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Accuracy of Urinalysis for Urinary Tract Infection in 6 Months to 18 Years Old Children along with Its Bacteriological Profile: Koja General Hospital 2016-2017

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Abstract **Background:** Accurate diagnosis of urinary tract infection (UTI) in children is crucial, nevertheless it is an intricate process. Combination parameters such as leukocyte esterase (LE) and leukocyte count in urinalysis as initial laboratory exam for a suspected UTI reported to have a high sensitivity and specificity. Urine culture as the gold standard may take some time, while prompt treatment is imperative. **Methods:** From July 2016 to June 2018 paired urinalysis and urine culture data from in-patient in Koja General Hospital age 6 months to 18 years old were retrieved. Diagnostic study was done for each individual component i.e. LE, nitrite, bacteria, and leukocytes. Urinary pathogen and antibiotic susceptibility patterns were descriptively analyzed. **Results:** One-hundred-seventeen data were eligible for analysis. Median age of subjects was 2 years old (6 month-18 years), of which 51.3% were boy. Nitrite had the best specificity (98.8%) and accuracy (77.4%) while bacteriuria had the best sensitivity (34.5%). Pyuria and LE had the lowest sensitivity (31% and 17.2% respectively). Bacteria isolated from the culture were all gram negative. *Escherichia coli* was the most prevalent bacteria, represented 44.8% of the positive cases. Amikacin had the best sensitivity among the antibiotics tested. **Conclusion:** While in theory pyuria and LE might be used in diagnosing UTI, several factors may distort its value. This should be taken into consideration when a child is suspected of having a UTI.

Keywords: *pediatric urinary tract infection, bacteriological profile, accuracy of urinalysis*

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1. Introduction

Accurate diagnosis of urinary tract infection (UTI) notably in children is clinically important though the process is quite challenging. [1,2] Clinical manifestation varies widely between different age group, but no single sign or symptom is specific enough. [3,4] Combination parameters in urinalysis as initial laboratory examination in children suspicious for UTI are reported to have high sensitivity and specificity. [4] Urine culture as the gold standard have its own issues such as it is an invasive procedure to obtain a representative sample and waiting for the final result might delay treatment of which early management is paramount to prevent complications.

The challenge could escalate in referral hospital especially in those area where prudent antibiotic use has not been established. Excessive usage of antibiotic with low compliance may end up with a high bacterial resistance and perplexing cases, thus treatment should be tailored based on bacteriological profile and antibiotic sensitivity pattern for each region. Empirical treatment for area which diagnostic modalities are not readily available should be based on regional pattern. [5]

The aim of this paper is to perform a diagnostic study of urinalysis with the bacteriological profile and antibiotic susceptibility pattern in Koja General Hospital, a referral hospital in North Jakarta, Indonesia.

2. Subjects and Methods

Urinalysis and urine culture data from patient age 6 months – 18 years old who was admitted in Koja General Hospital from July 2016 to June 2018 were retrieved.

Urinalysis individual component i.e. LE, nitrite, bacteriuria, and pyuria were assessed with semi-automated urinalysis analyzer. Pyuria defined as the presence of >5 white blood cells (WBCs) per high-power field (HPF). Diagnostic study was done for each of the components. Urine culture as the gold standard were paired with the urinalysis data. UTI was defined as a bacterial growth of ≥100,000 CFUs/mL since the culture specimen was obtained from a mid-stream urine. Antibiotic resistance was tested using automated identification following interpretation based on Clinical Laboratory Standard Institute (CLSI) guideline. Urinary pathogen and antibiotic sensitivity pattern were descriptively analyzed.

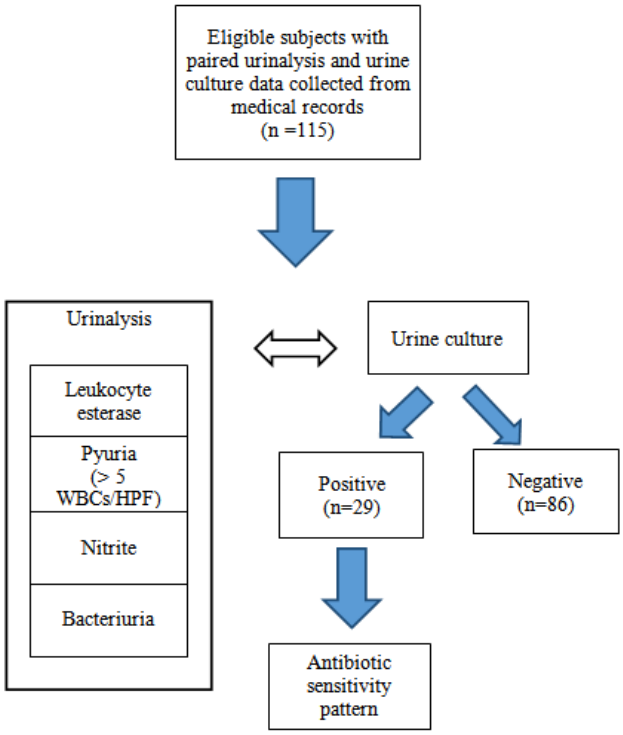

Figure 1. Flow of method

3. Results

One-hundred-seventeen data were eligible for analysis. Median age of subjects was 2 years old (6 month-18 years) with male predominance (51.3%). Thirty-one subject was diagnosed as UTI but 2 of them were then disregarded due to identification growth of *Staphylococcus haemolyticus* which considered as sample contamination. Individual parameters of urinalysis in relation to UTI diagnosis is shown in Table 1.

Diagnostic study was done on each urinalysis parameters. Nitrite shown to has the best specificity (98.8%) and accuracy (77.4%) while bacteriuria had the best sensitivity (34.5%). This study demonstrates that combination of nitrite, pyuria, or bacteriuria give a better result as oppose to combination of all parameters (Table 2).

Table 3 show the urine culture results, all of which were gram negative bacteria. *Escherichia coli* was the most common identified isolates. The best in vitro susceptibility profile in this study has been shown by Amikacin (Table 4).

Table 1. Urinalysis Result Based on UTI status

Parameter (n=115)	UTI [n (%)]	No UTI [n (%)]	p
LE concentration			
Small (trace or 1+)	2 (6.5)	5 (5.8)	0.773*
Moderate (2+)	2 (6.5)	5 (5.8)	
Large (3+)	1 (3.2)	3 (3.5)	
Negative result	24 (82.8)	73 (84.9)	
Nitrite			
Positive	4 (13.8)	1 (1.2)	0.014**
Negative	25 (86.2)	85 (98.8)	
Pyuria			
Positive (>5 WBCs/HPF)	9 (31)	31 (36)	0.624***
Negative (≤ 5 WBCs/HPF)	20 (69)	55 (64)	
Bacteriuria			
Small (+1)	6 (20.7)	13 (15.1)	
Moderate (+2)	4 (13.8)	5 (5.8)	0.093****
Large (+3)	0 (0)	1 (1.2)	
Negative	19 (65.5)	67 (77.9)	

* Fisher exact test after regrouping (Positive vs Negative)
** Fisher exact test
*** Chi-square
**** Chi-square after regrouping (Positive vs Negative)

Table 2. Diagnostic Value of Urinalysis Parameters

Parameters	Sensitivity (%)	Specificity (%)	Accuracy (%)
LE	17.2 (3.49 to 30.99)	84.9 (77.31 to 92.45)	67.8 (59.29 to 76.36)
Nitrite	13.8 (1.24 to 26.34)	98.8 (96.57 to 100)	77.4 (69.75 to 85.04)
Pyuria	31.0 (14.20 to 47.87)	64.0 (53.81 to 74.10)	55.7 (46.57 to 64.73)
Bacteriuria	34.5 (17.18 to 51.78)	77.9 (69.14 to 86.68)	66.9 (58.36 to 75.55)
LE OR Nitrite OR Pyuria OR Bacteriuria	44.8 (26,73 to 62,93)	58.1 (47.71 to 68.57)	54.8 (45.69 to 63.88)
Nitrite OR Pyuria OR Bacteriuria	44.8 (26.73 to 62.93)	59.3 (48.92 to 69.69)	55.7 (46.57 to 64.73)

Table 3. Microorganism from Urine Culture Result

Culture Result (n=29)	**n**
Escherichia coli	13
Pseudomonas Aeruginosa	4
Klebsiella pneumoniae	4
Acinetobacter baumannii	3
Enterobacter cloacae	3
Morganella morganii	1
Proteus mirabilis	1

Table 4. Antibiotic sensitivity of all antibiotic tested

Antibiotic (n)	**Sensitive (%)**
Cefazolin (27)	4 (14.8)
Piperacillin Tazobactam (27)	15 (55.6)
Tigecycline (27)	**20 (74.1)**
Ampicillin (27)	0 (0)
Aztreonam (27)	6 (22.2)
Gentamycin (29)	18 (62.1)
Amikacin (29)	**27 (93.1)**
Amoxicillin (29)	1 (3.4)
Ampicillin Sulbactam (29)	6 (20.7)
Ceftazidime (29)	9 (31)
Ceftriaxone (29)	6 (20.7)
Cefotaxime (2)	1 (50)
Cefepime (29)	10 (34.5)
Ciprofloxacin (29)	18 (62.1)
TMP-SMX (29)	10 (34.5)
Nitrofurantoin (27)	9 (33.3)
Meropenem (29)	**25 (86.2)**

4. Discussion

It is widely known that urinalysis shown to be an important addition to urine culture in the detection of UTI in children and adults. Pyuria which a representation of inflammation may assist the determination of either contamination, colonization, asymptomatic bacteriuria or bacteremic UTI. [6] Indonesian Pediatric Association Consensus on UTI affirm that bacteriuria $>10^5$ CFU/mL found in urine culture from mid-stream specimen is interpreted as significant. Further it stated that clinical diagnosis of UTI can be made and be treated with empirical antibiotic before urine culture result is acquired if there is fever with urinalysis abnormality such as pyuria, positive nitrite, and or LE. [7] Schroeder et al found that LE had the highest sensitivity even when trace LE was excluded (95.7%) and nitrites had the highest specificity of 100%. A very strict criteria of pyuria >10 WBCs/HPF had sensitivity of 80.7%. [6] A study by Tzimenatos et al [8] showed similar result where sensitivity for any LE was at 92% and pyuria of >5 WBCs/HPF was at 82%. These findings are in concordance with American Academy of Pediatrics guideline that suggest pyuria should be present when diagnosing UTI. [9] Nevertheless this paper revealed different result of individual urinalysis parameters accuracy compared to the previous studies, particularly for pyuria and LE which showed a very low sensitivity.

Roberts [10] disclosed the history of urine culture as gold standard for the diagnosis of UTI. Definition of "positive" in urine culture and the role of urinalysis came from publication by Edward Kaas in 1956 which conclude that "for survey purposes, a count of 10^5 bacteria or more per ml of urine has been designated arbitrarily as the dividing line between true bacilluria and contamination". At that time, people had not acknowledged asymptomatic bacteriuria yet. Applying colony count from urine culture result without taking into consideration the host response in the form of inflammation can be misleading. Schoeder et al [6] derived to a conclusion that urinalysis is highly sensitive in young infants with bacteremic UTI and suggest that the suboptimal urinalysis sensitivity in other studies may be explained by urine culture result that do not reflect true UTI.

Shaikh et al [11] demonstrate that certain urinary pathogens fail to elicit pyuria reliably. They found that children with Enterococcus species, Klebsiella species and *Pseudomonas aeruginosa* were significantly less likely to exhibit pyuria than children with *Eschericia coli*. Our study found that 11 out of 29 positive urine culture were due to those pathogens that less likely to have positive LE or pyuria. It may be an addition explanation why the sensitivity of pyuria and LE in this study were low.

Technical approach in modern laboratory may alter the sensitivity of pyuria. This study employed spun urine specimens which then analyzed with semi-automated urinalysis system. Cut off of pyuria >5 WBCs/HPF is applied. Chaudhari et al [12] in their study found a threshold difference between spun urine (concentrated) sample for traditional microscopic urinalysis and unspun urine (dilute) sample for automated urinalysis system. They enunciate that urine concentration should be incorporated into the interpretation of automated microscopic urinalysis, because they found that the threshold for pyuria to be as lower as 3 WBCs/HPF in dilute urine. This can make the 'old believe' using >5 as cut off for pyuria can be inaccurate. Spun urine is used in this study, hence technical consideration was not a confounder.

Our study showed that positive urine culture was low (25.2%), all yielded gram-negative bacteria. *Eschericia coli* was the predominant growth (45%), followed by *Pseudomonas aeruginosa* (13.7%) and *Klebsiella pneumoniae* (13.7%). This is similar with other study from India, Iran, and Cambodia which use similar method of collecting urine specimens. [5,13,14,15] We did not exclude the pre-treated child and no preceding antibiotic data were obtained. Study by Badhan et al [5] and Motamedifar et al [14] also had similar low positive culture result after excluded all children who receive antibiotic either as prophylactic or therapy.

A study by Singh et al [15] from Nepal showed higher positive rate (45.2%) by obtaining urine culture only from those specimens which had pre-examination WBCs ≥5/HPF. Haris et al [16] from Indonesia demonstrated positive culture rate of 41.2% using the same method. Our study still generated low positive culture rate of 21.6% even after omitted specimens with WBCs<5/HPF while losing 21 out of 29 positive culture result.

Another study from Indonesia by Subandiyah [17] had higher positive culture rate (49.02%) by excluding patient who received antibiotic more than 2 days prior to specimen collection. The study showed significantly lower positive result infant 1 month to 1 year old (7.6%), while this number were much higher in other study (15% [16] and 26.7% [19]).

E. coli is the most common microorganism revealed in most studies with the exception of Haris et al who found that *Pseudomonas aeruginosa* was more prevalent than *E. Coli* in one of the hospitals in Aceh. Some of the subjects in their study were children with malignancy that can be infected by *Pseudomonas aeruginosa* as a nosocomial pathogen. We found that all of microorganism yielded were gram negative pathogen though others showed that gram positive bacteria also play a role in causing UTI in children. [5,13-18]

The most sensitive oral antibiotic was Ciprofloxacin, which was not recommended for children due to its safety concerns. Amikacin (93.1%) had the highest sensitivity followed by Meropenem (86.2%) and Tigecycline (74.1%). Amoxicillin, Cephalosporin and TMP-SMX are the most widely used antibiotics in practice, nonetheless the susceptibility is only at 3.4-34.5%. The need of intravenous antibiotic can be a burden for society since outpatient parenteral antimicrobial therapy (OPAT) was not widely available yet, so hospitalization is a must. Studies reported that most of UTI pathogens are sensitive to nitrofurantoin. [5,13,14,15,17,18] Our study showed nitrofurantoin sensitivity was only at 33.3%.

It is evidence from this study there is an increase of resistance of the uropathogens in paediatric population. Studies around the world reported comparable findings which make periodic bacteriological profile and antibiotics susceptibility pattern evaluation is imperative. Over-the-counter antibiotics use, which is a common practice in our population, is one of the risk factors which evoke this phenomenon. [19,20]

Our data was based only on laboratory records which lead to an inadequate analysis of prior antibiotic exposure. Literature showed that there is an association between antibiotics prescription up to 3 months prior and a UTI episode due to resistant *E. coli*. [21]

References

[1] Finnell SME, Carroll AE, Downs SM, Subcommittee on Urinary Tract Infection. Technical report — Diagnosis and management of an initial UTI in febrile infants and young children. Pediatrics [Internet] 2011; 128(3): e749-70.

[2] Shaikh N, Morone NE, Bost JE, Farrell MH. Prevalence of urinary tract infection in childhood: A meta-analysis. Pediatr Infect Dis J 2008; 27(4): 302-8.

[3] Miesien M, Tambunan T, Munasir Z. Profil klinis Infeksi Saluran Kemih pada Anak di RS Dr. Cipto Mangunkusumo. Sari Pediatri 2017; 7(4): 200.

[4] Robinson JL, Finlay JC, Lang ME, et al. Urinary tract infection in infants and children: Diagnosis and management. Paediatr Child Health 2014; 19(6): 315-9.

[5] Badhan R, Singh DV, Badhan LR, Kaur A. Evaluation of bacteriological profile and antibiotic sensitivity patterns in children with urinary tract infection: A prospective study from a tertiary care center. Indian J Urol 2018; 32(1): 50-6.

[6] Schroeder AR, Chang PW, Shen MW, Biondi EA, Greenhow TL. Diagnostic Accuracy of the Urinalysis for Urinary Tract Infection in Infants, 3 Months of Age. Pediatrics 2018; 135(6).

[7] Pardede SO, Tambunan T, Alatas H, Trihono PP HE. Konsensus infeksi saluran kemih pada anak. Jakarta: Badan Penerbit IDAI; 2011.

[8] Tzimenatos L, Mahajan P, Dayan PS, et al. Accuracy of the Urinalysis for Urinary Tract Infections in Febrile Infants 60 Days and Younger. Pediatrics [Internet] 2018; 141(2). Available from: http://www.ncbi.nlm.nih.gov/pubmed/29339564.

[9] Subcommittee on Urinary Tract Infection, Steering Committee on Quality Improvement and Managements, KB. R. Urinary Tract Infection: Clinical Practice Guideline for the Diagnosis and Management of the Initial UTI in Febrile Infants and Children 2 to 24 Months. Pediatrics [Internet] 2011; 128(3): 595-610.

[10] Roberts KB. The Diagnosis of UTI : Liquid Gold and the Problem of Gold Standards. Pediatrics 2015; 135(6): 5-8.

[11] Shaikh N, Shope TR, Hoberman A, Vigliotti A, Kurs-Lasky M, Martin JM. Association between Uropathogen and Pyuria. Pediatrics. 2016; 138(1).

[12] Chaudhari PP, Monuteaux MC, Bachur RG. Urine Concentration and Pyuria for Identifying UTI in Infants. 2016; 138(5).

[13] Gupta P, Mandal J, Krishnamurthy S, Barathi D, Pandit N. Profile of urinary tract infections in paediatric patients.Indian J Med Res 2015; (April): 473-7.

[14] Motamedifar M, Zamani K, Hassanzadeh Y, Pashoutan S. Bacterial Etiologies and Antibiotic Susceptibility Pattern of Urinary Tract Infections at the Pediatric Ward of Dastgheib Hospital, Shiraz, Iran:A Three-Year Study (2009-2011) Arch Clin Infect Dis. 2016; 11(2): 2-6.

[15] Singh SD, Madhup SK. Clinical profile and antibiotics sensitivity in childhood urinary tract infection at Dhulikhel Hospital. Kathmandu Univ Med J [Internet] 2013; 11(44): 319-24.

[16] Haris S. Kejadian Infeksi Saluran Kemih di Ruang Rawat Inap Anak RSUD Dr. Zainoel Abidin Banda Aceh. Sari Pediatri. 2012; 14(4): 235-40.

[17] Subandiyah K. Bacterial etiologic agents of urinary tract infections in children at Saiful Anwar Hospital, Malang. J Kedokt Brawijaya 2004; XX(2): 57-61.

[18] Moore CE, Sona S, Poda S, et al. Antimicrobial susceptibility of uropathogens isolated from Cambodian children. 2016; 113-7.

[19] Stultz JS, Doern CD, Godbout E. Antibiotic Resistance in Pediatric Urinary Tract Infections. Curr Infect Dis Rep [Internet] 2016; 1-9.

[20] Gökçe İ, Çiçek N, Güven S, et al. Changes in bacterial resistance patterns of pediatric urinary tract infections and rationale for empirical antibiotic therapy. Balkan Med J 2017; 34(5): 432-5.

[21] Global prevalence of antibiotic resistance in paediatric urinary tract infections caused by Escherichia coli and association with routine use of antibiotics in primary care: systematic review and meta-analysis. BMJ 2016; 352: i939.