Urinary tract infection in obstetrics and gynaecology

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Abstract

Urinary tract infections are an important cause of morbidity affecting women of all ages. *Escherichia coli* is the most common causative pathogen for urinary tract infections. Diagnosis is best made by symptoms or culture as dipstick testing for leucocytes and nitrites is unreliable.

There is an increased risk of UTIs in pregnancy. They are common and warrant investigation and treatment as even asymptomatic bacteria can be associated with adverse pregnancy outcomes. Fetal complications include preterm labour, still birth and low-birth weight. The maternal complication of pyelonephritis has a high recurrence rate.

Urinary tract infection is one of the main differentials for pelvic pain in a gynaecological patient. In addition, UTIs must be excluded before diagnoses of overactive bladder or bladder pain syndrome are made.

UTIs are most commonly treated using antibiotics, however, research is underway into further novel treatment options for UTI which may be available in the future.

Keywords asymptomatic bacteriuria; cystitis; pyelonephritis; recurrent urinary tract infections; urinary tract infection

Introduction

Worldwide each year 150 million people suffer from urinary tract infections (UTI). UTIs can either results from a bladder infection in the lower urinary tract (cystitis) or a kidney infection of the upper tract known as pyelonephritis. Typical features of urinary tract infection are urgency, frequency, and dysuria. The woman may feel generally unwell and her urine may be odorous, cloudy or contain blood. UTIs are a significant public health burden and substantially affect the quality of life of affected individuals. Females are more susceptible to UTIs; about 10–20% of all women will experience a symptomatic UTI in their life time. The high incidence of UTI in young women means UTIs are commonly seen in obstetrics and gynaecology with associated morbidity and mortality both in and outside pregnancy.

The scope of this review is to highlight the current evidence of surrounding urinary tract infections in obstetrics and gynaecology. The focus of this review will be uncomplicated UTIs affecting the lower urinary tract.

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Predisposing factors

The female urethra is short in comparison with males and therefore the chance of bacteria ascending into the bladder to cause an infection is higher. The interplay in the embryological development of the urinary and genital tracts means women with uterine anomalies may have co-existing urinary tract anomalies. Abnormalities of the renal tract and neurological conditions such as multiple sclerosis all predispose to UTI. Any condition affecting the immune system will also contribute to an increase susceptibility to urinary tract sepsis e.g. Diabetes which affects women of all ages. Other genetic and acquired immune deficiency (e.g. HIV) will likewise increase the chances of developing a UTI. Sexual intercourse can encourage ascending bacteriuria. There was an association between coital frequency and UTI in a cohort of unmarried women. Women with mothers prone to UTIs are more susceptible and any condition that results in the bladder not emptying completely e.g. cystocele will predispose to urinary tract infection.

Catheterisation and instrumentation of the bladder increase the risk of a urinary tract infection with UTIs accounting for about 40% of all hospital acquired infections. Each time a catheter is passed into the bladder there is a 1–2% risk of urinary infection (EUA guidelines). Catheterisation is done routinely in obstetrics for caesarean sections and in laparoscopic gynaecology to protect the bladder. The ability to manage urinary tract infection is therefore an important skill in an obstetrician and gynaecologist.

Investigations

Urinalysis

When a UTI is suspected the first investigation is dipstick urinalysis testing for the presence of nitrites and leucocyte esterase. Studies have reported a wide range of sensitivity and specificity for dipstick investigations when diagnosing UTIs. 70 publications were included in a meta-analysis by Deville et al. this showed that the sensitivity of the urine dipstick for nitrites was low (45%–60%) and the specificity ranged between 85% and 98%. The dipstick test sensitivity of leucocyte esterase again was low (48%–86%) and the specificity of leucocyte esterase had a very large range of specificities between studies (17%–93%). It is possible to increase the specificity and sensitivity by combining these tests.

Mid-stream urine microscopy & culture

Sample: In order to accurately diagnose a UTI it is recommended that contamination of the sample is minimised. Most clinicians opt for diagnosis with a clean catch mid stream urine culture. As this method is better tolerated than suprapubic bladder aspiration or catheter samples.

Microscopy: The presence of 10 or more white blood cells (WBC)/mm^3 in fresh urine (pyuria) can be associated with UTI.

However, infection may not always show pyuria. Although bacterial count correlates with pyuria, 15% of samples from urine with bacterial counts of $>10^5$ do not have pyuria at microscopy.

Many laboratories will test for the presence of pyuria before going on to perform a culture. It is possible to underestimate pyuria rates as there is a decline in the wcc following sampling with 40% of white cells are still lost by 4 hours. Refrigeration and boric acid slow this process but there will often be a delay between a specimen being produced and arrival and processing in the laboratory. This could result in a sample being discarded as being free from infection.

Culture: A urine culture can show the concentration of bacteriuria, identify the organism responsible and the antibiotic sensitivity of that pathogen. Assuming that the sample is collected, stored and analysed appropriately there is a high sensitivity and specificity for urine cultures to be used to diagnose significant bacteriuria. Routine culture is not recommended for uncomplicated urinary tract infections in the non-pregnant women. However, where there is non-resolution of symptoms, complications or in the pregnant women cultures should be sent. Clean catch mid-stream urine cultures can guide the choice of antimicrobial therapy and provide a diagnosis where there is clinical uncertainty. Currently a urinary tract infection by MSU culture is diagnosed where $\geq 10^5$ colony forming units per millilitre (CFU/ml) of a single species of bacteria are isolated from direct-plating of the urine sample. Routine hospital MSU culture in the United Kingdom is performed in aerobic conditions looking for known uropathogens. Some less common pathogens require longer incubation times and prefer anaerobic conditions. Studies have shown positive routine blood cultures in women with acute pyelonephritis to be between 15 and 17%.

Imaging: There is no role for imaging in an uncomplicated urinary tract infection. However, in recurrent UTIs imaging may be undertaken, if the history is suggestive, to rule out structural anomalies. There is, however, a low rate of detecting an abnormality in uncomplicated recurrent UTIs. Recurrent UTIs in pregnancy likewise can be an indication to image the upper renal tract. If a uterine anomaly (e.g. didelphys) is diagnosed the upper renal tract should be checked for co-existing anomalies.

Pathogens

The vast majority of UTIs are caused by bacteria. *Escherichia coli* is the most common cause of UTI. An international study of the urinary cultures from 4734 women with UTI found *E. coli* to be implicated in 53.3%. The next most common pathogen was *Proteus mirabilis* at 4.4%. Other common species to cause UTIs include *Staphylococcus saprophyticus* a coagulase negative cocci, *Klebsiella pneumonia*, *Enterococci* and *Pseudomonas*. Other pathogens include *Staphylococcus aureus* and *Mycobacterium tuberculosis* can be haematologically inoculated. The bacteria responsible for UTI in pregnancy are similar to those in non-pregnancy.

Urinary tract infections have also been shown to be caused by other bacteria that are not identified by routine culture. *Actinobaculum schaalii* has been found to be a cause of urinary tract infection in the elderly. This bacterium is a slow growing facultative anaerobe. Other rarer causes of urinary tract infections include non-bacterial infections such as Chlamydia and *Candida albicans*.

It is understood that in many infections there is an initial phase in which the pathogen attaches to a particular site of the host. This early adhesion helps the pathogen to compete effectively with the host's own micro-flora and helps overcome other factors that might inhibit the pathogen becoming established. This ability confers an important factor in the virulence of the bacteria. Bacterial cell surface structures that are responsible for the promotion of adhesion are known as adhesins. These are often encoded by plasmids and may be in the form of fimbriae and non-fimbrial adhesins.

Extracellular substances, pili, flagella and extracellular DNA are able to form a biofilm scaffold which might support a multicellular bacterial community. In this way protecting the pathogens from antimicrobials, immune response and other stressors enabling them to persist and cause recurrent infections. Within this micro-ecosystem a variety of microbial strains may exist and co-operate in order to efficiently derive nutrition. *Pseudomonas aeruginosa* is an important cause of UTIs associated with catheter use. It forms biofilms on catheters by producing auto-inducers that bind to transcriptional regulators up regulating exopolysaccharides that promote a biofilm matrix. *P. aeruginosa* can also adopt a filamentous morphology and flagella promoting pathogenesis.

Traditionally urine was thought to be sterile, however, there is increasing evidence that there is a healthy flora of bacteria, or microbiome, that co-exist in the healthy bladder without causing an infection. These bacteria are present at much lower levels than are detected by routine hospital cultures but have been identified by using expanded culture techniques and next generation sequencing of the gene for the 16S RNA subunit present in all bacteria.

UTIs in obstetrics

UTIs have three main presentations in pregnancy. Asymptomatic bacteriuria is the persistent colonisation of the urinary tract by a significant number of bacteria in women without symptoms. Acute cystitis on the other hand is defined as the presence of symptoms including dysuria, urgency, frequency, nocturia, haematuria and suprapubic discomfort with no evidence of systemic illness. The third presentation is pyelonephritis – significant bacteriuria in the presence of systemic illness which may include pyrexia, rigors, renal angle pain, nausea and vomiting and fetal tachycardia.

Increased risk in pregnancy

There are a unique set of circumstances in pregnancy which contribute to the increase in susceptibility to UTIs. There is an increase in bladder volume and a coexisting decrease in detrusor tone. Progesterone can cause ureteric dilatation due to relaxation of smooth muscle and the gravid uterus may also compress the ureters causing hydronephrosis. Predominantly this is seen on more on the right side (the left is protected by the sigmoid colon). The kidney in pregnancy allows more glucose into the urine with the majority of women developing glycosuria, this may