ORIGINAL RESEARCH PAPER

Volume-7 | Issue-10 | October-2018 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

NEUTROPHIL-LYMPHOCYTE RATIO AS A MARKER OF URINARY TRACT INFECTION IN CHILDREN CAUSED BY BACTERIA

Nephrology

Harida Panduwita Sinaga* Department of Child Health, Faculty of Medicine, Universitas Sumatera Utara, Haji Adam Malik General Hospital, Medan, North Sumatera, Indonesia *Corresponding Author

Oke Rina Ramayani Department of Child Health, Faculty of Medicine, Universitas Sumatera Utara, Haji Adam Malik General Hospital, Medan, North Sumatera, Indonesia

Johannes Harlan Saing Department of Child Health, Faculty of Medicine, Universitas Sumatera Utara, Haji Adam Malik General Hospital, Medan, North Sumatera, Indonesia

ABSTRACT

Background. Urine culture, gold standard of urinary tract infection (UTI), takes time. Alternative parameters are needed. Neutrophil-lymphocyte ratio (NLR) can be counted from complete blood tests. This study aimed to determine the NLR as bacteria-caused UTI marker in children.

Methods. A cross sectional study in 50 patients with suspected UTI and leukocyturia in Adam Malik and USU Hospital Medan, September 2017 to January 2018. Urine culture and NLR were taken from all patients. NLR cut off point was determined based on the receiver-operating characteristic (ROC) curve, with p-value <0.05 was significant.

Results. Positive urine culture was found in 35 children (70%) with suspected UTI and leukocyturia. ROC analysis showed NLR insignificant to be used as bacteria-caused UTI marker (p = 0.073). Cut off point of NLR for bacteria-caused UTI was 4.55, with area under curve 0.665 (CI 95%: 0.515-0.815).

Conclusion. NLR cannot be used as bacteria-caused UTI marker in children.

KEYWORDS

Neutrophil-lymphocyte Ratio, Urinary Tract Infection, Children

INTRODUCTION

Urinary tract infection (UTI) is the most common bacterial infection that causes an inflammatory response and can cause serious death in infants and children.[1] Urinary tract infections can be caused by bacteria, fungi and viruses, however E.coli are the most common cause of UTI[2].

In a study conducted in Bali from 2010 to 2012, UTI mostly occurred in children under 2 years and 27% cases of UTI occured in children aged over 5 years[3]. The diagnosis of UTI in infants and children is not easy, especially in children under 3 years because the symptoms and signs arise were not specific.[1]

Diagnosis of UTI is established based on history, physical examination and investigations and confirmed by urine culture.[1] Urine culture result takes time, so it has been studied several various parameters to predict rapidly the cause of UTI which to be used as a guideline in the treatment of UTIs.

A study conducted in UK in 2014 showed that NLR has been used as a guideline to determine prognosis in some cases such as community-acquired pneumonia, ischemic heart disease and several types of cancer.[4] Thus, NLR are expected to be used as a significant diagnostic indicator and prognostic factors in UTI, but there are no studies on the usefullness or relationship of NLR in children with UTI. Various studies have shown increased neutrophils and decreased lymphocytes immediately after tissue injury.

The neutrophil-lymphocyte ratio is very easy to calculate and obtained based on the results of a complete blood tests.[5] This study aimed to determine the value of the NLR which to be used as a marker of UTI in children caused by bacteria.

MATERIAL AND METHOD

Patients selection

This study was a cross sectional study in patients with suspected UTI who were admitted to Haji Adam Malik and USU General Hospital Medan from September 2017 to January 2018. Patients with suspected urinary tract infection and leukocyturia, aged 1-18 years, parents or caregivers were willing to be interviewed and participate in research were included to this study consecutively. The suspected urinary tract infection defined when the following clinical signs and symptoms were found: (1) children aged> 1 year to <3 years: fever, abdominal pain, vomiting, dysuria, frequency, loin tenderness, (2) children aged> 3 years : fever, abdominal pain, vomiting, dysuria, frequency, loin tenderness, cloudy urine, smelly urine. Leukocyturia defined as the presence of leukocytes in the urine > 10 cells/μL urine or > 5 cells/high power field (hpf). Patients who met the inclusion criteria were examined for urine culture and performed complete blood test to assess the NLR value. Positive urine culture was defined as those with significant microbial growth determined (presence growth of bacteria $\geq 10^5$ CFUs/ mL), collected by midstream, urine catheterization and urine collector.

Exclusion criteria were patients with infections other than UTI, patients who were currently taking antibiotics or taking antibiotics 1 week prior the study, immunocompromised conditions (HIV, malignancy, using corticosteroids), and patients during menstrual period. Informed consent was obtained from all the participants and this study had been approved by the Research Ethical Committee Faculty of Medicine Universitas Sumatera Utara.

Data analysis

Demographic data such as gender, age, weight, body length and nutritional status were collected. Urine collection was performed by urine collector for younger children and midstream urine or urine catheterization for older children. All samples were stored in a sterile container. Examination of urinalysis was analyzed by urine analyzer Cobas U 411 ROCHE and urine culture was done at the Microbiology Laboratory using urine 0.01 ml and incubated in blood agar and eosine methylene blue agar.

Complete blood tests were analyzed using a Sysmex XT1800i / XT-2000i machine. The neutrophil-lymphocyte count ratio was obtained from neutrophil / lymphocyte calculation results.

Statistical method

Demographic data were analysed by univariate analysis using computer statistical software with SPSS 20 version with a 95% confidence interval. The cut-off value from NLR was determined by the ROC curve. All differences were considered significant at a value of $p<0.05$.

Results

This study enrolled 50 children, consisting of 35 children with UTI and 15 children non UTI. Of the UTI group, 57.1% were girls. UTI patients had an average age of 108 months, with nutritional status in most subjects (60%) were well-nourished children (Table 1).

TABLE 1. Characteristics of Subjects

Variable	UTI (n=35)	Non-UTI (n=15)
Gender, n(%)		
Boys	15 (42.9)	5 (33.3)
Girls	20 (57.1)	10 (66.7)
Age (months),median (min-max)	10 (12-214)	120 (14-216)
Weight (kg), median (min-max)	21 (5.4-60)	29.5 (8-51)
Height (cm), median (min-max)	121 (65-156)	126.5 (70-153)
Nutritional Status, n (%) Well-nourished Undernourished Malnourished	21 (60) 11 (31.40) 3 (8.6)	11 (73.3) 4 (26.7) 0 (0)
Neutrophil, %, mean (SD)	74.2 (12)	67.4 (11.8)
Lymphocyte, %, median (min-max)	16.4 (9.1-39.1)	21.1 (12.6-29.1)
NLR, %, median (min-max)	4.8 (1.3-8.9)	3.2 (1.8-6.4)
Leukocyturia, hpf, median (min-max)	15 (8-30)	10 (6-25)
Clinical manifestation, n(%)		
Fever	17 (48.6)	6 (40)
Dysuria	9 (25.7)	5 (33.3)
Poor urine flow	5 (14.3)	2 (13.3)
Cloudy urine	4 (11.4)	0
Vomiting	2 (5.7)	0
Loin tenderness	0	1 (6.7)
Frequency	0	1 (6.7)

The NLR cut-off value of ≥ 4.55 obtained from the study subjects was not significant to be used as a bacteria-caused UTI marker (p = 0.073), with a sensitivity value of 0.51 and a specificity value of 0.48 **(Figure 1).**

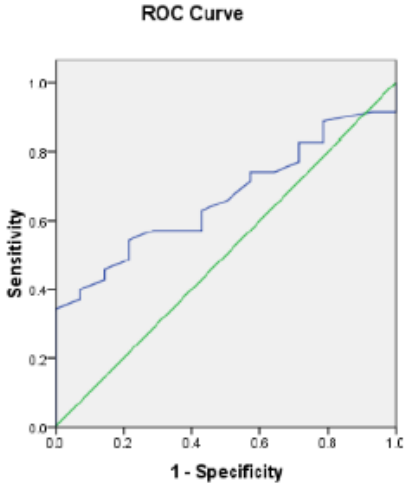

FIGURE 1. ROC curve of NLR value as a marker of UTI in children caused by bacteria (p = 0.073; AUC = 0.665)

DISCUSSION

The neutrophil- lymphocyte ratio is a simple marker of inflammation. The inflammatory response will then activate the apoptotic pathway. Under normal condition, circulating neutrophils have a short life (7-12 h in vivo) and are generally functionally quiescent. Neutrophil life-span is dynamically influenced during inflammation to enhance the anti-microbial action of the neutrophil. This is typified by the increased half-life of neutrophils stimulated with inflammatory agents such as tumor necrosis factor. Once their physiological function has been fulfilled in the tissues, they undergo spontaneous apoptosis, a programmed cell death that occurs to preserve neutrophil membrane integrity and prevent the uncontrolled release of toxic cell contents.[6,7]

A study in Turkey in 2015 showed the value of NLR in critically ill patients is very important and accurate NLR values can be used as a guideline in the selection of appropriate antibiotics.[7]

Studies on the value of NLR had been conducted in several countries, NLR originally studied in patients with lung cancer[8], community acquired pneumonia[9], appendicitis[8], critically ill children[10]. This study is the first study which discuss NLR as a marker of UTI in children caused by bacteria.

Treatment should be given early to eradicate infection, prevent bacteremia, improve clinical outcomes, reduce the probability of renal involvement during the acute phase of infection and reduce the risk of renal scarring.[11] Initial antibiotic therapy in UTI is empirical therapy while waiting for urine culture results.[12] Results of urine culture takes longer, in this study the results of culture were obtained within 3 to 5 days. The value of NLR ratio can be obtained easily and quickly from complete blood tests and is expected to be a guide in providing further therapy in children with UTI.

Study in Korea in 2010 to 2014 found that the cut off value of NLR (2.5 ± 2.3) was a good diagnostic marker for acute pyelonephritis incidence and a good predictor of the incidence of vesicoureteral reflux (VUR) in children.[5]

In this study, the optimal cut-off value of NLR ≥ 4.55 was obtained, this value was not significant when used as a marker of UTI in children caused by bacteria. Previous studies on NLR in children with UTI have never been done so researchers do not have a reference to the NLR cut-off value as a comparison.

Study in Turkey in 2015 got the NLR cut-off value ≥ 5 has a good value for detecting bacterial infections.[7] Studies in the UK from 2009 to 2010 got a cut-off value of NLR> 10 as a predictor of bacteremia in the emergency unit.[4] The weaknesses in this study were the researchers did not differentiate between upper and lower UTI and did not perform any imaging to see anatomical or functional abnormalities of the kidneys and urinary tract.

Further studies are needed to differentiate between upper and lower UTI with more specific age group. Detection of anatomical or functional abnormalities of the kidney and urinary tract with imaging studies is very important to look for predisposing factors for UTI.

Conclusion

The neutrophil-lymphocyte ratio cannot be used as a marker of UTI in children caused by bacteria.

REFERENCES

[1] National collaborating centre for women's and children's health. Urinary tract infection in children: diagnosis, treatment and long-term management. NICE clinical guideline. London: RCOG press; 2007. H. 1-137
[2] Koufadaki AM, Karavanaki KA, Soldatou A, Tsentidis Ch, Sourani MP, Sdogu T, et al. Clinical and laboratory indices of severe renal lesions in children with febrile urinary tract infection. Acta Paediatr. 2004;103:404-9.
[3] Sampurna M, Nilawati GAP, Adi-Tarini M. Clinical profile and bacterial pattern of urinary tract infection in children at Sanglah General Hospital Bali Indonesia. JCMID. 2014;1:1-5
[4] Lowsby R, Gomes C, Jarman I, Lisboa P, Nee PA, Vardhan M, et al. Neutrophil to lymphocyte count ratio as an early indicator of blood stream infections in the emergency department. Emerg Med J. 2015;32:531-4.
[5] Han SY, Lee I, Park SJ, Kim JH, Shin J. Usefullness of neutrophil-lymphocyte ratio in young children with febrile urinary tract infection. Korean J Pediatr. 2016;59(3):139-44.
[6] Fox S, Leitch A, Haslett C, Rossi A. Neutrophil apoptosis: relevance to the innate immune response and inflammatory disease. J Innate Immun. 2010;2:216-27.
[7] Gurol G, Citci IH, Terzi HA, Atasoy AR, Ozbek A, Koroglu M. Are there standardized cutoff values for neutrophil-lymphocyte ratios in bacterimia or sepsis?. J Microbiol biotechnol. 2015;25(4):521-525.
[8] Faraj FH, Karim SA, Fattah FH. Role of neutrophil/lymphocyte ratio in diagnosis of acute appendicitis. JSMC. 2015;5(2):85-93.
[9] Jager CP, Wever P, Gemen E, Kusters R, Lafeber A, Poll T, et al. The neutrophil-lymphocyte count ratio in patients with community-acquired pneumonia. Plos One. 2012;7:1-8.
[10] Zahorec R. Ratio of neutrophil to lymphocyte counts--rapid and simple parameter of systemic inflammation and stress in critically ill. Bratisl Lek Listy. 2001;102:5-14
[11] Silva AC, Oliveira EA. Update on the approach of urinary tract infection in childhood. J Pediatr. 2015;91:S2-S10.
[12] Jantausch B, Kher K. Urinary tract infection. In: Kher KK, Schnaper HW, Makker SP, editor. Clinical Pediatric Nephrology 2nd Edition. United States: Mc.Graw Hill; 2007.p. 553-70.