Reliability of microscopic urinalysis in predicting urinary tract infection in Children.

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ABSTRACT
Urinary tract infections (UTIs) are associated with potentially serious long-term consequences. Up to 7 percent of girls and 2 percent of boys will have a symptomatic, culture-confirmed UTI by six years of age. Most UTIs in children result from ascending infections, colonic bacteria responsible for most of cases. Urinary tract infection may be suspected because of urinary symptoms in older children or because of fever, nonspecific symptoms, or failure to thrive in infants. Eighty one child of age 3.5months -10 years with variable presentation and high clinical suspicion of UTI were recruited for evaluation of UTI on out patient bases over nine –months period, data regarding age , sex was obtained . Urine samples were collected by clean- catch or urine bags .UA was done by microscope for pus cells and urine cultures were carried out.
UTIs seems to be highly prevalence among studied children and vary with age and sex and the sensitivity of UA is high(77%)but the specificity is low( 33%) , in agreement with other studies.
UA can rule out UTI if the result is negative in cases with low clinical suspicion and positive result is insufficient to diagnose UTI because false positive results are common. However, proper urine culture which required invasive procedure is necessary for diagnosis of urinary tract infections , so the criteria for its use should be optimized.
Key words: UA-urinalysis, UC-urine culture, UTI-urinary tract infection, CFU- colony-forming units

INTRODUCTION
Urinary tract infections (UTIs) are the most common source of serious bacterial infection in young children and are associated with potentially serious long-term consequences of renal scarring, hypertension, and chronic renal failure\(^1\). Overall, 3% to 5% of girls and 1% of boys have UTIs\(^1\). Up to 7 percent of girls and 2 percent of boys will have a symptomatic, culture-confirmed UTI by six years of age\(^2,3\).
The prevalence of UTI vary with age and sex ,it is greater in younger age
with a rate of nearly 7% among febrile newborns\textsuperscript{2,4}. It more common in male during the 1\textsuperscript{st} year of life while beyond 1-2 yr there is striking female preponderance\textsuperscript{1}. Beyond the diagnosis and treatment of UTIs, the identification of a UTI in a young child prompts investigation for vesicoureteral reflux and other urinary tract anomalies that may predispose patients to long-term renal complications.\textsuperscript{1,4, 5}

Most UTIs in children result from ascending infections, although hematogenous spread may be more common in the first 12 weeks of life, most UTIs in children are mono microbes, often caused by Escherichia coli (60 to 80 percent of cases), Proteus (more common in boys and in children with renal stones), Klebsiella, Enterococcus ,and coagulase-negative staphylococci\textsuperscript{2,4,6}

There are numerous risk factors for UTI in children ,UTIs were associated with constipation, encopresis, bladder instability, infrequent voiding, bathing and back-to-front wiping , anatomical abnormalities, uncircumcision and others\textsuperscript{1,2,7,8}.

Older children with UTIs may have dysuria, frequency, urgency, hesitancy, small volume voids, or lower abdominal pain (cystitis ),flank pain ,malaise, fever , nausea ,vomiting and occasionally diarrhea(pyelonephritis) . Infants with UTI more commonly present with nonspecific symptoms such as fever, irritability, jaundice, vomiting, or failure to thrive\textsuperscript{1,2}. Unusual odor of the urine is not helpful in predicting UTI\textsuperscript{9}.

Other manifestations are asymptomatic bacteriuria refers to child who have bacteriuria without manifestations\textsuperscript{1}. asymptomatic bacteriuria is detected in 0.5 -1% of children with urine culture\textsuperscript{6}.

A UTI may be suspected based on symptoms or finding on urinalysis, or both, but a urine culture is necessary for confirmation and appropriate therapy, the diagnostic threshold depends on the method of urine collection, thus the diagnoses of UTI depending on having the proper sample of urine, There are several ways to obtain urine sample ;some are more accurate than others\textsuperscript{1,2}.

A urinalysis should be obtained from the same specimen as that cultured .Pyuria (Leukocytes in the urine ) suggest infection, but infection can occur in the absence of pyuria ,consequently , this finding is more confirmatory than diagnostic .conversely ,pyuria can be present without UTI\textsuperscript{1}.

Nitrites and leukocyte esterase ± microscopy are usually positive in infected urine. Microscopic hematuria is common in acute cystitis .White blood cell casts in the urinary sediment suggest renal involvement ,but these are rarely seen.

If the child is asymptomatic and the urinalysis result is normal .it is unlikely that the urine is infected .However ,if the child is symptomatic a UTI is possible .even urinalysis result is negative\textsuperscript{1}. Screening urine cultures in non symptomatic child are generally discouraged because differentiating asymptomatic bacteriuria from true UTI with no or minimal signs of inflammation can be difficult but repeated urine cultures are often helpful\textsuperscript{6}.

AIM OF THE STUDY
We undertook this study to measure the sensitivity of the standard UA(microscopy) for detecting UTI, to determine if sensitivity varies by age of the patient, and to offer recommendations for, when a urine culture, and not just a screening UA, should be obtained.

SUBJECTS AND METHODS
Eighty one children who were consider to be at risk of UTIs were recruited in this study. The results of urine samples collected from those enrolled in this study (61
female, 20 boys, all boys are circumcised, aged 3.5 months to 10 years for 9 consecutive months (January to Sept 2007), were analyzed, those patients presented to clinic because of fever {50 (61.7%) patients with out any other focus of infection} others attended the clinic because of fever and abdominal pain, chronic diarrhea, decrease in appetite, ill health, few {10 (22.3%) patients} of them complain from classical symptoms of urinary tract infection as urgency, frequency, dysuria and some presented with failure to thrive without obvious cause.

All urine specimens were collected as clean-catch or midstream urine sample in younger and older children, respectively, and as clean-catch or by using adhesive, sealed, sterile collection bag in infant and children who were still in diapers. Clean-catch urine collection from infant requires more patience and effort than the use of bag, but this method is reasonably accurate and rates of contamination are low. In girls disinfection of the skin of the perineum was carried out.

Demographic data of age, sex was recorded, beside body temperature. The child was febrile when temperature equal or greater than 38°C. The samples were delivered fresh (within 1 hour of voiding) to the laboratory for microscopy and culture, cultures obtained from the same specimen as that analyzed. A 8 samples were analyzed but cultures were not done.

Catheterization and supra pubic aspirate were not done, the families regarded them as invasive procedures and we can’t persuade them.

Test employed in the study is:
Simple microscopy of fresh uncentrifuged urine for pus cells done by the microbiology laboratory. It was the practice of the laboratory to report the results recorded as positive if there were 5 and more of pus cells/ high power field, and negative if there were <5 pus cells/ high power field. (Dipstick for leukocyte esterase and nitrite was not done by microbiology laboratory because not available).

Urine cultures were done regardless the result of UA except for 8 specimens in which UA was done without cultures.

A positive UA result was defined as positive for pyuria (5 cells or >5 cells/high power field).

A positive UC consider as UTI regardless the result of UA.

The results of the UA was compared with final urine culture reports. A urine culture was reported as positive when there were greater than 100,000 colonies of a single pathogen or if there were 10,000 colonies also of single pathogen in symptomatic child this regarding clean catch urine collection. Results above, it is considered UTI. For collection from bag, if the UA is positive, the patient is symptomatic, and there is single organism cultured with a colony count greater than 100,000 CFU per ml we regard it as UTI.

Statistical analyses were conducted using the Statistical Program for the Social Sciences version 6.1.1 (SPSS, Chicago, IL).

RESULTS
Eighty one children with variable presentation (fever no apparent focus of infection, failure to thrive after exclusion of other causes), classical urinary tract symptoms were evaluated for urinary tract infections. 61 (75%) were girls and 20 (25%) were boys, the age range 3.5 months—10 years. A UA was performed on 81 (100%) patients. Urine cultures were obtained from 73 (90%) patients. Paired UA and urine culture were evaluated for those 73 child.

Fifty two (71.2%) cultures results were positive, 38 female and 14 male,
and 21 (28.8%) cultures were negative, 17 female and 4 male.
Eight specimens cultures were not done, 2 male, 6 female.
45 (85%) of the positive urine cultures were obtained by clean void specimen and 7 (15%) by bag. {36 of 45 and 4 of 7 were positive on UA also} Organism isolated were 35(67%) E-coli, 8(15%) klebsiella, 5(10%) proteus, 2 (4%) staphylococcus epidermidis, 1 (2%) staphaureaus, 1 (2%) enterobacter. Pyuria was observed in 62(77%) samples (52 female and 10 male). 40(74%) specimens with pyuria yield positive and 14 (22%) yield negative results on culture in addition 8 samples all of them were positive for pyuria were not send for cultures.
Microscopy UA was negative (no pyuria) in 19 samples (9 females and 10 males), of which 12 (63.2%) yield positive and 7 (36.8%) produce negative culture.
40 specimens of Those with pyuria were paired positive on UA and culture 33 females and 7 males. 22 with pyuria 14 were negative on culture (2 male 12 female) and 8 of them culture was not done (2 male and 6 female).
Pyuria was observed in (77%) of those with UTI (40 from 52) and no pyuria in (23%) 12 from 52.
The prevalence of UTI presented in table (1)
The positive and negative predictive value presented in the table (2).
The sensitivity and specificity of the UA by age is presented in table 3
Use of study patients for detected prevalence of UTI, determine sensitivity and specificity of UA in figure (A)

Table (1)
Detected prevalence of UTIs by age and sex

<table>
<thead>
<tr>
<th>Age group in years</th>
<th>NO. of children</th>
<th>% of children with UC</th>
<th>Prevalence</th>
<th>Prevalence%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>&lt;1</td>
<td>12</td>
<td>10/12 83%</td>
<td>70</td>
<td>75</td>
</tr>
<tr>
<td>&gt;1-5</td>
<td>59</td>
<td>53/59 90%</td>
<td>68</td>
<td>61</td>
</tr>
<tr>
<td>&gt;5-10</td>
<td>10</td>
<td>10/10 100%</td>
<td>90</td>
<td>50</td>
</tr>
<tr>
<td>Total</td>
<td>81</td>
<td>73/83 90%</td>
<td>72</td>
<td>62</td>
</tr>
</tbody>
</table>

In 8 specimens cultures were not don

Table (2)
The positive and negative predictive values (expressed as percentage) of UA microscopy.

<table>
<thead>
<tr>
<th>Total number of urine samples</th>
<th>Number (%) of positive urine cultures</th>
<th>Number (%) of negative urine cultures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microscopy for pus cells</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>54</td>
<td>40 (74%)</td>
</tr>
<tr>
<td>Negative</td>
<td>19</td>
<td>12 (63%)</td>
</tr>
</tbody>
</table>

8 samples were positive on UA but cultures were not done
This mean that 74% from those with pyuria suffer from UTI while 37% of those with negative UA are truly not having UTI.
Table 3: Sensitivity of the standard UA (microscopy) for identifying UTI by age.

<table>
<thead>
<tr>
<th>Age Group Years</th>
<th>No. (%) of paired UA-UC</th>
<th>No. (%) of UTIs/paired UA-UC</th>
<th>Sensitivity of microscopy</th>
<th>Specificity of microscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1</td>
<td>10</td>
<td>4 (40%)</td>
<td>57</td>
<td>33</td>
</tr>
<tr>
<td>&gt;1-5</td>
<td>53</td>
<td>28 (52%)</td>
<td>76</td>
<td>30</td>
</tr>
<tr>
<td>&gt;5-10</td>
<td>10</td>
<td>8 (80%)</td>
<td>89</td>
<td>100</td>
</tr>
<tr>
<td>Total</td>
<td>73</td>
<td>40 (71%)</td>
<td>77</td>
<td>33</td>
</tr>
</tbody>
</table>

Figure (A)

81 patients

8 laboratory UA

8 No culture obtained

8 No culture proven UTI

52 Culture proven UTI

Detected prevalence: NO. of UTIs / tested children

Use of study patients for (1) determining test characteristic of urine analysis (UA) and measuring prevalence.
DISCUSSION
Because the signs and symptoms of UTI are mostly non-specific or absent especially in young children, the decision to investigate the urine as possible cause of fever or other odd complain, it need to rely on the prior probability of UTI as determined by age and Sex. However, whether those children require a screening UA or urine culture regardless the UA result is controversial. This decision is magnified by the invasiveness of proper culture testing compared with non invasive bag specimens that can be used for screening UA.

Three issues must be addressed first 1-the prevalence of UTI which varies by age and sex. 2-the sensitivity of UA in detecting UTI 3- the likelihood of missing UTI if clinician accepts a negative UA result as sufficient evidence that culture is not needed.

The prevalence of UTI has been previously reported, but the study populations, definitions of UTI, and urine collection methods have varied. In large population-based study in Sweden, marid and jodal found accumulative incidence rate for symptomatic UTI to be 6.6% for girls and 1.8 for boys among children younger than 6 yr. Hoberman et al. found an overall prevalence of 7.5% among those without another potential source of fever and 17% for white girls with temperature higher than 39, Shaw et al. collect catheterize urine specimens for culture from febrile infant who did not have source of fever, they found the prevalence of UTI was(3.3%). In other studies the prevalence 2%,7 % in boys and girls respectively by 6 yr of age and it is greater with younger age and among febrile new born.

In our study the prevalence is high among our patients included in this study as in table (1), this might be explained on base of the high likelihood of UTI in those enrolled in our study, that those children were selected as suffering from UTI depend on clinical finding and according to these finding they were evaluated by UA and most of those submitted for culture they have positive UA. Our study show high prevalence among male during 1st year of age and then girls predominant in agreement with other studies. Investigator have reported on sensitivity of the various component of the UA to detect UTI, including dipstick leukocyte esterase and nitrite, microscopy for pus cells and gram stain. We used only microscopy for pus cells because the other component are not available in our laboratory whether private or in the hospital. Lohr found the sensitivity of UA( dipstick and microscopy)to be 88% in children grouped together from 1month to16 years of age. Hoberman found sensitivity of 54% for pyuria in febrile infant younger than 1 year. Shaw et al reported the sensitivity of UA( dipstick and microscopy)to be 83%. Crain and Gershel found the sensitivity of UA (pyuria and bacteriuria) to be 48%. Richard Bacher found the sensitivity of UA to be 82% and it constant for age subgroup in 1st 2yrs. In our study we found the sensitivity of UA (Microscopy for pyuria) is 77% in children group together from 3.5 months to 10years and it vary with age as in table (3), this finding is comparable with some studiers but not with others studies and not in agreement for age variation. It is less might be related to use of both dipstick, microscopy and gram stain all together in some studies and high in comparism for other studies might be related to that must of patients included in our study are at high risk of UTIs in addition to methods of collection of urine samples. Regarding the variation of sensitivity of UA with the age may be related to the effect of the method of urine collection where the sensitivity is less in those less than one year of age and
high in those more than 5 years old, where the possibility of contamination is high in infant if non proper methods of collection are used (suprapubic and catheterization).\textsuperscript{1,4,6}

Our study was conducted on 81 fresh urine samples reliably tested for pus cells on microscopy, it was found that 62 (77\%) samples were positive for pyuria and 52 (72.2\%) were culture positive from all samples (73) regardless the result of UA as in figure A. 40 (75\%) of samples with pyuria were culture positive and 14 (25\%) of samples with pyuria were culture negative While 7 (37\%) of those with negative UA yield negative UC which mean that 37\% are truly not having UTI among the whole negative UA and 12 (63\%) from those who were negative UA have positive UC. 74\%, 37\% represent the positive and negative predictive value respectively as shown in table (2). This support the observation that positive microscopy UA doesn't confirm diagnosis of UTI, but will be of practical value in the process of selecting samples for cultures, and negative UA might result in missing UTI if cultures were not done and the values will be changed if we used more than one screening tests as dipstick and microscopy\textsuperscript{17,18}. low negative predictive value may be adequate in asymptomatic older children, but in ill febrile child is an adequate and high negative predictive value of more than one screening test (dipstick and microscopy) is required to exclude urinary tract infection\textsuperscript{18,19}.

The probability of a missed UTI because of false negative UA can occur, so exclusion of UTI should be interpreted on clinical variables, screening tests (better to use more than one --dipstick and microscopy) and cultures provided that urine samples were collected in proper ways regarding the age\textsuperscript{13,15,16,17,20}. An acceptable risk of UTI is not a mathematical or statistical function, but a clinician-dependent function. Clinicians should consider the likelihood of UTI in a particular patient based on all of the clinical variables and then decide whether the patient needs to be tested for a UTI. The clinician must then decide whether a negative UA result is sufficient or whether the risk of missing a UTI is still significant enough to warrant obtaining a urine culture. From a practical standpoint, the risk of missing a UTI in practice is much higher when a patient is not considered to be at risk for a UTI (i.e., no UA is done) than because of a false-negative UA result\textsuperscript{18,19}. Widespread use of the new dipsticks, coupled with microscopy for pus cells performed on fresh samples by adequately trained doctors, would dramatically cut down the number of samples sent for culture and this, in turn, would cut down on costs.

**Conclusion**

The sensitivity of UA (microscope only) is high 77\% but the specificity is low 36\%, Positive predictive value is high while negative predictive value is low and to get high results better to be combined with dipstick test and proper ways of urine collection.

Confirmation or exclusion of UTI is not absolute according to the result of UA. There is possibility of missing UTI because of negative UA. Possibility of missing UTI is much higher when no UA is done and the patient not considered to be at risk of urinary tract infection.

Clinicians can therefore use the patient-specific estimates of risk for a UTI to determine when the UA is an adequate screening test and which patients will require a urine culture.

**Recommendations:**

Urine culture should be obtained for diagnosis of UTI if there is high clinical suspicion, or positive UA, symptomatic child.
We should use dipstick and other measures with microscopy in standard UA, to increase sensitivity and specificity of UA.

REFERENCES