

# Urinary tract infection in pregnancy

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# Objectives

- 1) Define, classify and describe the epidemiology UTI in pregnancy
- 2) Understand the UT changes in pregnancy that increase the risk of UTI
- 3) Identify the risk factors and causes of UTI in pregnancy
- 4) Rationalize the diagnosis and management of UTI in pregnancy
- 5) Outline the maternal and neonatal complications of UTI in pregnancy

# UTI in pregnancy

- Definition
  - presence  $\geq 100,000$  organisms/mL of urine in *asymptomatic* or  $> 100$  organisms/mL of urine with pyuria ( $>7$  WBC/mL) in *symptomatic* patient.
- Classification
  - Upper (pyelonephritis) vs lower (cystitis and urethritis)
  - Asymptomatic (asymptomatic bacteriuria) vs Symptomatic (acute urethritis, cystitis and pyelonephritis)
- Epidemiology
  - Asymptomatic- 2-10% prevalence in pregnancy, untreated leads to cystitis (30%) and pyelonephritis (50%)
  - Symptomatic-acute cystitis 1–4%, acute pyelonephritis 0.5% to 2%

# Urinary tract changes that increase risk of UTI

- The renal pelvis and ureters - hydroureter and hydronephrosis
  - progesterone- reduce ureteral tone, peristalsis, and contraction pressure
  - hypertrophy of Waldeyer's sheath (the connective tissue that surrounds the ureters within the true pelvis) may prevent hormone-induced dilatation below the pelvic brim
  - mechanical compression of the ureters at the pelvic brim- by enlarged vessels in the suspensory ligament of the ovary

# Urinary tract changes that increase risk of UTI

- Hydroureter and hydronephrosis
  - more prominent on the right than the left-
    - right ureter affected by dextrorotation of the uterus by the sigmoid colon
    - kinking of the ureter as it crosses the right iliac artery, and/or proximity to the right ovarian vein
  - the resulting urinary stasis can serve as a reservoir for bacteria

# Urinary tract changes that increase risk of UTI

- Bladder
  - edematous and hyperemic mucosa
  - progesterone induces bladder wall relaxation and increased capacity
  - the enlarging uterus displaces the bladder superiorly, anteriorly, and flattens it, which can decrease capacity
  - increased incidence of microhematuria
- Intermittent vesicoureteral reflux
  - incompetence of the vesicoureteral valve from bladder flaccidity
  - increased intravesical pressure
  - decreased intraureteral pressure

# Urinary tract changes that increase risk of UTI

- Postpartum changes from trauma during labor and delivery
  - mucosal congestion and submucosal hemorrhage
  - decreased bladder sensitivity/sensation
  - detrusor atony, increased postvoidal residual urine, bladder overdistention, and urinary retention
- Impaired tubular function
  - reduced fractional reabsorption of glucose, amino acids, and beta microglobulin results in higher rates of urinary excretion-hence glucosuria and aminoaciduria

## Increased risk of UTI in women vs men

- Shorter urethra
- Lower third of the urethra is continually contaminated with pathogens from the vagina and the rectum
- Incomplete bladder emptying
- Intercourse-expose urogenital system to bacteria during intercourse

# Urinary tract changes that mimic UTI

- Urinary frequency (voiding  $>7$  X per day)
  - due to changes in bladder function and increase in urine output
- Nocturia (voiding  $\geq 2$  X at night)
  - due to excretion of larger amounts of sodium and water during the night than nonpregnant women and nocturnal mobilization of edema later in pregnancy
- Urgency and stress incontinence
  - uterine pressure on the bladder
  - hormonal effects on the suspensory ligaments of the urethra
  - altered neuromuscular function of the urethral striated sphincter

# Etiology

- Two main sources
- *Enterobacteriaceae* including *Escherichia coli* and other coliforms:
  - normal vaginal and perineal flora introduced into the urethra during intercourse/wiping after bowel movement
- *Neisseria gonorrhoeae* and *chlamydia trachomatis*
  - sexually transmitted

# Etiology/microbiology

- Escherichia coli: 80-90% as ascending infection from periurethral fecal flora
- Urea-splitting bacteria e.g. Proteus (7%), Klebsiella (5%) Pseudomonas, and coagulase-negative staphylococcus, alkalinize the urine, may be associated with struvite stones.
- Enterobacter species (3%)
- Staphylococcus saprophyticus (2%), aggressive community acquired likely to be persistent/recurrent
- Group B beta-hemolytic Streptococcus (GBS; 1%) leads to neonatal sepsis and death
- Gram-positive: Enterococcus faecalis
- Chlamydia causes sterile pyuria and up to 30% of atypical pathogens.

# Asymptomatic Bacteriuria (ASB)

- Definition

- persistent, actively multiplying bacteria within the UT without urinary symptoms
- defined by  $>100,000/10^5$  CFU of a single organism
- prevalence in pregnancy no higher than non-pregnant population (2-7%)

- Significance

- if untreated increases the risk of symptomatic UTI (20-40%) as acute cystitis/pyelonephritis

# ASB-risk factors

- age (1% increase/decade of life)
- multiparity
- sexual activity
- chlamydia infection
- lower socioeconomic status
- UTI prior to prenatal care
- history of recurrent UTI
- DM
- sickle cell disease (renal damage),
- anatomic or functional GU abnormalities e.g. diversion
- preeclampsia
- Ccesarean delivery/catheterization

# ASB-screening

- Urine culture by clean catch at initial visit or by 12-16 weeks
  - clean the vulvar from front to back to avoid contamination of the urine sample
  - collect MSSU
- Dipslide (semi-quantitative dip inoculum method)
  - a special agar-coated dipstick first placed in urine and then used as culture plate
- Urinalysis and urine dipstick
  - PH- range 4.5 to 8 but normally is slightly acidic (5.5 to 6.5), alkaline urine suggests urea-splitting organism
  - leukocyte esterase and nitrite-inadequate, lower sensitivity, and high specificity
    - many gram-negative and some gram-positive organisms reduce urinary nitrates to nitrites
    - false-negative results from non-nitrate-reducing organisms and low-nitrate diet
    - leucocyte esterase produced by neutrophils and may signal pyuria from UTI

# Acute urethritis/acute urethral syndrome

- Causes:
  - *Escherichia coli* and other coliforms
  - *Neisseria gonorrhoeae*, and *Chlamydia trachomatis*
- Symptoms
  - frequency, urgency, and dysuria, hesitancy, dribbling, mucopurulent urethral discharge
- Investigations
  - urine microscopy: white blood cells, bacteria
  - urine culture: low colony counts of coliforms
  - culture urethral discharge: for gonorrhoea and chlamydia
  - a rapid diagnostic test e.g. NAAT preferred for gonorrhoea and chlamydia

# UTI: treatment

- Asymptomatic bacteriuria
  - Coliforms
    - empiric
    - PO antimicrobials
    - 3-7 days preferred over single day course: amoxicillin, cephalosporin, nitrofurantoin
    - Cephalexin 500 mg 4 times daily, Ampicillin 500 mg 4 times daily, Nitrofurantoin 100 mg 4 times daily, Sulfisoxazole 1 g 4 times daily
  - Treatment failures: nitrofurantoin for 21 days
  - Persistence or recurrence: suppress, nitrofurantoin at bedtime until delivery

# Treatment: gonococcal

- Dual therapy preferred
  - ceftriaxone 250 mg IM single dose PLUS azithromycin 1 g PO single dose
  - cefixime 400 mg orally as a single dose PLUS azithromycin 1 g PO single dose
- Single therapy -use local resistance data for susceptibility
  - e.g. spectinomycin 2 g IM

Higher dosages for recurrence

# Treatment: chlamydia

- Azithromycin 1 g PO as a single dose/**doxycycline** 100 mg PO twice a day for 7 days
- OR
  - **tetracycline** 500 mg orally four times a day for 7 days
  - erythromycin 500 mg orally twice a day for 7 days
  - **ofloxacin** 200–400 mg orally twice a day for 7 days and other fluoroquinolones contraindicated in pregnancy due to fetal cartilage development disorders
- In pregnancy
  - azithromycin preferred over erythromycin or amoxicillin
  - amoxicillin preferred over erythromycin

Higher dosages for recurrence

# Acute cystitis

- Inflammation of the bladder from bacterial or nonbacterial causes (e.g. radiation or viral infection)
- Prevalence :1-2%
- Symptoms and signs
  - Suprapubic discomfort
  - Dysuria, urgency, nocturia and frequency
  - Pyuria and bacteriuria
  - Microscopic hematuria and occasionally gross hematuria from hemorrhagic cystitis
- Significance
  - Precede 40 % of acute pyelonephritis in pregnancy
- Treatment
  - 3-7 days and not single-dose therapy needed as for ASB

# Treatment: acute cystitis

- Antibiotic choice depends on
  - Sensitivity patterns
  - Ampicillin, amoxicillin, cephalexin, amoxicillin-clavulanic acid affect normal bowel and vaginal flora to cause diarrhea or monilial vulvovaginitis
  - Nitrofurantoin has minimal effect on vaginal and bowel flora, and effective against the common uropathogens, except Proteus species
  - Amoxicillin-clavulanic acid and trimethoprim-sulfamethoxazole best for resistant pathogen
  - Amoxicillin-clavulanic acid concern about neonatal necrotizing enterocolitis
  - Sulfonamides not used in the first trimester due to teratogenicity, and immediately prior to delivery due to displacement of bilirubin from protein binding sites and resultant neonatal jaundice

# Acute pyelonephritis

- The most common serious medical complication of pregnancy
- About 10–20% of women with pyelonephritis have bacteremia
- Prevalence: 1-2 % and most common in the 2nd and 3rd trimesters
- Location: right (75%-80%), left (10% -15%) or bilateral
- Symptoms and signs
  - urinary symptoms-frequency, and dysuria
  - fever, flank pain, nausea, vomiting, shaking chills
  - CVA/renal angle tenderness
  - signs of preterm labor, septic shock, and ARDS
- Labs:
  - Bacteriuria- 1–2 per HPF in unspun urine or >20 in centrifuged urine
  - Pyuria
  - WBC casts
  - Leukocytosis
  - Blood cultures –septicemia in 10–20%

# Acute pyelonephritis: general management

- Admit
- Intravenous hydration to ensure adequate urinary output
- Antipyretics/cooling blanket. Hyperthermia in early pregnancy is teratogenic and can lead to early labor or fetal compromise/NRFS
- Closely monitor urinary output, BP, PR, Temp, and oxygen saturation.
- Investigations: CBC, UEC, urine culture, BGAs in ARDS
- Renal US for failed/persistent or complicated infections: can identify obstruction/perinephric abscess
- In selected cases
  - plain abdominal radiograph identify nearly 90% of radiopaque calculi
  - modified one-shot intravenous pyelogram—a single radiograph 30 minutes after contrast; CT urogram; MRI if no response to RX
  - cystoscopy and retrograde pyelography

# Acute pyelonephritis: specific management

- Parenteral antibiotics until defervescence and culture obtained within 48-72 hours
- Then oral antibiotics for a total of 10 to 14 days
- Options:
  - cefazolin +/-gentamicin
  - cefuroxime
  - ceftriaxone

# UTI: prevention

- Primary prevention: screening for and treating ASB, repeat screening after treatment for ASB in subsequent trimesters
- Behavioral:
  - front-to-back wipes after micturition or bowel movt, wash hands before and after the toilet, washcloths to clean the perineum, liquid soap to prevent colonization from bar soap, clean urethral meatus first when bathing
- Secondary prevention
  - suppressive therapy for
    - ASB: no response to initial and subsequent 7-10 day therapy
    - Recurrent bacteriuria after initial clearance of ASB
    - $\geq 2$  symptomatic UTIs
    - Acute pyelonephritis
    - UTI only after sexual intercourse
  - Options-bedtime antibiotic dose
    - Nitrofurantoin 100 mg
    - Cephalexin 250 mg
    - Amoxicillin 250mg

# UTI: differential diagnosis

- Labour
- Chorioamnionitis
- Appendicitis
- Placental abruption
- Degeneration of leiomyomas
- Musculoskeletal pain
- Costochondritis

# UTI: maternal complications

- Accompany late/sub-optimal treatment and include
  1. Fever
  2. Bacterial endotoxemia, endotoxic septic shock, sepsis
  3. Transient renal insufficiency/acute kidney injury
  4. Hemolysis
  5. Anemia
  6. Leukocytosis
  7. Thrombocytopenia
  8. Elevated fibrin split product levels
  9. Postpartum endometritis
  10. Pulmonary dysfunction
    1. minimal (mild cough and slight pulmonary infiltrate)
    2. severe ADRS
    3. pulmonary edema

# Complications: ARDS

- bacterial endotoxins increase alveolar permeability leading to pulmonary edema
- increased risk in the presence of: tachycardia, tachypnea, blood transfusion, temp > 103 degrees, tocolytics, excessive IV fluids
- awareness, prompt and aggressive management needed
- intensive care may be needed
- Other complications from bacterial toxins include systemic inflammatory response and endothelial injury

# UTI: Fetal/neonatal complications

- preterm labor and prematurity
- FGR
- low birth weight
- fetal death

# UTI: recurrence

- Recurrence occurs in 30 to 40 %
- Relapse
  - recurrent infection from the same species and type-specific strain present before treatment; a treatment failure.
  - occur <2 weeks after completion of RX
- Reinfection
  - recurrent infection due to a different strain of bacteria after successful treatment of the initial infection
  - occurring >3 weeks after completion of RX