IMMATURE TO TOTAL NEUTROPHIL RATIO (I/T RATIO) ON NORMAL AND SEPSIS RISK NEONATUS FACTOR AT ULIN GENERAL HOSPITAL BANJARMASIN

Muhammad Rifky Ersadian Noor[1], F.X. Hendriyono[2], Ari Yunanto[3]

[1] Medical Study Program of Medical faculty, Lambung Mangkurat University Banjarmasin
[2] Clinical Pathology Department of Medical faculty, Lambung Mangkurat University Banjarmasin / Ulin General Hospital Banjarmasin
[3] Pediatrics Department of Medical faculty, Lambung Mangkurat University Banjarmasin / Ulin General Hospital Banjarmasin

Corresponding Email: rifkyersadian@gmail.com

Abstract: ***Neonatal sepsis is the main cause of morbidity and mortality in neonates.*** *Early diagnostic and appropriate treatment can reduce the mortality and morbidity rate. Immature neutrophil ratio tand total neutrophil (I/T ratio) can be used as one of early diagnostic tool of neonatal sepsis. The purpose of this research was to find difference of I/T ratio between normal neonates and neonates with sepsis risk factor at Ulin General Hospital Banjarmasin on April – June 2016. It was an analytic observational study and collected by accidental sampling. From 39 neonates, there was 23 normal neonates and 16 neonates with sepsis risk factor who diagnosed by competence pediatrics based on mayor and minor risk factor. Mean I/T ratio from normal neonates is 0,06 and neonates with sepsis risk factor is 0,16. From statistical test with independent T-test, there is significant difference p=0,000 (p<0,05). In conclusion, there is a difference of I/T Ratio between normal neonates and neonates with sepsis risk factor.*

Keywords: *neonatal sepsis, I/T ratio, risk factor, neonates.*

INTRODUCTION

Neonatal sepsis is defined as the clinical syndrome of systemic disease and the acquisition of pathogenic bacteria in the bloodstream that occurs in neonates. Globally, sepsis remains one of the major causes of neonatal morbidity and mortality in neonates. More than 40% death of toddler in the world occurs in the neonatal period or 3.1 million newborn deaths each year.[1,2]

Most of these deaths usually occur in low-income countries and nearly 1 million of these deaths are associated with infectious causes including neonatal sepsis, meningitis, and pneumonia. Meanwhile, survivors of neonatal sepsis are susceptible to long-term neurodevelopmental morbidity.[1]

The incidence of neonatal sepsis in the world ranges from 1 to 8 per 1000 live births. In developed countries like America, the incidence of sepsis since 1980 varies between 2-4 per 1000 live births while in developing countries like India, the incidence rate is 34-37 per 1000 live births.[2] The incidence of neonatal sepsis in some referral hospitals in Indonesia ranged from 1.5% -3.72% and the death rate ranged from 37.09% -80%.[3] Based on previous research, the incidence of neonatal sepsis at Ulin General Hospital Banjarmasin reached 17.3%.[4,5]

The diagnosis and management of sepsis is a major challenge facing neonatologists. If the diagnosis of sepsis only based on clinical signs, it will be difficult to enforce and not specific. Besides, the laboratory examination will take a long time.[1] Blood cultures are a gold standard for diagnosis of neonatal sepsis, but complete blood cultures take a long time, thus, the management of neonatal sepsis will also be delayed. Assisting the allegation of neonatal sepsis can be done with several examinations including Immature to Total Neutrophil Ratio (I/T Ratio), C-Reactive Protein (CRP), and ESR microstructure. I/T Ratio has higher level of effectiveness and sensitivity. The cost of using I/T Ratio is also more economical compared to other examinations in early diagnosis of neonatal sepsis.[3,5]

RESEARCH METHODS

Population is the whole subject who will be studied. The population in this research was all neonates recorded in the medical record and have been treated in the lotus room of Ulin General Hospital Banjarmasin period 1 April - 30 June 2016.

Subjects in this research were determined by the following inclusion criteria:

1. All normal neonates (neonates with no sepsis risk) are born at Ulin General Hospital Banjarmasin.
2. All neonates who have risk factors with major and minor criteria of neonatal sepsis at Ulin General Hospital Banjarmasin.
3. Parents of neonates who are willing to be subject of this research by signing *informed consent*.

Exclusion criteria in this research are as follows:

1. Newborns with severe congenital abnormalities.
2. The placenta is damaged, such as in placental abruption, placental abruption, placental retention, and placental insufficiency.
3. The placenta is deformed, such as the placenta succenyata, placenta spuria, bilobus placenta, and trilobus placenta.
4. Blood samples are not sufficient.
5. Blood samples are freezing.
6. Parents of neonates are not willing to be subject of research.

Sampling was done by using *non probability sampling* technique, as known as *accidental sampling*. This research was conducted on April 1 - June 30, 2016 at Ulin General Hospital Banjarmasin.

RESULTS AND DISCUSSION

The calculation result of I/T Ratio in Clinical Pathology laboratory in this research is as fig.1.

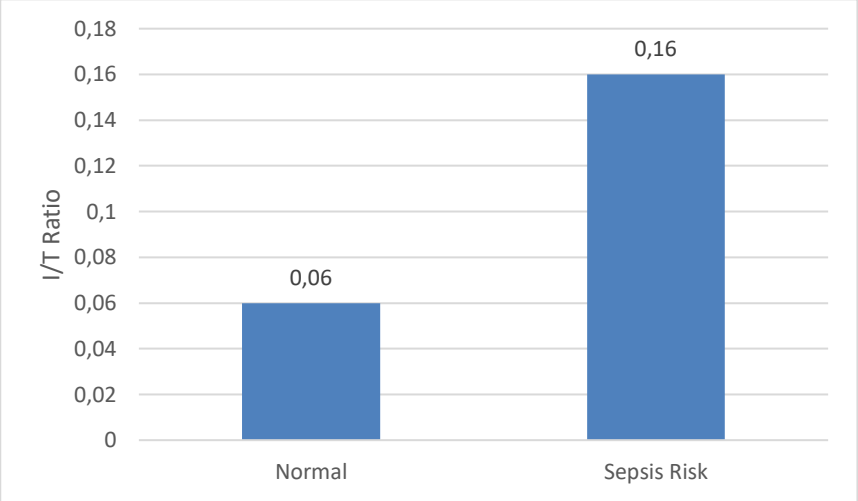

Figure 1 Data I/T Ratio at Ulin General Hospital Banjarmasin Period April-June 2016.

The data from research result was analyzed by using Saphiro-Wilk test to know the distribution of data because the number of research subjects is <50. From Saphiro-Wilk test, it was obtained that p = 0.221 in normal neonates and p = 0.901 in neonates with sepsis risk factor showed that the data distribution is normal because p> 0,05, as shown in table 2:

Table 2 Data of Normality Test Results Using *Shapiro -Wilk* Test.

	Amount (n)	Mean	p value
Normal Neonates	23	0,06	0,221
Neonates with Sepsis Risk	16	0,16	0,901

After performing normality test by using Saphiro-Wilk test, then the data was analyzed by using unpaired T test to know the difference of I/T ratio in normal neonate and neonate with neonatal sepsis risk factor because of normal data distribution. From the unpaired T test, it was obtained that p=0,000 which indicated that there was significant difference of I/T ratio in normal neonate and neonate with noenatus sepsis risk factor because p <0,05, as shown in table 3. Therefore, the hypothesis in this research was accepted.

Table 3 Data Analysis Using Unpaired T Test with I/T Ratio in Normal Neonates and Neonate with Sepsis Risk.

	Amount (n)	*p value*
Normal Neunates	23	
Neunates with Sepsis Risk	16	0,000

From Immature to Total Neutrophil Ratio (I/T Ratio) of 16 subjects with risk factor of neonatal sepsis, there were 7 (43,75%) neonatus having I/T ratio ≥ 0,2 with mean value of I/T ratio 0,217. According to Desai' study on 2014, it was reported in India that 70% of 100 neonates suspected sepsis neonatorum which has an I/T ratio ≥ 0.2 while research results of Ade on 2015, it was reported that at Arifin Achmad General Hospital Riau that there were 50.5% neonates have I/T ratio ≥ 0.2 from 97 neonates with sepsis neonatorum risk factors.[6,7] The increase of I/T ratio is because of the microorganisms that cause neonatal sepsis enter into the blood circulation which resulting the release of immature neutrophils from the bone marrow. The release of neutrophils is due to stimulants from IL-3 and GM-CSF. The number of neutrophils in sepsis is removed from the bone marrow to tens of thousands which resulting the release of all neutrophils including immature neutrophils which should also be excluded even though neutrophil cell differentiation from G-CSF is underway.[8,9] Neonates with I/T ratio <0.2 were found in 12 (56.25%) neonates with a mean value of 0.108. It is suspected that there is still no release of immature neutrophils, but if there is an increase, the immediate action is needed although the risk factor of neonatal sepsis and I/T ratio is still within the normal range <0.2.

The difference of this research results is because of blood collection through the umbilical cord basically should be fast and precise but when this research was conducting, it was still difficult to distinguish between the artery and vein on the umbilical cord. Therefor, the accuracy in taking blood samples is still lack. The appropriate blood sampling is the arterial vein on the umbilical cord to represent the neonatal blood sample.[10] In addition, the number of samples and neonate characteristics observed from each hospital is also different, as well as the varying interpretation of peripheral blood readings at the microscope by health personnel in the laboratory of Clinical Pathology. Less peripheral of blood smear results also affect the results of the I/T ratio.

From 19 subjects with risk factors of neonatal sepsis, there were the most common risk factors found at Ulin General Hospital Banjarmasin, it is premature rupture of membranes (KPD)> 24 hours as shown in Table 1.4. Utomo's research also reported that at the Soetomo Hospital, there were 97 neonates suspected sepsis neonatorum, it was obtained that the risk factors that are closely related to the incidence of neonatal sepsis is premature rupture of membranes (KPD).[11]

Table 4 Criteria for Risk Factors of Neonatal Sepsis Occurring in Neonates with Neonatal Sepsis Risk at Ulin General Hospital Banjarmasin Period 1 April - 30 June 2016

Risk Factor	Suspect of neonatal sepsis	
	n	%
Major criteria		
Premature rupture of membranes (KPD)> 24 hours	8	50
Intrapartum fever> 38 ° C	6	37,50
Amniotic smelling	5	31,25
Minor Criteria		
Whitish is itchy and smelly	4	25
Gestational age <37 weeks	3	18,75
BBLSR (< 1500 gram)	2	12,50
Intrapartum fever> 37.5 ° C	2	12,50

Early rupture of membranes is the highest cause of neonatal sepsis because when rupture of the membranes, microorganisms in the vagina or other pathogenic bacteria may reach the amniotic fluid and fetus. This allows the occurance of chorioamnionitis and aspiration by the fetus.[12] Mothers with intrapartum fever of> 38ºC are biased because it depends on antibiotics given to fevery mothers, thus, it reduces the risk of neonatal sepsis. Fetal heart rate (DJJ)> 160x / min is a sign of stress on the fetus. A persistent FHR may also be biased because beside neonatal sepsis such as placenta previa and old partus, there may also be an increase in FHR. Therefore, this criterion is not sufficient as a sign of neonatal sepsis and should be reinforced by other risk factors.[13]

Premature neonates or gestational age <37 weeks usually coincide with the case of BBLSR (<1500 grams) and at risk for neonatal sepsis events because immune system formation is still imperfect, therefore, the release of immature neutrophils from the bone marrow becomes more increased for the phagocytic process of microorganisms that enter the bloodstream. Similarly, in BBLSR infants have a risk of neonatal sepsis due to maturation of organs such as the imperfect liver.[14] A low APGAR score does not yet have a major role in the risk of neonatal sepsis. According to Winny's research on 2013 at RSUP Prof. Dr. R. D. Kandou Manado also stated that APGAR score <7 risk of neonatal sepsis was statistically inadequate.[15]

CONCLUSIONS

Based on the research results of Immature to Total Neutrophil Ratio (I/T Ratio) in normal neonates and neonates wuth neonatal sepsis risk at Ulin General Hospital Banjarmasin period April-June 2016, *I/T Ratio* in normal neonates has a mean of 0.06, neonates with neonalal sepsis risk has a mean of 0,15 and there was a significant difference between normal neonate and neonate with neonatal sepsis risk factor at Ulin General Hospital Banjarmasin period April - June 2016.

Suggestions for this research are there should be a longer research to have more varied data, the precision of blood sampling in arteries on the umbilical cord should be considered to represent neonatal blood, a correlation between I/T ratio with blood culture as the gold standard in the diagnosis of neonatorum sepsis is required.

REFERENCES

1. Eman RSE, El-Sokkary MMA, Bassiouny MR, et al. Epidemiology of neonatal sepsis and implicated pathogens: a study from Egypt.

BioMed Research International. 2015; 10(1): 1-11.
2. Pusponegoro TS. Sepsis pada neonatus. Jakarta: Sari Pediatri, 2000.
3. Setyawati, Ariningrum D, Sari IUS, et al. Penampilan diagnostik parameter-parameter hematologis untuk diagnosis sepsis neonatal. Berkala Ilmu Kedokteran. 2006; 38(1): 30-40.
4. Yunanto A. Kualitas pelayanan bayi baru lahir di RSUD Ulin Banjarmasin. Simposium Pencegahan Preeklampsi dan Penatalaksanaan Kegawatan Bayi Baru Lahir Menuju Keamanan Persalinan dan Kesehatan Bayu Baru Lahir. Perinasia Kalimantan Selatan, 2010.
5. Rosalina DR, Idham A, Nasrulloh MH. Penelitian awal : faktor risiko pada sepsis neonatorum awitan dini. Jakarta: Departemen Ilmu Kesehatan RS Cipto Mangunkusumo, 2013.
6. Reslina AN, Fatmawati, Wisnumurti DA. Gambaran rasio neutrofil imatur/ neutrofil total (Rasio I/T) pada tersangka sepsis neonatorum yang dirawat di instalasi perawatan neonatus RSUD Arifin Achmad Provinsi Riau. JOM FK. 2015; 2(2): 1-10.
7. Desai P, Shah AN, Pandya T. C-reactive protein immature to total neutrophil ratio and micro ESR in early diagnosis of neonatal sepsis. IJBAR. 2014; 5(8): 364-6.
8. Glogauer M, Hartwig J, Stossel T. Two pathways through CDC 42 couple the N-formyl receptor to actin nucleation in permeabilized human neutrophils. J Cell Bio. 2007; 150(1): 785-9.
9. Jackson GL, Engle WD, Sendelbach DM. Are complete blood cell counts useful in the evaluation of asymptomatic neonates exposed to suspected chorioamnitis?. J of Pediatrics. 2004; 113(5): 1173-80.
10. Richard A. Management of neonates with suspected of proven early-onset bacterial sepsis. The American Academy of Pediatrics. 2012; 129(1): 1006-15.
11. Utomo MT. Risk factor of neonatal sepsis : a preliminary study in Dr. Soetomo Hospital. Indonesian Journal of Tropical and Infectious Disease. 2010; 1(1): 23-6.
12. Chiesa C. Panero A, Osborn JF. Diagnostic of neonatal sepsis: a clinical and laboratoty challenge. Clin Chem. 2004; 50(1): 297-87.
13. Wilar R, Kumalasari E, Suryanto DY. Faktor risiko sepsis awitan dini. Fakultas Kedokteran Universitas Sam Ratulangi. 2010; 12(4): 265-9.
14. Raden NS. Pengaruh antara bayi berat badan lahir rendah dengan terjadinya sepsis neonatorum di RSUD dr. Moewardi [skripsi]. Surakarta: Program Pendidikan Dokter, 2008.
15. Carsolus W, Rompis J, Willar R. Hubungan APGAR skor dan berat badan lahir dengan sepsis neonatorum. Manado: Fakultas Kedokteran Universitas Ram Ratulangi, 2013.