Association Between Urinary Tract Infection in Pregnant Women

Research Project

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Abstract

Urinary tract infection (UTI) is a common problem during pregnancy, affecting about 8% of pregnancies worldwide. This study examines pregnant women's knowledge and attitudes concerning UTIs. UTIs are caused by infections, primarily bacteria like Escherichia coli, that travel from the urethra to the bladder and kidneys. Physiological changes during pregnancy, such as ureteral dilation and urine stasis caused by elevated progesterone levels, enhance the incidence of UTIs. Asymptomatic bacteriuria is a major risk factor, and if left untreated, it can escalate to symptomatic infections, causing maternal and fetal problems. Screening for asymptomatic bacteriuria is advised during prenatal care visits. The diagnosis is based on symptoms, urine dipstick testing, and urine cultures. Treatment and prognosis vary according on the severity of the infection, which can range from asymptomatic bacteriuria to severe cystitis and pyelonephritis. Understanding pregnant women's knowledge and attitudes concerning UTIs is critical for developing effective preventive and management plans.

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1. Introduction

Urinary tract infection (UTI) is one of the most common infective sequels associated with pregnancy. The urinary tract is the system that includes kidneys, ureters, bladder and urethra (Thalava, 2021). Globally, urinary tract infection and its associated problems are the cause of nearly 150 million deaths per year. The disease can progress in 40-50% of women Urinary tract infection (Nwosu et al., 2015). (UTI) is one of the more common perinatal complications, affecting approximately 8% of pregnancies (Graseck et al., 2023). This is because pregnancy is associated with a rapid increase in progesterone levels which leads to ureteric dilatation and urinary stasis which increases the risk of bacteriuria. Mechanical pressure from the gravid uterus and the physiological changes that occur in pregnancy further increase the risk of asymptomatic bacteriuria and in turn ascending infection (Amer and Almasri, 2023). Urinary tract infections (UTIs) are infections that can occur in the urethra (urethritis), bladder (cystitis), or kidneys (pyelonephritis) (McCann et al., 2020, Flores-Mireles et al., 2015). The urinary system plays a key role in removing the waste products of metabolism from the bloodstream. Other important functions performed by the system are the normalization of the concentration of ions and solutes in the blood and the regulation of blood volume and blood pressure (Mancuso et al., 2023). In healthy people, urine is sterile or contains very few microorganisms that can cause an infection (Wolfe and Brubaker, 2015). The probability of bacteria reaching the bladder before getting removed by urination are greater in women as the space between the opening of the urethra and the bladder is shorter. The chances of development of bacterial colonies are greater in women because of the presence of vaginal cavity and the close proximity of the rectum to the urethral opening. Another significant fact about these bacterial colonies is that even if they reach the urinary bladder where they get a chance to multiply, the symptoms of UTIs are seldom visible(Kaur and Kaur, 2021). As many UTIs are initially asymptomatic, checking pregnant women's urine for asymptomatic bacteriuria (ASB) is recommended in many countries as 20-30% of patients showing ASB are at risk of subsequently developing symptomatic kidney infections (Balachandran et al., 2022).

Chronic UTIs are microbiologically and immunologically intricate. Little is known regarding the etiopathogenesis or the role of the host immune system in the natural history, progression, and resolution of this disease in humans. The pathogenesis of infection is muddied by the multiplicity of pathogenic and commensal organisms found in the urinary tract and their virulence mechanisms capable of circumventing immune detection. The urinary bladder also

appears to exhibit an atypical adaptive immune response to infection (Chan et al., 2013, Wu et al., 2020).

The pathogens that cause UTI in pregnancy are the same as in the general population, especially bacteria of bowel provenance. Dominantly involved are Gram-negative bacilli as *Escherichia coli* (75-90%), Proteus mirabilis, *Klebsiella pneumoniae* and Gram-positive cocci (5%) as Enterococcus, Group B (Glaser and Schaeffer, 2015, Nelson-Piercy, 2020, Koirokpi et al., 2020). Factors that have been associated with a higher risk of bacteriuria include history of prior urinary tract infection, pre-existing diabetes mellitus, increased parity, and low socioeconomic status (Michelim et al., 2016).This pathology can be at the origin of multiple feto maternal complications (acute pyelonephritis, maternal sepsis, premature birth, intrauterine growth restriction – IUGR), fact that justifies the systematic screening during pregnancy. Common symptoms of UTI include high frequency of urination and pain associated with burn sensation when discharging urine (Glaser and Schaeffer, 2015). Severe UTI forms can also associate fever, nausea, vomiting and chills (Glaser and Schaeffer, 2015, Ghouri and Hollywood, 2020)

Diagnosis of UTI is traditionally based on presence of typical symptoms, positive urine dipstick and growth of uropathogenic bacteria on urine culture (Edwards et al., 2023)**.**The treatment and the prognosis differ according to the gravity, as UTI can be divided in asymptomatic bacteriuria, acute cystitis and acute pyelonephritis (Glaser and Schaeffer, 2015, Nelson-Piercy, 2020, Koirokpi et al., 2020).

Aim of the study This study aimed to assess knowledge And attitudes among pregnant women regarding Urinary tract infection

2. Literature review

2.1 Definition

Biology of urinary tract Urinary tract infection affects the parts of the urinary tract which includes the upper and lower urinary tract and the occurrence is high in females due to their reproductive anatomy (Vasudevan, 2014). Urinary tract infections (UTIs) are the inflammatory disorders of the urinary tract caused by the abnormal growth of pathogens (Nicolle, 2016). Urinary tract infection (UTI) is a collective term that describes any infection involving any part of the urinary tract, namely the kidneys, ureters, bladder and urethra. The urinary tract can be divided into the upper (kidneys and ureters) and lower tract (bladder and urethra) (Odoki et al., 2019)Urinary tract infection (UTI) is one of the most common infective sequels associated with pregnancy (Thalava, 2021).Urinary tract infections (UTIs) are the second most common ailment of pregnancy after anemia and, at the same time, the most common type of infection during pregnancy (Amiri et al., 2015).

2.2 Epidemiology

Incidence of bacteriuria in pregnant women is roughly the same as in non-pregnant women; however, recurrent bacteriuria is more frequent during pregnancy. Additionally, the incidence of pyelonephritis is higher than in the general population, likely as a result of physiologic changes in the urinary tract during pregnancy (Michelim et al., 2016). UTIs are studied to be 14 times more frequent in women than in men. Bacteriuria occurs in 2 to 7 percent of pregnancies, particularly in multiparous women, a similar prevalence as seen in non-pregnant women. The prevalence of UTI during pregnancy increases with maternal age. As the organisms responsible for infection (in terms of species and virulence factors) are observed to be same in pregnant and non -pregnant women, the basic mechanism of entry of bacteria into the urinary tract is likely to be the same for both groups (Rahiman et al., 2015). The most significant factor predisposing women to UTI in pregnancy is asymptomatic bacteriuria (ASB). ASB is defined as more than 100,000 organisms/mL on a clean catch urinalysis obtained from an asymptomatic patient. The rate of asymptomatic bacteriuria in non-pregnant women is 5% to 6% which compares similarly to estimated rates in pregnancy of 2% to 7%. ASB is seen more frequently in parous women and women of low socioeconomic status. Women who are carriers for sickle cell trait also have a higher incidence of ASB (Hudson et al., 2022). Bacteriuria often develops in the first month of pregnancy and is frequently associated with a reduction in

concentrating ability, suggesting involvement of the kidney. The smooth muscle relaxation and subsequent ureteral dilatation that accompany pregnancy are thought to facilitate the ascent of bacteria from the bladder to the kidney. As a result, bacteriuria during pregnancy has a greater propensity to progress to pyelonephritis (up to 40 percent) than in non-pregnant women (Rahiman et al., 2015)

2.3 Types of urinary tract infection

Can be classified into asymptomatic or symptomatic , "Asymptomatic bacteriuria is defined as growth of same species of more than 105 colonies/ ml of urine in a clean catch midstream urine sample in women without any symptoms (Nalam and Gopalan, 2021). If asymptomatic bacteriuria is untreated in pregnancy, the rate of subsequent UTI is approximately 25%. Due to both to the high rate and potential seriousness of pyelonephritis, it is recommended that all pregnant women be screened for ASB at the first prenatal visit. This is most often done with a clean catch urine culture (Hudson et al., 2022). Asymptomatic bcateriuria rates in the pregnant and non-pregnant population are similar, however bacteriuria during pregnancy has a greater tendency to progress to ascending infection than in the non-pregnant woman (Amer and Almasri, 2023). This is because pregnancy is associated with a rapid increase in progesterone levels which leads to ureteric dilatation and urinary stasis which increases the risk of bacteriuria. Mechanical pressure from the gravid uterus and the physiological changes that occur in pregnancy further increase the risk of asymptomatic bacteriuria and in turn ascending infection (Amer and Almasri, 2023). Symptomatic urinary tract infections are further divided:

Upper urinary tract infection: pyelonephritis or infection involving kidney and urethra (Urethritis):

- Pyelonephritis is a condition suggested when at least 100,000 bacteria /mL of a single uropathogen in a midstream MSSU culture is identified with associated inflammation of the renal parenchyma, calices and pelvis in the presence of systemic illness. It can progress to maternal sepsis, preterm labor and premature delivery. Symptoms include flank or renal angle pain, pyrexia, rigor, chills, nausea, vomiting and hip pain. Symptoms of lower tract infection, such as frequency and lack of urination, may or may not be present (Rahiman et al., 2015).

- Urethritis is the Infection of urethra with bacteria, protozoa, viruses, or fungi. This occurs when organisms gain an access to it periurethral glands in the bulbous and pendulous portions of the male urethra and in the entire female urethra (Rahiman et al., 2015).

Lower urinary tract infection: cystitis or infection of urinary bladder

- Cystitis is the infection of bladder, it is more common in women, in whom cases of uncomplicated cystitis are usually preceded by sexual intercourse. It is also defined as significant bacteriuria with associated bladder mucosal invasion, and is distinguished from asymptomatic bacteriuria by the presence of symptoms such as dysuria, urgency, frequency, nocturia, haematuria and suprapubic discomfort in afebrile women with no evidence of systemic illness (Rahiman et al., 2015).

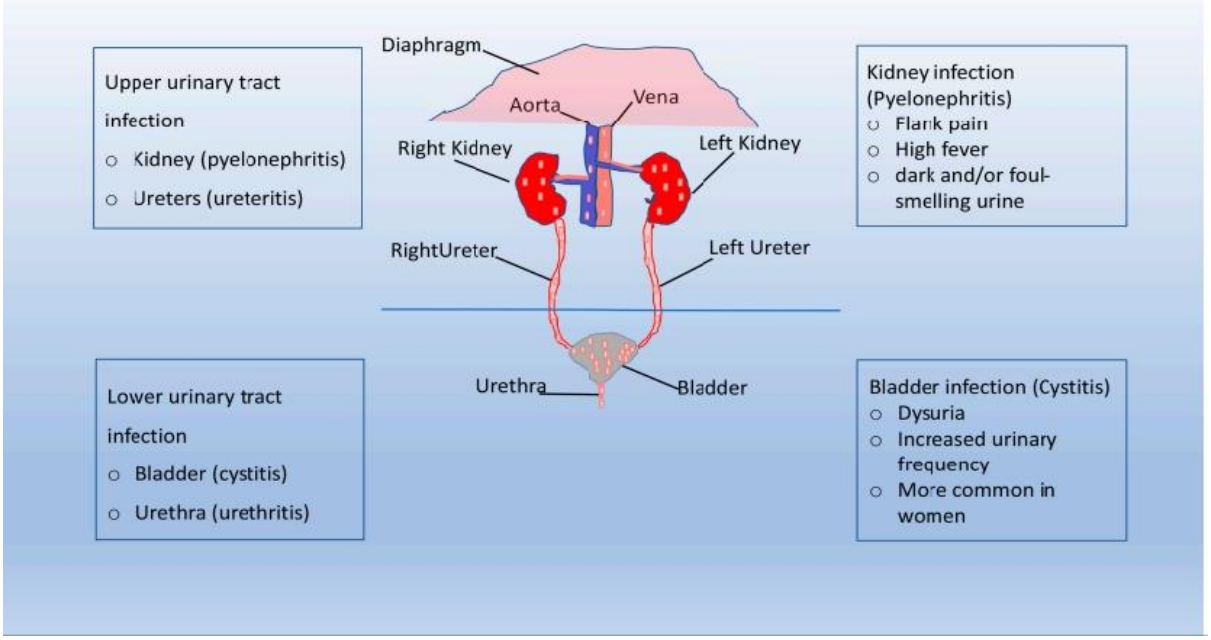

Figure 1. Types of urinary tract infection and Pathogenesis of UTI (Mancuso et al., 2023).

2.4 Symptoms of UTIs

Common symptoms during pregnancy include nausea, vomiting, frequent urination, dysuria, early birth, and low birth weight (Patnool et al., 2022). According to the types of UTI the symptom is divided into acute pyelonephritis, urethritis, Cystitis. In acute pyelonephritis, symptoms may be the same as those of cystitis. One third of patients has frequency and dysuria.

However, with pyelonephritis, symptoms typically include chills, fever, flank pain, colicky abdominal pain, nausea, and vomiting. If abdominal rigidity is absent or slight, a tender, enlarged kidney is sometimes palpable. Costovertebral angle percussion tenderness is generally present on the infected side. In urethritis, the main symptoms are dysuria and urethral discharge. Discharge can be purulent, whitish, or mucoid. Characteristics of the discharge, such as the amount of purulence, do not reliably differentiate gonococcal from non-gonococcal urethritis. Cystitis onset is usually sudden, typically with frequency, urgency, and burning or painful voiding of small volumes of urine. Nocturia, with suprapubic pain and often low back pain, is common. The urine is often turbid, and microscopic hematuria can occur. A low-grade fever may develop. Pneumaturia can occur when infection results from a vesicoenteric or vesicovaginal fistula or from emphysematous cystitis. Since the frequent urge to urinate is common during pregnancy, it may be hard to tell the presence of cystitis, especially if symptoms are mild. A doubt of an infection should be clarified, because untreated cystitis puts the patient at high risk for getting a kidney infection, especially while pregnancy (Rahiman et al., 2015).

.2.5 Physiological changes of pregnancy and it is association with urinary tract infections

Pregnancy increases the risk of UTIs. At around 6^{th} week of pregnancy, due to the physiological changes of pregnancy the ureters begin to dilate. This is also known as “hydronephrosis of pregnancy”, which peaks at 22-26 weeks and continues to persist until delivery (Loh and Sivalingam, 2007). Physiological changes related to increased levels of progesterone place pregnant women at the risk of developing UTI. High progesterone level causes smooth muscle relaxation, resulting in reduced ureteric peristalsis and increased bladder capacity, thus favoring physiological ‘hydronephrosis’ and urinary stasis (Ansaldi and de Tejada Weber, 2022). Increased plasma volume during pregnancy leads to decrease urine concentration and increased bladder volume. The combination of all these factors lead to urinary stasis and uretero-vesical reflux. Glycosuria in pregnancy is also another well-known factor which predisposes mothers to UTI (Loh and Sivalingam, 2007)

2.6 Causes of Urinary Tract Infection UTI

Infection is the penetration of a pathogenic organism into the tissues of the host body, as well as the host's tissues' response to the pathogens and their toxins. Infectious diseases account for 3% of the top ten causes of death and 16% of all deaths per year. Infectious diseases

are now one of the leading causes of death worldwide (Saxton and Cancian, 2021).The Causes of Urinary Tract Infection during pregnancy women have a narrow urethra and their urinary tract can be easily contaminated with fecal microbes, they are more vulnerable to UTIs than men. Pregnancy and sexual activity are two other major variables that increase the risk of UTI in women. Women develop glycosuria during pregnancy as a result of the normal increase in plasma volume and decrease in urine concentration, eventually leading to bacterial growth in the urine. The three most common clinical manifestations of UTI in pregnancy are asymptomatic bacteriuria, acute cystitis, and acute pyelonephritis. (Patnool et al., 2022). Urinary tract infections are caused by microorganisms; normally, dead bacteria penetrate the urethra and bladder, causing inflammation and infection. While urethral and bladder infections are the most common, bacteria may also pass through the ureters and invade the kidneys. Escherichia coli, a bacterium usually found in the intestine, is responsible for more than 85-90% of bladder infections –cystitis (Alkhafaji and Jayashankar, 2022).

2.7 Microbiology

In normal physiological circumstances, the genitourinary tract is sterile. The microorganisms causing UTIs usually originate from the gastro-intestinal flora of the host. For example, during pregnancy bacteriuria can occur when bacteria from a fecal source gains access to the bladder by ascending the relatively short female urethra (Bradley et al., 2017).Pathogens causing bacteriuria are similar in both pregnant and non-pregnant women (Amer and Almasri, 2023). UTIs are mainly caused by bacteria, while the involvement of other microorganisms, such as fungi and viruses, is quite rare. *Candida albicans* is the most common type of fungus that causes UTIs (Olin and Bartges, 2015, Paduch, 2007). Although virtually every organism can be associated with UTIs, certain organisms predominate as a result of specific virulence and host susceptibility factors. The most common agent implicated in uncomplicated UTIs is *Escherichia coli*, which accounts for 85% of non-hospital setting infections. Other microorganisms such as *Staphylococcus saprophyticus* (5% to 15% of cases), *Gardnerella vaginalis, Chlamydia trachomatis, Klebsiella pneumoniae,* Proteus Spp., *Pseudomona Aeruginosa,* Enterococcus spp. (5% to 10%), *Ureaplasma urealyticum* and lactobacilli have also been associated with UTIs. Although the clinical significance of these organisms on UTIs during pregnancy was not yet appreciated, a few small studies have reported improved outcomes following therapy against these agents. The consensus Is that during gestation, most UTIs are caused by a single organism(Amer and Almasri, 2023).

2.8 Pathogenesis of UTI

Urinary tract infections (UTIs) begin when gut-resident uropathogens colonize the urethra and subsequently the bladder through the action of specific adhesins. If the host's inflammatory response fails to eliminate all bacteria, they begin to multiply, producing toxins and enzymes that promote their survival. Subsequent colonization of the kidneys can evolve into bacteremia if the pathogen crosses the kidney epithelial barrier. In complicated UTIs, infection by uropathogens is followed by bladder compromise, which occurs with catheterization. A very common situation is the accumulation of fibrinogen on the catheter as a result of the strong immune response induced by catheterization. Uropathogens, through the expression of fibrinogen-binding proteins, bind to the catheter. Bacteria also multiply as a result of biofilm protection, and if the infection is left untreated, it can progress to pyelonephritis and bacteremia. The spread of UTIs is closely linked to the effectiveness of a number of strategies that uropathogens have developed to adhere to and invade host tissues (Lewis et al., 2017, Mancuso et al., 2023). Often, the infection does not seem particularly severe, especially in the early stages, but it can worsen significantly in the presence of complicating factors (Zagaglia et al., 2022, Storme et al., 2019). Complicating factors that are involved in the progression of UTI are biofilms, urinary stasis due to obstruction, and catheters. UTIs comprise a heterogeneous group of clinical disorders that vary in terms of the etiology and severity of conditions (Storme et al., 2019, Craven et al., 2019) . A urine culture with ≥105 colony-forming units/mL without any specific UTI symptoms is defined asymptomatic bacteriuria, as it usually resolves spontaneously and does not require treatment (Wiley et al., 2020) . Asymptomatic UTIs should be treated only in selected cases, such as pregnant women, neutropenic patients, and those undergoing genitourinary surgery, as antibiotic treatment may contribute to the development of bacterial resistance (Luu and Albarillo, 2022, Ourani et al., 2021) . In contrast, symptomatic UTIs are commonly treated with antibiotics that can alter the intestinal and vaginal microbiota, increasing the risk factors for the spread of multidrug-resistant microorganisms (Ourani et al., 2021, Meštrović et al., 2020, Mancuso et al., 2023) .

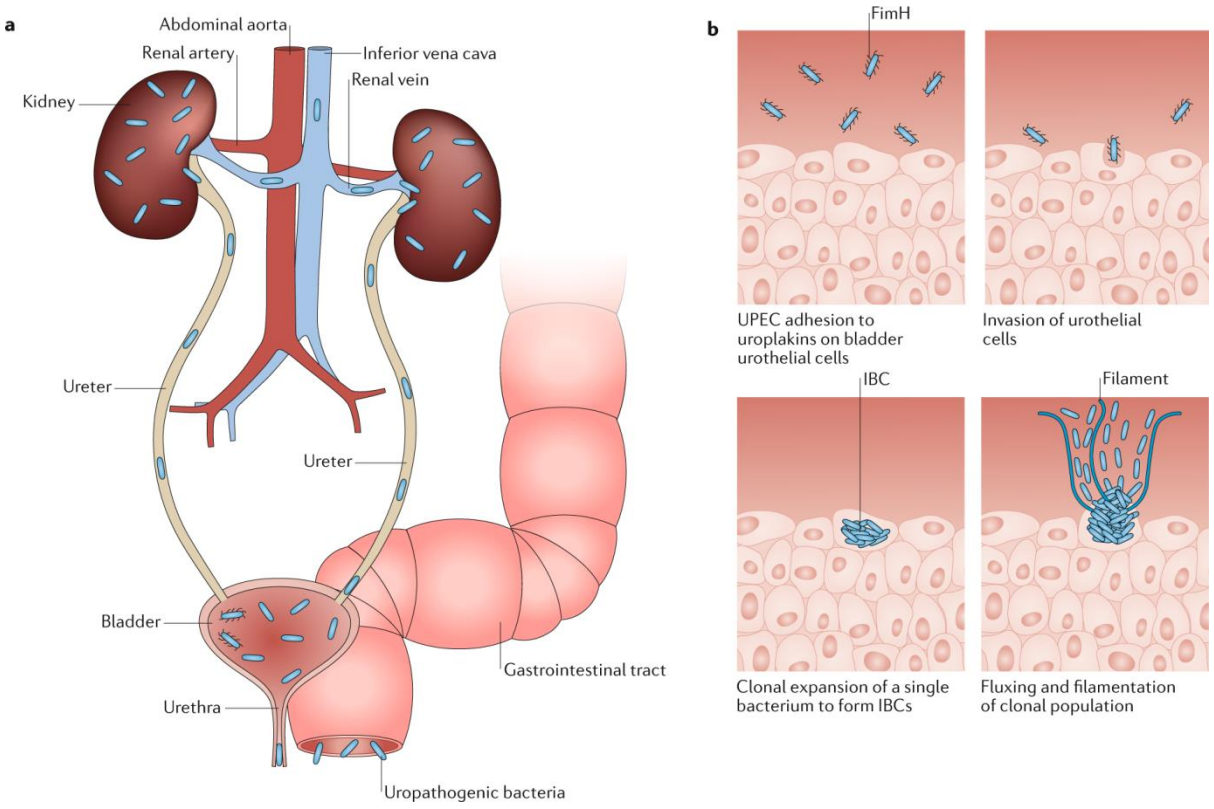

Figure 2. Pathogenesis (Klein and Hultgren, 2020)

2.9 Physiopathology

For many years, pregnancy was seen as a period that naturally predisposes to all forms of UTIs. This was explained by the fact that genito-urinary anatomical and physiological changes induced by gestation predispose women with asymptomatic bacteriuria to develop symptomatic UTIs, leading to the impression that the number of UTIs was higher during this period of life. Nowadays, it is known that gestation itself is not the only responsible for the increased risk of UTIs. Throughout pregnancy, UTIs often persist, owing to reinfection. During gestation the urethra is colonized by bacteria originated from the gastro-intestinal and perineal flora. Other factors that can predispose urethral colonization include the use of some methods of contraception before pregnancy, such as spermicides and diaphragms (Amer and Almasri, 2023). Although there is evidence that bladder infections follow colonization of the urethra, the mode of ascent of the microorganisms is not completely elucidated. After reaching the bladder, the organisms quickly multiply and can ascend the ureters to the kidneys. This sequence of events is more likely to occur if reflux of urine into the ureters and kidneys is present. Bacterial colonization is facilitated as early as the renal pelvis and ureters begin to dilate (eighth week of gestation), and the bladder is displaced superiorly and anteriorly inside

the intra-abdominal cavity. Mechanical compression caused by the enlarging uterus is the principle cause of this dilatation, but smooth muscle relaxation induced by progesterone may also play a role. The main consequences of these changes are the decrease in peristalsis of the ureters, followed by an increase in bladder capacity and urinary stasis. It is known that the decreased renal capacity to concentrate urine during pregnancy reduces the antibacterial activity of this fluid, leading it to excrete smaller amounts of potassium and higher amounts of glucose, amino acids and hormone degradation products. These biochemical alterations turn the urine into an alkaline solution, thus providing a suitable environment for bacterial growth. Additionally, the increase in the estrogen induced by gestation, contribute to the adhesion of certain E. coli strains to the type 1 uroepithelial cells. Host protective factors such as the low glucose concentration of the urine, stability of the vaginal lactobacilli population, the influence of estrogens, the activity of Tamm-Horsfall protein, the presence of urinary mucus or slime (called glycosaminoglycan) and the immunologic defense mechanisms, makes the normal urinary tract generally resistant to invasion and efficient in rapidly eliminating microorganisms that reach the bladder. Specific subsets of E. coli clones identified with O, K and H antigens were shown to have increased propensity to cause UTIs. An important virulence factor of bacteria is their ability to adhere to urinary epithelial cells, resulting in colonization of the urinary tract, bladder infections, and pyelonephritis. Uropathogenic E. coli have such virulence factors, known as fimbrias or pilli. These are adherence proteins (adhesins) expressed on the bacterial wall surface that promote binding to the epithelium of the vagina and urethra, thus increasing E. coli ability to cause UTIs. Hemolysis provides E. coli a possible selective advantage by releasing iron from lysed erythrocytes and thus, enhancing pathogenicity by destroying phagocytic and epithelial cells (Amer and Almasri, 2023).

2.10 Immune response in urinary tract infection

In contrast to the study of bacteria in the pathogenesis of UTI, there is a paucity of research into host immune factors, particularly the adaptive immune responses elicited in chronic UTI. The bladder sloughs off its epithelial layers upon infection as a bacterial clearance mechanism, and the cell regeneration that follows seems to limit inflammatory processes required for complete killing of pathogens. Vaccines and immunostimulants have been developed in an effort to harness a targeted immune response, but none has proven to be fit for widespread use thus far (Chieng et al., 2023). The kidneys, upstream of the bladder in the urinary system, have a robust dendritic cell–mediated immune response predominated by neutrophils and macrophages with interferon-γ as the key inflammatory cytokine during

infection (Tittel et al., 2011, Shaikh et al., 2019, Steiner et al., 2021). A bladder infection also induces similar neutrophil-driven responses as a result of interleukin (IL)-8 produced by uroepithelial cells (Chieng et al., 2023). The role of broad-spectrum antimicrobial peptides that are either constitutively expressed or upregulated during UTI (Spencer et al., 2014). Upon re-infection with the same bacteria, the kidneys are able to produce bacterial species-specific antibodies, but this secondary memory response is not observed where the prior infection is restricted to the bladder alone (Chan et al., 2013). Further immune activation that stimulates epithelial cells to produce IL-6 for neutrophil recruitment is dependent on the presence of lipopolysaccharide, showing that the bladder is capable of recognizing a common antigen present in Gram-negative bacteria and mounting an immune response (Jhang et al., 2021). Use of vaccines and immunostimulants are attractive non-antibiotic alternatives in the clinical management of UTI. the design of an efficacious formulation with the specific goal of preventing or treating a target health condition is technically difficult. There are multiple factors to be considered, including route of administration, dosage, duration, timing, type of adjuvant, and the identification of biomarkers that signal successful immunity (Chieng et al., 2023).

2,11 Risk factors associated with urinary tract infections

Urinary tract infection during pregnancy is common and high in age group between 26-35 years. The high incidence of UTI in the young reproductive age group is due to early pregnancy particularly in the remote settings. Many studies considered advances in age a risk factor for getting UTI in pregnancy because there is decline in glycogen level, deposition and decrease in the Lactobacillus as part of ageing progression which increases bacterial adherence and attack by pathogens and make them more vulnerable. Majority of urinary tract infection among pregnant women is well-known in age group 26-30 years, followed by 21-25, and 31-35years. The youngest among those studied was 18 years and oldest 45 years (Tadesse et al., 2014). Lower levels of education and low socio-economic grade have correlation with higher prevalence of ASB in many studies and reports(Obeagu et al., 2023). The prevalence of urinary tract infection was found to vary with socio-economic status of respondents. The prevalence was higher in women with low socio-economic status compared to middle and higher classes (Obeagu et al., 2023). According to, urinary tract infection in pregnancy was more common among women with first pregnancies (53.85%) compared to multi-gravidae (46.15%). This study shows that nulliparous women are more susceptible to UTI compared to multiparous women. Pregnant women in their third trimester of current pregnancy and those having more

than one child were mostly susceptible to acquire urinary tract infection. Numerous anatomical and hormonal variations in pregnant women lead to urethral dilation and urinary inertia which increased changes of developing UTI (Oladeinde et al., 2015). Studies have shown that with respect to trimester, majority of the pregnant women with UTI were in third trimester, followed by second trimester and first trimester (Lawani et al., 2015). The presence of P-antigens on ABO blood group in the uro-epithelial cells act as receptors for E. Coli adhesion. In people with secretor status, ABO blood group antigens are secreted in body fluids to cover the receptors for E. Coli adhesion. Therefore, such persons hardly suffer from UTI. Comparatively, for persons having no secretor status, the receptors for E. Coli adhesion are uncovered and exposed for attachment of bacteria hence resulting into recurrent UTI. Metabolic factors like diabetes mellitus are associated with a high prevalence of perianal colony by potential pathogens. Presence of glucose in urine increases occurrence and severity of infection in mothers with diabetes mellitus (Obeagu et al., 2023). Physiological changes in pregnancy that diminish the renal reabsorption of glucose causing glycosuria and urine alkalinization contribute furthermore to the high frequency of these infections (Matuszkiewicz-Rowińska et al., 2015)

2.12 The complications of urinary tract infections in pregnancy

Preterm birth or delivery under 37 weeks of gestation represents a great public health issue with a prevalence of 11-12% in United States. Even though the exact mechanism of pathogenesis is not known, recent studies have shown there is a direct correlation between untreated UTI in pregnancy and preterm birth abnormal placentation associated with systemic inflammation caused by infections may slow the rate of fetal growth and influence the future wellbeing after birth. The risk of preterm birth, also detected in untreated UTI, is related with low birth weight newborns (Nelson-Piercy, 2020). The emotional impact of UTI in pregnancy is very high and it is based on the prenatal attachment to the fetus and the knowledge that untreated, it could harm the future baby (Ghouri et al., 2019). Preeclampsia (PE) represents a multi systemic vascular syndrome that arise frequently after 20 weeks gestation and is defined by tensional values equal or exceeding 140 mmHg for systolic and 90 mmHg for diastolic. Even though the actual etiology of PE has not yet been established, it is highly believed that the systemic inflammatory response plays a key role in this pathology, so each trigger of the immune system can be at the origin of its occurrence in pregnancy (Yan et al., 2018, Rezavand et al., 2016). There is evidence showing that the systemic inflammation has a negative influence on placentation by favoring uteroplacental acute apheresis, which affects the spiral arteries and

is defined by intramural deposits of lipids, with high incidence in PE (Alnaes-Katjavivi et al., 2020). As the most frequent infection that occurs in pregnancy, UTI is probably one of the main activators of the immune system, making the screening and rapid treatment of UTI in pregnancy a priority of a good medical practice (Yan et al., 2018, Guibert, 2019). Due to a higher cardiac output and lowered peripheral vascular resistance in pregnancy, renal blood flow increases by 60-80% and leads to the increase in GFR by 40-65%. This in turn causes an average fall in the blood creatinine level from 0.8 to 0.5 mg/dL. Therefore, altered pharmacodynamics of drugs as a result of the altered renal metabolism should be taken into account in the treatment of pregnant patients (Szweda and Jóźwik, 2016).

2.13 Diagnosis

All UTI cases can be classified as either asymptomatic or symptomatic. An asymptomatic UTI is diagnosed based on urinalysis results (Czajkowski et al., 2021). Major efforts are being taken for rapid detection, monitoring and quantification of uropathogens. When left undetected in early stages, UTIs can cause serious health implications. UTI are detected by analysis of bacteria culture in the urine of the patient. Positive sign of symptomatic UTI is generally defined when bacteria count is >105 cfu/ml in free collection of urine (Kaur and Kaur, 2021).

There are many techniques used to detect UTIs, such as phenotypical biochemistry or culture identification strategy, which is considered to be slow due to time taken by bacteria to grow. Another technique is PCR or immunoassay technique, which is rapid, but former has the limitation of background contamination by exogenous sources of DNA, and the latter one require sensitivity, antigen amounts and time for seroconversion. A gold standard technique is quantitative urine culture, but it gives results in approximately 24hours, and antibiotic susceptibility testing requires another 24hours. As a result, broad spectrum antibiotics are often prescribed in this case. Surfaceenhanced Raman spectroscopy, a rapid diagnostic method based on spectra of bacterial strains grown in urine sample, is the latest technique which is being used to detect UTI (Premasiri et al., 2017). When dealing with pregnant patients, it is recommended to take a culture sample at the start of treatment due to increased risk of premature birth associated with urinary tract infections as well as limited antibiotic treatment options compatible with pregnancy(Czajkowski et al., 2021).

2.14 Management and Treatment of UTI

As previously mentioned, UTI in pregnancy need to be treated adequately (Ghouri and Hollywood, 2020). UTI during pregnancy are divided in three classes, according to their clinical gravity: asymptomatic bacteriuria, acute cystitis, acute pyelonephritis. There are numerous antibiotics that can safely be used taking in account the urine culture result and the necessity of urgent treatment initiation. While asymptomatic bacteriuria can wait the antibiogram result, acute cystitis and acute pyelonephritis need rapid start of therapy with subsequent adjustment (Kalinderi et al., 2018).

2.14.1 Lower UTI (asymptomatic bacteriuria and acute cystitis)

The first-choice antibiotic in lower UTI in pregnant women (acute cystitis and asymptomatic bacteriuria) is nitrofurantoin. Nitrofurantoin should be avoided in the first trimester or in pregnancy at term, in the few weeks before birth, because it is related to the risk of neonatal hemolysis. The treatment should be administrated for a period of 7 days, with a dosage of 100 mg given twice a day (Nelson-Piercy, 2020, Health and Excellence, 2018). Other antibiotics, recommended as second-line choice, are penicillins (amoxicillin) and cephalosporines (cefalexin). They have to be indicated if the first-line choice antibiotic does not relieve the symptoms or if the symptoms worsen after at least 48 hours of treatment. The advised antibiotherapy is 7 days, with amoxicillin 500 mg administrated three times a day and cefalexin 500 mg twice a day (Health and Excellence, 2018). Trimethoprim is not recommended in pregnancy because being a folate antagonist, it has a teratogenic risk in the first trimester. However, when there is no other option for treatment of UTI, but trimethoprim, this could be offer together with folic acid 5mg daily in the first trimester (Koutora et al., 2021, Bakdach and Elajez, 2020). Fosfomycin is an exception to this principle, it has shown good efficacy as a single-dose treatment for both ASB and symptomatic acute cystitis, making it a reasonable choice for 1-day treatment of ASB. Although 3-day treatment durations are recommended and commonly used for acute cystitis in non-pregnant women, there are no studies assessing a 3-day treatment duration for ASB (Graseck et al., 2023). Although there have been made several trials which concluded there are no adverse effects of the drug in pregnancy, adequate research is to be made taking in account the ethical considerations (Glaser and Schaeffer, 2015, Matuszkiewicz-Rowińska et al., 2015, Widmer et al., 2015). The follow up of the case implies repeating the urine culture one week after termination of treatment, with subsequent bacteriuria clearance. If the bacterial growth is present (more than 105 cfu/ml) and

if the pathogen remains the same, it can be reinitiated the initial antimicrobial therapy for a longer time, or the antibiotic can be changed with the conventional length of treatment.

2.14.2 Upper UTI (acute pyelonephritis)

Pyelonephritis is one of the most common reasons for hospitalization in pregnancy. Timely recognition and diagnosis are essential to initiate treatment. Given the associated risks, inpatient management is recommended for patients with acute pyelonephritis (Graseck et al., 2023). When pyelonephritis is diagnosed, parenteral broad-spectrum antibiotics need to be given rapidly and implies hospitalization for at least 48 hours. If there are no signs of gravity, the treatment can be initiate with cephalosporines (ceftriaxone, cefepime, cefotaxime), aztreonam or amoxiclav. Severe forms of pyelonephritis associated with obstacle, septicemia, or immunosuppression, need a more aggressive therapy with ticarcillin associated with clavulanic acid, piperacillin associated with tazobactam, meropenem, ertapenem or doripenem (Matuszkiewicz-Rowińska et al., 2015). After 48 hours without fever, the therapy should be adapted to the antibiogram result and pass to oral administration. The duration of the treatment should be 2 weeks (Koutora et al., 2021, Matuszkiewicz-Rowińska et al., 2015, Gupta, 2022). If there is no clinical improvement after 24 to 48 hours of parenteral antibiotic, it is necessary to perform a renal ultrasound and to collect a new sample for the urine culture, in order to exclude a pathology of the urinary tract or an infection with a resistant pathogen to the antimicrobial therapy (Gupta, 2022). Nitrofurantoin and fosfomycin are not appropriate oral agents to complete treatment for pyelonephritis, because they work within the lower urinary tract only and do not penetrate to reach therapeutic levels in the renal parenchyma, where the foci of infection reside. Urine culture should be obtained after completion of antibiotics to ensure no residual infection (Graseck et al., 2023).

2.14.3 Risks and prognosis

Urinary tract infections if mismanaged increase the risk of systemic maternal infection and severe acute pyelonephritis. These maternal complications influence the evolution of the pregnancy and could result in affecting the fetus as well by preterm birth, low birth weight, preeclampsia (Abou Heidar et al., 2019). A positive urine culture for group b streptococcus should not be overlooked, as it is closely associated with fetal infection, premature rupture of membranes and going in labor before term. Once identified this pathogen, peripartum antibiotic is required for preventing a neonatal infection (Abou Heidar et al., 2019, Szweda and Jóźwik, 2016, Angelescu et al., 2016). Antibiotic treatment given in pregnancy for UTI is necessary

and its administration has good prognostic value for the maternal and fetal outcome, reducing the prevalence of preterm labor and low birth weight infants (Azami et al., 2019, Angelescu et al., 2016, Groulx et al., 2016).

2.14.4 Natural Treatment of UTI

It is not known, what percentage of people are now using alternative therapies, but certainly large numbers of women are drinking cranberry juice or using herbal remedies to enhance their immune status or taking probiotics to restore the normal vaginal flora, which usually gets disturbed after an antibiotic therapy. Vaccine development for organisms other than *E. coli* still remains obscure (Das, 2020). Cranberry, mannose, and probiotics are frequently used for recurrent UTI, and berberine and uva ursi are prescribed for acute UTI. Potassium salt supplements reduce dysuria by alkalinizing the urine. Application of estriol cream and supplement of vitamins A and C were considered to be effective to prevent UTI (Head, 2008). Generally, people drink plenty of water to flush out the infectious bacteria. Application of curd water around the urethra can help in getting rid of urinary burning sensation. This present review enlists some ethnobotanicals, which are reported to be beneficial for UTI and other urinary disorders. It covers a list of potential herbs with urobactericidal activity, the in vitro/in vivo and clinical trial studies reported to prove the efficacy of cranberry in treating UTI. It also represents the synopsis of relevant natural therapeutics, those are proven to be useful in both prevention and cure of urological disorders (Das, 2020).

3.Conclusion

In conclusion, urinary tract infections (UTIs) pose a significant danger during pregnancy due to the potential repercussions. Although a variety of reasons, including physiological changes, gravidity, and genetic predispositions, the repercussions deserve special consideration. UTIs can lead to major health issues for both the mother and the fetus, such as hypertension, premature birth, low birth weight, and intrauterine growth restriction. These adverse effects underline the importance of a thorough diagnosis and treatment approach. Early detection of urinary tract infections (UTIs) and the capacity to discriminate between upper and lower UTIs are crucial for initiating the appropriate treatment, which may include antibiotic therapy if necessary. Moreover, understanding how to prevent UTIs without the use of antibiotics, the chance of problems linked with UTIs decreases. Finally, a comprehensive plan that focuses on preventing complication and management is crucial for protecting the health of both the mother and the fetus.

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