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Comparative validity of urine microscopy with dipstick leukocyte esterase and nitrite tests for the rapid diagnosis of urinary tract infections in children- Cross-sectional study

[1]Dr. Basil Joseph, Pediatrician, Community Health Centre, Vengola

[2]Dr. Deepa T. Unnikrishnan, Associate Professor, Pediatrics, Malankara Orthodox Syrian Church Medical College, Kolenchery, Ernakulam District, Kerala, India

[3]Dr. M.M Mathew, Professor, Pediatrics, Malankara Orthodox Syrian Church Medical College, Kolenchery, Ernakulam District, Kerala, India

Corresponding Author: Dr. Deepa T. Unnikrishnan, Associate Professor, Pediatrics, Malankara Orthodox Syrian Church Medical College, Kolenchery, Ernakulam District, Kerala, India

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Abstract

Background: Urinary tract infection (UTI) is one of the most common bacterial infections encountered in clinical practice both in community and hospital settings. Rapid diagnostic tests like Dipstick are economical, save valuable time and thus useful in high-end laboratories.

Methodology: We compared the performance of leukocyte esterase and nitrite reductase dipstick tests with microscopic examination for pus cells and bacteria in children with clinically suspected urinary tract infection (UTI) keeping Urine culture and sensitivity as the gold standard for diagnosis of UTI. Restructured proforma was used for data collection and urine samples were obtained by midstream clean catch method.

Results: 409 children of the age group 1 month to 18 years were included in the study. Results of urine dipstick tests and microscopy were compared with urine culture for each sample. Significant bacteriuria was found in 194 cases (47.4%). The dipstick leukocyte esterase and nitrite testing had a sensitivity of 72.16% and 28.35% and specificity of 78.14% and 93.95%, respectively. The positive predictive value of the tests was 69.65% and 80.88%, and the negative predictive value was 80.77% and 59.24%, respectively. A combination of LET and NT either of the two positives (dipstick positive) had higher sensitivity (75.77%) and specificity (74.8%) as compared to microscopy. We found that PPV and NPV were higher (73.13% and 77.4% respectively) for urine microscopy (66.3% and

71.01% respectively). The dipstick test had a higher positive likelihood ratio and DOR as compared to microscopy (3.01 vs 2.18) and (9.33 vs 4.83) respectively.

Conclusion: Urine dipstick can be used as a better cost-effective screening tool in the diagnosis of UTI. Dipstick, being a rapid test, saves time, is economical as compared to microscopy and decreases the laboratory burden especially in a tertiary care hospital Statistical analysis showed there is positive correlation at 0.05 significance level between leukocyte esterase – nitrite; leukocyte esterase – culture; nitrite – bacteria, and bacteria – culture. Strong positive correlation ($p = 0.01$) significance level seen between leukocyte esterase – bacteria and Dipstick – Microscopy tests.

Keywords: Urinary Tract Infection, Dipstick, Leukocyte Esterase, Nitrite, Urine Culture

Introduction

In developing countries, urinary tract infection (UTI) is a common bacterial infection met by clinicians in community and hospital settings. The risk of having a UTI before the age of 14 years is 1-3% in boys and 3-10% in girls [1]. UTI is the second most common bacterial infection in children, after otitis media [2]. It has become the most common hospital-acquired infection, accounting for as many as 35% of nosocomial infections, and is the second most cause of bacteremia in hospitalized patients [3].

It is necessary to identify children with UTI and treat them as soon as possible to avoid any long-term complications. UTI are categorized into either lower tract infection, affecting the bladder (cystitis) and/or urethra (urethritis), and upper tract infection, affecting the ureters, collecting system, and parenchyma (pyelonephritis). Any anatomic or functional abnormalities of the urinary tract may impede urinary flow and can increase the host susceptibility to UTI. Physiologic factors include dysfunctional voiding, infrequent voiding, incomplete bladder emptying, and constipation. Anatomic factors include phimosis, vulval synechiae, urinary incontinence etc.

Most of the symptoms like dysuria, back pain, abdominal pain, frequency, new-onset incontinence alone is not sufficient to prove UTI in verbal children [4]. These symptoms lead to a presumptive diagnosis of UTI, and a presence of pyuria shows probable UTI pending culture results. However, fever of an unexplained source in children usually shows UTI [5]. Because of these factors, much reliance is placed on laboratory tests to augment clinical impressions; even when clinical diagnoses are unequivocal. Enteric bacteria, particularly E. Coli remain the most frequent cause of UTI, although the distribution of pathogens that cause UTI is changing [6].

Prompt detection and treatment of urinary tract infection is especially important in children because the developing kidney is more prone than the adult kidney for formation of renal scars and later for development of chronic renal failure following delayed or improper treatment of the infection [7, 8]. Rapid dipstick-based tests, which detect leukocyte esterase and nitrite, are useful in screening for UTI. Dipstick tests on urine to detect gram negative bacteria (nitrite test) or WBC (leukocyte esterase test) are typically done together; if both are positive, the diagnostic sensitivity for UTI is about 93 to 97% and the specificity is about 72 to 93% [9]. Urine Culture and sensitivity stays the gold standard in the diagnosis of UTI.

Materials and methods

The aim of the study is to evaluate the validity of urine microscopy, dipstick leukocyte esterase and nitrite tests in diagnosing UTI in children.

Study Design: Descriptive validation of a diagnostic tool

Duration of Study: 1 year

Sample size

Sample size of 189 diseased subjects with a precision of 80% and alpha error of 5% was calculated comparing the sensitivity of new test & reference test with a difference - 5.099.

Study population

Children admitted in pediatric ward with symptoms of UTI (lethargy, irritability, poor feeding, failure to thrive, increased frequency, urgency, dysuria, suprapubic pain, back pain) or unexplained fever of 38°C or higher for > 48 hrs. Duration in the age group 1 month to 18 yrs.

Inclusion criteria

Children admitted with symptoms of UTI (Lethargy, irritability, poor feeding, failure to thrive, increased frequency, urgency, dysuria, suprapubic pain, loin pain) or unexplained fever of 38°C or higher for > 48 hrs. Duration in the age group 1 month to 18 years.

Exclusion criteria

Children taking antibiotics at the time of collection of samples. Children whose parents or care givers refused to give consent for the study.

Materials and Methods

Children admitted with symptoms of UTI (lethargy, irritability, poor feeding, failure to thrive, increased frequency, urgency, dysuria, suprapubic pain, loin pain) or unexplained fever of 38° C or higher for > 48 hrs. Duration were included.

A semi structured questionnaire was filled in while interviewing the patient or the mother/father. Detailed history with special regard to the onset and duration of symptoms of UTI was noted. Written informed consent was obtained from the parents. Clean catch mid-stream urine samples were collected from the patients. Urine dipstick test for leukocyte esterase and nitrites, Urine microscopy for Pus cells and bacteria and Urine culture and sensitivity were done on the samples collected.

Data including patient profile, dipstick, microscopy, and culture results were recorded and analyzed using Microsoft Excel software. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) and Likelihood ratio were calculated for each of the methods (microscopic pyuria / bacteriuria, dipstick LET/ NT) using standard formulae. Diagnostic odds ratio (DOR) was also calculated.

Results

Our study to evaluate the validity of urine microscopy and dipstick test in the diagnosis of UTI, had 409 samples in which 203 were males (49.63%) and 206 were females (50.37 %). Among the study population 194 cases were diagnosed with UTI by the gold standard test. Proportion of diseased males and females was 104: 90. (53.6 % vs 46.4 %).

The distribution of confirmed cases in our study was 44 % in the age group 1- 5 year followed by 37 % <1 year and 19 % above 5 years of age. In our study UTI was more common in males in the age group < 1 year and in females after infancy. Males' vs Females were 72.2 % vs 27.8 %, 46.5 % vs 53.5 % and 33.4 % vs 66.6 % respectively in the age group < 1 year, 1- 5 year, and more than 5 years.

Sensitivity, specificity, PPV, NPV of LET, NT, DIPSTICK (either LET/NT positive) were 72.1, 78.1,

69.6, 80.7%; 28.3, 93.9, 80.8, 59.2% and 75.7, 74.8, 73.1, 77.4% respectively, while sensitivity, specificity, PPV, NPV of pyuria, bacteriuria, microscopy (either of the two positive) were 67.5, 71.1, 67.8, 70.8 %; 22.1, 97.2, 87.7, 58 .0 % and 69, 68.3, 66.3, 71.0% respectively. The highest specificity was for bacteriuria in microscopy. A combination of LET and NT either of the two positives (dipstick positive) had higher sensitivity (75.77%) and specificity (74.8%) as compared to microscopy. We found that PPV and NPV were higher (73.13% and 77.4% respectively) for urine microscopy (66.3% and 71.01% respectively). The dipstick test had a higher positive likelihood ratio and DOR as compared to microscopy (3.01 vs 2.18) and (9.33 vs 4.83) respectively.

Statistical analysis showed there is positive correlation at 0.05 significance level between leukocyte esterase – nitrite; leukocyte esterase – culture; nitrite – bacteria, and bacteria – culture. Strong positive correlation (p = 0.01) significance level saw between Leukocyte esterase – bacteria and Dipstick – Microscopy tests

Table 1: Pearson's Correlation Coefficient between different diagnostic tests

	LET	NT	Dipstick	PC	Bacteria	Microscopy	Culture
LET	1.000						
NT	0.454*	1.000					
Dipstick	0.207	0.183	1.000				
Puss Cells	0.240	0.280	0.239	1.000			
Bacteria	0.995**	0.454*	0.207	0.240	1.000		
Microscopy	0.203	0.189	0.947**	0.373	0.203	1.000	
Culture	0.556*	0.299	0.387	0.298	0.526*	0.374	1.000

LET – Leukocyte esterase Test; NT – Nitrite Test; * Significance at 0.05 level PC – Puss Cells ** Significance at 0.01 level

Discussion

In our study, of the 409 samples studied 194 (47.4%) were disease positive and 215 (52.6%) were disease negative as diagnosed by the gold standard test. Overall, more males were diagnosed with UTI than females in our study (53.6 % vs 46.4%). The distribution of confirmed cases in our study was 44 % in the age group 1- 5 year followed by37 % <1 year and 19 % above 5 years of age.

Sex shows a preponderance of UTI in boys during the first year of life, but after the first year, UTI is more common in girls than boys [10]. We had similar outcome in which percentage of male's vs females was 72.2 % vs 27.8 %, 46.5 % vs 53.5 % and 33.4 % vs

66.6 % respectively in the age group < 1 year ,1- 5 year, and more than 5 years the sensitivity of leukocyte esterase test (LET) 72.16%, higher than microscopic pyuria (67.53%) and low for bacteriuria (22.16%) and for nitrite (28.35%) The highest sensitivity was for LET (72.16%) in our study and was comparable to the study by Taneja et al. (2009) (73.5%) [11] and Goldsmith et al. (1990) (76%) [12]. In our study we found that dipstick LET was more sensitive (72.16% vs 67.53%) than microscopic pyuria.

The specificity of LET, NT, microscopic pyuria and bacteriuria was 78.14, 93.95, 71.16, 97.21% respectively. Dipstick NT was more specific as compared to dipstick LET in our study. This was like the study by Taneja et al. (2009) (11) and Goldsmith et al. (12) (1990) the highest specificity was for the presence of bacteria in urine microscopy [12].

A combination of LET and NT either of the two positives (dipstick positive) had higher sensitivity (75.77) and specificity (74.8) as compared to microscopy. It was found that PPV and NPV were higher (73.13% and 77.4% respectively) for urine microscopy (66.3% and 71.01% respectively). The dipstick test had a higher positive likelihood ratio and DOR as compared to microscopy (3.01 vs 2.18) and (9.33 vs 4.83) respectively in this study, Sensitivity, and positive predictive value (PPV) of dipstick test were 76%and 72%respectively by Ayazi[13]. Another study by Hiraoka et al. (1994) [14] of 92 children found the combined tests (LET and NIT) to have a sensitivity and negative predictive value of 100%.

These results suggest that use of the dipstick test of LET and NT negative can avoid a large part of the cost incurred by urine culture and is useful for screening UTI in children by study by Hiraoka [14].

When both Leukocyte esterase and Nitrite are both positive, the diagnostic sensitivity for UTI is about 93 to 97% and the specificity is about 72 to 93% [15]. The specificity of the nitrite test is quite high (about 98%); a positive result on a freshly voided specimen is highly predictive of UTI., but its sensitivity is low in children because they void often, and the time to produce nitrites by bacterial metabolism is limited to give a positive nitrite test. Acute UTI can be missed in infants as frequent bladder emptying leads to lack of urinary nitrates.[5]

Contaminated urine is common in non-invasive samples collected from infants and children who are not toilet trained. In some cases, non-nitrite forming organisms (e.g., some pseudomonas strains and B. Hemolytic streptococcus) could theoretically give a negative strip test.

Dipstick tests have the advantage of being quick and easy to perform and can be carried out in primary care centers, giving an immediate result. Microscopic examination of urine samples for leukocytes or bacteria is more time consuming and labor intensive than the dipstick method by Upadhayay et al [16].

Statistical analysis showed there is positive correlation at 0.05 significance level between leukocyte esterase – nitrite; leukocyte esterase – culture; nitrite – bacteria, and bacteria – culture. Strong positive correlation ($p = 0.01$) significance level saw between leukocyte esterase – bacteria and Dipstick – Microscopy tests. Whiting et al [17], showed that test combination, that is, a dipstick test positive for both nitrite and LE, having highest positive likelihood ratio, could rule in disease and that negative for both LE and nitrite could rule out UTI.

In our country high rates of UTI with variations among regions have been reported. Still, in our study as expected, gram-negative bacteria were the most frequent, and E. Coli (53.09%) was the most common organism isolated followed by Klebsiella species (24.2%). The frequency of microorganisms was similar in all the age groups studied. Earlier studies proved that most frequent organisms in children were Escherichia coli (57.2 - 89.9%), Klebsiella species (2.1 - 10%), P. Mirabilis (1.2 - 10.9%), Enterobacter (1.2 - 12.7%), Pseudomonas (1 - 7%),

Staphylococcus (1.2 - 6.3%) and Enterococcus (3.7-

13.7%), by Schalger [18] and Riccaborne [19].

Conclusion

Rapid diagnosis and prompt therapy is critical in the prevention of long-term UTI sequelae. UTI must be considered, in any infant or child presenting with fever without any focus.[20]

In our study, sensitivities and PPV of urine dipstick were higher as compared to microscopy (75.7 vs 69.0% and 73.1 vs 66.3 % respectively). The dipstick test had a higher positive likelihood ratio and DOR as compared to microscopy (3.01 vs 2.18) and (9.33 vs 4.83) respectively. Hence urine dipstick can be used as a better cost-effective screening tool in the diagnosis of UTI.

Recommendations

Dipstick being a rapid test, saves time, is economical as compared to microscopy and decreases the laboratory burden especially in a tertiary care hospital. The specificity of the nitrite test is quite high (about 98%); a positive result on a freshly voided specimen is highly predictive of UTI, but in non-toilet-trained children, non-nitrite forming organisms (e.g., some pseudomonas strains and B. Hemolytic streptococcus) could theoretically give a negative strip. The results are more significant above one year of age dipstick tests have the advantage of being quick and easy to perform and can be carried out in primary care centers, giving an immediate result. Microscopic examination of urine samples for leukocytes or bacteria is more time consuming and labor intensive than the dipstick method [16]. Urine dipstick combining the presence of both leukocyte esterase and nitrites rules in UTI and may be the most practical approach in an outpatient setting [21]. So, both positive rules in UTI, while both negative rules out UTI, thus saving resources on urine cultures, and thereby reducing antibiotic resistance in children, by unnecessary start of antibiotics.

Figure 1: Comparison of sensitivity, specificity, PPV and NPV of LET, NT and Dipstick Test

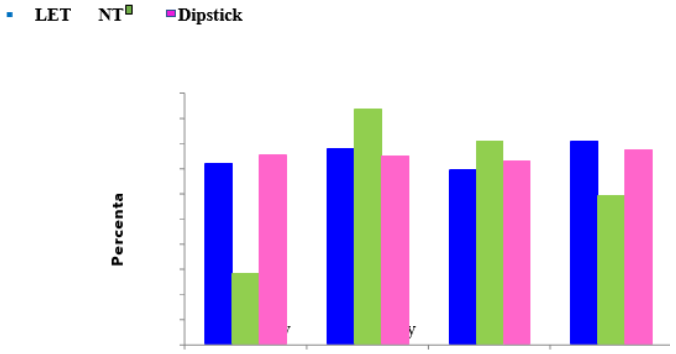

Figure 2: Comparison of sensitivity, specificity, PPV and NPV of Dipstick and microscopy

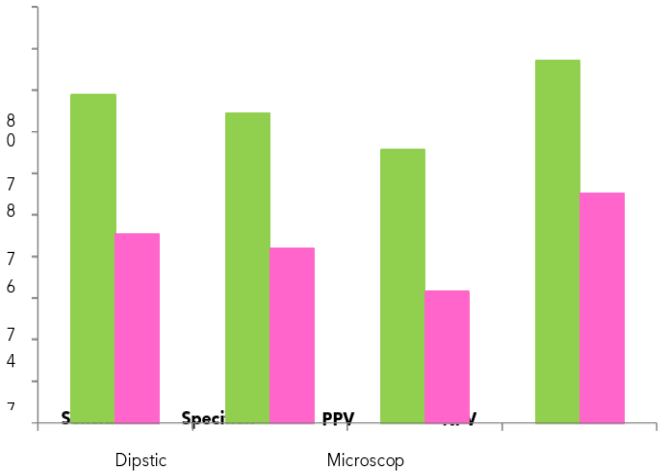

Table 2: Tabular descriptions of the total samples		
Total Number of Samples: 409		
Sex	Male: 203 (49.63%)	Female: 206 (50.37%)
Culture Positive	Male: 104 (53.61%)	Female: 90 (46.39%)

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	PLHR	NLHR	DOR
Leukocyte esterase	72.16	78.14	69.65	80.77	3.301	0.356	9.27
Nitrite	28.35	93.95	80.88	59.24	4.689	0.763	6.15
Dipstick	75.77	74.88	73.13	77.40	3.017	0.324	9.33
Pus Cells	67.53	71.16	67.88	70.83	2.342	0.456	5.13
Bacteria	22.16	97.21	87.76	58.06	7.942	0.801	9.92
Microscopy	69.07	68.37	66.34	71.01	2.184	0.452	4.83

PPV- Positive Predictive Value (%); NPV – Negative Predictive Value (%), PLHR – Positive Likelihood Ratio; NLHR – Negative Likelihood Ratio; DOR – Diagnostic Odds Ratio

Table 3: Tabular descriptions of the <1 year old samples

Total Number of Samples: 115		
Sex	Male: 71 (61.74%)	Female: 44 (38.26%)
Culture Positive	Male: 52 (72.22%)	Female: 20 (27.78%)

Pus Cells	61.11	74.42	80.00	53.33	2.389	0.523	**4.57**
Bacteria	22.22	93.02	88.89	41.24	3.185	0.836	**3.81**
Microscopy	62.50	74.42	80.36	54.24	2.443	0.504	**4.85**

PPV- Positive Predictive Value (%); NPV – Negative Predictive Value (%), PLHR – Positive LikelihoodRatio; NLHR – Negative Likelihood Ratio; DOR – Diagnostic Odds Ratio

Table 4: Tabular descriptions of the 1–5-year-old samples

Total Number of Samples: 172		
Sex	Male: 80 (46.51%)	Female: 92 (53.49%)
Culture Positive	Male: 40 (46.51%)	Female: 46 (53.49%)

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	PLHR	NLHR	DOR
Leukocyte esterase	75.00	83.72	65.85	88.89	4.607	0.299	**15.43**
Nitrite	27.78	97.67	83.33	76.36	11.944	0.739	**16.15**
Dipstick	75.00	83.72	65.85	88.89	4.607	0.299	**15.43**
Pus Cells	77.78	67.44	50.00	87.88	2.389	0.330	**7.25**
Bacteria	19.44	97.67	77.78	74.34	8.361	0.825	**10.14**
Microscopy	77.78	65.12	48.28	87.50	2.230	0.341	**6.53**

PPV- Positive Predictive Value (%); NPV – Negative Predictive Value (%), PLHR – Positive LikelihoodRatio; NLHR – Negative Likelihood Ratio; DOR – Diagnostic Odds Ratio

Table 5 Tabular descriptions of >5-year-old samples

Total Number of Samples: 122

Sex	**Male**: 52 (42.62%)			**Female**: 70 (57.38%)			
	Sensitivity (%)	**Specificity (%)**	**PPV (%)**	**NPV (%)**	**PLHR**	**NLHR**	**DOR**
Leukocyte esterase	75.00	83.72	65.85	88.89	4.607	0.299	15.43
Nitrite	27.78	97.67	83.33	76.36	11.944	0.739	16.15
Dipstick	75.00	83.72	65.85	88.89	4.607	0.299	15.43
Pus Cells	77.78	67.44	50.00	87.88	2.389	0.330	7.25
Bacteria	19.44	97.67	77.78	74.34	8.361	0.825	10.14
Microscopy	77.78	65.12	48.28	87.50	2.230	0.341	6.53

PPV- Positive Predictive Value (%); NPV – Negative Predictive Value (%), PLHR – Positive Likelihood Ratio; NLHR – Negative Likelihood Ratio; DOR – Diagnostic Odds Ratio

Table 5: Tabular description in children above 5years

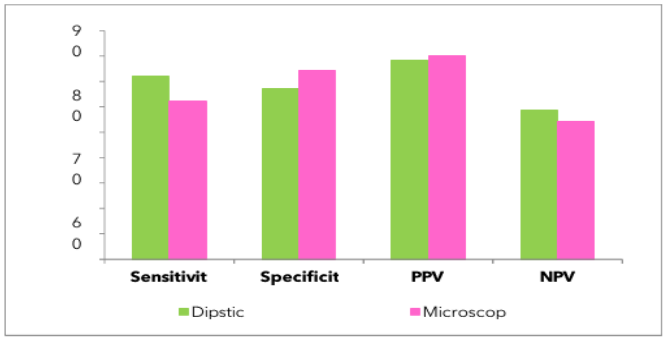

Figure 3: Showing sensitivity, specificity, PPV, NPV of Dipstick and Microscopy in less than 1 year

References

1. Indian society of pediatric nephrology. Revised statement on management of urinary tract infections. Indian pediatrics, 2011; 48: 709 – 717.
2. Becknell b., m. Schober, l. Korbel, j. D. Spencer the diagnosis, evaluation and treatment of acute and recurrent pediatric urinary tract infections. Expert rev. Anti infect ther., 2015; 13(1): 81-90.
3. Najar ms., saldanha cl., banday ka. Approach to urinary tract infections. Indian journal of nephrology 2009; 19(4): 129-139
4. Naeem akhtar. “urinary tract bacterial pathogens; their antimicrobial susceptibility patterns at bahawalpur.” (“urinary tract bacterial pathogens; their antimicrobial susceptibility ...”) (“prevalence of urinary tract infection in patients attending ... - iabcr”) the professional, 2000; 7(2):131-137.
5. Baumer jh, jones rwa urinary tract infection in children, national institute for health, and clinical excellence archives of disease in childhood - education and practice 2007; 92:189-192.
6. lindstorm, tc. Baerheim, a., flataas, as. Behaviour modification group-treatment of children with recurrent lower urinary tract infections. Scand j caring sci. 2000;14(4): 259-67.
7. Bakker, e., van sprundel, m., van der aurwera, jc., van gool, jd., wyndaele, jj. Voiding habits and wetting in a population of 4332 belgian schoolchildren aged between 10 and 14 years. Scand j urol nephrol. 2002; 36(5): 354-62.
8. Meadow, sr. Day wetting. Pediatr nephrol.1990; 4(2):178-84
9. Mazzola, bl., von vigier, ro., marchand, s., tonz, m., bianchetti, mg. Behavioral and functionalabnormalities linked with recurrent urinary tract infections in girls. J nephrol. 2003; 16(1):133-8
10. Tanagho, emil a., mcaninch, jack w., (eds). Smith's general urology. Mcgraw hill inc; 2004. Bacterial infections of the genitourinary tract p 203-227.
11. Taneja n., ss chatterjee, m. Singh, s. Sivapriya, m. Sharma, s.k sharma. Validity of quantitative unspun urine microscopy, dipstick test leucocyte esterase and nitrite tests in rapidly diagnosing urinary tract infections. 2010; japi. 58: 485-487.
12. Goldsmith bm, campos jm. Urine dipstick microscopy and culture for the detection of bacteriuria in children clin. Paedtr. 1990: 29: 2114 – 2118.
13. Ayazi p. And m.m. daneshi. Comparison of urine culture and urine dipstick analysis in diagnosis of urinary tract infections. Acta medica iranica, 2007; 45(6):501-504.
14. Hiraoka m1, hida y, hori c, tuchida s, kuroda m, sudo m. Rapid dipstick test for diagnosis of urinary tract infection. Acta paediatr jpn. 1994; 36(4):379-82.
15. Weinberg, g.a. urinary tract infection in children – pediatrics – merck manuel professional edition, 2015.Www.merckmanuals.com/professional/pediatrics
16. Upadhyay, j., bolduc, s., braga, l., farhat, w., bägli, d. J., mclorie, g. A., khoury, a. E., & el-ghoneimi, a. (2002). Impact of prenatal diagnosis morbidity is associated with ureterocele management. The journal of urology, 167(6), 2560–2565.
17. Whiting, p., westwood, m., watt, i., cooper, j., & kleijnen, j. (2005). Rapid tests and urine sampling techniques for the diagnosis of urinary tract infection (uti) in children under five years: a

systematic review. Bmc pediatrics, 5(1), 4. Https://doi.org/10.1186/1471-2431-5-4

18. Schalger, ta. Urinary tract infections in children younger than 5 years of age: epidemiology, diagnosis, treatment, outcomes, and prevention. Paediatr drugs. 2001; 3(3): 219-27.
19. Riccabona m. Urinary tract infections in children. Current opinion in urology, 2003; 13: 59-62.
20. becknell b, schober m, korbel l, spencer jd. “the diagnosis, evaluation and treatment of acute and recurrent pediatric urinary tract infections.” (“congenital anomalies of the kidney and urinary tract: a clinical review”) expert rev anti infect ther. 2015 jan;13(1):81-90. Doi: 10.1586/14787210.2015.986097.
21. National collaborating centre for women's and children's health (UK). (2007). “Urinary Tract Infection in Children: Diagnosis, Treatment and Long-term Management.” (“Prescribing Guidelines for Urinary Tract Infections”) RCOG Press.