TITLE: CORRELATION OF CLINICAL FEATURES OF URINARY TRACT INFECTION IN PREGNACY WITH ISOLATION OF UROPATHOGENS.

PURPOSE: M.MED DISSERTION IN OBSTETRICS AND GYNAECOLOGY, UNIVERSITY OF NAIROBI.

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DECLARATION

I, Dr. Ogindo Joacquem, declare that this research has been conducted, analysed and written by me under the guidance of my supervisors. It has not been presented at any other university and is now submitted as part of the fulfilment of M.Med, Obs/Gyn, University of Nairobi.

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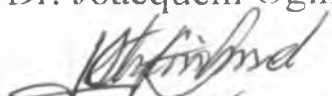
Signed : 

Date : 30/7/2008

CERTIFICATE OF SUPERVISION

This is to certify that this research study for long commentary in obstetrics has been conducted and written by Dr. Ogindo J, O under my guidance and supervision, and is submitted with my approval for M.Med. in Obstetrics and Gynaecology.

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DEDICATION

This book is dedicated to my father, and posthumously to my late mother for all they did to make sure I got an education and for the love and understanding they always showed. This also extends to my aunties, fiancée, siblings and cousins who did every little and big thing to make sure that I got all the moral, social and psychological support that I needed.

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To you all, I say thank you and may God bless you to continue with the good work.

DEFINITIONS AND ABBREVIATIONS

Definitions

Definition of Symptoms

Dysuria: Pain or burning sensation on passing urine.

Frequency: Passing urine more than 2 times at night.

Macroscopic hematuria: Passing of bloody urine.

Back pain: Low backache.

Flank pain: (lumbar/renal angle pain)/ Pain in the loin.

Suprapubic pain: Pain in the hypogastrium/ pain in the lower abdomen just above the pubic bone.

Urgency: A strong, persistent urge to urinate, which must be met immediately or else there will be dribbling.

Body hotness: Complaint by a patient of feeling hotness of the body.

Definition of Signs

Fever: Temperature > 37.5 0C

Costovertebral angle tenderness: Tenderness over the renal angle/loin/flank/lumbar area.

Suprapubic tenderness: Tenderness over the hypogastrium.

Other Definitions

Asymptomatic bacteriuria: Presence of $>10^5$ bacteria per mL of midstream specimen of urine in patients without urinary symptoms.

Symptomatic bacteriuria: Presence of $\geq 10^2$ per mL of midstream specimen of urine of patients with urinary symptoms.

Haematuria: Presence of blood in urine.

Microscopic haematuria: Presence of red blood cells in urine on microscopy.

Macroscopic haematuria: Presence of blood in urine on physical inspection.

Clinical diagnosis of UTI: Defined by a minimum of suprapubic tenderness with fever, or suprapubic tenderness with flank pain, or suprapubic pain with suprapubic tenderness, or suprapubic pain with flank tenderness, or dysuria, or hematuria, or flank pain with fever, or flank

pain and flank tenderness, or low back pain with fever, or flank tenderness with fever, or a combination of these, with or without other symptoms such as frequency, urgency and low backache.

Abbreviations

ANC – Antenatal clinic

ASB – Asymptomatic bacteriuria

CLED – Cystine Lecithin Electrolyte Deficient

GBS – Group B streptococcus

Hb – Haemoglobin

HBD-1 – Human beta defensin-1

HIV – Human immunodeficiency virus

KNH – Kenyatta National Hospital

RBC – Red blood cells

SB – Symptomatic bacteriuria

SGG – Sialosyl galactosyl globoside

T - Temperature

UTI – Urinary tract infection

VDRL – Venereal disease laboratories

WBC – White blood cells

ABSTRACT

Background: Urinary tract infection in pregnancy has prevalence rates of 2-10% and is associated with adverse maternal and neonatal outcomes. Diagnosis depends on clinical features and can be confirmed with urine culture. There is paucity of local data correlating clinical diagnosis of UTI with laboratory outcomes in order to give credence to empiric therapy. The evidence from this study will help make a simple clinical decision tree for syndromic management of UTI for use in resource constrained settings.

Objective: To correlate clinical features of UTI with uropathogen isolation among pregnant women with a clinical diagnosis of UTI.

Study Design: Cross-sectional analytical study.

Setting: Kenyatta National Hospital, Nairobi, Kenya.

Outcome Measures: Quanlitative urinalysis, urine culture and sensitivity.

Methodology: All consenting pregnant women seen in the antenatal clinic and labour ward with signs and symptoms of UTI were recruited into the study until the sample size of 137 was reached. The women completed a questionnaire that had sections on demographic and obstetric details, relevant past medical history and presenting complaints of the urinary tract, before being requested to provide a urine specimen. Midstream urine specimen was then obtained by the clean catch method and used for qualitative urine analysis, culture and sensitivity. Samples were processed and analysed at Kenyatta National Hospital microbiology laboratory. Laboratory data was then entered into the lab section of the questionnaire by the principal investigator. Data analysis was done using Statistical Package for Social Scientists (SPSS)/PC+ programme.

Results: The most common symptoms of UTI were suprapubic pain (97.1%), urgency (94.2%), frequency (92%) and loin pain (91.2%). Loin tenderness and suprapubic tenderness occurred in 62%. Leukocyte esterase was identified in 43% on dipstick urinalysis and bacteria detected in 41.2%. Presence of nitrite was associated with 66.7% bacterial isolation rates. Overall bacterial isolation rate was 41.6%, the commonest of which were E.coli (52.6%) and Staphyllococus (33.6%). Fever was associated with high bacterial isolation rate (77.8%) and suprapubic and loin tenderness 42% and 40.1% respectively. Urgency, suprapubic pain, loin pain, frequency and dysuria were associated with bacterial isolation rates of 39-47%. Nitrofurantoin, amoxicillin-clavulanic acid, cefuroxime were associated with bacterial sensitivity of 91.2%, 77.2% and 73.7%

of instances respectively.

Conclusion: There is a good correlation of clinical features of UTI with uropathogen isolation. These uropathogens are sensitive to simple antibiotics such as nitrofurantoin, amoxicillin-clavulanic acid and cefuroxime.

CORRELATION OF CLINICAL DIAGNOSIS OF UTI IN PREGNACY WITH ISOLATION OF UROPATHOGENS.

INTRODUCTION AND LITERATURE REVIEW

Urinary tract infections are due to bacterial invasion of the urinary tract, and can be lower (cystitis) or upper (pyelonephritis). They are the most common of all infections and can occur at any time in the life of an individual. (1, 2) They account for approximately 10% of office visits by women, and 15% of women will have a UTI at some time during their life. (3, 4)

Urinary tract infections are more common in women than men due to the anatomic and physiologic differences, that is, shorter urethra and shorter distance between the urethra and the anus in women, and its proximity to the vagina. Certain women may carry a compound called sialosyl galactosyl globoside (SGG) on the surface of kidney cells, which is a highly powerful receptor for *E. coli*. Some women have a genetic susceptibility to greater numbers of infecting organisms in the vaginal areas that adhere to the lining and some may be deficient in human beta-defensin-1 (HBD-1), believed to be a naturally occurring antibiotic. Pregnancy and certain conditions are known to increase susceptibility to UTI. Such conditions include diabetes mellitus, sickle cell disease, immunosuppressive treatment, urolithiasis, urinary tract anomalies like cystocoele, cystourethrocoele and urethral diverticula, and acquired immune deficiency syndrome. (1)

Urinary tract infections are known to be common in pregnancy with various studies reporting prevalence rates ranging from 2-10%. (6) The prevalence of UTI in pregnancy in our set up was found to be 23% in a study done in the year 2002 at Kenyatta National Hospital. (7) Physiological changes of pregnancy put pregnant women at an increased risk for urinary tract infection. Hormonal and mechanical changes put the pregnant women at an increased risk of urinary stasis and ureterovesical reflux. Increased urinary progestins and estrogens may lead to a decreased ability of the lower urinary tract to resist invading bacteria. The decreased ability to resist invading bacteria may be due to decreased ureteral tone or possibly by allowing some strains of bacteria to selectively grow. Additionally, glycosuria and aminoaciduria during pregnancy provide an

excellent culture medium in areas of urinary stasis. All these factors work in concert in predisposing to UTI during pregnancy. (3, 4, 5, 8, 9, 10)

However, currently it's not known whether there is a difference in the uropathogen and antibiotic sensitivity patterns as compared to the normal population.

PATHOGENESIS AND BACTERIOLOGY

Infection of the urinary tract is mostly by ascending, though may rarely occur by the haematogenous route. Uropathogens have special characteristics for urovirulence such as adhesions, fimbriae and toxins. These urovirulence characteristics allow colonization of the distal urethra to occur by adherence to the mucosal cells, from where there is ascension to the bladder mucosa. Some uropathogens possess certain special types of fimbriae that are renal tropic, and hence ascend up from the bladder and invade the renal mucosa causing acute tubular suppurative inflammation and focal necrosis. Some of the bacteria then invade the renal interstitium and parenchyma causing patchy interstitial and parenchymal suppurative inflammation. This suppurative inflammation of the renal tubules and parenchyma leads the costovertebral angle pain and tenderness, whereas the suppurative mucosal inflammation in the bladder and urethra lead to suprapubic pain and dysuria, respectively. The systemic evidence of infection in acute pyelonephritis, such as fever, malaise and vomiting result from the uropathogen toxins (hemolysin and cytotoxic necrotizing factor 1) which are released into the systemic circulation.

The commonest urinary pathogens are Escherichia coli, Klebsiella pneumoniae, and Proteus mirabilis. As many as 90 percent of uncomplicated cystitis episodes are caused by *Escherichia coli*. (11, 12, 13, 14, 15) Uropathogenic E. coli have special characteristics causing urovirulence. They most likely belong to phylogenic lineage B2. They usually possess specific adhesins such as P, S or Dr to facilitate their colonization in the urinary tract, toxins such as hemolysin and cytotoxic necrotizing factor 1 to provoke local and systemic inflammatory response that is responsible for the development of the UTI symptoms. (9) Less common organisms that may cause UTI include Gardenerella vaginalis and Ureaplasma urealyticum. (3, 4) In the local set up, a few studies have been carried out showing the prevalence of causative organisms of urinary tract infections. A study of UTI in pregnant mothers attending antenatal clinic at Kenyatta National Hospital in 2002 showed the following uropathogenic prevalence pattern; Escherichia coli

(34.4%), other enteric bacteria [Klebsiella and Proteus] (12.5%), Candida albicans (25%), Staphylococcus aureus (15.6%), Group B streptococci (6.25%), Streptococcus faecalis (6.25%). (7)

NATURAL COURSE OF UTI

UTI is an infectious disease which is caused by different uropathogens. Infectious diseases are known to have causative microbes (in this case the uropathogens) and the susceptible host (in this case the pregnant women). They are known to have certain natural courses, if these are not interrupted by use of antibiotics. Once there is exposure, there may follow infection. This is then followed by the incubation period during which there are no symptoms. In UTI, the incubation period of the different uropathogens is not adequately known and as such it's not known how long the infected women would remain asymptomatic before clinical features become evident. The incubation period is usually followed by the period of symptoms and then the recovery phase or disability or death (adverse outcomes). For UTI, the duration of symptoms and recovery is also not well defined. The period of bacteriuria is also not well defined. As well, there is no clarity on how long the recovery phase is and therefore how long there will be no bacteriuria while symptoms are still present during the convalescent period. The absence of literature on the natural course of UTI presents a big challenge in the correlation of signs and symptoms with uropathogen isolation. It's also not clear what proportion of those with symptoms actually have UTI. This background information shows therefore that UTI is a spectrum of infective disease ranging from those in the incubation period and thus asymptomatic, through the symptomatic phase in which there is bacteriuria to the convalescent phase in which there may or may not be bacteriuria. As such it may be difficult to define infection in terms of only the presence of uropathogen or symptoms. This therefore underscores the significance of signs and symptoms suggestive of UTI. The diagnostic accuracy of these signs and symptoms is not clear. (16, 17, 18)

DIAGNOSIS OF UTI

Diagnosis of urinary tract infections depend both on the clinical presentation and laboratory findings on urine specimen studies. (19) Many practical issues have yet to be fully addressed. What diagnostic threshold should be used to define infection and what is the diagnostic accuracy of clinical features of UTI? (11) Though symptoms suggestive of UTI constitute one of the most common reasons for women to visit clinicians, the diagnostic accuracy of the clinical assessment for UTI remains uncertain. (19)

Moreover, the spectrum of UTI ranges from those who are asymptomatic to the symptomatic. Whereas lack of symptoms may not imply absence of UTI, the presence of symptoms may be non-specific during pregnancy since some of the symptoms associated with UTI may have other causes such as pressure, labour and periurethral irritations.

An article in the American Family Physician journal of 2005 shows that in women who present with 1 or more symptoms of UTI, the probability of infection is approximately 50%. (4) Specific combination of symptoms (eg, dysuria and frequency without vaginal discharge or irritation) raise the probability of UTI to more than 90% effectively ruling in the diagnosis based on history alone. (4) Nocturia is a useful symptom for it is a more predictable marker for frequency, since most women will be able to remember how many times they woke up at night to pass urine than how many times they passed urine in the day. Signs of UTI include suprapubic tenderness, fever and costovertebral (renal) angle tenderness depending on whether it is a lower or an upper UTI. (4) Four symptoms and one sign significantly increases the probability of UTI. The important symptoms and signs include dysuria, frequency, haematuria and back pain, and costovertebral angle tenderness, respectively. (19) Urinary tract infections diagnosis is usually made through dipstick urinalysis and urine culture. The pre-test likelihood of UTI in asymptomatic pregnant women is 6%. (20) In this group the sensitivity and specificity of dipstick urine test is 68% and 87% respectively, with probability of UTI with a positive test being 58% and the probability of a UTI with a negative test being 5%. (20)

UTI is a spectrum ranging from those without symptoms to those with symptoms. The following clinical categories are used generally to describe UTI.

ASYMPTOMATIC BACTERIURIA

This is common with a prevalence of 10% during pregnancy. (12) It is defined as finding of 100,000 colony forming units per millilitre of urine. Significant bacteriuria may exist in asymptomatic patients. Untreated asymptomatic bacteriuria may lead to pyelonephritis in 50% of cases and acute cystitis in 30% of cases and is associated with an increased risk of intrauterine growth restriction and low-birth-weight infants. (3) The relatively high prevalence of asymptomatic bacteriuria during pregnancy, the significant consequences for women and for the pregnancy, plus the ability to avoid consequences with treatment, justify screening women for bacteriuria. Thus, routine screening for bacteriuria is advocated during pregnancy. Good evidence exists that screening pregnant women for asymptomatic bacteriuria with urine culture (rather than urinalysis) significantly reduces symptomatic urinary tract infections, low birth weight, and preterm delivery. A specimen obtained at 12 to 16 weeks' gestation will detect approximately 80 percent of patients with asymptomatic bacteriuria. The optimal frequency of subsequent urine testing during pregnancy is uncertain. (21, 22)A repeat of urine culture should be obtained during third trimester, because the urine of treated patients may not remain sterile for the entire pregnancy. (23) Whereas this is the routine practice, exposure to uropathogens may occur at any time during the course of pregnancy. It may therefore be prudent to have a high index of suspicion of UTI even in the absence of symptoms upon performing of routine dipstick urinalysis at every antenatal clinic visit. Those found to have predictive features of UTI should be put on treatment in case there is difficulty on obtaining urine culture. Obtaining urine culture in resource constrained settings may be difficult therefore making culture diagnosis of UTI an uphill task. Therefore, how do we identify asymptomatic bacteriuria in the absence of facilities for urine culture?

In treatment the choice of antibiotics should address the most common infecting organisms and should also be safe for the mother and the fetus. Antibiotic choice for asymptomatic bacteriuria should focus on the coverage of the common pathogens and can be changed after the organism is identified and sensitivities are determined. Antibiotic choices for treatment of UTIs during pregnancy could include nitrofurantoin, clavulanic acid-amoxycillin, fosfomycin, erythromycin and cephalosporins such as ceftriaxone, cefuroxime, ceftazidime, cefadroxil, and cephalexin. A seven to ten-day course of antibiotic treatment is usually sufficient, but this finding has not been studied in the obstetric population.

CYSTITIS

Cystitis occurs in approximately 1% of pregnant patients. It is distinguished from asymptomatic bacteriuria by the presence of symptoms such as dysuria, urgency, hematuria, suprapubic discomfort or pain and frequency in afebrile patients with no evidence of systemic illness. Examination may reveal suprapubic tenderness. However, these clinical features during pregnancy may have other causes other than UTI. Urine dipstick usually shows leukocyte esterase, nitrite, hematuria, and proteinuria. A urine culture may be positive for the incriminated organism. (3) The diagnosis should be confirmed by urinalysis with examination for pyuria and/or white blood cell casts and by urine culture. Facilities for urine culture to confirm UTI, may not be available or affordable in certain resource constrained settings.

Oral therapy should be considered in women with mild to moderate symptoms who are compliant with therapy and can tolerate oral antibiotics but do not have other significant conditions, including pregnancy and gastrointestinal upset. Since *E. coli* resistance to ampicillin, amoxicillin and first-generation cephalosporins exceeds 30 percent in most locales, these agents should not be used empirically for the treatment of pyelonephritis. (12) Treatment is usually initiated before the results of culture are available, which underscores the importance of diagnostic accuracy of clinical features in predicting UTI. Antibiotic choice should focus on the coverage of common pathogens and can be changed after the organism is identified and sensitivities are determined. Duration of antibiotic therapy is the same as that for asymptomatic bacteriuria. Acute cystitis is complicated by upper urinary tract disease (ie, pyelonephritis) 15-50% of the time. (3)

PYELONEPHRITIS

Pyelonephritis is a serious maternal illness that can progress to maternal sepsis, preterm labour and premature delivery. (3) Diagnosis is made by the presence of significant bacteriuria (100 organisms per mL of urine) accompanied by systemic symptoms such as fever, flank pain, chills nausea and vomiting or the presence of 100,000 organisms per mL of urine in asymptomatic clients. The diagnostic accuracy of these features remains uncertain as they are mainly non-specific, especially during pregnancy. Symptoms of lower tract infection (i.e. dysuria and frequency) may or may not be present. Pyelonephritis occurs in 2% of pregnant women; up to 23%

of these women have a recurrence during the same pregnancy. (3, 24, 25) Blood cultures are positive in up to 20 percent of women who have this infection. With the exceptions of white cell casts on urinalysis, and bacteremia and flank pain on physical examination, none of the physical or laboratory findings are specific for pyelonephritis. (12) Pregnant women with pyelonephritis should be hospitalized. Initially, these patients should receive intravenous antibiotic therapy. (12) Ceftriaxone, a third-generation parenterally administered cephalosporin, is a suitable agent for inpatient treatment. (12) Early aggressive treatment with i.v antibiotics and i.v fluids may be initiated before the results of urine culture and sensitivity. Parenteral treatment should continue until the patient becomes afebrile. Most patients respond to hydration and prompt antibiotic treatment within 24-48 hours. (26) The total duration of treatment for patients with acute pyelonephritis is uncertain, but at least two weeks is recommended. (25, 26)

LABORATORY DIAGNOSIS OF UTI

In the laboratory physical examination of the specimen, urinalysis, Gram stain and microscopy, and cuture and sensitivity are carried out. Urine specimen is to be collected by obtaining a midstream, clean-catch specimen from all patients with urinary tract symptoms as well as from the asymptomatic participants. The specimen is to be sent to the lab for evaluation as soon as possible. Refrigerate the sample at 4 degrees centigrade if it cannot be transported immediately. (2) Diagnosis of urinary tract infection is made through urinalysis and urine culture. In urinalysis, the presence of nitrites, leukocyte esterase, WBCs, RBCs, and protein are suggestive of a UTI. Bacteria found in the specimen can help with the diagnois. Urinalysis has a specificity of 97-100% with a sensitivity that ranges from 25-67% when compared to culture in the diagnosis of asymptomatic bacteriuria. (3, 27, 28) Several reports describe the use of urine dip for nitrites and leukocyte esterase in the evaluation of asymptomatic bacteriuria. (3) Sensitivities range from 50-92%, and specificity 86-97% when compared to culture in the diagnosis of asymptomatic bacteriuria. Urine culture is the criterion gold standard for the evaluation of urinary tract infection in pregnancy. Colony count of 100,000 colony forming units per mL of urine in asymptomatic bacteriuria and counts of 100 per mL in symptomatic patients are considered significant. Culture results can be used to identify specific organisms and antibiotic sensitivities. (3)

TREATMENT OF UTI IN PREGNANCY

Antibiotics are very effective at clearing urinary tract infections in pregnancy, and complications are very rare if timely and appropriate antibiotic therapy is given. (4, 29, 30, 31) Uncomplicated UTIs in women are one of the most common indications for antibiotics. Cystitis should be treated on outpatient basis. Hospitalization is often indicated for acute pyelonephritis for intravenous antibiotics and intravenous fluids. Patients with complicated UTIs require at least a 10- to 14-day course of therapy. Follow-up urine cultures should be performed within 10 to 14 days after treatment to ensure that the uropathogen has been eradicated. Recent studies have shown that patients initially placed on parenteral therapy can be switched to oral therapy within 72 hours as long as they are clinically improving and able to tolerate the oral agent. (12) Antibiotic sensitivity of a study carried out on antenatal mothers at Kenyatta National Hospital in the year 2002 showed the following pattern. *Clavulanic acid- Amoxycillin* 100% effective against all the uropathogens isolated, *Nitrofurantoin* 100% effective against all the uropathogens isolated, except for E. coli (81.8% sensitivity) and Group B Streptococci (GBS) (50% sensitivity). *Cephalosporins*(cefuroxime and cephalexin) 100% effective against GBS. *Gentamycin* showed good efficacy except against GBS. This study recommended the use of clavulanic acid- amoxycillin and nitrofurantoin as first line drugs in treatment of patients with UTI.

EFFECTS OF UTI IN PREGNANCY ON MATERNAL AND NEONATAL OUTCOMES

UTI has adverse maternal and neonatal outcomes. If asymptomatic bacteriuria is not detected and treated promptly in pregnant women, as many as 25% develop pyelonephritis, which in turn increases the risk for premature birth, infant mortality, and later chronic kidney disease. (1, 3)Thirty percent of patients with untreated asymptomatic bacteriuria develop symptomatic cystitis and upto 50% develop pyelonephritis. (3) Schieve and associates (3, 4, 32, 33) conducted a study involving 25,746 pregnant women and found that the presence of UTI was associated with premature labour, hypertensive disorders of pregnancy, anaemia and amnionitis. (3, 4, 5, 34) A

risk of urosepsis and chronic pyelonephritis was also found. In addition acute pyelonephritis has been associated with anaemia. (3, 4, 5) Neonatal outcomes that are associated with UTI include sepsis and pneumonia, increased risk of mental retardation, delayed developmental milestones, preterm delivery, intrauterine growth restriction, cerebral palsy, high fetal mortality rate, low birth weight infants. (1, 3, 4, 23, 33, 35, 36, 37)

RATIONALE

Urinary tract infections are the commonest bacterial infections during pregnancy and are an important contributor to maternal and perinatal morbidity and mortality. Timely diagnosis and intervention is therefore essential to improve both maternal and neonatal outcomes.

Diagnosis of urinary tract infections depends on clinical suspicion and can be confirmed by laboratory findings. Culture of urine which is the gold standard in the diagnosis of urinary tract infections is expensive and it takes 48-72 hours to get results. Obtaining urine culture in resource constrained settings to confirm UTI may not be easy if not impossible. It is therefore useful to evaluate the diagnostic accuracy of clinical features in the management of symptomatic urinary tract infection, and thus help recommend syndromic management based on evidence.

As most urinary tract infections are caused by a predictable group of susceptible organisms, they can be treated empirically without the need for urine cultures in circumstances where culture facilities are not available. Local data is necessary to help objectively support use of empiric treatment of UTI in pregnancy. However, little has been done locally so far, to confirm the prevalence of uropathogens in those with clinical suspicion of UTI, especially by a second party, in order to give credence to empirical therapy and thereby confirm the diagnostic accuracy of clinical features. It is therefore not clear whether all women with suspected urinary tract infections should be put on empirical treatment or should wait for laboratory confirmation prior to initiating antibiotic therapy.

Antibiotic sensitivity of microorganisms is known to change time to time due to development of antibiotic resistance; hence it is appropriate to carry out periodic microbial antibiotic sensitivity studies. A review of the current antibiotic sensitivity of uropathogens is therefore deemed useful in revising antibiotic use in the treatment of urinary tract infection in pregnancy.

This study is designed to determine the correlation of various symptoms of UTI with laboratory outcomes in order to give credence to empirical therapy especially where resources for investigation are scarce.

RESEARCH QUESTION

Do clinical findings in women with a clinical diagnosis of UTI correlate well with laboratory findings to support routine empirical treatment of UTI in pregnancy?

OBJECTIVES

GENERAL OBJECTIVE:

To correlate clinical features of UTI in pregnancy with uropathogen isolation.

SPECIFIC OBJECTIVES:

1. To determine the frequency of various clinical presentations in clinical diagnosis of UTI.
2. To determine the frequency of indicators of UTI on urine analysis.
3. To determine the pattern of uropathogen isolates.
4. To correlate signs and symptoms of UTI with laboratory results.
5. To correlate sensitivity to antibiotics with clinical presentation.

METHODOLOGY

STUDY SITE

The study was conducted in the obstetric department (antenatal clinic, labour ward and antenatal wards), which is a unit in the obstetric and gynaecology department of Kenyatta National Hospital. Kenyatta National Hospital is a national referral and teaching hospital. It is made up of several specialist departments, the obstetric and gynaecology department being one of them. The obstetric unit is part of the obstetric and gynaecology department and is made up of the antenatal clinic no. 18, the labour ward, the obstetric wards GFA, GFB and 1A, and the family welfare clinic no. 66. Pregnant study participants were recruited at the antenatal clinic no. 18 and labour ward. Follow-up with the culture results was carried out at the antenatal clinic and in the antenatal wards.

STUDY DESIGN

This is a cross-sectional analytical study on pregnant women with symptoms and signs associated with urinary tract infection, designed to correlate clinical features with uropathogen isolation and hence recommend on empirical antibiotic therapy.

STUDY POPULATION

The study population consisted of pregnant women at any gestation who had a diagnosis of urinary tract infection made because of presenting with various urinary symptoms. They were either admitted to the maternity unit or in the antenatal clinic of the Kenyatta National Hospital. All of them were seen before starting them on empiric antibiotic therapy as it was necessary to take mid-stream specimen of urine for urinalysis, microscopy, culture and sensitivity. It was only then that the empiric therapy was started.

STUDY INSTRUMENT

The study instrument was a primarily coded questionnaire with two main areas. These were patient characteristics and outcomes of laboratory investigation. The patient characteristics section

consisted of sociodemographic and obstetric characteristics, and urinary clinical features. The laboratory section consisted of urinalysis, microscopy and culture and sensitivity sections. This was then used to collect data and the data obtained was completed into the questionnaire.

SAMPLE SIZE

The sample size was calculated using the formula for cross-sectional studies as follows.

n = sample size

Z=95% confidence intervals (= 1.96)

P=0.9 (the estimated prevalence of the uropathogen isolation in the population with symptoms of UTI taken at 90%)

d = Error range = 0.05

$$n=\frac{Z^2 \times P\,(1-P)}{d^2}$$

$$n=\frac{1.96^2 \times (0.9 \times 0.1)}{0.05 \times 0.05}=136.8$$

The calculated statistical sample size therefore is 137.

Therefore a sample size of 137 pregnant women with signs and symptoms of UTI was recruited into the study.

DATA COLLECTION

Data was collected at Kenyatta National Hospital antenatal clinic, the obstetric wards and microbiology lab of Kenyatta National Hospital. All antenatal mothers being seen at the antenatal clinic and labour ward with clinical features of UTI were asked to take part in the study and all those who consented were recruited into the study after meeting the eligibility criteria. By the time of recruitment, a diagnosis of UTI had already been made by practicing clinicians. Privacy was achieved by having patient privacy during the interview and clinical examination, and all the data obtained was kept private and only used for research purposes. Consent was obtained by explaining to the participants about the study, its procedure, purpose and benefits without any coercion. (See appendix 2)

The questionnaire was administered by the study assistants by interviewing the participants on sociodemographic and obstetric characteristics as well as symptoms of urinary tract infection. Clinical examination was subsequently performed. The information obtained was then entered into

the clinical section of the questionnaire. Sterile mid-stream urine specimen was then obtained from the participants in a sterile wide bore container and sent for urinalysis, microscopy, culture and sensitivity. The laboratory results were later obtained and then entered into the lab section of the questionnaire.

SAMPLING

Sampling Frame

Pregnant women attending antenatal clinic or being seen in labour ward of Kenyatta National Hospital.

Sampling Procedure

Sampling was conducted by recruiting all consenting pregnant women with signs and symptoms of UTI being seen both in the antenatal clinic and labour ward after meeting the eligibility criteria until a sample size of 137 was reached. Every pregnant woman with clinical features of UTI who came to the antenatal clinic or labour ward and met the eligibility criteria was asked to participate in the study and all those who consented were recruited.

Once a patient was clinically diagnosed with UTI by the practicing clinicians, they were recruited by two trained study nurses, one at the antenatal clinic and another in the labour ward. The clinical part of the questionnaire was completed by the trained study nurses. Once recruited, relevant suggestive of urinary tract infection as well as sociodemographic and past medical history was elicited and filled into the questionnaire. Samples were then collected and preserved in an ice box. All the samples collected were delivered to the microbiology department laboratory within 3 hours of collection. Lab results were collected three days after collection and the lab section of the questionnaire was then completed by the principal investigator.

ELIGIBILITY CRITERIA

Inclusion Criteria:

1. Consenting pregnant women with signs and symptoms of UTI. Not used antibiotics in the previous two weeks. Not in labour. Not having P.V bleeding. Not draining liquor.

Exclusion Criteria:

1. Refusal of informed consent. Those who declined to take part in the study after adequate explanation were excluded.
2. Women who had used systemic antibiotics within two weeks prior to the study. (Samples of locally commonly used antibiotics such as amoxyl, augmentin, septrin, nitrofurantoin, erythromycin, cefadroxyl, cefuroxime etc were carried and shown to the patients by the interviewer on questioning about antibiotic use.)
3. Women admitted with features of labour were excluded.
4. Those women who had par vaginal bleeding in the presence of urinary symptoms were excluded.
5. Those who had drainage of liquor were excluded.

MATERIALS

Sterile urine specimen bottles were supplied by the microbiology department of Kenyatta National Hospital. Two cooler boxes were bought.

Laboratory materials including uristix, culture media such as CLED (Cystine Lecithin Electrolyte Deficient) medium and blood-agar medium, bacterial identification antibiotic sensitivity discs and Gram stain.

Study nurses were trained on the data collection procedure prior to commencement of the study.

PROCEDURE

Two study assistants who were qualified nurses were trained on the study and questionnaire administration. Questionaire was then pretested to find out ease of administration, the ease of understanding it and to rule out any ambiguity. Recruitment of study participants was carried out after meeting the eligibility criteria. The questionnaire was administered to the study participants by the study assistants and the principal investigator. Relevant history that included presenting complaints, sociodemographic data, antenatal profile, obstetric and gynaecological history was taken, physical examination performed by the registrar on duty and this information was filled into the study questionnaire by the study assistant.

Specimen Collection

Urine specimen collection was then carried out. The participants were then given sterile urine bottles for collecting midstream specimen of urine. The following other instructions were given to the patient;

1. Not to touch the inside or the rim of the container.
2. Squat over the toilet and separate the labia with one hand.
3. Void the first portion of the urine into the toilet.
4. Collect the mid portion of the urine into the container and pass the excess into the toilet.

Urine specimens collected were transported to the Kenyatta National Hospital microbiology laboratory based at the Kenyatta National Hospital. in an ice box within 3 hours of collection. Specimen was processed by qualified laboratory technologists under the supervision of a consultant microbiologist in the microbiology lab.

The processing of the specimen involved the following.

i) Physical analysis of specimen.

The colour (turbidity) and smell of the urine was noted.

The specimen was divided into three equal portions by pouring it into sterile containers under aseptic conditions, and used for urinalysis, wet preparation and Gram staining, and culture.

ii) Quantitative urine analysis

On dipstick urinalysis the following are reported;

Leucocytes, nitrites, pH, protein. glucose, ketones, blood, urobilinogen, bilirubin and haemoglobin.

iii) Examination of wet preparation and Gram staining.

This portion was centrifuged at 1000 revs/minute for minutes. The supernatant was poured off and a drop of the deposit placed under the cover slip on a glass slide. The specimen was examined for RBCs, pus cells, casts, epithelial cells, crystals and micro-organisms. Gram staining was also carried out on this specimen.

Results were tabulated as below;

Bacteria, white blood cells, red blood cells, yeast cells, epithelial cells, casts, crystals and parasites.

iv)Culture

Quantitative culture was carried out in CLED culture medium.

v) Bacterial identification and antibiotic sensitivity.

These were done using standard identification methods and antibiotic discs respectively. The bacteria studied are the ones that were isolated from the urine specimens.

The antibiotics studied are the ones currently available on antibiotic discs used for urine culture and in the microbiology laboratory of Kenyatta National Hospital. The listed antibiotics are those currently used for treatment of UTI both locally and in the international scene, based on currently known sensitivity. (6, 19, 20. 27). These are the same antibiotics currently available on antibiotic discs used for urine culture and sensitivity in the microbiology laboratory of Kenyatta National Hospital. These antibiotics are also currently the most commonly used for treatment of UTI, based on currently known antibiotic sensitivity.

Amikacin

Cefuroxime

Ciprofloxacin

Ceftazidime

Clavulanic acid-Amoxycillin

Gentamycin

Nalidixic acid

Nitrofurantoin

BENEFIT TO THE PATIENT

The antibiotic sensitivity pattern helped to confirm that the patient was on the correct antibiotic to which the organism was sensitive, and if not then changed appropriately.

STUDY LIMITATIONS

There were not many limitations in the study. Obtaining uncontaminated urine specimen may have been difficult due to anatomical reasons. However effort was made to explain how to collect the urine specimen to the participants and to ensure that they understood the instructions before giving a sterile wide bore container. The instructions were to squat over the toilet, separate the labia with one hand, void the first portion of the urine into the toilet and collect the mid portion of the urine into the container. Population was drawn from labour ward and antenatal clinic and there may have been slight differences in the population characteristics. However, its assumed that all are pregnant

women and pregnancy is a risk factor for UTI.

DATA MANAGEMENT

Data was collected using the questionnaire. Then data entry into the computer was done. Cleaning and validation of the data was carried out. Relevant statistical analysis was done using the Statistical Package for Social Scientists (SPSS).

Presentation of the results was done in tables with descriptions as appears below.

ETHICAL CONSIDERATIONS

There were no serious ethical issues as the data collected was not highly sensitive. Confidentiality was maintained throughout the study and there was no identification of the study participants. There was voluntarism and adequate explanation was given on the nature of the study. There were no invasive procedures involved. There was benefit to the participants when culture and sensitivity of urine showed antibiotic resistance by the isolated pathogen and thus the antibiotic treatment was changed appropriately. Approval of the study was obtained from the scientific and ethical review committee at Kenyatta National Hospital and the department of obstetrics and gynaecology of the University of Nairobi.

RESULTS

The study population consisted of 137 subjects.

Table 1 The study population by sociodemographic and obstetric characteristics (N=137)

Characteristic	No	%
Age group		
15-19 years	5	3.7
20 - 24 years	54	39.4
25 -29 years	47	34.3
30 -34 years	16	11.7
35 - 39 years	12	8.8
≥40 years	3	2.2
Marital Status		
Single	21	15.3
Married	116	84.7
Widowed	0	0
Parity		
0	51	37.2
1	43	31.4
2	17	12.4
3	16	11.7
4	4	2.9
≥5	6	4.4
Trimester		
First Trimester	10	7.3
Mid Trimester	55	40.1
Third Trimester	72	52.5)

Table 1 shows that the study population consisted of mainly those under 30 years (80%) with a modal age group of 20-24 years (40%). Eighty five percent were married. Most were of them were of low parity. Majority were either in second or third trimester (92.6%). The mean gestational age was 32 weeks with a range of 6 to 41 weeks. (Table 1)

Table 2 Frequency distribution of clinical presentation in the study population (N=137)

Clinical Presentation	No	%
Symptom		
Suprapubic pain	133	97.1
Urgency	129	94.2
Frequency	126	92
Loin pain	125	91.2
Dysuria	107	78
Hotness of the body	89	65
Haematuria	12	9
Sign		
Loin tenderness	85	62
Suprapubic tenderness	85	62
Fever	9	6.6

As can be seen in table 2, suprapubic pain was the most common presentating symptom (97.1%) followed by urgency (94.2%), frequency (92%), loin pain (91.2%) and dysuria (78%), in that order. Haematuria was present in only 9% of the study population. The common demonstrable signs were loin tenderness (62%) and suprapubic tenderness (62%). Fever was the least common sign (6.6%).

Table 3 Indicators of UTI on urinalysis (N=137)

Indicators	No	%
Dipstick Indicators		
Protein	27	19.7
Blood	27	19.7
Nitrite	9	6.6
Leukocyte esterase	59	43.1
Ketones	24	17.5
Microscopy Indicators		
Bacteria	57	41.6
Pus cells (>10/HPF)	95	69.3
Red blood cells	33	24.1

Table 3 shows the frequency distribution of urinalysis indicators of UTI upon urine dipstick analysis and microscopy. The presence of pus cells was the commonest finding (69.3%) followed by leukocyte esterase 43.1% and bacteria (41.6%). Proteinuria was present in 19.7% of the study population. Nitrite was the least common finding (6.6%). In nearly a quarter of the study population red blood cells presence was detected on urinalysis. (Table 3)

Table 4 Isolation of significant uropathogens

Uropathogens isolated	No	%
Overall isolation (N=137)		
Yes	57	41.6%
No	80	58.4%
By Species (N=57)		
Escherichia coli	30	52.6%
Staphylococcus spp	19	33.3%
Others*	8	14.1%
By Gram Stain (N=57)		
Gram -ve	35	61.4%
Gram +ve	22	38.6%

* Others included Citrobacter, Klebsiella and Streptococcus.

Table 4 shows that the overall prevalence of uropathogen isolation rates was 41.6%. The two commonest uropathogens were Escherichia coli (52.6%) and Staphylococcus spp (33.3%). Gram negative bacteria were the most commonly isolated uropathogens (61.4%) as compared to Gram positive bacteria (38.6%).

Table 5 Uropathogen isolation rates by clinical features

Clinical Feature	Isolation of uropathogen	
	No (%)	p value
Symptom		
Hotness of the body(N=89)	41 (46.1)	0.15
No hotness of the body(N=48)	16 (33.3)	
Urgency(N=129)	55 (42.6)	0.03
No urgency (N=8)	2 (25.0)	
Suprapubic pain(N=133)	50 (41.3)	0.99
No suprapubic pain(N=4)	4 (100)	
Loin pain(N=125)	51 (40.8)	0.33
No loin pain(N=12)	6 (50.0)	
Frequency(N=126)	51 (40.5)	0.14
No frequency(N=11)	6 (55.0)	
Dysuria(N=107)	42 (39.2)	0.25
No dysuria(N=30)	15 (50.0)	
Haematuria(N=12)	2 (16.7)	0.98
No haematuria(N=125)	55 (44.0)	
Sign		
Fever ($T \geq 37.5^0C$)(N=9)	7 (77.8)	0.0003
No fever(N=128)	50 (39.0)	
Loin Tenderness(N=85)	34 (40.0)	0.66
No loin tenderness(N=52)	23 (44.0)	
Suprapubic tenderness(N=85)	35 (41.2)	0.93
No suprapubic tenderness(N=52)	22 (42.0)	

The table 5 shows uropathogen isolation rates by clinical features. The overall correlation of clinical features of UTI with uropathogen isolation was 41.6%. The two most predictive markers of bacteriuria were found to be fever ($T \geq 37.5^0C$, 75%), body hotness (46.1%) and urgency at 42.6%.

Fever in the presence of other urinary symptoms and/or signs is the best predictor of uropathogen

upon culture followed by urgency (42.6%), suprapubic pain (41.3%), loin pain (40.8%), frequency (40.5%) and dysuria (39.2%) in that order. The significant markers for uropathogen isolation are fever (p=0.003) and urgency (p 0.03). (Table 5)

Table 6 Uropathogen isolation rates by urinalysis indicators of UTI

Indicator	Bacterial growth		
	No	(%)	P value
Dipstick Indicators			
Nitrite (N=9)	6	(66.7)	0.007
No nitrite (N=128)	51	(39.0)	
Leukocyte esterase (59)	31	(52.5)	0.035
No leukocyte esterase (N=78)	26	(33.0)	
Protein (N=27)	10	(37.0)	0.5
No protein (N -110)	47	(43.0)	
Blood (N=27)	12	(44.4)	0.75
No blood (N=110)	45	(41.0)	
Microscopy Indicators			
Bacteria (N=57)	40	(70.1)	0.00
No bacteria (N=80)	17	(21.2)	
Red blood cells (N=33)	17	(51.5)	0.17
No red blood cells (N=104)	40	(38.5)	
Pus cells (≥10/HPF) (N=95)	39	(41.1)	0.84
No pus cells (N=42)	18	(42.9)	

As can be seen in table 6, the study participants in whom nitrites were present by dipstick, 66.7% had bacterial isolates followed by leukocyte esterase (52.5%), blood (44.4%) and protein (37%). Of those who had bacteria on microscopy 70% had uropathogen isolates, followed by red blood cells (51.5%) and pus cells (41.1%). The significant urinalysis markers for uropathogen isolation are bacteria (p=0.00), nitrite (p=0.007) and leukocyte esterase (0.035).

Table 7 Sensitivity, Specificity, Positive Predictive Value (PPV) and Negative Predictive

Value (NPV) for the urinalysis indicators of UTI

Indicator	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Dipstick Indicators				
Nitrite	10.5	96.3	66.7	60.2
Protein	17.5	78.8	37.0	57.3
Leukocyte esterase	54.4	65.0	52.5	66.7
Microscopy Indicators				
Bacteria	70.2	78.8	70.2	78.8
Pus cells	68.4	30.0	41.1	80.0
Red blood cells	29.8	80.0	51.5	61.5

Table 7 above shows the sensitivity, specificity, positive predictive value and negative predictive value for the various urinalysis indicators for uropathogen isolation. The presence or absence of bacteria on microscopy had the average best values for all the four parameters for evaluating the diagnostic indicators, with these values ranging between 70% and 80%. Bacteria had a sensitivity of 70% while that for nitrites was 10%. However, nitrite had the best specificity of 96.3% followed by red blood cells (80%) and bacteria (79%).

Table 8 Antibiotic sensitivity of uropathogens by bacterial isolates

	Amikacin	Augmentin	Ciprofloxacin	Cefuroxime	Ceftazidime	Gentamycin	Nalidixic acid	Nitrofurantoin
ted	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
oli(N=30)	19(63.3%)	19(63.3%)	27(90.0%)	22(73.3%)	25(83.3%)	23(76.7%)	20(66.7%)	27(90.0%)
=19)	18(94.7%)	18(94.7%)	15(78.9%)	16(84.2%)	12(63.2%)	12(63.2%)	3(15.8%)	8(94.7%)
N=3)	2(66.7%)	2(66.7%)	3(100.0%)	2(66.7%)	3(100.0%)	3(100.0%)	2(66.7%)	2(66.7%)
(N=2)	0(0.0%)	2(100.0%)	2(100.0%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	2(100.0%)
=2)	2(100.0%)	2(100.0%)	1(50.0%)	2(100.0%)	2(100.0%)	2(100.0%)	1(50.0%)	2(100.0%)
s(N=1)	1(100.0%)	1(100.0%)	1(100.0%)	1(100.0%)	1(100.0%)	1(100.0%)	0(0.0%)	1(100.0%)

E. coli showed good sensitivity to most antibiotics with the sensitivities ranging between 63% and 90%. Staphylococcus spp, the second most common uropathogen, was found to have good

sensitivity to most antibiotics except to nalidixic acid with 16% sensitivity. Its sensitivity to the rest of the tested antibiotics ranged between 63% and 95%. The other isolated uropathogens had poorest sensitivity to nalidixic acid, but good sensitivity to the rest of other tested antibiotics. (Table 8)

Table 9 Overall sensitivity patterns of antibiotics among patients in whom there were uropathogens isolates (N=57)

	Proportion in whom there was sensitivity	
Antibiotic	No.	%
Amikacin	41	71.9%
Amoxycillin-Clavulanic acid	44	77.2%
Ciprofloxacin	48	84.2%
Cefuroxime	42	73.7%
Ceftazidime	41	71.9%
Gentamycin	40	70.2%
Nalidixic acid	24	42.1%
Nitrofurantoin	52	91.2%

As can be seen in table 9, the overall antibiotic sensitivity to uropathogens in subjects in whom there were uropathogens isolated was best with nitrofurantoin 91.2%, but least with nalidixic acid 42.1%. Amoxycillin-Clavulanic acid had sensitivity of 77% and cefuroxime 73.9%. The sensitivity study included ciprofloxacin, because the antibiotic discs currently available for uropathogens contain the quinolones.

DISCUSSION

The results indicate that there is some correlation between clinical features of UTI and isolation of uropathogens although there is some variability in correlation among the various signs and symptoms. The most common clinical features in order of frequency were fever, hotness of the body, urgency, suprapubic pain, suprapubic tenderness, loin tenderness, frequency, loin tenderness, dysuria and hematuria. This study shows that out of the 137 study participants 41.6% had uropathogen on culture. This is in agreement with other studies which have shown that urinary symptoms and signs are significant markers of bacteriuria. (4, 15) In this study there was a significant correlation of symptoms and signs of urinary tract infection with uropathogen isolation in pregnant women. The prevalence of uropathogen in this study population was 41.6%. The level of bacterial isolation was much lower than expected, the sample size having been calculated on prevalence assumption other than previous studies which were lacking.

There was a 41.6% uropathogen isolation rate in this study population. This implies that a pregnant woman with urinary symptoms and signs has 41.6% likelihood of uropathogen, a figure which is slightly below the 50% traditionally thought to be the correlation of symptoms with bacteriuria outside pregnancy. (4, 19) Better surrogates for uropathogen isolation were urgency (42.6%), suprapubic pain (41.3%), loin pain (40.8%), suprapubic tenderness (41.2%), fever {$T \geq 37.5^0C$} (77.8%) and hotness of the body (46.1%). Dysuria (39.2%), frequency (40.5%), haematuria (16.7%) and loin tenderness (40.8%) had below average correlation. Some of the symptoms and signs such as dysuria, hematuria and loin tenderness that have been traditionally used in clinical practice as features highly predictive of UTI have lower than average uropathogen isolation rates. Urgency, which during pregnancy has not been considered a useful marker has featured in this study as correlating well with uropathogen isolation (42.6%) compared to the other clinical features. Fever and urgency are the significant clinical markers for uropathogen isolation, which is in contrast to what is in routine clinical practice. (4, 19)

Microscopic and dipstick urine analysis add value in the diagnosis of UTI. The presence of bacteria on urine microscopy correlated highly with uropathogen isolation at 70.1%. The next significant urine analysis findings that correlated well with uropathogen isolation were nitrite, leukocyte esterase, red blood cells and pus cells in reducing order of correlation. Literature search

on objective value of urinalysis indicators of UTI reveal paucity of data in this area except for nitrite and leukocyte esterase whose sensitivities fall within the expected range. These parameters can thus be combined with clinical presentation to increase the accuracy of predicting uropathogen isolation. The significant urinalysis markers for uropathogen isolation are bacteria, nitrite and leukocyte esterase. This is agreement with previous publications. (27, 28)

From this study population, the organisms isolated in order of frequency were Escherichia coli (52.6%) and Staphylococcus species (33.3%) which are known as causative organisms for UTI. Thus E. coli was the commonest uropathogen followed by Staphylococcus species. E. coli is known to be the commonest cause of bacteriuria, causing more than 80% of asymptomatic bacteriuria whereas in this study it constituted 52.6% of the isolates. (4, 11, 12, 13, 15) This may imply that there may be a slight difference in the uropathogen distribution pattern between symptomatic and asymptomatic bacteriuria.

Commonly used antibiotics such as nitrofurantoin and amoxycillin-clavulanic acid were found to be efficacious against the isolated uropathogens. (4, 24, 29) Previous antibiotic sensitivity studies showed the uropathogens having good sensitivity to the used antibiotics. This trend is also reflected in this study in which there is good sensitivity of the isolated uropathogens to nitrofurantoin, cefuroxime, ceftazidime and amoxycillin-clavulanic acid. However there was lower sensitivity to gentamycin and nalidixic acid compared to previous studies. (7, 12, 13, 15)
Knowing that E. coli and Staphylococcus species are the commonest uropathogens with specific known antibiotic sensitivity, it's therefore possible to recommend a protocol for syndromic management of UTI, for use in resource constrained settings, where culture and sensitivity of urine may not be available or affordable to the majority of the population. This protocol would also be applied empirically in resource endowed settings while awaiting culture report.
In this study population UTI is common. Clinical features of UTI provide high index of suspicion for diagnosis of UTI to the clinician and they have a clinically good correlation with uropathogen isolation. Uropathogens are still sensitive to commonly used antibiotics except to gentamycin and nalidixic to which there is reduced sensitivity.

Nitrofurantoin followed by amoxycillin-clavulanic acid, cefuroxime, ceftazidime, amikacin and

gentamycin appeared as the most likely antibiotics to treat urinary tract infection effectively, as they showed the the highest sensitivity levels among women with bacterial isolates in urine, irrespective of the specific uropathogens.

The diagnosis of UTI was made by clinicians empirically, while analysis of symptomatology with laboratory findings was done by the investigators. Therefore, the study tests the accuracy of clinicians in making diagnosis of UTI in pregnancy in order to give credence to empirical antibiotic therapy, which is a very prevalent practice in Kenyatta National Hospital, assuming that bacterial isolation is the gold standard for diagnosis of UTI. This study has shown that there is reasonable correlation of clinical features of UTI with uropathogen isolation. Extensive literature search does not reveal this concept of other clinicians' opinion in clinical diagnosis of UTI in pregnancy. It can be noted that, whereas many studies show prevalence rates, (1, 3, 4, 5, 6, 7, 12, 31, 34) there is a paucity of data correlating symptomatology with laboratory findings.

CONCLUSION

1) A significant proportion of pregnant women who present with clinical features of UTI have uropathogens on culture, especially if they have fever, dysuria, frequency and urgency.
2) Urinalysis indicators of UTI, especially nitrite, leukocyte esterase, bacteria and red blood cells were highly correlated with bacterial isolates.
3) Escherichia coli is the most predominant cause of UTI showing sensitivity to most simple antibiotics such as nitrofurantoin.
4) Simple antimicrobials such as nitrofurantoin, amoxicillin-clavulanic acid and cefuroxime were found suitable for empiric treatment in most of those with bacterial isolates.

RECOMMENDATIONS

1) Empirical treatment of UTI, based on the common symptoms such as urgency, suprapubic pain, loin pain, hotness of the body, dysuria and frequency, should involve use of simple drugs such as nitrofurantoin, amoxicillin-clavulanic acid and cefuroxime since they are available, affordable and have good cover against uropathogens.

2) It is appropriate to make diagnosis of UTI, especially in the periphery, by doing urinalysis with or without microscopy through demonstrating bacteriuria, nitrites, leukocyte esterase, pyuria

and hematuria.

3) The most common symptoms that can be used to make a clinical diagnosis of UTI are urgency, suprapubic pain, loin pain, hotness of the body, dysuria and frequency, and this may be reinforced by urinalysis and microscopy, where applicable.

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APPENDIX 1.QUESTIONAIRE

Date

Serial number

Completed by

A. SOCIODEMOGRAPHIC DATA

1) What is your age?

2) What is your marital status?

Single _____

Married _____

Widowed _____

Divorced/ Separated _____

3) What is your level of education?

None _____

Primary _____

Secondary _____

Tertiary (college) _____

4) What is your occupation?

Housewife

Employed _____

Self employed _____

B) OBSTETRIC HISTORY

5) Parity : _____+_____

6) L.M.P : _____

7) Gestation by dates: _____ weeks

C) CLINICAL PRESENTATION

i) PAST MEDICAL HISTORY

8) Have you ever been told you have any of the conditions listed below?

a) Diabetes Mellitus: Yes____ No____

b) Sickle Cell Disease: Yes____ No____

c) Structural Urinary Tract Anomalies such as urinary divarticula and cystocele:

Yes____ No____

9) Prior to this pregnancy, have you ever been treated for urinary tract infection?

No____ Yes____

How many times?_____

ii) URINARY SYSTEM

10) In this pregnancy, have you been seen with complains of;

a) Pain on passing urine: Yes _____ No _____

b) Passing bloody urine: Yes _____ No _____

c) Pain at the loin with body hotness: Yes _____ No _____

d) Low back pain with body hotness: Yes _____ No _____

11) Do you have any of the complaints listed below;

a) Pain on passing urine Yes _____ No _____

b) Passing bloody urine Yes _____ No _____

c) Passing urine more than 2times at night Yes _____ No _____

d) Lower abdominal pain Yes _____ No _____

e) Flank pain(loin pain) Yes _____ No _____

f) Hotness of the body Yes _____ No _____

g) Nausea Yes _____ No _____

h) Vomiting Yes _____ No _____

i) A strong persistent urge to pass urine Yes _____ No _____

12) When was the last time you had sexual intercourse?

a) Same day of interview ____
b) Within 1 week ____
c) More than 1 week, but within 1 month ____

13) Do you have vaginal vischarge? No ____ Yes ____

What's the colour? _____

D) PHYSICAL EXAMINATION

14) Vital signs

a) Temperature ____
b) Pulse Rate ____
c) Blood Pressure ____
d) Respiratory Rate ____

15) Abdominal Examination

a) Fundal Height
   i) Corresponding to dates ____
   ii) > dates ____
   iii) < dates ____

b) Abdominal Tenderness
   i) Suprapubic ____
   ii) Loin ____
   iii) None ____

E) DRUGS PRESCRIBED

16) _____

_____

_____

_____

_____

_____

F) LABORATORY RESULTS

17) ANC Profile

a) VDRL Positive _____ Negative _____

b) HB (g/dl) _____

c) HIV Positive Negative

18) Urinalysis

a) Nitrites _____

b) Leucocyte esterase _____

c) **Pus** cells _____

d) Red blood cells _____

e) Protein _____

f) Bacteria _____

g) Blood _____

h) Ketones _____

i) pH _____

j) Specific Gravity _____

19) Urine culture

a) Colony count (No. of colony forming units) - _____

b) Specific organism(s) identified, for example*:-

Bacteria isolated	No. of colony forming units

c) Antibiotic sensitivity

	Bacteria isolated	Bacteria isolated	Bacteria isolated	Bacteria isolated
Amikacin*				
Augmentin*				
Cefadroxil*				
Cefuroxime*				
Cephalexin*				
Gentamycin*				
Nalidixic acid*				
Nitrofurantoin*				

* Sensitivity is to be marked by S= Sensitive **OR** by R= Resistant

APPENDIX 2. CONSENT FORM

We are asking you to be in a research study. The purpose of this consent form is to give you the information you will need to help you decide whether to be in the study. Please read this form carefully. You may ask questions about what we will ask you to do, the risks, the benefits and your rights as a volunteer, or anything about the research or in this form that is not clear. When all your questions have been answered, you can decide if you want to be in this study or not. This process is called "informed consent".

The decision on whether to join the study is entirely yours and is voluntary. You will not be denied any medical care or services due to you if you decide not to join the study. All the information you give will be treated as confidential.

This study will help us to know whether it is correct to put pregnant women with complaints suggestive of urinary tract infection on treatment while we wait for results of urine tests or whether it is better to wait for results before giving treatment.

We will invite pregnant women who have come for antenatal care and those admitted in the antenatal wards with complaints suggestive of urinary tract infections to participate in the study.

If you accept to participate in this study, you will sign this consent form. You will then be asked questions by the study nurse and doctor on your social, demographic, and reproductive history and on complaints of urinary tract infections. The study nurse and doctor will then take your temperature and perform an abdominal examination to assess the status of your pregnancy and to look for signs of urinary tract infection. You will then be given a container to provide a urine specimen of about 5mls. The urine sample will be taken to the laboratory to be tested for the presence of bacteria and for the antibiotics that would be most effective to kill the bacteria. If you have complaints suggestive of urinary tract infection you will then be put on treatment and asked to come back for the test results after one week at the antenatal clinic no 18. For women with no urinary complaints, they will receive their test results at their next clinic visit.

This study has been explained to me. I have had a chance to ask questions.

I volunteer to take part in this research.

Name _____ Sign _____

Date _____/_____/_____

Name of investigator _____ Sign _____

Date_____/_____/_____

APPENDIX 3 STUDY APPROVAL LETTER

KENYATTA NATIONAL HOSPITAL
Hospital Rd. along Ngong Rd.
P.O. Box 20723, Nairobi
Tel: 726300-9
Fax: 725272
Telegrams: "MEDSUP", Nairobi
Email: KNHplan@Kenhealthnet.org

Ref: KNH-ERC/ 01/ 4193

23rd March 2007

Dr. Ogindo Joacquem Otieno
Dept. of Obs/Gynae
School of Medicine
University of Nairobi

Dear Dr. Ogindo

RESEARCH PROPOSAL: "URINARY TRACT INFECTION IN PREGNANCY – CORRELATION OF CLINICAL FEATURES AND CULTURE AND SENSITIVITY IN PREGNANT WOMEN WITH SYMPTOMATIC U.T.I" **(P6/01/2007)**

This is to inform you that the Kenyatta National Hospital Ethics and Research Committee has reviewed and **approved** your above cited research proposal for the period 23rd March 2007 – 22nd March 2008.

You will be required to request for a renewal of the approval if you intend to continue with the study beyond the deadline given. Clearance for export of biological specimen must also be obtained from KNH-ERC for each batch.

On behalf of the Committee, I wish you fruitful research and look forward to receiving a summary of the research findings upon completion of the study.

This information will form part of database that will be consulted in future when processing related research study so as to minimize chances of study duplication.

Yours sincerely

PROF A N GUANTAI
SECRETARY, KNH-ERC

c.c. Prof. K.M.Bhatt, Chairperson, KNH-ERC
The Deputy Director CS, KNH
The Dean, School of Medicine, UON
The Chairman, Dept. of Obs Gynae, UON
Supervisor: Dr Z. Qureshi Dept.of Obs/Gynae, UON
Dr. J. Kinuthia Dept. of Obs/Gynae KNH