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SEPERTI SENARAI EDARAN

YBhg Datuk/Dato'/Dato'Indera/Datin/Tuan/Puan,

CONSENSUS GUIDELINES ON THE MANAGEMENT OF URINARY TRACT INFECTIONS IN PREGNANCY

Dengan segala hormatnya saya merujuk kepada perkara di atas.

2. *Urinary tract infection (UTI)* merupakan jangkitan yang kerap dialami oleh ibu hamil, dimana jangkitan yang serius boleh menyebabkan morbiditi dan mortaliti kepada ibu hamil serta komplikasi pada bayi. Sehubungan itu, Jawatankuasa Kematian Ibu Peringkat Kebangsaan (CEMD) telah menyediakan *Consensus Guidelines on the Management of Urinary Tract Infections in Pregnancy* sebagai panduan kepada anggota kesihatan di kinik kesihatan dan hospital dalam mengendali dan merawat ibu hamil yang menghadapi masalah berkenaan.

3. Bersama-sama ini disertakan *Consensus Guidelines on the Management of Urinary Tract Infections in Pregnancy* untuk digunapakai sebagai rujukan oleh anggota kesihatan di fasiliti kesihatan di bawah seliaan YBhg. Datuk/Dato'/Dato'Indera/Datin/Tuan/Puan. Diharap *consensus* ini dapat membantu mengurangkan morbiditi akibat UTI dalam kalangan ibu hamil, seterusnya meningkatkan lagi kualiti perkhidmatan ibu

selaras dengan matlamat kerajaan untuk mencapai *Sustainable Development Goal*.

Sekian, terima kasih

"WAWASAN KEMAKMURAN BERSAMA 2030"

"BERKHIDMAT UNTUK NEGARA"

Saya yang menjalankan amanah,

(TAN SRI DATO' SERI DR. NOOR HISHAM BIN ABDULLAH)

s.k: Timbalan Ketua Pengarah Kesihatan (Perubatan)

Timbalan Ketua Pengarah Kesihatan (Kesihatan Awam)

CONSENSUS GUIDELINES ON THE MANAGEMENT OF URINARY TRACT INFECTIONS IN PREGNANCY

National Technical Committee
Confidential Enquiries into Maternal Deaths
2021

CONSENSUS GUIDELINES ON THE MANAGEMENT OF URINARY TRACT INFECTIONS IN PREGNANCY

AIM:

These recommendations on the management of urinary tract infections in pregnancy are made for the guidance of all primary care physicians, internal medicine physicians and obstetricians managing antenatal mothers.

1. INTRODUCTION

Urinary tract infections (UTI) are common in pregnancy and continue to pose clinical problems and a great challenge for physicians. It can be asymptomatic, as well as symptomatic, thus complicating the diagnostic process. It is of importance to obstetricians because of its association with significant maternal and perinatal morbidity and mortality and subsequent long-term effects.

The overall incidence of pyelonephritis reaches up to 2% of all pregnancies (vs. < 1% in the general population).This is related to profound structural and functional urinary tract changes, typical for pregnancy. In about 80% of pregnant women, dilatation of the urinary tract combined with slight hydronephrosis is frequently observed. Urinary stasis and impairment of the physiological anti-reflux mechanism create conditions favorable for bacterial growth and ascending infections[1].

Common organisms implicated to the cause of UTIs are:

- Escherichia coli - 63–85%
- Klebsiella pneumoniae (~8%)
- Coagulase-negative Staphylococcus (up to 15%)
- S. aureus (up to 8%)
- Group B streptococci (GBS) (2–7%)

The organisms that cause UTIs during pregnancy are the same as those found in non-pregnant patients. *Escherichia coli* accounts for the majority of infections. Other gram-negative rods such as *Proteus mirabilis* and *Klebsiella pneumoniae* are also common. Gram-positive organisms such as group B streptococcus (GBS) and *Staphylococcus saprophyticus* are less common causes of UTI. GBS has important implications in the management of pregnancy with regards to neonatal infections; but the detail of it will not be discussed further here. Less common organisms that may cause UTI include enterococci, *Gardnerella vaginalis* and *Ureaplasma ureolyticum*.

If left untreated, patients with UTIs including asymptomatic bacteriuria (ASB) in pregnancy have been shown to be at risk of developing symptomatic cystitis to up to 30% of cases; increased risk of acute pyelonephritis in 30–50% in untreated patients as compared to 3–4% intreated patients[1].

As for the perinatal outcome, there is an increased risk of premature delivery and/or lower birth weight; and possibly increased risk of pre-eclampsia in untreated patients. A 2015

Cochrane review established that treatment reduces the risk of pyelonephritis in pregnancy and, consequently, the risks of preterm delivery and low birthweight[2].

This guideline will discuss on the general management of urinary tract infection in pregnancy which includes:

1. Asymptomatic Bacteriuria (ASB)
2. Lower Urinary Tract Infection
    i. Acute cystitis
    ii. Acute urethritis
3. Acute Pyelonephritis
4. Urosepsis

2. MANAGEMENT OF URINARY TRACT INFECTIONS IN PREGNANCY

2.1 Asymptomatic Bacteriuria (ASB)

Asymptomatic bacteriuria (ASB) is defined as the presence of bacteria in the urine of a person without signs or symptoms of a urinary tract infection. Among the general adult population, women (across all ages) have the highest prevalence of asymptomatic bacteriuria, although rates increase with age among both men and women. It is present in an estimated 2% to 10% of pregnant women[1].

2.1.1 Evidence on Benefits of Screening and Treatment of Pregnant Women

Henderson *et al*[3] in their systematic review of 12 trials of pregnant women screened for asymptomatic bacteriuria and randomized to either a treatment or control condition (placebo or no treatment) found that patients in the control groups had higher rates of pyelonephritis. Pooled analysis demonstrated a 76% reduction in pyelonephritis among the intervention groups (pooled relative risk [RR], 0.24 [95% CI, 0.14-0.40]; 12 studies; n = 2068) than those in the treatment groups. By screening for and aggressively treating pregnant women with asymptomatic bacteriuria, it is possible to significantly decrease the incidence of pyelonephritis during pregnancy.

Seven treatment studies reported on the incidence of low birth weight. The pooled analysis found statistically significant reductions in the incidence of infants with low birth weight (pooled RR, 0.64 [95%CI, 0.46-0.90]; 7 studies; n = 1522)[3]. Preterm birth and perinatal mortality were reported in 3 and 6 studies, respectively. For both outcomes, results were mixed and pooled estimates did not demonstrate statistical significance.

2.1.2 Evidence on Harms of Screening and Treatment of Pregnant Women

In the same analysis[3], 5 out of 7 studies (n = 961) reported on congenital malformations. All but one study reported fewer cases in the intervention group, although the number of cases was small and pooled estimates were not statistically significant. Other infant or foetal harms were sparsely reported and event rates were low, which limited comparisons.

Adverse reactions to medications and complications of pregnancy and delivery were inconsistently and sparsely reported, again, limiting any meaningful conclusions.

The overall global incidence of ASB is relatively small, which is around 2% to 10% of pregnant women. Due to cost effectiveness and the fear of inappropriate antibiotic use leading to the emergence of resistant micro-organisms, countries may not want to embark on mass screening for ASB in all their pregnant mothers. From the local perspective, a recent cross-sectional survey done was conducted by a group of Family Physicians on few states in Malaysia involving 628 pregnant mothers to determine the incidence of ASB in these groups. The investigators found that only 2.55% of them had ASB (*unpublished data*). However, in this survey the investigators used reagent strip rather than urine culture as the diagnostic test. Due to its lack of sensitivity in diagnosing true infection, this will result in underestimation of a true incidence of ASB in pregnancy in Malaysian women.

2.1.3 Screening Test

1. Reagent strip testing
This has the advantage of being rapid and inexpensive and requiring little technical expertise. Urine microscopy and reagent strip analysis have been postulated as alternatives to culture but concerns remain over the efficacy of these techniques. Most studies note a high false negative rate for Gram staining and microscopy (up to 19.4%) and reagent strip testing (up to 52.8%)[4]. This implies that, at best, reagent strip testing will detect around half of women with ASB.

2. Urine culture (midstream sample)
This technique has been used as the reference standard for diagnosis of ASB. The drawbacks include the time lag: results are not usually available for at least 24 hours; and of course, the cost.

2.1.4 Diagnosis of ASB

ASB is defined as bacterial monoculture in the quantity of $\geq 10^5$ CFU/ml in a single urine culture taken in women without urinary symptoms. For group B streptococcus, CFU of $> 10^4$ is an indicator of vaginal colonization and is commonly used as the threshold for treatment of infection in pregnancy (as a part of prevention of early-onset Group B Streptococcus disease in infant).
For borderline bacteriuria i.e CFU/ml of 10^3 to 10^4 or polybacterial culture, a repeat test is recommended after 1 week, to avoid unnecessary treatment.

2.1.5 Timing of the test

There is little evidence on the optimal timing and frequency of screening. The American College of Obstetricians and Gynaecologists recommends screening at the first prenatal visit[5]. Meanwhile, the Royal College of Obstetricians and Gynaecologists recommends routine midstream urine screening for asymptomatic bacteriuria in early pregnancy[6].

US Preventive Services Task Force recommended obtaining a urine culture between 12 and 16 weeks of gestation or at the first prenatal visit[7].The Canadian Task Force on Preventive

Health Care (2018) recommends screening in pregnant women with urine culture once during the first trimester[8].

It is noteworthy that women with no bacteriuria in their initial examination in the first trimester may develop bacteriuria during the later trimesters. More recent reports suggest that repeating the urine culture in each trimester improves the detection rate of ASB.

There are subsets of people that are more at risk to develop acute pyelonephritis; even in non-pregnant state. These include diabetes mellitus, those with underlying renal tract abnormalities, past or recent renal calculi, people with recurrent infection, young, less educated, nulliparous, late antenatal care booking, and active smoking during pregnancy[1].

Screening for ASB in these groups of people may be considered. However, up to now there has been no evaluation of a screening algorithm incorporating risk factors.

Recommendation 1:
Until further data is available, the committee does not recommend a routine screening for ASB on all pregnant mothers. Screening may be considered in selected high risk mothers.

2.1.6 Management of ASB

Preventing inappropriate antibiotic use has become an important aspect of programs to decrease the development of antimicrobial resistance. However, there is no evidence for an effective non-pharmacological therapy in women with asymptomatic bacteriuria.
The presence of ASB in a pregnant woman is an absolute indication for initiation of the treatment. The choice of antibiotics should address the most common infecting organisms (i.e., gram-negative gastrointestinal organisms). The antibiotics should also be safe for the mother and fetus.
Commonly accepted antibiotics used in treating UTIs during pregnancy, regardless of its period, include derivatives of penicillin and cephalosporin, particularly those with low protein-binding ability (such as cephalexin), all of FDA pregnancy category B.
Trimethoprim/sulfamethoxazole and nitrofurantoin are well tolerated and by some considered even first line agents. Their use is safe in the second and third trimester, except in the last week before delivery, when they may increase neonatal jaundice and predispose to kernicterus. They should be avoided during the first trimester due to a possible risk of fetal defects.
In a long term follow-up among children born to women who had received antibiotics, erythromycin and amoxicillin-clavulanate have been found to significantly increase the number of children with various functional impairments and cerebral palsy compared to placebo[9].

Table 1: Treatment recommendation for ASB in pregnancy

Suggested Regime		Duration	Remark
Preferred Agent	**Alternative Agent**		
Nitrofurantoin (macrocrystal) 50mg to 100mg QID/ Nitrofurantoin (monohydrate/ macrocrystal) 100mg BD Cephalexin 500mg QID Trimethoprim/ sulphamethoxazole 160/800mg BD	1.Cefuroxime 250mg BD 2.Amoxicillin/ Clavulanate 625mg TDS 3.Ampicillin/ Sulbactam 375mg - 750mg BD OR 4.Fosfomycin 3g OD 1 dose	Generally 5 – 7 days	Avoid nitrofurantoin in third trimester if another option is available. This is due to the small risk of hemolytic anemia in newborn. Amoxicillin/ Clavulanate is generally safe in pregnancy (Category B) except for an increasing incidence of necrotizing enterocolitis in preterm babies and in babies born after premature rupture of membrane.

*Adapted from National Antimicrobial Guideline 2019[8]

Treatment is usually short-term, between 5–7 days of oral antibiotic therapy. Shorter than 5 days treatment associated with higher rates of recurrence and/or treatment failure. Another Cochrane systematic review of short courses (3 days) found insufficient evidence to confirm treatment efficacy.

After patients have completed the treatment regimen, a repeat culture should be obtained to document successful eradication of bacteriuria.

Recommendation 2:
Narrow-spectrum antibiotics should be used for the treatment of ASB for at least 5 days duration.

2.2 Lower Urinary Tract Infection (LUTI)

Acute cystitis (urinary bladder infection) and acute urethritis (urethral infection) is commonly referred to as lower urinary tract infection (LUTI). All LUTIs in pregnancy is considered as complicated LUTIs.

2.2.1 Diagnosis

Acute cystitis/acute urethritis (AC/AU) is distinguished from asymptomatic bacteriuria by the presence of symptoms such as dysuria, cloudy urine, haematuria, abdominal or suprapubic discomfort/pain, urgency and frequency in afebrile patients with no evidence of systemic illness. Up to 30% of patients with untreated asymptomatic bacteriuria later develop symptomatic cystitis.

The diagnosis of AC/AU is confirmed by the presence of even small bacterial colony counts ($\geq 10^2$–10^3CFU/ml).

2.2.2 Management of AC/AU

In general, treatment of pregnant patients with acute cystitis is initiated before the results of the culture are available. Antibiotic choice, as in asymptomatic bacteriuria, should focus on coverage of the common pathogens and can be changed after the organism is identified and sensitivities are determined (refer **Table 2**). Under-treatment will lead to persistent infection and progression to pyelonephritis. The optimal duration of treatment is unknown, but longer courses (7–10 days) of the therapy are generally suggested.

Table 2: Treatment recommendation for acute cystitis/acute urethritis in pregnancy

Suggested Regime		Duration	Remarks
Preferred Agent	**Alternative Agent**		
Nitrofurantoin (macrocrystal) 50mg to 100mg QID/ Nitrofurantoin (monohydrate/ macrocrystal) 100mg BD	1.Cefuroxime 250mg BD 2.Amoxicillin/Clavulanate 625mg TDS 3.Ampicillin/ Sulbactam 375mg -750mg BD OR 4.Fosfomycin 3g OD 1 dose	Generally 5 -7 days	Obtain urine culture before starting treatment and repeat 1-2 weeks after treatment completion.

*Adapted from National Antimicrobial Guideline 2019[8]

2.3 Acute Pyelonephritis (AP)

Acute pyelonephritis is most common in late pregnancy, with 80–90% of cases occurring in the second and third trimester[4]. It is usually a consequence of undiagnosed or inappropriately treated LUTI, or a complication of untreated ASB.
About 15–20% of women with pyelonephritis have bacteremia. Acute pyelonephritis during pregnancy is a serious systemic illness that can lead to preterm labor, low birth weight and premature delivery. The various serious complications to mother include acute kidney injury, preeclampsia, urosepsis and septic shock and acute respiratory distress syndrome. All pregnancy associated pyelonephritis are regarded as complicated pyelonephritis.

2.3.1 Diagnosis

The diagnostic gold standard in pyelonephritis is renal biopsy but this is impractical in clinical practice. A combination of symptoms, full blood count, inflammatory markers, renal function tests, blood culture, urine culture and sensitivity testing are used. In practice, acute pyelonephritis is suggested by:
Presence of any of the symptoms:

A. Flank or renal angle pain, costo-vertebral tenderness or pyuria.
B. Fever and/ or other evidences of systemic illness (rigor, nausea and vomiting).
AND
C. The presence of even small bacterial colony counts (≥ 10^2–10^3 CFU/ml).

2.3.2 Management of Acute Pyelonephritis

Early, aggressive treatment is important in preventing complications from pyelonephritis. Since AP in pregnancy is considered a complicated AP, all suspected cases of AP should be hospitalized at least for the initial 48 h of treatment given the limited data evaluating its safety and the need for close monitoring of the patient.

Urine for culture, urinalysis and antimicrobial susceptibility should be performed to all patients suspected to have acute pyelonephritis. Pyuria is present in the majority of cases and its absence should prompt consideration of other diagnosis or complete obstruction. However, absence of pyuria does not rule out UTI if symptoms and urine culture are consistent with the diagnosis. Blood culture is recommended in all AP in pregnancy. A positive culture is highly supportive of the causative organism even though only small proportions will have significant bacteremia. It is especially useful in cases of suspected multi-drug resistant organisms.

Antibiotic therapy and intravenous fluids may be initiated before obtaining the results of urine culture and sensitivity. Several antibiotic regimens may be used (Refer **Table 2**). Intravenous antibiotic is the preferred mode of administration. Antibiotic can be converted to an oral regime 24-48 hours after resolution of symptoms and should be tailored to the susceptibility profile of the isolated organism.

Generally, antibiotic therapy is usually continued for 10–14 days[4]. In patients with slow resolution of fever or delayed in source control, urine culture must be repeated and renal ultrasound should be performed if not done earlier to rule out persistent infection and urinary tract pathology. The duration of antibiotic shall be extended beyond 14 days[4].
To prevent recurrence or to avoid sub-optimum treatment, urine sterility must be confirmed after the completion of antibiotic course.

Table 3: Treatment recommendation for acute pyelonephritis in pregnancy

Suggested Regime		**Duration**	**Remarks**
Preferred Agent	**Alternative Agent**		
IV Amoxycillin / Clavulanate 1.2g TDS IV Cefuroxime 750mg TDS IV Ampicillin/ Sulbactam 1.5-3.0g TDS	IV Ceftriaxone 1g OD	Not stated	Obtain urine culture before starting treatment. Perform ultrasound of the upper urinary tract to exclude obstructive pyelonephritis. May step down to oral antibiotic guided by culture and sensitivity result once patient can tolerate orally and being afebrile for ≥ 24 hours.

*Adapted from National Antimicrobial Guideline 201910

2.4 Urosepsis

Urosepsis implies clinically evident severe infection of the urinary tract with features consistent with systemic inflammatory response syndrome. It is a state of life threatening organ dysfunction caused by a dysregulated host response due to infection originating from the urinary tract. It is usually a complication of acute pyelonephritis, rarely cystitis/urethritis. Urosepsis accounts for up to 20-30% of sepsis cases and can be potentially leading to septic shock and associated with high mortality and morbidity.

2.4.1 Management of Urosepsis

Management of urosepsis comprises of four major aspects:-

1. Early diagnosis
2. Early Empiric Intravenous antimicrobial treatment
3. Identification and control of complicating factors
4. Adjunctive measures / Specific Sepsis Therapy

Early Diagnosis of Urosepsis

A. Patients with sepsis may show many different clinical symptoms and signs. The greatest challenge is to identify the presence of early organ dysfunction. Systemic Inflammatory Response Syndrome **(SIRS)** score has been widely used as a tool to diagnose sepsis. However, it may have some issue with pregnant women as normal pregnancy parameters may overlap with criteria of sepsis. However, no specific pregnancy specific score for sepsis has been universally accepted or validatedand it still remains a reliable indicator of sepsis. We propose to use SIRS score as a guide for early detection of sepsis (**Table 4**).

Table 4: Systemic Inflammatory Response Syndrome Scoring System

SIRS and Sepsis	
Temperature	> 38°C or < 36°C
Heart rates	> 90 beats/min
Respiratory rates or PCO_2	> 20 breaths/min < 32 mmHg
WBCs	> 12,000/mm^3 or < 4,000/mm^3
Sepsis Criteria	
- SIRS + source of infection	
Severe Sepsis Criteria	
- Lactic acidosis - SBP < 90 mmHg or (SBP drop > 40 mmHg)	
Septic Shock Criteria	
- Severe sepsis with hypotension despite adequate fluid resuscitation	

*Adapted from G Bonkat et al (2018)[11].

B. Blood and urine for culture should be obtained in all suspected cases of urosepsis. A positive culture is highly supportive of the causative organism. However, a negative culture does not exclude the diagnosis because the culprit organism is frequently not identified in up to 50% of the cases.
C. Serum lactate in sepsis is useful to determine the severity of the disease
D. Imaging investigations such as ultrasonography or CT scan should be performed early.

Early Empiric Intravenous antimicrobial treatment

Initial empiric antimicrobial antibiotic therapy should provide broad antimicrobial coverage against all likely causative agents. Antimicrobials must be administered no later than one hour after the diagnosis. Antimicrobial should be started at high dose with appropriate adjustment for renal function. No specific recommendation of antibiotic of choice for urosepsis/ severe pyelonephritis in pregnancy.
However, few factors for antibiotics consideration as listed below:

- Urosepsis-specific pathogen from local drug susceptibility patterns especially looking at the resistant organism;
- Previous urological interventions;
- Previous urinary tract infection;
- Hospitalization associated with previous antimicrobial administration;
- Presence of a urinary catheter.

Identification and control of complicating factors

In many cases, urosepsis is linked to few complicating factors:

- Underlying pathology or renal tract anomaly. Major or minor abnormality reached up to 32% of cases[12].
- renal or perinephric abscess
- renal calculi
- obstruction from any cause including foreign bodies

Obstruction in the urinary tract such as stones or foreign bodies such as urinary stent or catheters is the most frequent urological source of urosepsis. Drainage of obstruction and removal of foreign bodies is therefore the most important source control strategy. These are key components of the strategy. It is the most important strategy for source control and must be performed immediately[13].

Adjunctive measures / Specific Sepsis Therapy

Early involvement of appropriate specialists (radiologist, urologists/nephrologists, microbiologists/Infectious Disease specialists and intensivists) is strongly recommended.

I. Adjunctive measures

- Fluid therapy with crystalloids/colloids should be administered to increase blood pressure (up to 30ml/kg of fluid in the first 3 hours). Fluid therapy with albumin can be considered if cystalloids do not result in a sufficient increase in blood pressure.

- Serial blood lactate level monitoring.
- Blood products should be given to target a hemoglobin level of 7–9 g/dl.
- Glucose levels should be targeted at 10mmol/l.
- Vasopressors such as norepinephrine should be used primarily, or dobutamine in myocardial dysfunction to achieve a mean arterial pressure of ≥ 65mmHg.
- Glucose level should be targeted at 7.8 -10mmol/l.
- Measures to prevent Deep Veins Thrombosis should be applied. Subcutaneous Low Molecular Weight Heparin is recommended.
- Stress ulcers prophylaxis should be applied in patient at risk using proton pump inhibitor.
- Enteral nutrition should be started early (<48 hours).
- Mechanical ventilation should be applied with a tidal volume of 6 ml/kg, a plateau pressure of ≤ 30cmH20 and high positive end expiratory pressure.

II. Specific sepsis therapy

No specific recommendation of antibiotic of choice for urosepsis/ severe pyelonephritis in pregnancy. If the causative organism is known, the initial empirical antimicrobial antibiotic therapy should be de-escalated according to the susceptibility pattern of the organism. The duration of treatment is between 7 to 10 days but may be longer in certain conditions like slow resolution of fever, delay in source control or in patients with co-morbidities. **Table 5** shows the examples of commonly used antibiotics in urosepsis.

Table 5: Commonly used broad-spectrum antibiotics in urosepsis

Antimicrobial	Dose	Duration
Cefotaxime	2g TDS/QID	7 to 10 days. Treatment can be extended in the case of slow improvement.
Ceftriaxone	1-2g OD	
Ceftazidime	1g TDS	
Cefepime	2g BD/TDS	
Piperacillin/tazobactam	4.5g TDS	
Meropenem	1g TDS	
Imipenem	500mg TDS/QID	

*Adapted from G Bonkart et al (2018)[11]

Recommendation 3:
Empirical treatment of urosepsis should provide good coverage for most likely organisms. Once the result of culture and sensitivity is available, effort must be made to de-escalate the choice of antibiotic used.

Recommendation 4:
Drainage of obstruction and removal of foreign bodies are the most important strategy of source control.

3. RADIOLOGICAL DIAGNOSIS

The aim of imaging in urinary tract infections (UTI) is to detect conditions that must be corrected to avoid imminent deterioration of kidney function, or to prevent recurrent infections and long-term kidney damage. However, the routine performance of imaging studies in patients with UTI is reported to be of little value[14].

In patient with acute pyelonephritis, radiological diagnosis should be considered early if patient fails to respond to usual antibiotic regimen; or deteriorate despite of appropriate antibiotic treatment. What must be detected are complications of upper UTIs such as obstruction with potential risk of kidney function loss and abscess formation in the renal parenchyma or peri-renal space requiring surgical intervention. There is now a general consensus that ultrasonography (US) is the primary choice of imaging in most cases of suspected upper UTI due to its lack of harmful radiation, easy accessibility, and low cost. For the same reason, US have become the primary radiological investigation of choice for evaluation of the renal tract in pregnancy[15].

US of the upper urinary tract should also be arranged at the earliest opportunity(preferably within 48 hours of diagnosis) to exclude obstructive pyelonephritis and complications especially in patient with history of renal stones, symptoms of renal colic, repeated episodes of pyelonephritis, diabetes, history of urology surgery or urosepis. If present, drainage of obstruction or abscesses and removal of foreign bodies must be performed immediately as it is the most important strategy for source control.

CT scan is superior to ultrasonography in detecting parenchymal changes caused by acute pyelonephritis, the presence of which confirms the diagnosis. CT scan with contrast is superior to ultrasonography in differentiating the various forms of renal inflammation and complications, e.g. pyonephrosis and renal abscess. A CT scan should be considered as second-line imaging if ultrasound fails to detect urinary tract abnormalities; if the patient remains febrile after 72 hours of treatment or in patients with suspected complications e.g. sepsis.

Recommendation 5:
Early imaging investigations should be considered to exclude obstruction or abscess in high risk patients.

4. NON-PHARMACOLOGICAL TREATMENT OF URINARY TRACT INFECTION

4.1 Hygienic behaviour

Good hygiene is well known to protect against all types of infections. Results from studies show that increased sexual activity of greater than two or three times a week was linked to a high frequency of UTIs[16]. However, washing the genital area and voiding the bladder after intercourse had a protective effect. The direction of wiping the genital area after voiding the bladder was also found to be important and women who wiped from back to front had a

higher incidence of UTIs. Drinking inadequate amounts of fluid and delaying voiding of the bladder also increased the likelihood of UTIs.[16]

4.2 Cranberry juice

A Cochrane review in 2008 of ten studies showed that cranberry juice does decrease the number of UTIs over twelve months, but no data exists as to the optimum timing and quantity of cranberry juice that needs to be consumed to prevent infection.[17]Another Cochrane review published in 2012 which included a larger number of studies in their meta-analysis found cranberries to be ineffective in preventing UTIs in pregnancy.[18] Thus, although there has been interest in using cranberries for UTI prevention, the evidence does not support its efficacy. It can still be used as a self-care option, if preferred by women, because of its known safety in pregnancy.

4.3 Ascorbic acid

Ochoa-Brust et al.[19] concluded that daily ascorbic acid at a dose of 100mg was beneficial especially in areas with a high incidence of UTIs and antimicrobial resistance. This is a promising result but requires additional trials to strengthen the evidence before it can be recommended.
In the same systematic review[16], the authors concluded that, apart from cranberry juice and ascorbic acid, other approaches like immunisation and Canephron® N were also effective and safe. (Canephron® N is a phytotherapeutic medicine with antibacterial properties and contains three herbs namely rosemary, lovage and centaury). However apart from hygiene behaviours, the evidence behind these approaches is not robust enough to be recommended in practice.

Recommendation 6:
Hygienic behaviours should be promoted to pregnant women as a part of strategies to prevent urinary tract infection.

5. PREVENTION OF RECURRENT/PERSISTENT INFECTION

The majority of UTIs are caused by gastrointestinal organisms. Even with appropriate treatment, the patient may experience are infection of the urinary tract from the rectal reservoir. UTIs recur in approximately 4 to 5 percent of pregnancies[4], and the risk of developing pyelonephritis is the same as the risk with primary UTIs. Patients who are found to have urinary stones, which have more than one recurrent UTI or who have a recurrent UTI while on suppressive antibiotic therapy should undergo a postpartum evaluation.

Follow-up urine cultures are recommended 1–2 weeks after the treatment and then once a month.A repeat urine culture may be obtained during the third trimester, because the urine of treated patients may not remain sterile for the entire pregnancy.

In case of persistent or recurrent bacteriuria, longer antibiotic therapy using the same agent (e.g. 7 instead of 5 days of treatment) or another first line drug is recommended (Table

5).Subsequent treatment courses are administered until the bacterial counts drop to non-significant levels ($<10^2$ bacteria/ml).
Prophylaxis antibiotic may be given in the presence of 2 episodes UTI within 6 months or 3 episodes of UTI within a year.

Table 6: Prophylaxis regime for Recurrent UTI

	Preferred regime	Alternative
Prophylaxis for Recurrent UTI	Nitrofurantoin 50-100mg PO q6h (macrocrystals) or 100mg PO q12h (monohydrate/macrocrystals) OR Cephalexin 250mg PO ON	Trimethoprim/sulfamethoxazole 80/400 mg PO ON OR Trimethoprim 100mg PO ON Duration : 3-6 months

*Adapted from National Antimicrobial Guideline 2019[10]
Post coital prophylaxis is reasonable to use in case of recurrent UTI that appear to be temporally related to sexual intercourse.

- Single postcoital dose of Cephalexin 250 mg

Recommendation 7:
All pregnant women who had undergone treatment for urinary tract infection should have a repeat urine culture at least 2 weeks after treatment and at third trimester.

6. CONCLUSION

Significant bacteriuria in pregnancy is common and a serious cause of maternal and perinatal morbidity and mortality. Clinical presentations include asymptomatic bacteriuria, acute cystitis, acute urethritis, acute pyelonephritis and in the most severe form, urosepsis. All are amenable to investigation and treatment, substantially improving outcome. Pregnant women should be screened for asymptomatic bacteriuria by urine culture and treated with appropriate antimicrobials. Acute cystitis and pyelonephritis demand full assessment and treatment, with early involvement of other specialists in severe or systemic infection (urosepsis). All women should be reviewed to confirm post-treatment urine sterility.

Empirical antimicrobial treatments will be required in severe disease but any decision to treat should be re-evaluated once culture and sensitivity reports are available. It is not only important to choose the right drug, but also consideration should be given to selecting the right dose and treatment duration. When choosing an antimicrobial, the pharmacokinetics and bioavailability of the individual drug in pregnancy must be considered along with the resistance profiles of microorganisms in the local antenatal population. It is also vital to use treatments with an established safety profile and, most importantly, without teratogenetic risks. Local as well as international guidelines are available to guide clinician the most appropriate choice of antimicrobial for specific disease conditions.

7. GUIDELINE COMMITTEE

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