

Treatment of Urinary Tract Infection during Pregnancy

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ABSTRACT

Introduction: Pharmacotherapeutic treatment strategies of urinary tract infections (UTIs) in pregnancy needs legitimate diagnostic investigation and comprehensive knowledge of antimicrobial medications. This review aiming at obtaining the evidence about the effectiveness of antibiotic treatment for UTI among pregnant women that evaluated by included randomized controlled trials.

Methods: An Electronic search was conducted in Medline and Researchgate databases using simple search terms include (Pregnan* AND Infection AND Treatment). The search of the literature, after exclusion of irrelevant, duplicated and review studies, revealed 8 studies met the inclusion criteria.

Results: Most of the included studies used cephalosporins family of antibiotics. The cure rate of ceftibuten was 95.2% compared to 90% in fosfomycin. A cure rate of 96% after treatment by ceftriaxone and 94% after administration of cephazolin were reported. When gentamycin plus ampicillin used for the treatment of UTIs a cure rate of 93% was reported. **Conclusions:** This review found high effectiveness and cure rate of the antibiotics used in treatment of UTIs, however the recurrence rate varied between studied antibiotics. Nitrofurantoin and intravenous antibiotics reported very low recurrence rate in comparison to fosfomycin and cephalazolin with a clinically significant recurrence rate.

Keywords: Urinary Tract, Infections, Treatment, Antibiotics, Pregnancy.

INTRODUCTION

A definition UTIs is "the augmentation and multiplication of bacteria in the urinary tract," while the presence of bacteria in a collected urine sample is known as bacteriuria. Although all women are at risk to the advancement of UTIs, pregnant ladies are at higher risk than non-pregnant as a result of anatomical and hormonal differences which lead to ureteral dilatation and urinary stasis⁽¹⁾. The hormonal changes that associated with pregnancy may elevate the chance of getting UTIs include progesterone-mediated ureteral and vesicular smooth muscle relaxation⁽²⁾.

As pregnancy continued, from the sixth week to 22th to 24th week, around 90% of pregnant women infected by ureteral dilatation, which will continue to labor (pregnancy hydronephrosis)⁽³⁾. Elevated volume of bladder and reduced tone of bladder, along with reduced tone of ureters, lead to ureterovesical reflux and elevated urinary stasis⁽⁴⁾. Urinary tract infections, including pyelonephritis, are the most frequent health issues during pregnancy⁽⁵⁾. They occur in 17% to 20% of pregnancies. Pyelonephritis is the most frequent acute bacterial infection that contributes to perinatal and maternal inconveniences like premature labor, infants with low birth weight, fetal mortality, preeclampsia, pregnancy-initiated hypertension, anemia, thrombocytopenia, and transient renal inadequacy⁽⁶⁾. Enterobacteriaceae contribute to 90% of UTIs and the most effective antibiotics used are

Nitrofurantoin, Cefazolin, Cephalexin, Ceftriaxone, and Gentamicin. Pharmacotherapeutic treatment strategies of UTIs in pregnancy needs legitimate diagnostic investigation and comprehensive knowledge of antimicrobial medications to guarantee best maternal outcome, ensure wellbeing to the fetus, and avert drawbacks that lead to huge morbidity and mortality in both the woman and her fetus⁽⁷⁾.

Thu, schedule bacterial culture and antibiotic sensitivity test of mid-stream urine samples of pregnant ladies and other patients are recommended to be measured before the provision of the medications for the management of UTIs⁽⁸⁾. In this manner, development of uncommon microbial resistance among these strains could effortlessly be recognized, and thus, helped in better treatment and management of those contaminated by these bacteria⁽⁹⁾. This review aiming at obtaining the evidence about the effectiveness of antibiotic treatment for UTI among pregnant women that evaluated by included randomized controlled trials.

METHODS

Electronic search was conducted in Medline and Researchgate databases using simple search terms include (Pregnan* AND Infection AND Treatment). The search of the literature, after exclusion of irrelevant, duplicated and review studies, revealed 8 studies met the inclusion criteria. The relevant data were extracted from these articles using data extraction

sheet. Information about sample size, mean age of patients, the pregnancy trimester when treatment started, investigation of UTIs, symptoms of UTIs, antibiotic used for treatment infection, and the success rate of treatment.

The study was done after approval of ethical board of Umm Al-Qura University.

RESULTS

The search of the literature, after exclusion of irrelevant, duplicated and review studies, revealed 8 studies met the inclusion criteria. Included studies aimed to determine, from the best available evidence from randomized controlled trials (RCTs), which treatment is most effective for UTIs during pregnancy in terms of cure rates, recurrent infection, preterm delivery, premature rupture of membranes, admission to neonatal intensive care unit, need for change of antibiotic and incidence of prolonged pyrexia^(5, 10-14).

The number of patients recruited ranged from 41 pregnant women in the study by **Krcmery et al.**⁽⁵⁾ to 179 in the study by **Wing et al.**⁽¹⁴⁾. The total number of pregnant women in the included studies was 927. Only one study reported a mean age of the pregnant women

which was (22.5± 6.1) years old⁽¹³⁾. The reporting of pregnancy trimester in which treatment started found in four studies^(10-13, 15).

In regard to antibiotic treatment for UTIs among pregnant women, most of the included studies used cephalosporins family of antibiotics^(5, 10-14). However, the nitrofurantoin plus penicillin family used only by **Calderon-Jaimes et al.**⁽¹⁶⁾ for the treatment of urinary tract infection. Concerning effectiveness of antibiotics in the treatment of urinary tract infection, a cure rate of ceftibuten was found 95.2% compared to 90% in fosfomycin⁽⁵⁾. A cure rate of 96% after treatment by ceftriaxone and 94% after administration of cephalosporin were reported⁽¹³⁾. When gentamycin plus ampicillin used for the treatment of UTIs a cure rate of 93% was reported. The recurrence rate of UTIs was 4.76% with ceftibuten and 10% with fosfomycin⁽⁵⁾, while a recurrence rate of 0.16% and 0.9 was reported in nitrofurantoin, and intravenous antibiotics respectively⁽¹¹⁾. The recurrence rate in a study of **Wing et al.**⁽¹⁴⁾ was 5% with gentamycin plus ampicillin, 8% with cephalosporin, and 5% with ceftriaxone. Regarding reported secondary outcomes to the UTIs, 10% of women suffered pre-term delivery⁽¹⁴⁾.

Table 1: Summary of the findings

Study	Sample size	Time when treatment started	Types of UTIs	Symptoms	Antibiotic used for treatment of UTIs	Cure rate	Other important outcomes
Krcmery et al. ⁽⁵⁾	41 pregnant women	Not reported	Acute cystitis	Symptoms of lower UTI (dysuria, urgency, frequency, and suprapubic pain)	Fosfomycin, trometamol, and ceftibuten	Cure rate (sterile urine or growth < 10 ³ CFU/ml) (20/21 (95.2%) vs 18/20 (90.0%))	Persistence (growth of original bacterial strain ≥ 10 ³ CFU/ml) (1/21 (4.76%) vs 2/20 (10%))
Brost et al. ⁽¹¹⁾	67 pregnant women	22 weeks of gestation	Pyelonephritis	Symptoms of oral temperature of 38°C or greater, costovertebral angle tenderness.	Intravenous cephalosporin only or cephalosporin plus gentamicin or cephalosporin plus other antibiotic or ampicillin plus gentamicin or other antibiotic study group received nitrofurantoin The control group received no further oral antibiotic therapy	Cure rate in intravenous antibiotics plus nitrofurantoin cure rate=94%, in antibiotics only =87%.	Recurrent infection in intravenous antibiotics plus nitrofurantoin =16% and in intravenous antibiotics only = 9%

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Sanchez-Ramos <i>et al.</i> ⁽¹³⁾	178 pregnant women	23.6 to 24.1 weeks of gestation	Pyelonephritis E.coli	Febrile patients (temperature of 2 100.4" F) with chills and costovertebral angle tenderness	Ceftriaxone versus Cefazoline	Cure rates (ceftriaxone 96%, cefazolin 94%)	Recurrent pyelonephritis (ceftriaxone 48%, cephazolin 66%) and preterm delivery (ceftriaxone 10%, cephazolin 9%)
Ahmadinejad and Hantoooshzadeh ⁽¹⁰⁾	128 pregnant women	24 weeks of gestation	Acute pyelonephritis	Not reported	patient ceftriaxone versus inpatient ceftriaxone	Cure rate of initial treatment (inpatient= 86%) (outpatient =94%)	Recurrent pyelonephritis (Inpatient= 11%), (outpatient= 25%). Preterm delivery (inpatient=19%) (outpatient= 13%)
Ovalle <i>et al.</i> ⁽¹²⁾	111 pregnant women	Between 12 and 34 weeks of gestation	Acute pyelonephritis	Fever greater than 38°C, chills, low back pain	Cephadrine Cefuroxime	CFX is a more efficient therapy that CPD, with similar costs	Microbiological cure rate, clinical cure rate, recurrent infection, bacteriological failure rate, clinical cure failure
Calderón <i>et al.</i> ⁽¹⁶⁾	103 pregnant women	Not reported	Acute cystourethritis	Symptoms of dysuria, frequency, suprapelvic pain or tenderness	Nitrofurantoin versus ampicillin	Both regimens showed similar effectiveness with regard to cure rates, recurrence and treatment failure	Postpartum outcomes from each group were not presented
Wing <i>et al.</i> ⁽¹⁴⁾	179 pregnant women	Earlier than 24 weeks of gestation	Pyelonephritis	Fever, and costovertebral angle tenderness	Ampicillin with gentamicin versus cephazolin Versus ceftriaxone and cephalexin	Cure rates in ampicillin plus gentamicin= 93%, in cephazolin= 94.8%, in ceftriaxone= 16%);	Recurrent pyelonephritis in ampicillin plus gentamicin=5%, in cephazolin=8%, ceftriaxone=5%
Millar <i>et al.</i> ⁽¹⁵⁾	120 pregnant women	24 weeks of gestation	Pyelonephritis	Fever, flank pain, or costovertebral angle tenderness.	Ceftriaxone and cephalexin compared in outpatient and inpatient administration.	Cure rates in outpatients= 95%, in inpatients= 88%.	Recurrent pyelonephritis rate in inpatients=5%, and in outpatients=5%.

DISCUSSION

This review aimed to determine the effectiveness of the treatment of symptomatic UTIs during pregnancy in terms of cure rates, recurrent infection, and incidence of preterm delivery. Eight randomized controlled trials were included, where the intention was to allocate participants randomly to one of at least two alternative treatments for any symptomatic urinary tract infection. The critical appraisal of the included

studies revealed that all included trials have small sample size (<180) to detect significance differences between different treatment options. It is important to take into account that, in equivalence trials, failure to detect a difference does not imply equivalence between both treatments. Equivalence trials generally need to be larger than trials aimed to show that one treatment is better than other, because differences are

expected to be small, and therefore, bigger numbers are needed to increase statistical power for detection of any significant difference⁽³⁾. In all of the included studies, sample sizes were insufficient to detect at least a 10% difference in cure rates between 95% and 85%, which was considered the principal outcome for the review. To detect such difference, it would have been necessary to recruit at least 137 patients in each group, not taking into account dropouts and losses to follow-up⁽⁵⁾. In addition, the critical appraisal showed liability of selection bias in a study of **Ovalle *et al.***⁽¹²⁾ and unclear risk of bias related to allocation sequence in 3 studies^(5, 10, 11), which would significantly undermine the validity of conclusion made by these trials.

Finally the included studies were heterogeneous and in comparable in terms of antibiotics used for the treatment, their efficacy, route of administration, tolerability and side effects which fail to detect evidence of inferiority, data from non-pregnant women should be included which may be useful for decision-making in the absence of adequate data from pregnant women, but it is very important to take into account the quite different pharmacodynamics of some drugs during pregnancy in order to gather more information on comparative efficacy of different antibiotics used for symptomatic UTIs⁽⁷⁾. Most studies found a cure rate ranged between 90% - 96% of antibiotics such as cefitibuten, fosfomycin, ceftriaxone, cephazolin, gentamycin and ampicillin. However, a wide variation was reported in the recurrence rate of UTIs. It ranged from 0.16% to 0.9% in nitrofurantoin and intravenous antibiotics to 5% with gentamycin, ampicillin, and ceftriaxone to 8% and 10% in fosfomycin and cephazolin. This high recurrence rates can be attributed to the reduction in immunity status of pregnant women⁽⁹⁾.

CONCLUSION

This review found high effectiveness and cure rate of the antibiotics used in treatment of UTIs, however the recurrence rate varied between studied antibiotics. Nitrofurantoin and intravenous antibiotics reported very low recurrence rate in comparison to fosfomycin and cephazolin with a clinically significant recurrence rate. The lack of primary data with good quality and appropriate sample size, it is not possible to draw reliable conclusions on which is the best class, route or regimen of antibiotic to treat symptomatic UTIs during pregnancy. This review could not show that one treatment regimen is better than another.

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