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Antibiotics Used in Pregnency for Urinary Tract Infection

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ABSTRACT :
Urinary tract infections (UTIs) are common in pregnant women and pose a great therapeutic challenge, since the risk of serious complications in both the mother and her child is high. Pregnancy is a state associated with physiological, structural and functional urinary tract changes which promote ascending infections from the urethra. Unlike the general population, all pregnant women should be screened for bacteriuria with urine culture, and asymptomatic bacteriuria must be treated in every case that is diagnosed, as it is an important risk factor for pyelonephritis in this population. The antibiotic chosen should have a good maternal and fetal safety profile. In this paper, current principles of diagnosis and management of UTI in pregnancy are reviewed, and the main problems and controversies are identified and discussed.

KEYWORDS: pregnancy, asymptomatic bacteriuria, symptomatic bacteriuria, acute cystitis.

I. INTRODUTION :

Urinary tract infections (UTIs) in pregnant women continue to pose a clinical problem and a great challenge for physicians. Although the incidence of bacteriuria in this population is only slightly higher than in non-pregnant women, its consequences for both the mother and the unborn child are more severe. There is a much higher risk (up to 40%) of progression to pyelonephritis, and possibly increased risk of pre-eclampsia, premature birth and low neonatal birth weight [1]. That is related to profound structural and functional urinary tract changes, typical for pregnancy. In about % of pregnant women dilation of the urinary tract combined with slight hydronephrosis is observed, caused partly by a reduction in smooth muscle tone with slowing of ureteral peristalsis, and partly by urethral sphincter relaxation. This may be due to high levels of circulating progesterone [2]. Simultaneously, the enlarged uterus compresses the urina9999ry bladder, thus increasing the intravesical pressure, which may result in vesico-ureteral reflux and urine retention in the bladder after miction, commonly observed in pregnant women. Urinary stasis and impairment of the physiological anti-reflux mechanism create conditions favorable for bacterial growth and ascending infection. The additional predisposing factors include pregnancy-specific biochemical changes in urine, with higher amounts of glucose, amino acids and hormone degradation products, which increase urinary pH [3]

EPIDEMIOLOGY:

Urinary tract infections remain among the most common medical complications during pregnancy. It is estimated that the prevalence of ASB varies between 2% and 10–13%, similar to nonpregnant women [4]. There is a scarcity of data concerning acute cystitis in pregnancy; according to the available studies it is observed in 1–4% [5]. The prevalence of acute pyelonephritis in most reports ranges from 0.5% to 2% of pregnancies [6].

Many women acquire bacteriuria before pregnancy [7]. A large retrospective analysis with logistic regression modeling, embracing 8037 women from North Carolina, revealed that the two strongest predictors of bacteriuria at prenatal care at prenatal care initiation were: UTI prior to prenatal care initiation (OR = 2.5, 95% CI: 0.6–9.8 for whites, and OR = 8.8, 95% CI: 3.8–20.3 for blacks) and a pre-pregnancy history of UTI (OR = 2.1, 95% CI: 1.4–3.2) [8]. In a second analysis, prior antenatal UTI was found to be the strongest predictor of pyelonephritis after 20 weeks' gestation (OR = 5.3, 95% CI: 2.6–11.0) [9]. Other suggested risk factors for UTI during pregnancy are lower socioeconomic status, sexual activity, older age, multiparity, anatomical urinary tract abnormalities, sickle cell disease and diabetes, although the significance of some of them (age, parity or sickle cell trait) remains a matter of controversy [10].

PATHOGENESIS:

Pregnant women are at increased risk for UTIs. Beginning in week 6 and peaking during weeks 22 to 24, approximately 90 percent of

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pregnant women develop ureteral dilatation, which will remain until delivery (hydronephrosis of pregnancy). Increased bladder volume and decreased bladder tone, along with decreased ureteral tone, contribute to increased urinary stasis and ureterovesical reflux. Additionally, the physiologic increase in plasma volume during pregnancy decreases urine concentration. Up to 70 percent of pregnant women develop glycosuria, which encourages bacterial growth in the urine. Increases in urinary progestins and estrogens may lead to a decreased ability of the lower urinary tract to resist invading bacteria. This decreased ability may be caused by decreased ureteral tone or possibly by allowing some strains of bacteria to selectively grow. These factors may all contribute to the development of UTIs during pregnancy.

BACTERIOLOGY:

The organisms that cause UTIs during pregnancy are the same as those found in nonpregnant patients. Escherichia coli accounts for 80 to 90 percent of infections. Other gram-negative rods such as Proteus mirabilis and Klebsiella pneumoniae are also common. Gram-positive organisms such as group B streptococcus and Staphylococcus saprophyticus are less common causes of UTI. Group B streptococcus has important implications in the management of pregnancy and will be discussed further. Less common organisms that may cause UTI include enterococci, Gardnerella vaginalis and Ureaplasma ureolyticum.reus (up to 8%), and group B streptococci (GBS) (2–7%) [11].

CONSEQUENCES OF URINARY TRACT INFECTION IN PREGNANCY:

ASYMPTOMATIC BACTERIURIA:

The only serious maternal consequence of untreated ASB in pregnant women is a significant risk of acute pyelonephritis in later pregnancy (30–40% vs. 3–4% in treated patients) [12]. The results of the studies on perinatal outcomes of untreated ASB are controversial. Although a number of them demonstrated a relationship of ASB in pregnant mothers and the risk of premature delivery and/or lower birth weight, some other studies failed to prove the association [13].

The Cochrane Library meta-analysis revealed that antibiotic treatment was effective in reducing the incidence of low-birth-weight infants but not of preterm deliveries . However, the authors stressed the poor methodological quality of the available studies, their different design, lack of sufficient information about the randomization methods, different definitions used, low statistical power and some substantial biases, urging caution in drawing conclusions. A good example of these problems is presented by the Cardiff Birth Survey [14]. In a prospectively studied large cohort of 25 844 pregnancies, several demographic, social and medical factors (including bacteriuria) were significantly associated with preterm birth in the initial univariable analyses. However, after adjustments for other medical factors, bacteriuria retained an association of only borderline significance, and after further adjustment for demographic and social factors, the relationship completely disappeared. The results of the second analysis of the same cohort, aimed to compare associations of studied factors with spontaneous vs. indicated preterm birth, are even more interesting . Two separate multiple logistic regression analyses revealed that spontaneous and indicated preterm births have different overall profiles of risk factors, and only the last of them was associated with bacteriuria. The authors concluded that ASB, if it does not progress to symptomatic UTI, is not associated with preterm delivery.

Maternal GBS bacteriuria in a pregnant woman is considered a marker for genital tract colonization with this organism which poses a significant risk of preterm rupture of the membranes, premature delivery and early-onset severe neonatal infection .

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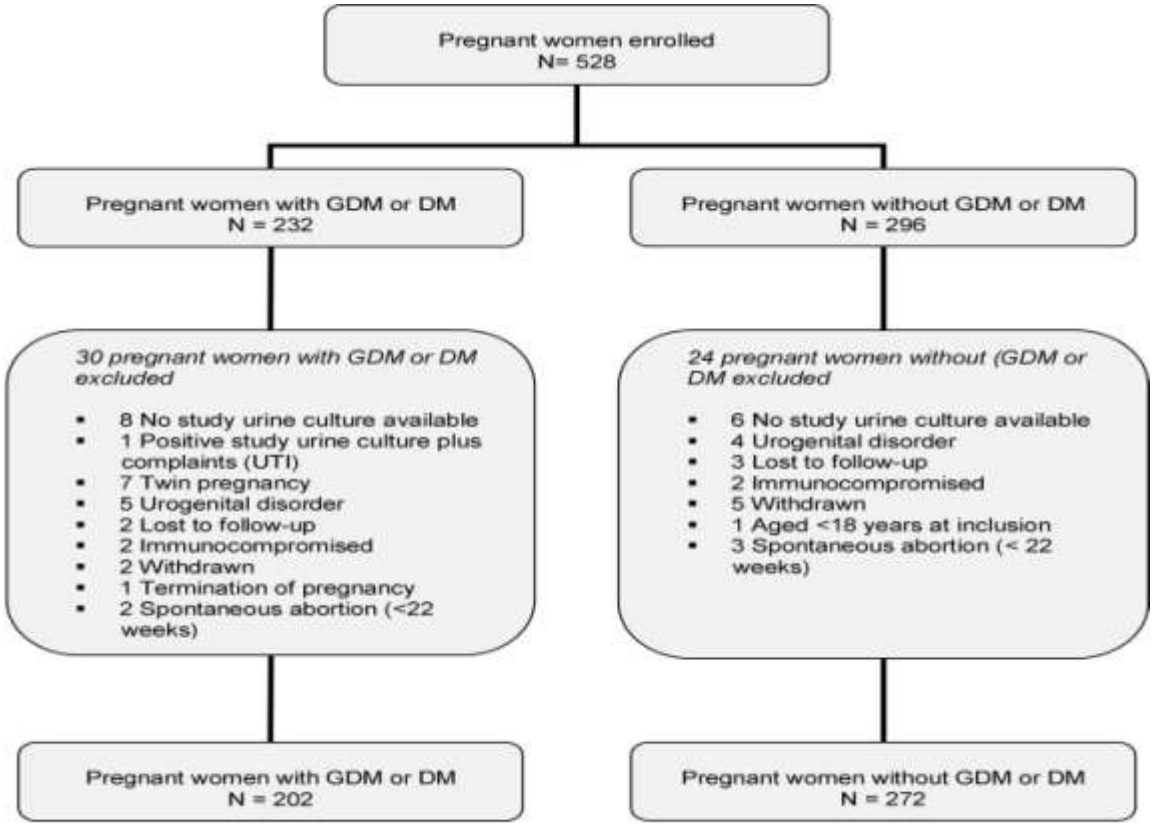

Abbreviations: (G)DM =(gestational) diabetes mellitus; UTI = urinary tract infection

FIG;1 Asymptomatic bacteriuia UTI for pregnancy

About 15–20% of women with pyelonephritis have bacteremia [15]. They may develop various complications, such as acute kidney injury, anemia, hypertension, preeclampsia, sepsis and septic shock, hemolysis, thrombocytopenia, and acute respiratory distress syndrome, particularly if treatment is initiated too late. Although these associations have not always been proved to be causal, most of the complications seem to be due to renal or other tissue damage caused by bacterial endotoxins and a systemic inflammatory response with endothelial injury .

SYMPTOMATIC URINARY TRACT INFECTION:

A number of observational studies have demonstrated the relationship between maternal symptomatic UTI and the risk of premature delivery and lower birth weight . The frequency of preterm deliveries in women with acute pyelonephritis is significantly higher than in women free of this complication, and pyelonephritis seems to be an important independent risk factor for delivery before 37 weeks' gestation . However, again, a substantial heterogeneity between these studies, together with many possible biases, makes it difficult to establish the overall contribution of UTI to preterm birth . A rare but severe complication is the transmission of the infection onto the newborn baby Very often the transmittedDuring Pregnancinfection originates from a heavily colonized birth canal, usually with GBS .

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ANTIBIOTIC USED IN UTI FOR PREGNANCY:

TABLE: 1 ANTIBIOTICS USED IN PREGNANCY FOR UTI :

Antibiotic	Pregnancy category	Dosage
Cephalexin (Keflex)	B	250 mg two or four times daily
Erythromycin	B	250 to 500 mg four times daily
Nitrofurantoin (Macrodantin)	B	50 to 100 mg four times daily
Sulfisoxazole (Gantrisin)	C*	1 g four times daily
Amoxicillin-clavulanic acid (Augmentin)	B	250 mg four times daily
Fosfomycin (Monurol)	B	One 3-g sachet
Trimethoprim-sulfamethoxazole (Bactrim)	C†	160/180 mg twice daily

SAFETY OF ANTI MICROBIAL TREATMENT:

TABLE:2 US Food and Drug Administration (FDA) categories of medications in pregnancy

Antibiotic	FDA risk category	Antibiotic	FDA risk category
Amoxicillin	B	Trimethoprim/sulfamethoxazol	C
Cephalosporins	B	Ciprofloxacin	C
Piperacillin/tazobactam	B	Levofloxacin	C
Daptomycin	B	Imipenem/cilastatin	C
Azithromycin	B	Linezolid	C
Erythromycin	B	Clarithromycin	C
EnemMerop	B	Spiramycin	C
Clindamycin	B	Gentamycin	C
Nitrofurantoin	B	Amikacin	D
Vankomycin iv.	B	Tobramycin	D
Metronidazol iv.	B	Netilmycin	D
Trimethoprim	c	Tetracyclines	D

A – Well-controlled studies available in humans with no adverse effects observed in human pregnancies; B – No adverse effects in well-controlled studies of human pregnancies with adverse effects seen in animal pregnancies OR no adverse effects in animal pregnancies without well-controlled human pregnancy data available; C – Human data lacking with adverse pregnancy effects seen in animal studies OR D – Adverse effects demonstrated in human pregnancies; benefits of drug use may outweigh the associate d risks [16]

SYMPTOMS:

A person who has a UTI may experience the following symptoms:

- urgent or frequent need to urinate
- burning sensation when urinating
- cloudy or strong smelling urine
- blood in the urine
- pain in the lower back, abdomen, and sides

People should tell their doctor straight away if they have blood in their urine, as this can be a sign of another condition.

In some cases, the bacterial infection causing a UTI can spread to the kidneys. A person who has a kidney infection may experience the following symptoms:

- back pain

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- fever
- chills
- nausea and vomiting

If people have these symptoms, they should see their doctor immediately. Kidney infections can be serious and require immediate medical treatment

TREATMENT:

Pregnant women should see their doctor if they have any symptoms of a UTI. Without treatment, a UTI can cause serious complications.

A 3-dayTrusted Source course of antibiotics may be necessary to treat a UTI during pregnancy. A doctor may prescribe one of the followingTrusted Source antibiotics:

- amoxicillin
- ampicillin
- cephalosporins
- nitrofurantoin
- trimethoprim-sulfamethoxazole

The American College of Obstetricians and Gynecologists (ACOG) advise that pregnant women avoid nitrofurantoin and trimethoprim-sulfamethoxazoleTrusted Source during the first trimester. These antibiotics can cause birth abnormalities if a person takes them at this stage of their pregnancy.

According to a 2015 reviewTrusted Source, studies show that both nitrofurantoin and trimethoprim-sulfamethoxazole are generally safe during the second and third trimesters. However, taking either antibiotic in the final weekTrusted Source before delivery may increase the risk of jaundice in newborns[17].

If pregnant women develop a kidney infection during pregnancy, they will need treatment in the hospital. This treatment will involve antibiotics and intravenous fluids.

A short course of antibiotics is unlikelyTrusted Source to cause any harm to a developing fetus. Research suggests that the benefits of taking antibiotics to treat a UTI far outweighTrusted Source the risks of leaving a UTI without treatment.

The presence of ASB in a pregnant woman is an absolute indication for initiation of the treatment. The benefits of such a strategy with bacteriological follow-up were summarized by Smaill and Vazquez for the Cochrane Library, on the basis of the results of 14 RCTs, embracing 2302 pregnant women with ASB, in which the effects of different antibiotics given for different duration were compared to placebo or untreated groups[18]

DIAGNOSIS OF URINARY TRACT INFECTION:

ASYMPTOMATIC BACTERIURIA:

CYSTITIS/URETHRITIES:

DIAGNOSIS:

The diagnosis is made on the basis of symptoms (cloudy urine, dysuria, frequency, urgency, abdominal or suprapubic pain) and the presence of even small bacterial colony counts ($\geq 10^2$–10^3 CFU/ml) .

MANAGEMENT:

In most cases of lower UTI, the treatment is similar to that used in ASB (Table II) and should be guided by antimicrobial susceptibility testing. The optimal duration of treatment is unknown, but longer courses (5–7 days) of the therapy are generally suggested Follow-up urine cultures are recommended 1–2 weeks after the treatment and then once a month. In women receiving chronic immunosuppression, management discussed in the section on ASB should be followed. In women with recurrent acute cystitis, antimicrobial urinary suppression based on daily use of a small dose of antibacterial drug during the symptom-free period is recommended or, in the case of an evident relationship of the disease with sexual activity, only after intercourse (e.g. nitrofurantoin 50–100 mg, cephalexin 250–500 mg) [19].

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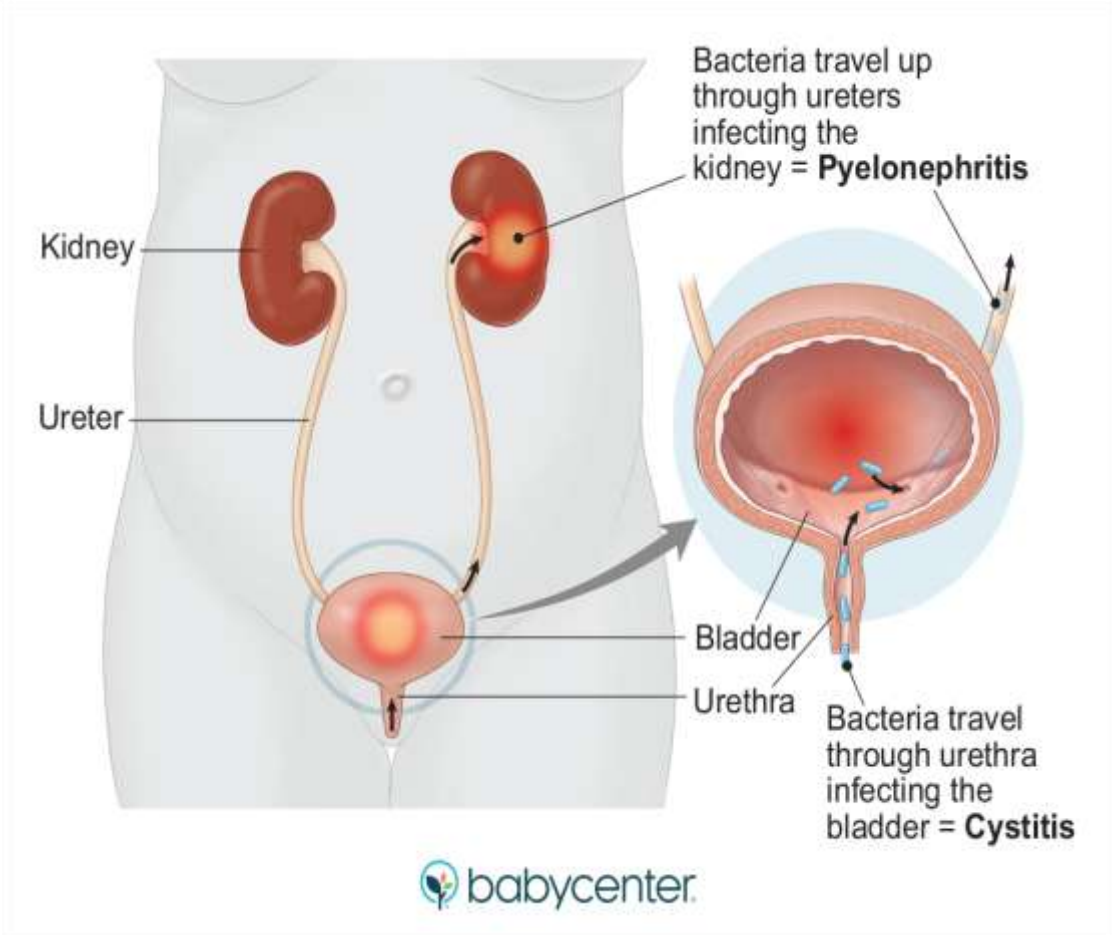

FIG;2 UTI IN PREGNANCY.

HOME REMEDIES:

Women who are pregnant and have symptoms of a UTI should see a doctor. As well as medical treatment, they may also wish to try the following at home to help speed up recovery:

- Drinking plenty of water: Water dilutes urine and helps flush bacteria out of the urinary tract.
- Drinking cranberry juice: According to a 2012 reviewTrusted Source, cranberries contain compounds that may help to stop bacteria from attaching to the lining of the urinary tract. This action helps to prevent and eliminate infection.
- Urinating when the urge arises: This helps bacteria pass out of the urinary tract more quickly.
- Taking certain supplements: A 2016 studyTrusted Source found that a combination of vitamin C, cranberries, and probiotics may help to treat recurrent UTIs in women.

Some women may choose the above treatments as an alternative to antibiotics. However, they should always consult their doctor before doing so. A doctor will monitor a pregnancy regularly to check the effectiveness of natural treatments and ensure a UTI does not worsen.[20]

II. CONCLUSION:

The use of antibiotics in pregnancy requires careful assessment and a discussion of risk versus benefit to mother and fetus, both short and long term. In general, many antibiotics are considered safe in pregnancy, especially beta-lactams, macrolides, clindamycin, and fosfomycin; however, additional data are needed for the majority of antibiotic classes. Emerging antibiotic resistance will certainly play a role in future use of broad-spectrum and alternative agents in pregnancy. Pharmacists play a prominent role in risk assessment and evaluation of available evidence for optimal antibiotic selection, dosing, duration of therapy, and monitoring. Pharmacists should also be aware of the new detailed product labeling for pregnancy that was implemented in the summer of 2015.

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