UTI in Pregnancy & Recurrent UTI in women

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23rd Feb 2014
Objectives

- Physiologic changes of the urinary tract in pregnancy.
- Significance of bacteriuria in pregnancy.
- Screening for bacteriuria in pregnancy.
- Range of UTIs associated with pregnancy.
- Treatment.
Introduction

• Pregnancy does not alter incidence of lower UTI.

• Physiological and anatomical changes alter course of infection.

• Increased risk of recurrent UTI and progression to acute pyelonephritis.

• 5% to 10% prevalence of asymptomatic bacteriuria in pregnancy.

• 20% to 40% will progress to symptomatic infection.

• Associated with maternal and fetal morbidity / mortality.
Changes of Urinary Tract in Pregnancy

- Renal size increases by 1cm and volume up to 30%.
- Due to increased interstitial volume and distended renal vasculature.

- Dilatation of the collecting systems > physiological hydronephrosis and hydroureter. (right > left).
- Due to mechanical obstruction by uterus and ovarian venous plexus.
- Smooth muscle relaxation by progesterone.

- Renal plasma flow increase by 75% at 16 weeks.
- Decline by 25% towards term.

- GFR increased by 50% by end of first trimester. Normal by 3 months postpartum.
Changes of Urinary Tract in Pregnancy

• Creatinine clearance increases.

• Glomerular hyperfiltration.

• Decrease in serum urea, creatinine and uric acid.

• Glycosuria.

• Increased urine output.
Changes of Urinary Tract in Pregnancy

- Bladder displaced anteriorly and superiorly.
- Raised estrogen and muscle hyperplasia.
- Associated increase in absolute and functional urethral length and pressures.

- LUTS.
- Frequency 80% to 90% incidence by third trimester.
- Urgency 60% incidence.
- Incontinence 10% to 20% incidence.
- Due to reduced functional capacity of bladder.
Risk Factors

• Previous history of recurrent UTIs.

• Preexisting anatomical or functional abnormality (eg. VUR).

• Diabetes mellitus.

• Parity.

• Lower socioeconomic status.
Epidemiology & Microbiology

- Bacteriuria usually reflect prior colonization rather than acquisition during pregnancy itself.

- *E.coli* implicated in 65% to 80%.

- Increased risk associated with virulence factor “Dr adhesin”.

- *Klebsiella* and *Proteus* species.

Significance of Bacteriuria During Pregnancy

• 1% to 2% without bacteriuria in first trimester develop symptomatic UTIs.
• Untreated asymptomatic bacteriuria associated with acute pyelonephritis in 20% to 40%.
• Treatment of asymptomatic bacteriuria decrease rate of symptomatic UTIs by 80% to 90%.

• Untreated asymptomatic bacteriuria associated with:
  - Preterm labour.
  - Low birth weight.
  - Preeclampsia.
  - Anemia in pregnancy.

• Strength of association subject to confounding factors (socioeconomic status)
Screening for Bacteriuria in Pregnancy

• Frequency, urgency and nocturia common in pregnancy.

• Screening for asymptomatic bacteriuria in pregnancy.

• 4% to 0.8% decrease in incidence of pyelonephritis.

• Single clean catch urine culture detects ASB in 80% cases.

• Midstream urine obtained at first antenatal visit (week 10).

• FEME and culture.

• EAU March 2013 – Pregnant women should be screened for bacteriuria during the first trimester.
Asymptomatic Bacteriuria

- 5% to 10% of pregnant women.

- Similar prevalence in non pregnant women.

- Diagnosed in case of two consecutive voided urine specimens with > 10.5cfu/ml of the same bacterial species; or a single catheterized specimen with >10.5cfu/ml of a uropathogen.

- Short courses of antibiotics therapy (3 days) should be considered for treatment of asymptomatic bacteriuria in pregnancy.

- Repeat urine culture one to two weeks after completion of therapy and at one other point before delivery.
Cystitis

• 1% to 3% of pregnancies.

• Symptomatic UTI with > 10.5cfu/ml midstream urine.

• Short courses of antibiotics therapy (3 days) should be considered for treatment of asymptomatic bacteriuria in pregnancy.

• Repeat urine culture one to two weeks after completion of therapy.

• Postcoital prophylaxis should be considered in pregnant women with a history of frequent UTIs before onset of pregnancy to reduce risk of UTI.
# Treatment regimens for asymptomatic bacteriuria and cystitis in pregnancy.

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>Duration of Therapy</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrofurantoin 100mg</td>
<td>Q12h, 3-5 days</td>
<td>Avoid in G6PD deficiency</td>
</tr>
<tr>
<td>Amoxicillin 500mg</td>
<td>Q 8h, 3-5 days</td>
<td>Increasing resistance</td>
</tr>
<tr>
<td>Co-amoxicillin/Clavulanate</td>
<td>500mg q12h, 3-5 days</td>
<td></td>
</tr>
<tr>
<td>Cephalexin 500mg</td>
<td>Q8h, 3-5 days</td>
<td>Increasing resistance</td>
</tr>
<tr>
<td>Trimethoprim</td>
<td>Q12h, 3-5 days</td>
<td>Avoid in first trimester/term.</td>
</tr>
</tbody>
</table>
Acute Pyelonephritis

- 1% to 2% of pregnancies.
- Most common in the third trimester.
- Most likely to affect the right side.
- Fever, flank pain, nausea/vomitting, often with elevated WBC.
- Ultrasound KUB is necessary in case of suspicion of pyelonephritis.
- Mild symptoms can be treated with appropriate antibiotics as outpatient with close follow up.
- Parenteral antibiotic and switch to oral therapy for total treatment duration of 7 to 10 days.
Treatment regimens for pyelonephritis in pregnancy.

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftriaxone</td>
<td>1-2g IV or IM q12h.</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>1g IV q8-12h.</td>
</tr>
<tr>
<td>Piperacilin+tazobactam</td>
<td>3,375-4.5g IV q6h.</td>
</tr>
<tr>
<td>Cefepime</td>
<td>1g IV q 12h.</td>
</tr>
<tr>
<td>Imipenem+cilastatin</td>
<td>500mg IV q6h</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>2g IV q6h.</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>3-5mg/kg/day IV in 3 divided doses</td>
</tr>
</tbody>
</table>
Recurrent UTI in women

- UTI affects 20% women 20 – 56 years of age annually.

- 40% - 50% will suffer at least one UTI in their lifetime.

- One in four will develop recurrence.

- Recurrent UTI = more than 2 infections in 6 months or 3 within 12 months.

- May be due to re-infection (infection by different organism) or bacterial persistence (infection by the same organism originating from a focus within the urinary tract.)
Bacterial Persistence

• Often there is an underlying functional or anatomical problems.

• Stones.
  • Atrophic or atrophic infected kidney.
  • Vesicovaginal or colovesical fistula.
  • Urethral diverticulum.

• Correct underlying cause.

• Frequent recurrence within days or weeks.
Bacterial re-infection

- Usually occurs after a prolonged interval (months) from previous infection.

- Different organism.

- Associated with increased vaginal mucosal receptivity for uropathogens and ascending colonization from fecal flora.

- 3 main risk factors.
  - Increased frequency of intercourse.
  - Use of spermicide and diaphragm.
  - Loss of estrogen’s effect in the vaginal and periurethral structures.
Management : Recurrent UTI due to re-infection

• KUB Xray, ultrasound and flexible cystoscopy to look for potential sources of bacterial persistence.

• Preventative and conservative management.

• Low-dose antibiotic prophylaxis.

• Post-coital antibiotic prophylaxis.

• Self-start therapy.
Recurrent UTI in women

- **Need to be diagnosed by urine culture.**

- **Excretory urography, cystography and cystoscopy not routinely recommended for evaluation of recurrent UTI.**

- **Antimicrobial prophylaxis for prevention of recurrent UTI should be considered only after counseling and behavioural modifications have been attempted.**
Re-infection: Preventative and Conservative Management

- High fluid intake.
- Voiding immediately after intercourse.

- Avoid spermicides used on condoms and diaphragms (contains nonoxynol-9, reduce normal flora and may enhance E.coli adherence).

- Cranberry juice or tablets (proanthocyanidins inhibit bacterial adherence).

- Estrogen replacement.
  - Topical or systemic.

- Natural yoghurt.

- Urine alkalinization help alleviate symptoms of cystitis.
Re-infection : Low dose Antibiotic Prophylaxis

- Trimethoprim, nitrofurantoin and low-dose cephalexin have minimal adverse effects on fecal and vaginal flora.

- Given at bedtime for 6-12 months.

- Reduced recurrence by 90% compared to placebo.

- Full therapeutic dose if symptomatic re-infection during prophylactic period.

- Before initiating prophylaxis regimens eradication of previous UTI should be confirmed by negative culture 1-2 weeks after treatment.
Low dose antibiotic prophylaxis: Trimethoprim

- Gut as reservoir for organisms that colonize the periurethral area.
- Causes acute cystitis.
- Eradicates Gram-negative aerobic flora from gut and vaginal fluid.
- Bactericidal concentration in urine following oral dose.
- Can increase serum creatinine by inhibiting tubular secretion.
- Side effects: nausea / vomiting, rash, suppresses hematopoiesis.
Low dose antibiotic therapy: Nitrofurantoin

• Presents in high concentration in urine.

•Repeated elimination of bacteria.

• Inactivated by upper gut and does not affect vaginal or intracoital colonization with Gram-negatives.

• Side effects: nausea / vomiting, pulmonary fibrosis, peripheral neuropathy.

• Increased risk of adverse reaction if > 50 years age.
Low dose antibiotic prophylaxis: Cephalexin

- 250mg on provides excellent prophylaxis.

- No bacterial resistance with low dosage.

- Side effects: nausea / vomiting, allergic reactions.
Low dose Antibiotic Prophylaxis: Fluoroquinolones

- Ciprofloxacin.
- Eradicates Enterobacteria from fecal and vaginal flora.
- Associated with C.Difficile colitis.
- Contraindicated in patients with tendon disorder due to association with tendon damage (rupture).
- Other side effects: Stevens Johnson syndrome, allergic reactions.
Re-infection: Post-coital antibiotic prophylaxis

- Intercourse important risk factor for acute cystitis.
- Higher risk in women using diaphragm.
- Single dose of antibiotic post-coital effectively reduces incidence of re-infection.
- Self-start therapy – women keep a home supply of an antibiotic and start treatment when develop symptoms suggestive of UTI.
Re-infection : Immunoactive Prophylaxis

- **OM-89 (Uro-Vaxom) is sufficiently well documented and has been shown to be more effective than placebo in several randomized trials.**

- Five different serotypes of heat-killed E.coli.

- *Can be recommended for immunoprophylaxis in women with recurrent UTI.*

- Solco Urovac – IM or vaginal suppository. Trials ongoing.

- Probiotics – Gaining momentum due to adverse reactions to antibiotics.
Recurrent UTI - Bacterial Persistence

- Often there is an underlying functional or anatomical problems.
- Stones.
- Atrophic or atrophic infected kidney.
- Vesicovaginal or colovesical fistula.
- Urethral diverticulum.
- Correct underlying cause.
- Frequent recurrence within days or weeks.
Management of Bacterial Persistence

• Aim to identify potential causes.

• KUB X-ray to detect radio-opaque stones.

• KUB Ultrasound.

• Post voiding volume.

• IVU or CTU.

• Flexible cystoscopy – stones, urethral or bladder neck stricture, or fistula.

• Treat underlying pathology.
Thank You