DIPSTICK TEST VERSUS URINE MICROSCOPY FOR SCREENING OF ASYMPTOMATIC BACTERIURIA DURING PREGNANCY

Thesis

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List of abbreviations

ANC……Antenatal care.
ASB ……Asymptomatic bacteriuria.
CFU ……Colony forming unit.
IL ……Interleukine.
LE ……Leukocyte esterase test.
Lesn ……combined leukocyte esterase test with nitrite test
ME …… Microscopic examination.
NPV ……Negative predictive value
PH ……Potential hydrogen
POR ……Prevalence odds ratio
PPROM ……Preterm premature rupture of membranes
PPV ……Positive predictive value
PTL ……Preterm labour
ROC……Receiver operating characteristic
SD ……Standard deviation
THP ……Tamm-Horsfall Protein
UTI ……Urinary tract infection.

List of tables

List of tables

Contents

Introduction

The changes that occur in the urinary tract in pregnancy predispose pregnant women to the development of urinary tract infection. Beginning in week 6 and peaking during week 22 and 24, approximately 90% of pregnant women develop ureteral dilatation (hydronephrosis of pregnancy), which persists until delivery. Other changes include reduction in ureteral tone, which contribute to increased stasis and ureterovesical reflux ***(Cardozo, 1995).*** Additionally, the physiological increase in plasma volume during pregnancy decreases urine concentration. Up to 70% of pregnant women develop glycosuria, which encourages bacterial growth in the urine. Increase in urinary progestin and estrogen may lead to a decreased ability of the lower urinary tract to resist invading bacteria. This decreased ability may be caused by decreases in ureteral tone or possibly by allowing some strains of bacteria to selectively grow ***(Lucas and Cunningham 1993).*** These factors predispose to urinary tract infection during pregnancy.

Urinary tract infection is the most common bacterial infection during pregnancy. It has three principal presentations: *Asymptomatic bacteriuria*, *acute cystitis* and *pyelonephritis*. Asymptomatic bacteriuria refers to persistent, actively multiplying bacteria within the urinary tract in asymptomatic women; it is defined as a finding of more than 100,000 CFU/mL of urine (significant bacteruria) in a clinically asymptomatic person ***(Delzell et al., 2000).***

The prevalence of asymptomatic bacteriuria during pregnancy ranges from about 2 to10% ***(Fiona, 2007)***.

There are a number of conditions associated with an increased prevalence of asymptomatic bacteriuria in pregnancy. Low socio-economic status, sickle trait, diabetes mellitus and grand multiparity have been reported; each is associated with two-fold increase in the rate of bacteriuria ***(Kiningham, 1993)***.

The organisms that cause urinary tract infection during pregnancy are the same as those found in non-pregnant patients. Escherichia coli accounts for 80 to 90 percent of infections. Other gram-negative rods such as Proteus mirabilis and Klebsiella pneumoniae are also common. Gram-positive organisms such as group B streptococcus and Staphylococcus saprophyticus are less common causes of urinary tract infection ***(John et al., 2000)***.

The maternal and neonatal consequences of urinary tract infection can be devastating. Some 30% of patients with untreated asymptomatic bacteriuria develop symptomatic cystitis and up to 30–40% develop pyelonephritis ***(Barnick and Cardozo, 1991).*** However, only 1% of women without asymptomatic bacteriuria develop symptomatic cystitis ***(Patterson and Audriole, 1987).***

Urinary tract infections during pregnancy have been associated with increased risks of chorioamnionitis and endometritis. With regards to the fetus it has been shown that urinary tract infection is associated with fetal growth

restriction, stillbirth, preterm labor, increased perinatal mortality, mental retardation and developmental delay ***(McCormick, 2008).***

A number of studies suggest that urinary tract infection during the course of gestation is associated with elevated risk for preeclampsia ***(AnatteKarmon et al., 2008)***.

The relatively high prevalence of asymptomatic bacteriuria during pregnancy and the significant consequences for women and for pregnancy and the likelihood that the sequelae can be avoided with treatment, justifies screening women for bacteriuria. ***The American Academy of Pediatrics and the American College of Obstetricians and Gynecologists (2007), as well as a U.S. Preventative Task Force (2010),*** recommend screening for bacteriuria at the first prenatal visit.

Most guidelines recommend a single urine culture at the first prenatal visit. Based on the results of their prospective studies, however, some authors have suggested that urine should be cultured in each trimester of pregnancy to improve the detection of asymptomatic bacteriuria, as up to half of the cases may be missed with just a single culture ***(Tugrul et al., 2005).***

The decision about how to screen asymptomatic women for bacteriuria has always been a balance between the cost of screening versus the sensitivity and specificity. Various methods exist for screening. Urine culture and sensitivity remains the gold standard for diagnosis. It has

been advocated as a screening procedure for urinary tract infection in pregnancy. It is however expensive, and takes 24–48 hours to obtain result. It also requires skilled personnel. The accuracy of faster screening methods (e.g., leukocyte esterase dipstick, nitrite dipstick, urinalysis and urine Gram staining) has been evaluated ***(Delzell et al., 2000)***.

Examination of the sediment by microscopic urinalysis to detect bacteria and white blood cells has also been evaluated as a screening test for bacteriuria ***(Bachman, 1993)***.The test is time consuming and requires skilled personnel and expensive equipment, which are not readily available in undeveloped countries.

The dipstick culture technique has excellent positive- and negative-predictive values ***(Mignini and co-workers, 2009).*** Standard urine cultures may not be cost effective when the prevalence is low, but less expensive screening tests such as the leukocyte esterase-nitrite dipstick are when the prevalence is 2 percent or less ***(Rouse and colleagues, 1995).***

The dipstick leukocyte esterase test, which detects esterases released from degraded white blood cells, is an indirect test for bacteriuria (leukocytes are lysed in urine at pH value >6.0) ***(Martina Franz et al., 1999)***.

Nitrite test depends on the ability of most enteric bacteria to reduce nitrates to nitrites ***(Mittendorf, 1992)***.

If the dipstick test is positive for both leukocytes and nitrites, then the probability of urinary tract infection is

higher than each alone; however if both are negative, the likelihood of urinary tract infection is less than 20% ***(Hurlbut, 1991).***

Unfortunately for the majority of people especially in the rural areas, appropriate investigations necessary for the diagnosis of urinary tract infection are not available at many health facilities within their reach.

RESEARCH OBJECTIVE (AIM OF THE WORK):

To compare sensitivity, specificity, positive predictive value and negative predictive value of the dipstick test versus urine microscopy, in comparison with the gold standard urine culture as screening tests for asymptomatic bacteriuria during pregnancy.

RESARCH QUESTION:

Is dipstick test not inferior to urine microscopy and urine culture in the screening of asymptomatic bacteriuria during pregnancy?

RESEARCH HYPOTHESIS:

The dipstick test is not inferior to the urine microscopy and urine culture in screening for asymptomatic bacteriuria during pregnancy.

MEDICAL APPLICATION

When compared with urine microscopy and urine culture the dipstick test has the advantages of being rapid (immediate results), readily available (can be used in the outpatient clinic), cost effective, doesn't require special equipments, and doesn't require skilled personnel.

Review of literature

Urinary tract infection:

Definition:

It is an inflammatory response of the urothelium to bacterial invasion that is usually associated with significant bacteriuria and pyuria (≥10 WBC/hpf). It is the most common bacterial infection during pregnancy. Although *asymptomatic bacteriuria*is the most common, symptomatic infection includes *cystitis*, or it may involve the renal calyces, pelvis, and parenchyma (*pyelonephritis)* ***(Schaeffer, 1998).***

Risk factors:

Some people are more prone to get a UTI than others. Any abnormality of the urinary tract that obstructs the flow of urine (a kidney stone, for example) sets the stage for an infection ***(Kavatha, 2003).***

People with diabetes have a higher risk of a UTI because of changes in the immune system. Any disorder that suppresses the immune system raises the risk of a urinary infection ***(Walsh et al., 1997).***Diabetics are especially susceptible to developing pyelonephritis (Czaja and colleagues, 2009).

There are a number of conditions associated with an increased prevalence of asymptomatic bacteriuria in pregnancy. Low socio-economic status, sickle trait,

diabetes mellitus and grand multiparity have been reported; each is associated with two-fold increase in the rate of bacteriuria ***(Kiningham, 1993)***.

UTI are rarely seen in boys and young men, women are significantly more likely to experience UTI than men, and nearly 1 in 3 women had at least one episode of UTI requiring antimicrobial therapy by the age of 24 years ***(Foxman., 2003).***

4 to 6% of young adult females have been shown to be bacteriuric on screening surveys and this rises by 1-2% for every decade of age reaching 10% at the age of 60s and the older the women the more likely they have a reinfection ***(Platt, 1987)***.

According to several studies, women who use a diaphragm are more likely to develop a UTI than women who use other forms of birth control. Recently, researchers found that women whose partners use a condom with spermicidal foam also tend to have growth of E. coli bacteria in the vagina ***(Uehling et al., 1995).***

Significant changes in both structure and function take place in the urinary tract during normal pregnancy. Urinary tract dilatation is one of the most significant anatomical alterations induced by pregnancy. It involves dilatation of the renal calyces and pelvis, as well as the ureters. These changes, which are more prominent on the right side, are secondary to both hormonal and mechanical obstructive factors. The latter creates urinary stasis, and may lead to serious upper urinary tract infections. Another factor predisposing to infection is increased vesicoureteral

reflux. Evidence for hypertrophy of renal function is apparent very soon after conception. It appears to be mediated by pregnancy-induced intrarenal vasodilatation. Effective renal plasma flow and glomerular filtration are increased on the average by 40 and 65 percent, respectively (***Cunningham et al., 2005).***

In the puerperium, several risk factors exist that predispose a woman to urinary infections. Bladder sensitivity to intravesical fluid tension is often decreased as a consequence of the trauma of labor as well as conduction analgesia. Sensation of bladder distension can also be diminished by discomfort caused by an episiotomy, periurethral lacerations, or vaginal wall hematomas. Normal postpartum diuresis may worsen bladder overdistension. Catheterization to relieve retention and distension commonly leads to urinary infection; however, there appear to be no long-term sequelae **(Yip and colleagues, 2002).**

Causative organisms:

The origin of urinary tract infection predominantly is via ascending bacteria from the periurethral micro flora ***(Kremery et al., 2001).***

The organisms that cause urinary tract infection during pregnancy are the same as those found in non-pregnant patients. Escherichia coli accounts for 80 to 90 percent of infections. Other gram-negative rods such as Proteus mirabilis and Klebsiella pneumoniae are also common. Gram-positive organisms such as group B streptococcus and Staphylococcus saprophyticus are less