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Frequency of Urinary Tract Infection in Females with Preterm Labor

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ABSTRACT

Introduction: Preterm labor is defined as the onset of labor before 37 completed weeks of pregnancy and is a leading cause of neonatal morbidity and mortality worldwide. The substantial increase in shortened gestations noted in the last decades occurred late in the preterm period, between 34 and 36 weeks (late preterm), and in deliveries in weeks 37 and 38 (early term). The rationale of this study is to determine frequency of urinary tract infection in females with preterm labor

Objective: To determine the frequency of urinary tract infection in females with preterm labor

Study Setting: Emergency Department of Gynecology, Lady Atchison Hospital, Lahore.

Duration of Study: May 25, 2018 to November 25, 2018

Study Design: Cross-Sectional Study

Subjects & Methods: A total of 357 cases fulfilling inclusion criteria was taken from Emergency Department of Gynecology, Lady Atchison Hospital, Lahore. SPSS v22.0 was used to enter and analyze data using descriptive statistics like Mean±S.D and frequency and percentage. Mean±S.D was used for quantitative data like age, gestational age and parity. Frequency and percentage were used for categorical data like UTI. Data was stratified for age, gestational age and parity to address effect modifiers. Post-stratification, Chi-Square test was used and p-value ≤0.05 was considered as significant.

Results: The urinary tract infection compare with the age 57 having urinary tract infection was from 18-30 years age group and 58 having urinary tract infection was from 31-40 years age group. In gestational age the 58 patients having urinary tract infection was from 22-30 weeks gestational age group and 57 having urinary tract infection was from 31-37 weeks gestational age group. The parity results was as 57 patients having urinary tract infection were from less than 3 groups and 58 was from the more than 3 groups.

Conclusion: UTI in pregnancy (whether symptomatic or asymptomatic) is a risk factor for adverse outcomes that endanger the health of both mother and fetus. Multiple sources of evidence strongly support screening and treatment of UTI as a valuable approach for improving birth outcomes.

Keywords: Urinary Tract Infection (UTI); Preterm Birth, Lahore

Abbreviations: UTI: Urinary Tract Infections; PRM: Prolonged Rupture of Membranes; OCD: Orthotopic Continent Diversion; STI: Sexually Transmitted Infections; STD: Sexually Transmitted Disease; PID: Pelvic Inflammatory Disease; CP: Control and Prevention; EA: Endovaginal; TA: Transabdominal; MRI: Magnetic Resonance Imaging; CT: Computed Tomography; AUA: American Urological Association; AF: Antiproliferative Factor

Introduction

Preterm labor is defined as the onset of labor before 37 completed weeks of pregnancy and is a leading cause of neonatal morbidity and mortality worldwide [1]. The substantial increase in shortened gestations noted in the last decades occurred late in the preterm period, between 34 and 36 weeks (late preterm), and in deliveries in weeks 37 and 38 (early term) [2]. Preterm birth is the main cause of morbidity and mortality during the perinatal period. Classical risk factors are held responsible for only 1/3 of preterm births and no current intervention has produced an appreciable reduction of this event [3]. Various maternal demographic, behavioral, and clinical characteristics have been associated with PTB including maternal race/ethnicity, maternal age at either extreme, cigarette smoking, low pre-pregnancy weight, psychosocial stress, previous PTB, and maternal intrauterine infections [4]. Pregnancy is a state associated with physiological, structural and functional urinary tract changes which promote ascending infections from the urethra [5].

The urinary tract is a common site of infection in humans. During pregnancy, urinary tract infection (UTI) is associated with increased risks of maternal and neonatal morbidity and mortality, even when the infection is asymptomatic [6]. Urinary tract infections (UTI) are among the most common bacterial infections in humans. UTI is commonly diagnosed based on clinical findings of bacteriuria (bacteria in midstream urine) counts of > 105colony forming units (cfu)/mL along with patient-reported symptoms. Lower bacterial counts are considered clinically significant when urine is collected by catheterization. Cystitis, or infection of the bladder, is typically accompanied by painful urination (dysuria), urgency, and frequent urination. A more severe infection of one or both kidneys, called pyelonephritis, is often accompanied by fever and flank pain, often in addition to symptoms of cystitis [6].

A study reported urogenital infections in the preterm labor included urinary tract infection in 36.7% of women [7]. Another study reported urogenital infection was seen in 19 women in PTB as 36.54 % [8]. Another study reported that frequency of UTI in females with preterm birth was 6.2% [4]. The rationale of this study is to determine frequency of urinary tract infection in females with preterm labor. The study is planned on local population as no local data is available and existing global data has no consensus i.e. 6.2%.[4] - 36.7% [7].Through this study if we find higher frequency then in future, it can be recommended that unlike the general population, all pregnant women was screened for UTI and asymptomatic bacteriuria should be treated in every case that is diagnosed to minimize the risk of preterm birth especially that is a leading cause of neonatal morbidity and mortality.

Review of Literature

Pregnancy causes numerous changes in the woman's body that increase the likelihood of urinary tract infections (UTIs). Hormonal and mechanical changes can promote urinary stasis and vesicoureteral reflux. These changes, along with an already short urethra (approximately 3-4 cm in females) and difficulty with hygiene due to a distended pregnant belly, help make UTIs the most common bacterial infections during pregnancy. UTIs during pregnancy are associated with risks to both the fetus and the mother, including pyelonephritis, preterm birth, low birth weight, and increased perinatal mortality. In general, pregnant patients are considered immunocompromised UTI hosts because of the physiologic changes associated with pregnancy. These changes increase the risk of serious infectious complications from symptomatic and asymptomatic urinary infections even in healthy pregnant women. Oral antibiotics are the treatment of choice for asymptomatic bacteriuria and cystitis. The standard course of treatment for pyelonephritis is hospital admission and intravenous antibiotics. Antibiotic prophylaxis is indicated in some cases. Patients treated for symptomatic UTI during pregnancy should be continued on daily prophylactic antibiotics for the duration of their pregnancy. Annual health costs for UTI exceed $1 billion. Although the condition-specific cost of asymptomatic bacteriuria or UTI in pregnancy is unknown, screening for these conditions in pregnant women is cost-effective, compared with treating UTI and pyelonephritis without screening. Goals for future research include targeting low-income groups and women in developing countries for screening and early treatment, as well as determining whether a causal relation exists between maternal UTI and childhood neurologic consequences.

Definitions of Key Terms

Urinary Tract Infection

UTI is defined as the presence of at least 100,000 organisms per milliliter of urine in an asymptomatic patient, or as more than 100 organisms/mL of urine with accompanying pyuria (> 7 white blood cells [WBCs]/mL) in a symptomatic patient. A diagnosis of UTI should be supported by a positive culture for a uropathogen, particularly in patients with vague symptoms [9].

Asymptomatic Bacteriuria

Asymptomatic bacteriuria is commonly defined as the presence of more than 100,000 organisms/mL in 2 consecutive urine samples in the absence of declared symptoms. Untreated asymptomatic bacteriuria is a risk factor for acute cystitis (40%) and pyelonephritis (25-30%) in pregnancy. These cases account for 70% of all cases of symptomatic UTI in unscreened pregnant women.

Acute Cystitis

Acute cystitis involves only the lower urinary tract; it is characterized by inflammation of the bladder as a result of bacterial or nonbacterial causes (eg, radiation or viral infection). Acute cystitis develops in approximately 1% of pregnant patients, of whom 60% have a negative result on initial screening. Signs and symptoms include hematuria, dysuria, suprapubic discomfort, frequency, urgency, and nocturia.

These symptoms are often difficult to distinguish from those due to pregnancy itself. Acute cystitis is complicated by upper urinary tract disease (ie, pyelonephritis) in 15 50% of cases.

Acute Pyelonephritis

Pyelonephritis is the most common urinary tract complication in pregnant women, occurring in approximately 2% of all pregnancies. Acute pyelonephritis is characterized by fever, flank pain, and tenderness in addition to significant bacteriuria. Other symptoms may include nausea, vomiting, frequency, urgency, and dysuria. Furthermore, women with additional risk factors (eg, immunosuppression, diabetes, sickle cell anemia, neurogenic bladder, recurrent or persistent UTIs before pregnancy) are at an increased risk for a complicated UTI.

Pathophysiology

Infections result from ascending colonization of the urinary tract, primarily by existing vaginal, perineal, and fecal flora. Various maternal physiologic and anatomic factors predispose to ascending infection. Such factors include urinary retention caused by the weight of the enlarging uterus and urinary stasis due to progesterone-induced ureteral smooth muscle relaxation. Blood-volume expansion is accompanied by increases in the glomerular filtration rate and urinary output. Loss of ureteral tone combined with increased urinary tract volume results in urinary stasis, which can lead to dilatation of the ureters, renal pelvis, and calyces. Urinary stasis and the presence of vesicoureteral reflux predispose some women to upper urinary tract infections (UTIs) and acute pyelonephritis. Calyceal and ureteral dilatation are more common on the right side; in 86% of cases, the dilatation is localized to the right. The degree of calyceal dilatation is also more pronounced on the right than the left (average 15 mm vs 5 mm). This dilatation appears to begin by about 10 weeks' gestation and worsens throughout pregnancy. This is underscored by the distribution of cases of pyelonephritis during pregnancy: 2% during the first trimester, 52% during the second trimester, and 46% in the third trimester. [10] Although the influence of progesterone causes relative dilatation of the ureters, ureteral tone progressively increases above the pelvic brim during pregnancy. However, whether bladder pressure increases or decreases during pregnancy is controversial. Glycosuria and an increase in levels of urinary amino acids (aminoaciduria) during pregnancy are additional factors that lead to UTI. In many cases, glucose excretion increases during pregnancy over non pregnant values of 100 mg/day. Glycosuria is due to impaired resorption by the collecting tubule and loop of Henle of the 5% of the filtered glucose, which escapes proximal convoluted tubular resorption.

The fractional excretion of alanine, glycine, histidine, serine, and threonine is increased throughout pregnancy. levels of cystine, leucine, lysine, phenylalanine, taurine, and tyrosine are elevated in the first half of pregnancy but return to reference range levels by the second half. The mechanism of selective aminoaciduria is unknown, although its presence has been postulated to affect the adherence of Escherichia coli to the urothelium [11].

Etiology

Infection

E coli is the most common cause of urinary tract infection (UTI), accounting for approximately 80-90% of cases. It originates from fecal flora colonizing the periurethral area, causing an ascending infection. Other pathogens include the following [12]

- Klebsiella pneumoniae (5%)
- Proteus mirabilis (5%)
- Enterobacter species (3%)
- Staphylococcus saprophyticus (2%)
- Group B beta-hemolytic Streptococcus (GBS; 1%)
- Proteus species (2%)

Gram-positive organisms, particularly Enterococcus faecalis and GBS, are clinically important pathogens. Infection with S saprophyticus, an aggressive community-acquired organism, can cause upper urinary tract disease, and this infection is more likely to be persistent or recurrent. Urea-splitting bacteria, including Proteus, Klebsiella, Pseudomonas, and coagulase-negative Staphylococcus, alkalinize the urine and may be associated with struvite stones. Chlamydial infections are associated with sterile pyuria and account for more than 30% of atypical pathogens. GBS colonization has important implications during pregnancy. Intrapartum transmission that leads to neonatal GBS infection can cause pneumonia, meningitis, sepsis, and death. Current guidelines recommend universal vaginal and rectal screening in all pregnant women at 35-37 weeks' gestation rather than treatment based on risk factors. Incidental documentation of GBS bacteriuria suggests a higher colonization count than is revealed by a screening vaginal or rectal culture. Beta-streptococcal colonization in the urine warrants immediate treatment and antibiotic prophylaxis when the patient presents in labor. Whether beta streptococci are associated with preterm labor is controversial. In a prospective study, McKenzie et al found no relation between beta-streptococcal bacteriuria and preterm labor, but they described the use of urinary antibodies to identify at-risk women [13]. In 2043 consecutive women, those with E coli antibodies at the initial visit and at 28 weeks' gestation and women with beta-streptococcal antibodies at 28 weeks' gestation had a significantly higher chance of preterm delivery.

Cesarean Delivery

Cesarean delivery is associated with UTI (increasing the likelihood 2.7-fold), but this association may be confounded by bladder catheterization or prolonged rupture of membranes (PROM). The incidence of symptomatic UTI is 9.3%, and that of asymptomatic bacteriuria is 7.6%.

Orthotopic Continent Urinary Diversion

Many women who, in the past, would have been counseled against pregnancy are now attempting pregnancy. In orthotopic continent diversion (OCD), an ileal-ascending colon conduit is made (OCD, Kock pouch) and reattached to the in-situ urethra (OCD) or a continent abdominal stoma (Kock pouch). Typical candidates are patients born with congenital exstrophy of the bladder in whom primary reconstruction has failed. Recurrent UTI and hydronephrosis are common because of outflow obstruction of the orthotopic stoma secondary to uterine compression or uterine prolapse. Indwelling catheterization of the urethra or continent stoma may be necessary, particularly during the later stages of pregnancy. In rare cases, a percutaneous nephrostomy tube or antegrade passage of a ureteral stent may be indicated.

Epidemiology

United States Statistics

The frequency of urinary tract infection (UTI) in pregnant women (0.3-1.3%) is similar to that in nonpregnant women [14]. Changes in coital patterns (eg, position, frequency, postcoital antibiotics) can offset recurrence in at-risk individuals. Overall, UTIs are 14 times more frequent in women than in men. This difference is attributed to the following factors:

- The urethra is shorter in women
- In women, the lower third of the urethra is continually contaminated with pathogens from the vagina and the rectum
- Women tend not to empty their bladders as completely as men do
- The female urogenital system is exposed to bacteria during intercourse

A difference between pregnant and non-pregnant women is that the prevalence of asymptomatic bacteriuria in pregnant women is 2.5-11%, as opposed to 3-8% in non-pregnant women. In as many as 40% of these cases, bacteriuria may progress to symptomatic upper UTI or pyelonephritis; this rate is significantly higher than that seen in non-pregnant women [15]. Several patient-level factors are associated with an increased frequency of bacteriuria during pregnancy. Compared with non-indigent patients, indigent patients have a 5-fold increased incidence of bacteriuria. The risk is doubled in women with sickle cell trait. Other risk factors for bacteriuria include diabetes mellitus, [1] neurogenic bladder retention, history of vesicoureteral reflux (treated or untreated), previous renal transplantation, [16] and a history of previous UTIs.

International Statistics

Versi et al described a higher prevalence of bacteriuria in pregnant white women (6.3%) than in pregnant Bangladeshi women (2%). Pregnancies that resulted in preterm deliveries were strongly associated with bacteriuria in white women; this association was not observed in Bangladeshi women. The authors hypothesized that the difference could be due to variation in hygiene practices and clothing. A large population-based study of nearly 200,000 pregnant Israeli women demonstrated a 2.5% rate of asymptomatic bacteriuria and a 2.3% rate of symptomatic UTI. [17] In this population, asymptomatic bacteriuria was found to have an association with multiple pregnancy complications, including hypertension, diabetes, intrauterine growth retardation, prolonged hospitalization, and preterm labor. The authors suggested that these findings may be a marker for intensity of prenatal care rather than a specific causal effect of the urinary infection. Additionally, their follow-up study examining women with symptomatic UTI showed a clear association between UTI and low birth weight and preterm delivery, a finding consistent with those of multiple previous investigations [18].

Age- and Race-Related Demographics

The prevalence of UTI during pregnancy increases with maternal age. A retrospective analysis of 24,000 births found the prevalence of UTI during pregnancy to be 28.7% in whites and Asians, 30.1% in blacks, and 41.1% in Hispanics. When socioeconomic status is controlled for, no significant interracial differences seem to exist. A survey-based analysis of self-reported UTI found similar trends. This study also considered Native American women and found the highest prevalence of UTI in this population (24.2%) as compared with Asian (10.3%), white (16.6%), Hispanic (18.3%), and black (20.3%) women [19]. UTI is associated with preterm delivery in persons of all races. The adjusted odds ratio in infants with very low birth weight is 2.8 in blacks and 5.6 in whites, adjusted for parity, body mass index, maternal age, marital status, cigarette smoking, education, and prenatal care. The overall relative risk of bacteriuria in blacks or whites is estimated at 1.5-5, and the relative risk of preterm birth in women with bacteriuria is 1.8-2.3.

Prognosis

In most cases of bacteriuria and urinary tract infection (UTI) in pregnancy, the prognosis is excellent. The majority of long-term sequelae are due to complications associated with septic shock, respiratory failure, and hypotensive hypoxia (ie, extremity gangrene). Maternal UTI has few direct fetal sequelae because fetal bloodstream infection is rare; however, uterine hypoperfusion due to maternal dehydration, maternal anemia, and direct bacterial endotoxin damage to the placental vasculature may cause fetal cerebral hypoperfusion. Untreated upper UTIs are associated with low birth weight, prematurity, premature labor, hypertension, preeclampsia, maternal anemia, and amnionitis [9]. A retrospective population-based study by Mazor-Dray et al showed that UTI during pregnancy is independently associated with intrauterine growth restriction, preeclampsia, preterm delivery, and cesarean delivery [20]. A prospective cohort study of pregnant patients also suggested an association between maternal UTI and childhood asthma.

Preeclampsia

A case-control study demonstrated an increased odds (1.22-fold) of preeclampsia in women with any UTI during pregnancy versus those without UTI [21]. A multicenter retrospective study found that the presence of UTI in pregnancy, particularly in the third trimester, is strongly associated with preeclampsia. Rates of preeclampsia in patients with UTI compared with those without reported UTI were 31.1% vs 7.8%, respectively ($P < 0.001$). The authors hypothesize that the increased maternal inflammatory burden from UTI enhances the risk of preeclampsia.

History

The presentation varies according to whether the patient has asymptomatic bacteriuria, a lower urinary tract infection (UTI; ie, cystitis) or an upper UTI (ie, pyelonephritis). Burning with urination (dysuria) is the most significant symptom in pregnant women with symptomatic cystitis. Other symptoms include frequency, urgency, suprapubic pain, and hematuria in the absence of systemic symptoms. The usual complaints of increased frequency, nocturia, and suprapubic pressure are not particularly helpful, because most pregnant women experience these as a result of increased pressure from the growing uterus, expanding blood volume, increased glomerular filtration rate, and increased renal blood flow [22]. Pyelonephritis symptoms on presentation vary. They often include fever (>38°C), shaking chills, costovertebral angle tenderness, anorexia, nausea, and vomiting. Right-side flank pain is more common than left-side or bilateral flank pain. Patients may also present with hypothermia (as low as 34°C). Lower UTI symptoms are common but not universal.

Physical Examination

During the physical examination, the findings should be considered in relation to the duration of pregnancy. The differential diagnoses may change from one trimester to the next, and the increasing size of the gravid uterus may mask or mimic disease findings. A thorough physical examination is recommended, with particular attention to the abdomen. Suprapubic or costovertebral tenderness may be present. In asymptomatic bacteriuria, no physical findings are typically present. Symptoms may arise intermittently, only to be overlooked because of lack of persistence or severity. Pelvic examination is recommended in all symptomatic patients (with the exception of third-trimester patients with bleeding) to rule out vaginitis or cervicitis. In patients with cystitis, tenderness can often be elicited with isolation of the bladder on pelvic examination. Patients with pyelonephritis have fever (usually >38°C), flank tenderness upon palpation, and an ill appearance. Flank tenderness occurs on the right side in more than half of patients, bilaterally in one fourth, and on the left side in one fourth. Pain may also be found suprapubically with palpation. Assessment of the fetal heart rate on the basis of gestational age should be included as part of the evaluation. Often, owing to maternal fever, the fetal heart rate is elevated to more than 160 beats/min.

Complications

The primary complication of bacteriuria during pregnancy is cystitis, though the primary morbidity is due to pyelonephritis. Other complications may include the following:

- Perinephric cellulitis and abscess
- Septic shock (rare)
- Renal dysfunction (usually transient, but as many as 25% of pregnant women with pyelonephritis have a decreased glomerular filtration rate)
- Hematologic dysfunction (common but seldom of clinical importance)
- Hypoxic fetal events due to maternal complications of infection that lead to hypoperfusion of the placenta
- Preeclampsia [23]
- Premature delivery leading to increased infant morbidity and mortality

Pulmonary injury may also complicate UTI in pregnancy. Approximately 2% of women with severe pyelonephritis during pregnancy have evidence of pulmonary injury due to systemic inflammatory response syndrome and respiratory insufficiency. Endotoxins that alter alveolar-capillary membrane permeability are produced; subsequently, pulmonary edema and acute respiratory distress syndrome develop.

Diagnostic Considerations

The differential diagnosis of urinary tract infection (UTI) in pregnancy includes the following:

- Cervicitis
- Chlamydial Genitourinary Infections
- Cystitis, Nonbacterial
- Ectopic Pregnancy
- Interstitial Cystitis
- Nephrolithiasis
- Trichomoniasis
- Trigonitis
- Urethritis
- Vaginitis

Other disorders to consider include the following:

- Glomerulonephritis
- Group B streptococcal colonization

- Sexually transmitted infection (eg, gonorrhea, nongonococcal urethritis)
- Threatened or incomplete miscarriage
- Urge incontinence

Vaginal infections can cause or mimic UTIs, which are common in women of reproductive age, affecting 25-35% of women aged 20-40 years. Discriminating between the 2 depends on the results of vaginal and urinary cultures.

Cervicitis

Cervicitis is an inflammation of the uterine cervix, characteristically diagnosed by: [1] a visible, purulent or mucopurulent endocervical exudate in the endocervical canal or on an endocervical swab specimen and/or [2] sustained, easily induced endocervical bleeding when a cotton swab is gently passed through the cervical os. [24].

Non-Infectious Cervicitis

Non-infectious cervicitis can be caused by the following:

- Local trauma - eg, cervical irritation caused by tampons, a cervical cap, the string from an intrauterine contraceptive device, a pessary, or a diaphragm
- Radiation
- Chemical irritation - eg, vaginal douches, latex exposure, or contraceptive creams
- Systemic inflammation - eg, Behçet syndrome
- Malignancy

Infectious Cervicitis

The infectious etiologies of cervicitis, all of which are sexually transmitted infections (STIs), are significantly more common than the noninfectious causes. This article focuses on the infectious etiologies of cervicitis. Infectious cervicitis may be caused by Chlamydia trachomatis, Neisseria gonorrhoeae, or herpes simplex virus (HSV). In most cases of cervicitis, however, lab tests fail to isolate an organism; this is particularly true in women with low risk factors.

Chlamydia (Chlamydial Genitourinary Infections)

Chlamydial infection can cause disease in many organ systems, including the genitourinary tract. Chlamydiae are small gram-negative obligate intracellular microorganisms that preferentially infect squamocolumnar epithelial cells. They include the genera Chlamydia (of which the type species is Chlamydia trachomatis) and Chlamydophila (eg, Chlamydophila pneumoniaeand Chlamydophila psittaci).

C trachomatis can be differentiated into 18 serovars (serologically variant strains) on the basis of monoclonal antibody–based typing assays. These serovars are associated with different medical conditions, as follows:

- Serovars A, B, Ba, and C – Trachoma, a serious eye disease endemic in Africa and Asia that is characterized by chronic conjunctivitis and can lead to blindness
- Serovars D-K – Genital tract infections
- Serovars L1-L3 – Lymphogranuloma venereum (LGV), which is associated with genital ulcer disease in tropical countries.

C trachomatis infection affects the cervix, urethra, salpinges, uterus, nasopharynx, and epididymis [25,26]; it is the most commonly reported bacterial sexually transmitted disease (STD) in the United States and a leading cause of infertility in women. C trachomatis infection causes other diseases as well, including conjunctivitis, pneumonia or pneumonitis, afebrile pneumonia syndrome (in infants born vaginally to infected mothers), Fitz-Hugh-Curtis syndrome, and trachoma (the world's leading cause of acquired blindness). C pneumoniae infection is spread via respiratory droplets and causes pharyngitis, bronchitis, and pneumonia. C psittaci infection is spread by bird droppings and aerosols and causes psittacosis. These infections are not discussed in this article. At present, fewer than 50% of sexually active young females in the United States are screened for the presence of chlamydiae. Nationally, the annual screening rate increased from 25.3% in 2000 to 43.6% in 2006, then decreased slightly to 41.6% in 2007. [5] The US Preventive Services Task Force recommends routine screening for chlamydial infections. The USPSTF recommends screening for chlamydia in sexually active females aged 24 years or younger and in older women who are at increased risk for infection. Routine Chlamydiascreening of sexually active young women is recommended to prevent consequences of untreated chlamydial infection (eg, pelvic inflammatory disease (PID), infertility, ectopic pregnancy, and chronic pelvic pain) [27]. A guideline synthesis is also available from the National Guideline Clearinghouse.

Nonbacterial and Noninfectious Cystitis

Nonbacterial cystitis is a catchall term that encompasses various medical disorders, including infectious and noninfectious cystitis, as well as painful bladder syndrome/interstitial cystitis (PBS/IC). PBS/IC describes a syndrome of pain and genitourinary symptoms (eg, frequency, urgency, pain, dysuria, nocturia) for which no etiology can be found. There are many controversies regarding nonbacterial cystitis, including possible etiologic agents, methods of diagnosis, and treatment, especially for noninfectious causes.

Infectious nonbacterial cystitis includes the following forms of the disease:

- Viral
- Mycobacterial
- Chlamydial
- Fungal
- Schistosomal

Non-infectious nonbacterial cystitis includes the following forms of the disease:

- Radiation induced
- Chemical
- Autoimmune
- Hypersensitivity

General symptoms of cystitis include urgency, frequency, dysuria, and, occasionally, hematuria, dyspareunia, abdominal cramps, and/or bladder pain and spasms. Establishing or excluding a specific diagnosis often requires repeated cultures and various urologic procedures, including cystoscopy with bladder biopsies, various bladder tests, and immune system function examinations. Some conditions, such as carcinoma in situ, bladder calculi, and urethral foreign bodies, may result in symptoms that mimic those of nonbacterial cystitis.

Ectopic Pregnancy

Overview

Ectopic pregnancy continues to be the leading cause of first-trimester maternal death. Although diagnosis and management have improved, the incidence of this disease has continued to climb since the US Centers for Disease Control and Prevention (CDC) started collecting data in 1970 [28]. This increase is likely due to a continued rise in the prevalence of predisposing risk factors. Ectopic pregnancy has additional significance in that the associated mortality with this condition usually affects an otherwise healthy segment of the population.

Preferred Examination

To diagnose an ectopic pregnancy, beta-HCG tests are required. A negative beta-HCG result effectively excludes the diagnosis of an ectopic or intrauterine pregnancy. In unstable patients, surgical evaluation and/or laparoscopy should be performed with or without culdocentesis. In patients with a stable clinical condition, transabdominal (TA) and endovaginal (EV) ultrasonography are performed [29]. The demonstration of an intrauterine gestational sac effectively excludes the diagnosis of an ectopic pregnancy. A search for a possible ectopic pregnancy as part of a heterotopic pregnancy should be attempted. Medical management is often associated with follow-up imaging [30,31]. Follow-up ultrasonography, along with follow-up beta-HCG levels, can be helpful if the diagnosis is unclear. A normal intrauterine pregnancy should demonstrate a 48-hour beta-HCG doubling time. Magnetic resonance imaging (MRI) has been used as a problem-solving tool in patients in stable condition and with special circumstances [32-35]. Active research continues in an attempt to elucidate an ectopic-specific serum marker. Multiple markers show some diagnostic benefit in attempting to discriminate an ectopic pregnancy from a normal intrauterine gestation; however, their use is still widely in the investigative stage. Some of the many markers investigated include progesterone, cancer antigen-125 (CA-125), pregnancy-associated plasma protein A (PAPP-A), and activin A.

Limitations of Techniques

TA and EV ultrasonography are recommended in all studies. In a patient in stable condition, a full bladder should be present as a proper TA ultrasonography window. In unstable patients in whom an expeditious diagnosis is needed, the time delay for the bladder to fill may be undesirable. TA and/or EV ultrasonography may be performed in these patients with an empty bladder. Both TA and EV examinations should still be performed with the acknowledgment of the limited, yet important, aspects of the TA portion of the examination. TA examination enables better evaluation of the superior uterus and superiorly positioned adnexa. It may aid detection of free peritoneal fluid and/or hemorrhage beyond the cul-de-sac. Transvaginal examination provides a detailed evaluation of the endometrial cavity and ovaries, but the high-frequency transducer that allows improved near-field resolution compared with TA examinations suffers from limited sound penetration (far-field imaging). MRI examination is time consuming and costly. Computed tomography (CT) scan findings are nonspecific in ectopic pregnancies and pose a hazard of ionizing radiation, which may be harmful to normal pregnancies.

Interstitial Cystitis

Interstitial cystitis is a clinical syndrome characterized by daytime and nighttime urinary frequency, urgency, and pelvic pain. Interstitial cystitis has no clear etiology or pathophysiology, and diagnostic criteria for the syndrome remain undefined. Despite considerable research, universally effective treatments do not exist; therapy usually consists of various supportive, behavioral, and pharmacologic measures. Surgical intervention is rarely indicated [36]. The International Continence Society has coined the term painful bladder syndrome (suprapubic pain with bladder filling associated with increased daytime and nighttime frequency, in the absence of proven urinary infection or other obvious pathology) and reserves the diagnosis of interstitial cystitis for patients with characteristic cystoscopic and histologic features of the condition [37]. An international consensus panel was able to generally agree on the following definition of interstitial cystitis/bladder pain syndrome (IC/BPS): unpleasant sensation (pain, pressure, discomfort) perceived to be related to the urinary bladder and associated with lower urinary tract symptoms of more than 6 weeks' duration, in the absence of infection or other identifiable causes. American Urological Association (AUA) guidelines published in 2011 and amended in 2014 use an evidence-based approach to provide a clinical framework for the diagnosis and management of this condition. [3] The Canadian Urological Association issued a guideline on diagnosis and treatment of IC/BPS in 2016.

Despite years of intensive research, there are no specific clinical or urinary markers currently clinically available; no absolutely specific radiographic, laboratory, or serologic findings; and no biopsy pat-

terns that are pathognomonic for interstitial cystitis. The syndrome remains a diagnosis of exclusion. Intensive study has been done to attempt to identify biomarkers for IC/BPS. Some interesting studies have shown that bladder nitric oxide is an accurate marker for Hunner lesions, but these are not present in all patients, and the test requires specific equipment, which has limited widespread clinical use. Differences in levels of cytokines and chemokines, specifically CXCL-10, have shown some ability to differentiate patients with and without Hunner lesions. Other studies of ulcerative IC/BPS have shown that numerous other cytokines and chemokines are up-regulated as well, heralding a possible urinary test to identify patients. Perhaps the most promising urinary biomarker for IC/BPS is antiproliferative factor (APF). This small 8–amino-acid peptide has been associated with suppression of cell growth, increases in transcellular permeability, and lowering of levels of proteins that form intercellular junctional complexes. APF is synthesized and secreted by bladder epithelial cells from patients with IC/BPS and may play a key role in pathophysiology. In vitro studies have shown that removal of APF from cell culture media restored cell proliferation and membrane integrity. Studies have also suggested a role for APF in the therapeutic effect of hydrodistension in patients with IC/BPS, although further confirmatory studies are necessary [38].

Treatment

The most important element in treating patients with interstitial cystitis is education and emotional support. Periodic exacerbations are managed as they occur because no long-term therapy has been shown to prevent or delay recurrent episodes. Therefore, the purpose of treatment is to palliate and alleviate symptoms. Because no discrete pathognomonic pathologic criteria exist for assessing and monitoring disease severity, indications and goals for treatment are based on the degree of patient symptoms. Assessing patient response to treatment is also complicated because of the subjective nature of symptoms; the waxing and waning nature of symptoms without treatment; and the lack of objective serologic, physical, or histopathologic findings. Conservative measures and oral or intravesical treatments are considered first-line treatment

Nephrolithiasis

Nephrolithiasis specifically refers to calculi in the kidneys, but renal calculi and ureteral calculi (ureterolithiasis) are often discussed in conjunction. The majority of renal calculi contain calcium. The pain generated by renal colic is primarily caused by dilation, stretching, and spasm because of the acute ureteral obstruction.

Signs and Symptoms

The classic presentation for a patient with acute renal colic is the sudden onset of severe pain originating in the flank and radiating inferiorly and anteriorly; at least 50% of patients will also have nausea and vomiting. Patients with urinary calculi may report pain, infection, or hematuria. Patients with small, non-obstructing stones or those with staghorn calculi may be asymptomatic or experience moderate and easily controlled symptoms.

The location and characteristics of pain in nephrolithiasis include the following:

- Stones obstructing ureteropelvic junction: Mild to severe deep flank pain without radiation to the groin; irritative voiding symptoms (eg, frequency, dysuria); suprapubic pain, urinary frequency/urgency, dysuria, stranguria, bowel symptoms
- Stones within ureter: Abrupt, severe, colicky pain in the flank and ipsilateral lower abdomen; radiation to testicles or vulvar area; intense nausea with or without vomiting
- Upper ureteral stones: Radiate to flank or lumbar areas
- Midureteral calculi: Radiate anteriorly and caudally
- Distal ureteral stones: Radiate into groin or testicle (men) or labia majora (women)
- Stones passed into bladder: Mostly asymptomatic; rarely, positional urinary retention

Diagnosis

The diagnosis of nephrolithiasis is often made on the basis of clinical symptoms alone, although confirmatory tests are usually performed.

Examination in patients with nephrolithiasis includes the following findings:

- Dramatic costovertebral angle tenderness; pain can move to upper/lower abdominal quadrant with migration of ureteral stone
- Generally unremarkable abdominal evaluation: Possibly hypoactive bowel sounds; usually absence of peritoneal signs; possibly painful testicles but normal-appearing
- Constant body positional movements (eg, writhing, pacing)
- Tachycardia
- Hypertension
- Microscopic hematuria

Testing

The European Association of Urology (EAU) recommends the following laboratory tests in all patients with an acute stone episode [39]

- Urinary sediment/dipstick test: To demonstrate blood cells, with a test for bacteriuria (nitrite) and urine culture in case of a positive reaction
- Serum creatinine level: To measure renal function

Other laboratory tests that may be helpful include the following:

- CBC with differential in febrile patients
- Serum electrolyte assessment in vomiting patients (eg, sodium, potassium, calcium, PTH, phosphorus)
- Serum and urinary pH level: May provide insight regarding patient's renal function and type of calculus (eg, calcium oxalate, uric acid, cystine), respectively
- Microscopic urinalysis
- 24-Hour urine profile

Imaging Studies

The following imaging studies are used in the evaluation of nephrolithiasis:

- Noncontrast abdominopelvic CT scan: The imaging modality of choice for assessment of urinary tract disease, especially acute renal colic
- Renal ultrasonography: To determine presence of a renal stone and the presence of hydronephrosis or ureteral dilation; used alone or in combination with plain abdominal radiography
- Plain abdominal radiograph (flat plate or KUB): To assess total stone burden, as well as size, shape, composition, location of urinary calculi; often used in conjunction with renal ultrasonography or CT scanning
- IVP (urography) (historically, the criterion standard): For clear visualization of entire urinary system, identification of specific problematic stone among many pelvic calcifications, demonstration of affected and contralateral kidney function
- Plain renal tomography: For monitoring a difficult-to-observe stone after therapy, clarifying stones not clearly detected or identified with other studies, finding small renal calculi, and determining number of renal calculi present before instituting a stone-prevention program
- Retrograde pyelography: Most precise imaging method for determining the anatomy of the ureter and renal pelvis; for making definitive diagnosis of any ureteral calculus
- Nuclear renal scanning: To objectively measure differential renal function, especially in a dilated system for which the degree of obstruction is in question; reasonable study in pregnant patients, in whom radiation exposure must be limited [40-42].

Management

Supportive Care and Pharmacotherapy

Medical treatment of nephrolithiasis involves supportive care and administration of agents, such as the following:

Acute Stone Attacks (Renal Colic):

- IV hydration
- NSAIDS (eg, ketorolac, ketorolac intranasal, ibuprofen)
- Nonnarcotic analgesics (eg, APAP)
- PO/IV narcotic analgesics (eg, codeine, morphine sulfate, oxycodone/APAP, hydrocodone/APAP, dilaudid, fentanyl)
- Alpha blockers (eg, tamsulosin, terazosin)
- Antiemetics (eg, metoclopramide, ondansetron)
- Antibiotics (eg, ampicillin, gentamicin, trimethoprim-sulfamethoxazole, ciprofloxacin, levofloxacin, ofloxacin)

Stone Prevention/Chemolysis

- Uricosuric agents (eg, allopurinol)
- Alkalinizing agents (eg, potassium citrate, sodium bicarbonate): For uric acid and cysteine calculi
- Thiazide diuretics- helps treat hypercalcicuria

Surgical Options

Stones that are 7 mm and larger are unlikely to pass spontaneously and require some type of surgical procedure, such as the following:

- Stent placement
- Percutaneous nephrostomy
- Extracorporeal shockwave lithotripsy (ESWL)
- Ureteroscopy
- Percutaneous nephrostolithotomy (PCNL) or mini PNCL
- Open nephrostomy- more historical
- Anatrophic nephrolithotomy- for large complex stag horn calculi that cannot be cleared by an acceptable number of PCNLs.Typically now done via laparoscopic or robotic approach

Trichomoniasis

Trichomoniasis is a sexually transmitted infection (STI) caused by the motile parasitic protozoan Trichomonas vaginalis. It is one of the most common STIs, both in the United States and worldwide. [6,43,44] The high prevalence of T vaginalis infection worldwide and the frequency of coinfection with other STIs make trichomoniasis a compelling public health concern. Notably, research has shown that infection with T vaginalis increases the risk of HIV transmission in both men and women. Trichomoniasis is also associated with adverse pregnancy outcomes, infertility, postoperative infections, and cervical neoplasia [45]. Humans are the only known host of T vaginalis. Transmission occurs predominantly via sexual intercourse. The organism is most commonly isolated from vaginal secretions in women and ure-

thral secretions in men. It has not been isolated from oral sites, and rectal prevalence appears to be low in men who have sex with men [46]. Women with trichomoniasis may be asymptomatic or may experience various symptoms, including a frothy yellow-green vaginal discharge and vulvar irritation. Men with trichomoniasis may experience nongonococcal urethritis but are frequently asymptomatic.

Trichomoniasis is thought to be widely underdiagnosed due to a variety of factors, including a lack of routine testing, the low sensitivity of a commonly used diagnostic technique (wet mount microscopy), [47,48] and nonspecific symptomatology. Self-diagnosis and self-treatment or diagnosis by practitioners without adequate laboratory testing may also contribute to misdiagnosis. Testing is recommended for T vaginalis in all women seeking care for vaginal discharge and screening for T vaginalis in women at high risk of STI. Sex partners of infected women should also be treated. Both patient and partner should abstain from sex until pharmacological treatment has been completed and they have no symptoms. Infected women who are sexually active have a high rate of reinfection; thus, rescreening at 3 months post treatment should be considered. Currently, no data are available on rescreening men. Oral metronidazole (Flagyl) remains the treatment of choice for trichomoniasis. In cases in which the first-line agent is ineffective, other nitroimidazoles or high doses of metronidazole may be used. Topical metronidazole and other antimicrobials are not efficacious and should not be used to treat trichomoniasis.

Trigonitis

Trigonitis refers to the nonkeratinizing squamous metaplastic changes in the bladder trigone. The trigone is the triangular area of the bladder bound by the ureteral orifices and the internal urethral sphincter, which is normally lined by urothelium, a type of transitional epithelial tissue. This entity was first described by Heymann in 1905 as cystitis trigoni and was subsequently described by Cifuentes as a true trigonal membrane. [49] It is also referred to in the literature as pseudomembranous trigonitis or vaginal metaplasia. Squamous metaplasia of the trigone occurs almost exclusively in women of childbearing age. It is almost nonexistent in children. Although the exact cause of trigonitis is unknown, the condition usually occurs in response to an irritative (eg, chronic indwelling catheter) or infectious process. Trigonitis is a benign lesion without malignant potential. It does not require follow-up cystoscopy. However, it should be distinguished from keratinizing squamous metaplasia (leukoplakia), which does require follow-up.

Urethritis

Urethritis is defined as infection-induced inflammation of the urethra. The term is typically reserved to describe urethral inflammation caused by a sexually transmitted disease (STD), and the condition is normally categorized as either gonococcal urethritis (GU) or nongonococcal urethritis (NGU).

Signs and Symptoms

Many patients with urethritis, including approximately 25% of those with NGU, are asymptomatic and present to a clinician following partner screening. Up to 75% of women with Chlamydia trachomatis infection are asymptomatic.

Signs and symptoms in patients with urethritis may include the following:

- Urethral discharge: May be yellow, green, brown, or tinged with blood; production unrelated to sexual activity
- Dysuria (in men): Usually localized to the meatus or distal penis, worst during the first morning void, and made worse by alcohol consumption; typically, not present are urinary frequency and urgency
- Itching: Sensation of urethral itching or irritation between voids
- Orchalgia: Heaviness in the male genitals
- Worsens during menstrual cycle (occasionally).
- Systemic symptoms (eg, fever, chills, sweats, nausea): Typically, absent

Diagnosis

Most patients with urethritis do not appear ill and do not present with signs of sepsis. The primary focus of the examination is on the genitalia. Examination in male patients with urethritis includes the following:

- Inspect the underwear for secretions
- Penis: Examine for skin lesions that may indicate other STDs (eg, condyloma acuminatum, herpes simplex, syphilis); in uncircumcised men, retract the foreskin to assess for lesions and exudate
- Urethra: Examine lumen of the distal urethral meatus for lesions, stricture, or obvious urethral discharge; palpate along urethra for areas of fluctuance, tenderness, or warmth suggestive of abscess or for firmness suggesting foreign body
- Testes: Examine for evidence of mass or inflammation; palpate the spermatic cord, looking for swelling, tenderness, or warmth suggestive of orchitis or epididymitis
- Lymphatics: Check for inguinal adenopathy
- Prostate: Palpate for tenderness or bogginess suggestive of prostatitis
- Rectal: During the digital rectal examination, note any perianal lesions

Examine female patients in the lithotomy position. Include the following evaluation:

- Skin: Assess for lesions that may indicate other STDs
- Urethra: Strip the urethra for any discharge
- Pelvis: Complete pelvic examination, including the cervix

Testing

Urethritis can be diagnosed based on the presence of one or more of the following:

- A mucopurulent or purulent urethral discharge
- Urethral smear that demonstrates at least 5 leukocytes per oil immersion field on microscopy
- First-voided urine specimen that demonstrates leukocyte esterase on dipstick test or at least 10 WBCs/hpf on microscopy

All patients with urethritis should be tested for Neisseria gonorrhoeae and C trachomatis. Laboratory studies may include the following:

- Gram stain
- Endourethral and/or endocervical culture for N gonorrhoeae and C trachomatis
- Urinalysis: Not useful test in urethritis, except to help exclude cystitis or pyelonephritis
- Nucleic acid–based tests: For C trachomatisand N gonorrhoeae (urine specimens) and other Chlamydia species (endourethral samples)
- Nucleic acid amplification tests (eg, PCR for N gonorrhoeae, Chlamydia species)
- KOH preparation: to evaluate for fungal organisms
- Wet mount preparation: To detect the movement/presence of Trichomonas
- STD testing for syphilis serology (VDRL) and HIV serology
- Nasopharyngeal and/or rectal swabs: For gonorrhea screening in men who have sex with men
- Pregnancy testing: In women who have had unprotected intercourse.

Imaging Studies

Imaging studies, specifically retrograde urethrography, are unnecessary in patients with urethritis, except in cases of trauma or possible foreign body insertion.

Procedures

Patients with urethritis may undergo the following procedures:

- Catherization: In cases of urethral trauma; to avoid urinary retention and tamponade urethral bleeding
- Cystoscopy: In cases when catherization is not possible, for placement of a catheter; to remove foreign body or stone in the urethra
- Dilation of urethral strictures with filiforms and followers
- Placement of suprapubic tube: In severe cases of urethral trauma that prevent placement of urethral catheters or in the absence of adequate facilities for emergent cystoscopy; temporizing measure to divert urine and relieve patient discomfort [50-53].

Management

Symptoms of urethritis spontaneously resolve over time, regardless of treatment. Administer antibiotics that cover both GU and NGU. Regardless of symptoms, administer antibiotics to the following individuals:

- Patients with positive Gram stain or culture results
- All sexual partners of the above patients
- Patients with negative Gram stain results and a history consistent with urethritis who are not likely to return for follow-up and/or are likely to continue transmitting infection

Antibiotics used in the treatment of urethritis include the following:

- Azithromycin
- Ceftriaxone
- Cefixime
- Ciprofloxacin
- Ofloxacin
- Doxycycline
- Moxifloxacin

Vaginitis

Vaginitis (inflammation of the vagina) is the most common gynecologic condition encountered in the office. It is a diagnosis based on the presence of symptoms of abnormal discharge, vulvovaginal discomfort, or both. Cervicitis may also cause a discharge and sometimes occurs with vaginitis. Discharge flows from the vagina daily as the body's way of maintaining a normal healthy environment. Normal discharge is usually clear or milky with no malodor. A change in the amount, color, or smell; irritation; or itching or burning could be due to an imbalance of healthy bacteria in the vagina, leading to vaginitis. The most common causes of vaginitis in symptomatic women are bacterial vaginosis (40-45%), vaginal candidiasis (20-25%), and trichomoniasis (15-20%); yet 7-72% of women with vaginitis may remain undiagnosed. [54-57] The workup for patients with vaginitis depends

on the risk factors for infection and the age of the patient. Accurate diagnosis may be elusive, and care must be taken to distinguish vaginitis from other infectious and noninfectious causes of symptoms. All women presenting with abnormal vaginal discharge should have a careful pelvic examination. Condition-specific tests (ie, colposcopy and cervical biopsies) are indicated for suspected cervical cancer. Studies that may be performed in cases of suspected vaginitis include saline wet mount, the so-called whiff test, pH testing, culture, nucleic acid amplification testing, and a number of other second-line tests. Treatment of vaginitis varies by cause and is directed at the relevant pathogen. Inpatient care usually is not indicated, unless serious pelvic infections arise or evidence of systemic infection in an immunocompromised host is present.

Urinary Tract Infections in Pregnancy Treatment & Management

Because of the dangers of maternal and fetal complications, acute care (eg, in the emergency department [ED]) should focus on identifying and treating asymptomatic and symptomatic bacteriuria, along with ensuring that an alternate process is not the cause of the symptoms. Treatment of asymptomatic bacteriuria in pregnant patients is important because of the increased risk of urinary tract infection (UTI) and its associated sequelae. [22] ED care may involve the following:

- Administration of appropriate antibiotics
- Administration of fluid if the patient is dehydrated
- Admission if any indication of complicated UTI exists

Behavioral Methods

Any discussion of treatment should be prefaced with a discussion of behavioral methods that may be used to ensure good hygiene and reduce bacterial contamination of the urethral meatus, thereby preventing inadequate treatment and recurrent infection.

Behavioral methods include the following:

- Avoid baths
- Wipe front-to-back after urinating or defecating
- Wash hands before using the toilet
- Use washcloths to clean the perineum
- Use liquid soap to prevent colonization from bar soap
- Clean the urethral meatus first when bathing.

Antibiotic Therapy

Oral antibiotics are the treatment of choice for asymptomatic bacteriuria and cystitis. Appropriate oral regimens include the following:

- Cephalexin 500 mg 4 times daily
- Ampicillin 500 mg 4 times daily
- Nitrofurantoin 100 mg twice daily
- Sulfisoxazole 1 g 4 times daily

The resistance of Escherichia coli to ampicillin and amoxicillin is 20-40%; accordingly, these agents are no longer considered optimal for treatment of UTIs caused by this organism. Fosfomycin, a phosphonic acid derivative, is useful in the treatment of uncomplicated UTIs caused by susceptible strains of E coli and Enterococcus species. Fosfomycin is a US Food and Drug Administration (FDA) category B agent in pregnancy (ie, animal studies have not demonstrated a risk to the fetus and there are no adequate and well-controlled studies in pregnant women). Although 1-, 3-, and 7-day antibiotic courses have been evaluated, 10-14 days of treatment is usually recommended to eradicate the offending bacteria. For example, studies with cephalexin, trimethoprim-sulfamethoxazole, and amoxicillin have indicated that a single dose is as effective as a 3- to 7-day course of therapy, but the cure rate is only 70%.

A systematic review that compared single-dose antibiotic treatment with 4- to 7-day treatments concluded that single-dose regimens may be less effective than a short-course regimen, but until more data become available from large trials, pregnant women with asymptomatic bacteriuria should be treated with the standard regimen [58-62]. Treatment success depends on eradication of the bacteria rather than on the duration of therapy. A test-for-cure urine culture should show negative findings 1-2 weeks after therapy. A nonnegative culture result is an indication for a 10- to 14-day course of a different antibiotic, followed by suppressive therapy (eg, nitrofurantoin 50 mg at bedtime) until 6 weeks postpartum. Mathai et al suggest the need for disseminated guidelines for practitioners in developing countries such as India. [24] Their study documented inappropriate use of antibiotics in terms of safety, cost, susceptibility, and threat for developing resistance.

Treatment of Pyelonephritis

The standard course of treatment for pyelonephritis consists of hospital admission and intravenous (IV) administration of cephalosporins or gentamicin. IV fluids must be administered with caution. Patients with pyelonephritis can become dehydrated because of nausea and vomiting and need IV hydration. However, they are at high risk for the development of pulmonary edema and acute respiratory distress syndrome (ARDS). Fever should be managed with antipyretics (preferably, acetaminophen) and nausea and vomiting with antiemetics. Most antiemetics can be used for adverse effects caused by antibiotics, but doxylamine, Emetrol (Wellspring, Sarasota, FL; pregnancy class A), dimenhydrinate, and metoclopramide (pregnancy class B) are preferred. Preterm labor and delivery are additional risks associated with pyelonephritis. These risks must be evaluated and treated early in the course of admission. In a randomized, controlled trial of outpatient treatment of pyelonephritis in pregnancy, Millar et

al concluded that outpatient therapy is as safe and effective as inpatient care in the treatment of pyelonephritis before 24 weeks' gestation. However, the prevailing view is still that aggressive inpatient hydration and parenteral antibiotics are necessary. Pyelonephritis places the patient at risk for spontaneous abortion in early pregnancy and for preterm labor after 24 weeks' gestation.

In their study, Millar et al treated outpatients with 2 doses of intramuscular (IM) ceftriaxone and 10 days of oral cephalexin [63]. Initial outpatient therapy and traditional inpatient therapy failed to cure equal numbers of patients. Benefits include the obvious cost savings and the psychosocial benefits for the patient. Risks include septic shock and respiratory insufficiency at home during outpatient therapy. Strict guidelines for an observation period before ED discharge, patient education, and home nursing have been discussed. In addition, approximately two thirds of the outpatient treatment group did not complete the study because the subjects developed 1 or more complications. If outpatient therapy is considered, only selected patients in their second trimester should be considered. More study is necessary before a change in the physician's practice pattern is considered.

Antibiotic Selection

Antibiotic selection should be based on urine culture sensitivities, if known. Often, therapy must be initiated on an empirical basis, before culture results are available. This requires clinical knowledge of the most common organisms and their practice-specific or hospital-specific sensitivities to medications. Institution-specific drug resistances should also be considered before a treatment antibiotic is chosen. For instance, with E coli infection alone, resistance to ampicillin can be as high as 28-39%. Resistance to trimethoprim-sulfamethoxazole has been described as 31%, and resistance to first-generation cephalosporins may be as high as 9-19%. Maternal physiologic changes that influence pharmacokinetics include increased glomerular filtration rate (GFR) and renal plasma flow, increased volume of distribution, decreased gastric motility and emptying, and decreased albumin levels. Serum levels of antibiotics are lower in pregnancy because of the gross increase in blood volume and the increased GFR.

Some antibiotics should not be used during pregnancy, because of their effects on the fetus. These include the following:

- Tetracyclines (adverse effects on fetal teeth and bones and congenital defects)
- Trimethoprim in the first trimester (facial defects and cardiac abnormalities)
- Chloramphenicol (gray syndrome)
- Sulfonamides in the third trimester (hemolytic anemia in mothers with glucose-6-phosphate dehydrogenase [G6PD] deficiency, jaundice, and kernicterus) Fluoroquinolones are to be used with caution in pregnancy.

Both ciprofloxacin and levofloxacin have been assigned pregnancy category C by the FDA (fetal risk is not confirmed by human studies but has been shown in some animal studies). Although not a first-line option for treatment of UTI in pregnancy, in certain clinical situations the benefits of using a fluoroquinolone may outweigh the risks to the developing fetus. Risks to the mother from fluoroquinolones must also be considered. In May 2016 the FDA advised that the risks of fluoroquinolones generally outweigh the benefits for patients with uncomplicated infections, including UTIs, and recommended reserving fluoroquinolones for patients who do not have alternative treatment options. Disabling and potentially permanent serious adverse effects associated with fluoroquinolones have involved tendons, muscles, joints, nerves, and the central nervous system [64-67]. Nitrofurantoin is safe and effective; however, poor tissue penetration has limited its use in pyelonephritis. In the past, nitrofurantoin was completely avoided in the third trimester because of hemolytic effects on the newborn.

Currently, restriction of this agent is limited to the last several weeks of pregnancy. Use during this period can cause hemolytic anemia in the fetus or neonate as a consequence of their immature erythrocyte enzyme systems (glutathione instability). Nitrofurantoin is also safe and effective for once-daily prophylactic therapy during pregnancy. Macrolides are not first-line agents for UTI in pregnancy. However, they are well tolerated by mother and fetus. A meta-analysis concluded that although antibiotic treatment is effective in patients with UTIs, the data are insufficient to recommend any specific regimen for treatment of symptomatic UTIs during pregnancy [68-71]. All of the antibiotics studied were effective in terms of both increasing cure rates of UTI in pregnancy and decreasing the incidence of associated adverse outcomes.

Current regimens are summarized below.

First-line therapy

- Nitrofurantoin monohydrate/macrocrystals 100 mg orally twice daily for 5-7 days or
- Amoxicillin 500 mg orally twice daily (alternative: 250 mg orally three times daily) for 5-7 days or
- Amoxicillin-clavulanate 500/125 mg orally twice daily for 3-7 days (alternative: 250/125 mg orally three times daily for 5-7 days) or
- Cephalexin 500 mg orally twice daily for 3-7 days

Second-line therapy

- Fosfomycin 3 g orally as single dose with 3-4 oz. of water

Surgical Treatment

Surgical care is rarely indicated, unless one of the pathologic causes listed in the differential diagnoses is suspected. In patients with urethral or bladder diverticulum, bladder stones, urethral syndrome,

lower urinary tract trauma, interstitial cystitis, or bladder cancer, cystoscopy may aid in establishing the diagnosis. A retrograde stent or a percutaneous nephrostomy tube should be placed to relieve ureteral colic or decompress an obstructed infected collecting system. More invasive procedures, such as ureteroscopic stone extraction, [29] are rarely indicated. Extracorporeal shock wave lithotripsy (ESWL) is contraindicated in pregnancy. In the rare patient for whom invasive surgical therapy is indicated, the operation should be planned for the second trimester. Surgical intervention during the first trimester is associated with miscarriage; surgery in the third trimester is associated with preterm labor. Urgent surgical intervention in the third trimester should coincide with delivery of the fetus.

Preterm Labor

Preterm labor is defined as the presence of uterine contractions of sufficient frequency and intensity to effect progressive effacement and dilation of the cervix prior to term gestation. Occurring at 20-37 weeks' gestation, preterm labor precedes almost half of preterm births and is the leading cause of neonatal mortality in the United States.

Risk of Preterm Labor

The exact mechanisms of preterm labor are largely unknown but are believed to include the following:

- Decidual hemorrhage such as abruption and mechanical factors such as uterine overdistention from multiple gestation or polyhydramnios
- Cervical incompetence (eg, trauma, cone biopsy)
- Uterine distortion (eg, müllerian duct abnormalities, fibroid uterus)
- Cervical inflammation as a result of, for example, bacterial vaginosis (BV) or trichomonas
- Maternal inflammation/fever (eg, urinary tract infection)
- Hormonal changes (eg, mediated by maternal or fetal stress)
- Uteroplacental insufficiency (eg, hypertension, insulin-dependent diabetes, drug abuse, smoking, alcohol consumption) [72-76].

Risk Assessment During Pregnancy

Physical Assessment

The integrity of the cervix and the extent of any prior injury to the cervix may be assessed by speculum and digital examination. The presence of asymptomatic bacteriuria, sexually transmitted disease (STD), and symptomatic BV may be investigated

History

A history of prior preterm deliveries places the patient in the high-risk category. Of the predictors of preterm birth, past obstetric history may be one of the strongest predictors of recurrent preterm birth.

Cervical Length

A short cervical length in the early or late second trimester has been associated with a markedly increased risk of preterm labor and delivery. In a study, a cervical length of 25 mm or less at 28 weeks had a 49% sensitivity for prediction of preterm delivery at less than 35 weeks [77-79].

Laboratory Tests

In patients with a history of midtrimester loss, laboratory tests for risk assessment include the following:

- Rapid plasma reagin test
- Gonorrheal and chlamydial screening
- Vaginal pH/wet smear/whiff test
- Anticardiolipin antibody (eg, anticardiolipin immunoglobulin [Ig] G and IgM, anti-beta2 microglobulin)
- Lupus anticoagulant antibody
- Activated partial thromboplastin time
- One-hour glucose challenge test

In addition, one should consider TORCH (toxoplasmosis, other infections, rubella, cytomegalovirus infection, herpes simplex), immunoglobulin G, and immunoglobulin M screening whenever the historical or clinical suspicion is present.

Diagnosis

Contractions of sufficient frequency and intensity to effect progressive effacement and dilation of the cervix at 24-37 weeks' gestation are indicative of active preterm labor. If the diagnosis of preterm labor is suspected, but not confirmed, it may be prudent to first obtain a vaginal fetal fibronectin (FFN) sample before pelvic cervical examination. If the diagnosis remains in doubt after the exam, the FFN specimen can be sent to the lab for analysis [80-82].

Management

Progesterone

Studies support the use of progesterone supplementation to reduce preterm birth in patients at high risk for recurrent preterm delivery.

Tocolytic Agents

Criteria that indicate consideration of tocolytic therapy include more than 6 contractions per hour resulting in a demonstrated cervical change or presumed prior cervical change (transvaginal cervical length < 25 mm, >50% cervical effacement, or cervical dilation ≥20

mm). If contractions are present without cervical change, management options include continued observation or therapeutic sleep for the patient (eg, morphine sulphate 10-15 mg subcutaneous).

The most common tocolytic agents used to treat preterm labor include the following:

- Magnesium sulfate (MgSO4): Widely used as the primary tocolytic agent because it has similar efficacy to terbutaline (one of the previous agents of choice), with far better tolerance
- Indomethacin: An appropriate first-line tocolytic for early preterm labor (< 30 wk) or preterm labor associated with polyhydramnios
- Nifedipine: Despite its unlabeled status, several randomized studies have found nifedipine to be associated with a more frequent successful prolongation of pregnancy than other tocolytics [83-87].

Overview

Preterm labor is defined as the presence of uterine contractions of sufficient frequency and intensity to effect progressive effacement and dilation of the cervix prior to term gestation (between 20 and 37 wk). Preterm labor precedes almost half of preterm births and preterm birth occurs in approximately 12% of pregnancies and is the leading cause of neonatal mortality in the United States. In addition, preterm birth accounts for 70% of neonatal morbidity, mortality, and health care dollars spent on the neonate, largely due to the 2% of American women delivering very premature infants (< 32 wk). [88-90] Despite the current use of material, effort, and money in perinatal medical technology, neonatal mortality rates for newborns born in the United States (5 per 1,000 babies) may rank as low as 32nd among the 33 industrialized nations, superior only to Latvia. [91,92] Successful reduction of perinatal morbidity and mortality associated with prematurity may require the implementation of effective risk identification and behavioral modification programs for the prevention of preterm labor; these in turn require both an improved understanding of the psychosocial risk factors, etiology, and mechanisms of preterm labor and programs for accurate identification of pregnant women at risk for premature labor and delivery. In fact, recent evidence suggests that early identification of at-risk gravidas with timely referral for subspecialized obstetrical care may help identify women at risk for preterm labor and delivery and decrease the extreme prematurity (< 32 wk) rate, thereby reducing the morbidity, mortality, and expense associated with prematurity.

Goals of Management

The focus of this article is the prevention, diagnosis, and treatment of preterm labor with intact membranes. The management of preterm labor associated with ruptured membranes is reviewed in Premature Rupture of Membranes; however, the overall goals of both management schemes are similar. Goals of obstetric patient management of preterm labor should include

(1) Early identification of risk factors associated with preterm birth,

(2) Timely diagnosis of preterm labor,

(3) Identifying the etiology of preterm labor,

(4) Evaluating fetal well-being,

(5) Providing prophylactic pharmacologic therapy to prolong gestation and reduce the incidence of respiratory distress syndrome (RDS) and intra-amniotic infection (IAI),

(6) Initiating tocolytic therapy when indicated, and

(7) Establishing a plan of maternal and fetal surveillance with patient/provider education to improve neonatal outcome.

Risk of Preterm Labor

The exact mechanism(s) of preterm labor is largely unknown but is believed to include decidual hemorrhage, (eg, abruption, mechanical factors such as uterine overdistension from multiple gestation or polyhydramnios), cervical incompetence (eg, trauma, cone biopsy), uterine distortion (eg, müllerian duct abnormalities, fibroid uterus), cervical inflammation (eg, resulting from bacterial vaginosis [BV], trichomonas), maternal inflammation/fever (eg, urinary tract infection), hormonal changes (eg, mediated by maternal or fetal stress), and uteroplacental insufficiency (eg, hypertension, insulin-dependent diabetes, drug abuse, smoking, alcohol consumption) [93-96]. A genome wide association study that included 43,568 European women identified six genes (BF1, EEFSEC, AGTR2, WNT4, ADCY5, and RAP2C) that were associated with gestational duration, of which, three genes were associated with preterm birth (EBF1, EEFSEC, and AGTR2). Although prediction of preterm delivery remains inexact, a variety of maternal and obstetric characteristics are known to increase the risk, presumably via one of these mechanisms. Finally, the fetus plays a role in the initiation of labor. In a simplistic sense, the fetus recognizes a hostile intrauterine environment and precipitates labor by premature activation of a fetal-placental parturition pathway. Risk factors for preterm birth include demographic characteristics, behavioral factors, and aspects of obstetric history such as previous preterm birth. Demographic factors for preterm labor include nonwhite race, extremes of maternal age (< 17 y or >35 y), low socioeconomic status, and low pre-pregnancy weight.

Preterm labor and birth can be associated with stressful life situations (eg, domestic violence; close family death; insecurity over food, home, or partner; work and home environment) either indirectly by associated risk behaviors or directly by mechanisms not completely understood. Many risk factors may manifest in the same gravida. Methods used for predicting preterm birth include home uterine activity monitoring (HUAM), assessments of salivary estriol, fetal fibronectin (FFN), the presence of BV, and cervical length assessment.

- While hospital tocodynamometry has been effective for monitoring uterine contractions to evaluate preterm labor, HUAM has not been proven valuable in detecting or preventing preterm birth and is not currently recommended for use.

- The proposed use of salivary estriol measurements in detecting preterm labor was based on the belief that the adrenal gland production of dehydroepiandrosterone increases before the onset of labor, which results in an increase of maternal estriol. Unfortunately, maternal estriol levels show diurnal variation, peaking at night, and are suppressed by betamethasone administration, thereby decreasing the predictive value of salivary estriol in the detection of preterm delivery risk.

- FFN is a basement membrane protein that helps bind placental membranes to the decidua. While a negative FFN is helpful in predicting women who are not destined to deliver preterm, a positive FFN has limited value in predicting women who will deliver preterm. Nevertheless, FFN has a predictive value in identifying patients who will or will not deliver within the subsequent 1-2 weeks.

- While the presence of BV has been associated with the risk of preterm delivery, prospective treatment trials eradicating asymptomatic BV failed to reduce the risk of preterm delivery.

- Longer term prediction of the risk of preterm delivery is achieved by cervical length measurements. A short cervical length in the early or late second trimester has been associated with a markedly increased risk of preterm labor and delivery. The prediction of preterm delivery may potentially be improved by combining FFN testing with measurements of cervical length.

Pre-Conceptual Evaluation

While the risk for preterm birth in nulliparous patients is hard to determine, past obstetric experience and personal behavior may provide significant insight into future pregnancy outcome in multiparous women. Identifying at-risk patients pre-conceptually may allow additional treatment options. Women who seek birth control have a 30% chance of becoming pregnant in the next 2 years, suggesting that these women represent one potential opportunity for intervention. The presence of the following risk factors should be addressed prior to pregnancy.

Cervical Trauma

The most common etiologies for cervical injury are elective abortion, surgeries to treat cervical dysplasia, and injury occurring at delivery. A single uncomplicated elective abortion at less than 10 weeks' gestation does not increase the risk of mid trimester loss or preterm birth unless the cervix has been forcibly dilated to more than 10 mm at the time of the abortion. However, patients with a history of multiple first-trimester elective terminations or one or more second-trimester elective abortions may be at increased risk for preterm delivery. Cervical dilatation with laminaria or cervical ripening agents, such as misoprostol, appears to be less traumatizing to the cervix than mechanical dilation. Cervical dysplasia should be treated appropriately whenever diagnosed. However the incidence of preterm birth and cervical incompetence may be increased 200-300% after preconceptual surgical treatment (eg, cold knife cone, cryoconization, laser cone, LEEP) of cervical intraepithelial neoplasia (CIN). The risk of subsequent preterm delivery may be proportional to the amount of cervical tissue removed during surgery. Surprisingly, the ease of performing LEEP for relatively minor abnormalities may have paradoxically led to more cervical injury than was observed with the relatively more invasive cone biopsy. Obstetric trauma may be underestimated as a risk for mid trimester loss or preterm birth. While women may relate a history of cervical laceration, often they are unaware of the injury and the obstetric records of the previous delivery may be misleading as to the extent of the cervical injury. Therefore, visual inspection of the cervix is important to assess the degree of injury and risk. Defects that involve more than 50% of the cervical length may indicate a higher risk for mid trimester loss [97]. The accuracy of transvaginal ultrasonic measurements to determine risk of cervical incompetence, specifically in the presence of a history of cervical trauma, has yet to be determined.

Genital Tract Infection

The young gynecology patient diagnosed with gonorrhea, chlamydia, or trichomoniasis has an approximate 25% risk of reinfection during the subsequent 12 months, but a clear association between these organisms and preterm delivery has not been established. BV is a vaginal syndrome associated with an alteration of the normal vaginal flora rather than an infection specific to any one organism and a lack of vaginal inflammation is evident when compared with vaginitis. The diagnosis of BV should be suspected with a positive Gram stain result or the presence of 3 of 4 traditional diagnostic signs (homogenous gray-white discharge, >20% clue cells on saline wet smear, positive whiff test, and a vaginal pH >4.50) Patients should be treated per the US Centers for Disease Control and Prevention guidelines, with test-of-cure sampling and subsequent treatment if necessary.

Preterm Labor/Birth History

A history of prior preterm deliveries places the patient in the high-risk category. Of the predictors of preterm birth, past obstetric history may be one of the strongest predictors of recurrent preterm birth. Given a baseline risk of 10-12%, the risk of recurrent preterm birth after 1, 2, and 3 consecutive preterm births may be increased to approximately 15%, 30%, and 45%, respectively. Pre-conceptual counseling should help encourage patients to make informed decisions concerning future pregnancy in light of prematurity risk in the presence of previous preterm delivery. Often the best time to counsel the patient is at her 4- to 6-week postpartum check after a preterm delivery. Lykke et al found that spontaneous preterm delivery, preeclampsia, or fetal growth deviation in a first singleton pregnancy

predisposes women to those complications in their second pregnancy, especially if the complications were severe. In a registry-based cohort study of 536,419 Danish women, delivery between 32 and 36 weeks of gestation increased the risk of preterm delivery in the second pregnancy from 2.7% to 14.7% (odds ratio [OR] 6.12; 95% confidence interval [CI], 5.84-6.42) and increased the risk of preeclampsia from 1.1% to 1.8% (OR 1.60; 95% CI, 1.41-1.81). A first delivery before 28 weeks increased the risk of a second preterm delivery to 26.0% (OR 13.1; 95% CI, 10.8-15.9) and increased the risk of preeclampsia to 3.2% (OR 2.96; 95% CI, 1.80-4.88). The optimal method of preventing preterm birth in multiple gestations has yet to be proven. Cervical cerclage, prophylactic bed rest, and empiric use of tocolytics have not been successful.

Most recently, a randomized controlled trial by Lim et al suggests that the use of 17α-hydroxyprogesterone caproate does not prevent neonatal morbidity or preterm birth in multiple pregnancies. Preeclampsia in a first pregnancy with delivery between 32 and 36 weeks increased the risk of preeclampsia in a second pregnancy from 14.1% to 25.3% (OR 2.08; 95% CI, 1.87-2.31) and increased the risk for a small for gestational age infant from 3.1% to 9.6% (OR 2.82; 95% CI, 2.38-3.35). Fetal growth 2 to 3 standard deviations below the mean in a first pregnancy increased the risk of preeclampsia from 1.1% to 1.8% (OR 1.62; 95% CI, 1.34-1.96) in the second pregnancy.

Mid-trimester Loss

Mid-trimester loss has many etiologies, including infection (eg, syphilis), anti-phospholipid syndrome, diabetes, substance abuse, genetic disorders, congenital müllerian abnormalities, cervical trauma, and cervical incompetence. Unfortunately, many mid-trimester losses remain unexplained. A complete workup may be of value in selected patients following a mid-trimester loss [98-100].

Objective

To determine the frequency of urinary tract infection in females with preterm labor.

Operational Definitions

Preterm Labor

It was labeled if females present as four uterine contractions in 20 min or eight in 60 min plus progressive change in the cervix; cervical dilatation greater than 1 cm; and cervical effacement 80% or greater at gestation <37 completed weeks.

UTI

UTI is commonly diagnosed based on clinical findings of bacteriuria (bacteria in midstream urine) counts of >105colony forming units (cfu)/mL.

Materials and Methods

Study Setting

This study was conducted at Emergency Department of Gynecology, Lady Atchison Hospital, Lahore.

Duration of Study

May 25, 2018 to November 25, 2018.

Study Design

It was a Cross-Sectional Study.

Sampling Technique

Non-Probability Consecutive Sampling.

Sample Size

A total of 357 females were estimated using an expected percentage of UTI in preterm labor as 36.7%.(7) We used 95% confidence level and 5% margin of error.

Sample Selection

Inclusion Criteria

- Pregnant females aged 18-40 years
- Gestational age above 22 weeks and < 37 weeks (was estimated on USG)
- Any parity
- Patients presenting with pre-term labor (as per operational definition).

xclusion Criteria

- Cases with history of Rh- isoimmunization (on clinical record)
- Multiple gestations (on USG)
- Structural uterine abnormalities (on clinical examination)
- Pregnancies complicated with medical disorders like hypertension (BP > 80 / 140)
- Chronic renal disorders (on history).

Data Collection Procedure

A total of 357 cases fulfilling inclusion criteria was taken from Emergency Department of Gynecology, Lady Atchison Hospital, Lahore. After taking informed consent form all subjects or attendants they was taken in this study. Their basic demographic information (like age), contact details, gestational age, parity was taken. From each female, urine sample was taken in sterilized container and was sent to hospital Laboratory for complete urinalysis and culture/sen-

sitivity. UTI was diagnosed as per operational definition. All females was managed according to standard protocol to lengthen their gestational age.

Data Analysis Plan

SPSS v22.0 was used to enter and analyze data using descriptive statistics like Mean±S.D and frequency and percentage. Mean±S.D was used for quantitative data like age, gestational age and parity. Frequency and percentage was used for categorical data like UTI. Data was stratified for age, gestational age and parity to address effect modifiers. Post-stratification, Chi-Square test was used and p-value ≤0.05 was considered as significant.

Results

This study was carried out to determine frequency of urinary tract infection in females with preterm labor. The total patients of our study was 357, information was collected and analyzed the results of analysis are as follows. The mean age of patients was 28.45 ± 4.44 years in our study. Total patients of our study was 357 with minimum age in years was 18 and the maximum age in year was 40. The mean gestational age of patients was 28.80 ± 4.32 weeks in our study. Total patients of our study was 357 with minimum gestational age was 22 weeks and the maximum gestational was 36 weeks. The mean value of parity in our patients was 3.36 ± 1.76. The minimum value of parity was 1 in our study and the maximum value of parity was 6 in our study. The results of urinary tract infection of our study patients are as, the frequency distribution showed that out of 357 patients 115 (32,2%) have urinary tract infection and 242 (67.8%) have not urinary tract infection. After stratification of age the frequency distribution results showed that 228 (63.9%) was from 18-30 years age group and 129 (36.1%) was from 31-40 years age group. More was belongs to 18-30 years age group.

Similarly after stratification of gestational age the results of frequency distribution showed that out of 357 patients 170 (47.6%) was from 22-30 weeks gestational age group and 187 (52.4%) was from 31-37 weeks gestational age group. More was from 31-37 weeks gestational age group. In parity the results of frequency distribution showed that out of 357 patients 205 (57.4%) was from less than 3 group and 152 (42.6%) was from more than three groups. More patients was from less than 3 group. When urinary tract infection compare with the age 57 having urinary tract infection was from 18-30 years age group and 58 having urinary tract infection was from 31-40 years age group. The p value of chi square showed a significant results between age and urinary tract infection as the value is less than level of significance. In gestational age the 58 patients having urinary tract infection was from 22-30 weeks gestational age group and 57 having urinary tract infection was from 31-37 weeks gestational age group. The p value of chi square showed non-significant results as the p value is greater than the level of significance. The parity results was as 57 patients having urinary tract infection was from less than 3 group and 58 was from the more than 3 groups. The p value of the chi square showed significant results between urinary tract infection and parity as the value is less than the level of significance (Tables 1-7).

Table 1: Frequency distribution of urinary tract infection.

Urinary Tract Infection	Frequency	Percent
Yes	115	32.2
No	242	67.8
Total	357	100.0

Table 2: Frequency distribution of age.

Age groups	Frequency	Percent
18-30 years	228	63.9
31-40 years	129	36.1
Total	357	100.0

Table 3: Frequency distribution of gestational age.

Gestational age	Frequency	Percent
22-30 weeks	170	47.6
31-37 weeks	187	52.4
Total	357	100.0

Table 4: Frequency distribution of Parity.

Parity	Frequency	Percent
Less than 3	205	57.4
More than 3	152	42.6
Total	357	100.0

Table 5: Stratification of UTI with respect to age.

Age groups	Urinary Tract Infection		Total	p-value
	Yes	No		
18-30 years	57	171	228	0.0001
	25.0%	75.0%	100.0%	
31-40 years	58	71	129	
	45.0%	55.0%	100.0%	
Total	115	242	357	
	32.2%	67.8%	100.0%	

Table 6: Stratification of UTI with respect to gestational age.

Gestational age	Urinary Tract Infection		Total	p-value
	Yes	No		
22-30 weeks	58	112	170	0.463
	34.1%	65.9%	100.0%	
31-37 weeks	57	130	187	
	30.5%	69.5%	100.0%	
Total	115	242	357	
	32.2%	67.8%	100.0%	

Table 7: Stratification of UTI with respect to parity.

Parity	Urinary Tract Infection		Total	p-value
	Yes	No		
Less than 3	57	148	205	0.038
	27.8%	72.2%	100.0%	
More than 3	58	94	152	
	38.2%	61.8%	100.0%	
Total	115	242	357	
	32.2%	67.8%	100.0%	

Discussion

As the main objective of our study was to determine frequency of urinary tract infection in females with preterm labor. Urinary tract infection is the common of all bacterial infections, affecting human beings throughout their life span especially in women. Around 20% women in the age range 20-65 years suffer from at least one episode per year, while 50% develop urinary tract infections within their lifetime.(69) Not surprisingly infections of the urinary tract are the most common bacterial infections encountered during pregnancy. Plausible explanation of increasing risk of UTI and peaking during weeks 22 to 24, was due to uretheral dilatation, decreased tone, decreased urine concentration and increased stasis, plus hormonal changes, all these factors contribute to the increased risk with increased pregnancy duration.(79) The mean age of patients was 28.45 ± 4.44 years in our study. The mean gestational age of patients was 28.80 ± 4.32 weeks in our study. The mean value of parity in our patients was 3.36 ± 1.76. In urinary tract infection of our study patients out of 357 patients 115 (32.2%) have urinary tract infection and 242 (67.8%) have not urinary tract infection. Results are matched with a study.(90) The prevalence of UTI increases with age by 1% to 1.5% per decade and that the frequency of UTI is directly proportional to gravidity. The numbers of patients were not sufficiently large to determine which effect that of age or that of gravidity was greater. In other population-based study, on non-pregnant women, however, age was found to have a greater effect than gravidity on the prevalence of bacteriuria (36).

Urinary tract infections (UTIs) are common in pregnant women and pose a great therapeutic challenge, since the risk of serious complications in both the mother and her child is high. Pregnancy is a state associated with physiological, structural and functional urinary tract changes which promote ascending infections from the urethra. Unlike the general population, all pregnant women should be screened for bacteriuria with urine culture, and asymptomatic bacteriuria must be treated in every case that is diagnosed, as it is an important risk factor for pyelonephritis in this population. The antibiotic chosen should have a good maternal and fetal safety profile The age frequency distribution results showed that 228 (63.9%) was from 18-30 years age group and 129 (36.1%) was from 31-40 years age group. More was belongs to 18-30 years age group. Similar results also find in a study.(89) The gestational age showed that out of 357 patients 170 (47.6%) was from 22-30 weeks gestational age group and 187 (52.4%) was from 31-37 weeks gestational age group. More was from 31-37 weeks gestational age group. The parity showed that out of 357 patients 205 (57.4%) was from less than 3 group and 152 (42.6%) was from more than three groups. More patients was from less than 3 group. The urinary tract is a common site of infection in humans. During pregnancy, urinary tract infection (UTI) is associated with increased risks of maternal and neonatal morbidity and mortality, even when the infection is asymptomatic. By mapping available rates of UTI in pregnancy across different populations, we emphasize this as a problem of global significance.

Many countries with high rates of preterm birth and neonatal mortality also have rates of UTI in pregnancy that exceed rates seen in more developed countries. A global analysis of the etiologies of UTI revealed familiar culprits as well as emerging threats. Screening and treatment of UTI have improved birth outcomes in several more developed countries and would likely improve maternal and neonatal health worldwide. However, challenges of implementation in resource-poor settings must be overcome. Our study furthermore strengthens the association between urinary tract infections with adverse fetal outcomes. Health education about personal hygiene, urine cultures early in pregnancy and during the third trimesters especially for low socioeconomic pregnant women must be considered in routine clinical practice.

Conclusion

UTI in pregnancy (whether symptomatic or asymptomatic) is a risk factor for adverse outcomes that endanger the health of both mother and fetus. Multiple sources of evidence strongly support screening and treatment of UTI as a valuable approach for improving birth outcomes. Resource availability appears to be the primary hurdle for eventual reductions in adverse pregnancy outcomes associated with UTI. Where the resources are available, we encourage maternal and child health organizations and local governments to consider, or

reconsider ASB screening and treatment as part of a package of infection prevention strategies (including sexually transmitted infections) to reduce pregnancy complications. It is our hope that the information compiled here will increase awareness of the global significance of UTI in maternal and neonatal health and embolden governments, nongovernmental organizations, and researchers to do their part to make urine screening and UTI treatment a reality for all pregnant women.

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