

ORIGINAL RESEARCH ARTICLE

Detection of Pyuria by Microscopic Urinalysis as a Marker of Pediatric Urinary Tract Infection

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Abstract

Globally, different diagnostic tests of urinary tract infection (UTI) are in clinical practices. A reliable test can increase the efficiency of the healthcare system, especially in a developing country like Nepal, reducing cost and time. Thus, we accessed the possibility of pyuria detected by microscopic urinalysis as a marker of pediatric UTI. The prospective study was conducted from July 2014 to January 2015 at Alka hospital, Lalitpur. Microscopic urinalysis of 353 clean-catch urine samples was done by the wet mount method, followed by urine culture by a semi-quantitative method. We confirmed 64 (18.1%) UTI cases by culture, the gold standard for UTI diagnosis. Fever was the most common clinical manifestation in UTI cases. The sensitivity, specificity, positive predictive value and negative predictive value of pyuria detected by microscopic urinalysis to identify UTI were 50%, 70.9%, 27.6% and 86.5% respectively. In 318 febrile cases, the sensitivity, specificity, positive predictive value and negative predictive value of pyuria detected by microscopic urinalysis to identify UTI were 73.2%, 72.6%, 28.3% and 94.8% respectively. The findings suggest pyuria detected by microscopic urinalysis as not a worthwhile marker of pediatric UTI. But it is a trust worthy marker in febrile pediatric cases.

Keywords: febrile, marker, microscopic urinalysis, pediatrics, pyuria, UTI

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Introduction

Urinary tract infection (UTI) is a common infection in all age groups [1-3] and affects at least 1% of boys and 3% of girls [4]. UTI is difficult to diagnose in children, as symptoms are non-specific [5-7]. Complications of UTI in children lead to renal scarring and terminal kidney damage [8]. UTI management varies with evolving research findings [8]. The diagnosis of UTI should be clinically and confirmed by urine culture [9]. Urine culture is a gold standard for the diagnosis of UTI, but it takes up to 24 hrs for final reporting [10]. Using microscopic urinalysis allows starting antimicrobial treatment 24 hours sooner than waiting for culture results [11]. Microscopic urinalysis can thus be a useful test for the rapid diagnosis of UTI in children [10]. But, no single cut-off count of leucocytes exhibits high sensitivity and specificity [5, 12]. At least 5

leucocytes per high power field (HPF) of centrifuged urine is commonly considered as pyuria [13]. Pyuria is mostly observed as a result of inflammation, thus it is a common sign of UTI [14]. This makes pyuria a suitable marker of UTI. This study aimed to access the utility of microscopic urinalysis as a potential marker to diagnose pediatric UTI.

Materials and Methods

The cross-sectional prospective descriptive study was conducted from July 2014 to January 2015 at Alka Hospital, Lalitpur, Nepal. The ISO 9001:2008 accredited hospital is a referral hospital at Kathmandu valley. A total of 8,692 urine samples were submitted to the microbiology laboratory for culture during the study period. Only 353 non-repetitive, clean catch urine samples from infants and children patients, under 13 years of age and with symptoms of UTI, were included in the study.



Table 1. Clinical symptoms in patients

Symptoms	Suspected UTI cases (% of 353 cases)	Confirmed UTI cases (% of 64 cases)
Abdomen pain	212 (60.1)	33 (51.6)
Dysuria	233 (66.0)	32 (50.0)
Fever	318 (90.1)	49 (76.6)
Frequency of urine	222 (62.9)	32 (50.0)
Malodorous urine	71 (20.1)	46 (71.9)

The symptoms were abdomen pain and/or dysuria and/or fever and/or frequency of urine and/or malodorous urine. For infants and younger children, symptoms were fever and parental reporting of malodorous urine. The children who were already on antibiotics therapy were excluded. The clean-catch urine samples were collected in a sterile container. In infants and non-toilet-trained children, a sterile plastic bag was attached to genitalia for clean catch urine collection. In toilet-trained children, voided midstream urine sample was collected. Each sample was first subjected to microscopic urinalysis by the wet mount method. In brief, 10mL of urine was centrifuged at 3000rpm for 5min. The supernatant was discarded, and the sediment was re-suspended in 500µL urine. This native urine sediment was dropped on a glass slide and covered by a coverslip. The microscopic examination was performed by the bright-field microscopy (x400). The threshold value of at least 5 pus cells/HPF, which corresponds to at least 25 leukocytes per mL of

non-centrifuged urine, was considered as pyuria[13]. In parallel, each sample was subjected to urine culture by a semi-quantitative method. In brief, 1µL urine was streaked on MacConkey agar (HiMedia Ltd, India) and blood agar plate (HiMedia Ltd, India) using a calibrated loop of 2mm size. Growths were observed after 18-48hrs of aerobic incubation at 37°C. The growth of at least 100 colonies on the agar plate, which corresponds to at least 10⁵ colony-forming units (CFU) per mL of urine, were considered as culture-positive [15]. Data were entered and stored using Microsoft Excel (version 2010, Microsoft Corporation, USA). Chi-square test of variables was performed whenever applicable and p values below 0.05 were considered significant.

Results

The mean age of patients was 5±3.5 years (ranging from 1 month to 12 years; variance= 12.5). In our study, the male to female ratio of UTI suspected cases was 1:1.4. UTI was confirmed by culture in 64(18.1%) out of 353 patients. Meanwhile male to female ratio of UTI confirmed cases was 1:1.2. Fever was the most common clinical symptom in UTI confirmed cases, 49 (76.6%) followed by malodorous urine, 46 (72%) (Table 1).

In 18 (62.1%) of 29 males and 14 (40%) of 35 females who were confirmed of UTI did not have pyuria (Table 2).

Of 64 UTI cases, 32 (50%) cases showed pyuria and 32 (50%) cases did not show pyuria. This was statistically significant since pyuria was associated with an increased risk of bacteriuria (p<0.05) (Table 3).

Table 2: Number of pus cells/HPF and bacteriuria in male and female patients

Pus cells/HPF	No. of sample	Male		Female	
		Culture negative	Culture positive	Culture negative	Culture positive
<3	181	70	14	86	11
3-5	56	23	4	26	3
5-8	39	13	3	21	2
8-10	14	2	2	9	1
10-15	20	5	1	12	2
≥15	43	7	5	15	16
Total	353	120	29	169	35

Table 3: Relationship between microscopic urinalysis and culture in all suspected cases

Pyuria	Urine culture		Total (%)
	Culture positive (%)	Culture negative (%)	
Pyuria	32 (50)	84 (29.1)	116 (32.9)
Nonpyuria	32 (50)	205 (70.9)	237 (67.1)
Total	64 (100)	289 (100)	353 (100)

Sensitivity=50%

Specificity=70.9%

Positive predictive value=27.6%

Negative predictive value=86.5%

Table 4: Relationship between microscopic urinalysis and culture in febrile cases

Pyuria in febrile cases	Urine culture		Total (%)
	Culture positive (%)	Culture negative (%)	
Pyuria	30 (73.2)	76 (27.4)	106(33.3)
Nonpyuria	11 (26.8)	201 (72.6)	212(66.7)
Total	41(100)	277(100)	318(100)

Sensitivity=73.2%

Specificity=72.6%

Positive predictive value=28.3%

Negative predictive value=94.8%

Of 41 febrile UTI cases, only 30 (73.2%) cases showed pyuria and 11(26.8%) did not show pyuria. This was statistically significant since pyuria was associated with an increased risk of bacteriuria in febrile cases ($p < 0.05$) (Table 4)

Discussion

UTI can only be accurately diagnosed by a combination of clinical and laboratory investigations. Wide ranges of practices are seen among physicians [16]. Over diagnosis of UTI had been a common problem that had led to aggressive antibiotic therapy [1].

We first classified the pool of 353 cases, as UTI and non-UTI, depending on the culture. Thus, 18.1% of cases were confirmed to have UTI. The discordance of clinical and laboratory investigations could have resulted in low growth positivity. In our study, male to female ratio of suspected cases was 1:1.4, this was involuntary recruitment bias. Meanwhile male to female ratio of UTI confirmed cases was 1:1.2. The natural epidemiology pattern of UTI shows more prevalence in females [17]. The urethra of females are colonized with colonic Gram-negative bacteria as they are shorter in length and are in close proximity to the anus, thus females are more frequently affected by UTI [18]. In our study, fever was the common symptom, manifested in 76.6% of UTI cases.

This was similar to reports from other studies [19-21].

There is no unison in the cut-off value of pus cells to consider as pyuria. The cut-off value of ≥ 5 pus cells/HPF was considered pyuria [13]. Out of total 237 samples without pyuria, 13.50% were culture positive; and of 116 samples with pyuria, 27.6% were culture positive. The relationship of pyuria and culture was statistically significant ($p < 0.05$). Culture positive without pyuria often occurs in patients with diabetes, enteric fever of bacterial endocarditis whereas pyuria with sterile culture occurs in patients with prior antibiotic use, renal tuberculosis, corticosteroid administration, analgesic nephropathy, or renal calculi [18]. In our study, since no distinction of samples from patients was made on these criteria, both bacteriuria without pyuria and pyuria without bacteriuria may have occurred. The sensitivity, specificity, positive predictive value and negative predictive value of pyuria to diagnose UTI were 50%, 70.9%, 27.6% and 86.5% respectively. This was slightly lower but comparable with reports from other studies [19, 22-24]. Our study revealed pyuria with less sensitivity and high specificity. This finding indicates that the presence of pyuria may not suggest UTI but the absence of pyuria can exclude UTI. Furthermore, positive predictive

value and negative predictive value suggest that using pyuria to diagnose UTI in children will result in a significantly larger number of false-positive and lower false-negative results. Therefore our study suggests that pyuria detected by microscopic urinalysis is a less reliable marker for pediatrics UTI but can be used to exclude UTI as a single test modality. Some authors still agree that microscopic urinalysis can identify only a third to half of the patients with positive urine culture [25-27].

We further accessed the reliability of pyuria detected using microscopic urinalysis by dividing the study population based on the presence or absence of symptom fever to improve predictive scores. Out of total 318 febrile cases, 9.4% were culture positive along with pyuria and 3.5% samples were culture positive without pyuria. The relationship of pyuria and culture in febrile cases was statistically significant ($p < 0.05$). Thus, in febrile cases, the sensitivity, specificity, positive predictive value and negative predictive value of pyuria to diagnose UTI increased to 73.2%, 72.6%, 28.3% and 94.8% respectively. Our study revealed pyuria with higher sensitivity and specificity in febrile cases. This finding indicates that the presence of pyuria in febrile cases can suggest UTI; similarly, the absence of pyuria in febrile cases can exclude UTI. Furthermore, low positive predictive value and high negative predictive value suggest that using pyuria to diagnose UTI in febrile children can result in a higher number of false-positive but lower false-negative results. This suggests that pyuria detected by microscopic urinalysis is a worthwhile marker for UTI in febrile children. Furthermore, our study suggests pyuria detected by microscopic urinalysis can serve as a reliable marker of UTI in pediatrics in a primary healthcare setting where prevalence is much lower. This can omit unnecessary tests, thus can increase effective diagnosis and cost in the healthcare system. Nitrate reduction test and leucocyte esterase (LE) test as recommended by the National Institute for Health and Care Excellence (NICE) can further be used to improve this diagnosis accuracy [5].

Nevertheless, our study doesn't underrate the importance of culture for UTI diagnosis in children. But reliable marker can increase the effectiveness of diagnosis excluding unnecessary tests. Critical cases need a quick diagnosis for prompt treatment that cannot wait culture result which usually demands 18-48 hours. In an economy lagged country like Nepal, this can help to improve and outreach the healthcare facility especially in a primary healthcare system where there is a fundamental lack of enough resources for investigations; and treatment is primarily based on clinical suspicion. Thus, pyuria detected by microscopic urinalysis can be a standalone diagnostic test in febrile cases in such settings.

Conclusion

Our findings suggest pyuria detected by microscopic urinalysis entertain less sensitivity and specificity, thus pyuria is not the reliable marker of UTI in pediatrics. However, the reliability of the pyuria detected by microscopic urinalysis was higher to diagnose UTI in febrile pediatric cases, which can be a single test model in low resource settings like the primary healthcare system.

Conflict of Interest

None declared

Acknowledgments

None

Consent to publish

Not applicable

Ethical approval and consent to the participant

The study was a laboratory-based study and a part of the study was a routine patient care investigation. No patient-related data were collected except the demographic parameters, thus ethical approval was not required. Oral informed consent was taken from a guardian on behalf of the patients.

Availability of data and materials

All data generated or analyzed during this study are included in the article. Raw data can

be made available upon request to the corresponding author.

Funding

None

Authors' Contributions

All authors made substantial contributions to the study. DS, VKS, and PKS conceived and designed the study. DS, PT, BB and HP collected samples, investigated and recorded the laboratory findings at the laboratory. VKS and PKS supervised and provided methods for the study. DS, BB, HP and PC reviewed works of literature and drafted the manuscript. DS, PT, BB and PC compiled, curated and interpreted data. DS, PT and DB critically reviewed and revised the manuscript by compiling, formatting, editing and writing the final version of the manuscript. All authors read and approved the final manuscript.

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