulanic acid *# (4) | 187 (124.25) | 3.5 (1) | 1.75 (0.5) | 3 | 1 |
| Ceftriaxone-Tazobactam # (1) | 1 | 2 | 2 | - | 1 |
| Cefuroxime * (4) | 375 (144.3) | 4.5 (1) | 2 | 4 | - |
| Cefuroxime axetil *# (10) | 350.15 (174.4) | 5 (1.05) | 2 | 9 | 1 |
| Ceftriaxone # (3) | 1 | 4.3 (1.15) | 2.3 (0.6) | - | 3 |
| Cefotaxime # (2) | 1.1 (0.14) | 4.5 (0.7) | 2 | - | 2 |
| Cefixime* (1) | 200 | 5 | 2 | 1 | 0 |
| Nitrofurantoin* (14) | 100 | 8 (6.75) | 2.07 (0.7) | 14 | 0 |
| Linezolid* (1) | 600 | 2 | 2 | - | 1 |
| Fluconazole* (1) | 150 | 3 | 1 | 1 | - |

*Milligram

Gram

Conclusion

It is concluded from the present study that all pregnant women with UTI during pregnancy should be treated. It is imperative that early screening of bacteriuria in pregnancy must be considered as a part of routine antenatal care. Cephalosporins were most commonly prescribed antimicrobials followed by Nitrofurantoin. Dose, duration, route and frequency of administration varied between the drugs.

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