**Neutrophil-Lymphosit Rasio as a Pedictor Outcome of Elective Pediatric Surgery for Clean and Clean Contaminated Operation: Single Centre Study**

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**Abstract:**
**Background:** Neutrophil-Limfosit Ratio (NLR) is a simple indicator for study inflammatory status easily in patient. An increasing value of neutrophils and decreasing value of lymphocytes is a physiological response in the immune system to systemic inflammation. **Methods:** This study was an analytical observational quantitative study using a prospective cohort approach, involving 51 patients pediatric surgery from age ≥1 months until ≤18 years who had done elective operation clean and clean contaminated criteria and after 6 hours operation, the subject had differential counted blood examination. Then we checked the outcome after first, third and seventh day after surgery, whether the condition improved (without complication) or worsen conditions (with complication). **Results:** From the total 51 patients, there was a significant result for gender in variable post operation in this research (OR=3.968; 95%CI=1.160-13.579; p=0,028), whether female patient were more risky 3.968 times to become worsen condition (with complication) than male patient. 34 patients with RNL ≤5 consists of 25 patients (73.5%) got improved condition (without complication), whether 17 patients who got worsen condition (with complication) with RNL >5 consist of 12 patients (70,6%). Sensitivity rate was 0,735, and specificity rate was 0,706 and prevalence ratio was 1,716. From this research we got RNL>5 (OR=6,667; 95%CI=1,832-24,264; p=0,004) were more risky 6.667 times to become worsen (with complication) than RNL≤5. From chi square result we got p value=0,003 (p<0,05) that’s mean there was a significant relationship between RNL and outcome of pediatric surgery patients age ≥1 months until ≤18 years who had done elective operation. Normal value of NLR would give better outcome. **Conclusions:** There was a significant relationship between RNL and outcome in pediatric surgery patients age ≥1 month- ≤18 years that was done elective operation with clean and clean contaminated surgery criteria, whether normal value of NLR would give improved outcome (without complication).

**Keywords:** Neutrophil-Lymphosit Rasio, Prediector Operation Outcome

**INTRODUCTION**
Neutrophil-Lymphocyte Ratio (NLR) is a simple parameter to easily assess the inflammatory status of a patient, by dividing the absolute value of neutrophils by the absolute value of lymphocytes. An increase in the value of neutrophils and a decrease in the value of lymphocytes is a physiological response in the immune system to systemic inflammation. In endotoxemic patients after 4-6 hours there would be a decrease in the number of lymphocytes by about 85% and neutrophils would increase by about 300%.\(^1\) As a result of increasing the number of neutrophils and decreasing the number of lymphocytes, there would be an increase in the absolute ratio of neutrophils and lymphocytes when compared to patients who do not experience a systemic inflammatory reaction.

NLR = Absolute value of Neutrophyl
Absolute value of Lymphocyte

Interpretation of NLR :\(^2\)
- 1-3 = Normal
- 4-5 = Borderline
- 6-9 = Mild Stres (example: patient with acute appendicitis/ without complication)
- ≥ 9 = Seriously ill

Based on National Academy of Sciences/ National Research Council Wound Classification\(^3\), the degree of contamination at operation wound consist of:

<table>
<thead>
<tr>
<th>Degree of Contamination</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

\(^1\) Based on National Academy of Sciences/ National Research Council Wound Classification; \(^2\) Interpretation of NLR; \(^3\) Degree of Contamination.
Clean Wounds  
Uninfected operative wounds in which no inflammation is encountered and the respiratory, alimentary, genital or uninfected urinary tracts are not entered. In addition, clean wounds are primarily closed and, if necessary, drained with closed drainage. Operative incisional wounds that follow nonpenetrating (blunt) trauma should be included in this category if they meet the criteria.

Clean–Contaminated Wounds  
Operative wounds in which the respiratory, alimentary, genital or urinary tract is entered under controlled conditions and without unusual contamination. Specifically, operations involving the biliary tract, appendix, vagina and oropharynx are included in this category, provided no evidence of infection or major break in technique is encountered.

Contaminated Wounds  
Include open, fresh, accidental wounds, operations with major breaks in sterile technique or gross spillage from the gastrointestinal tract, and incisions in which acute, non-purulent inflammation is encountered.

Dirty or Infected Wounds  
Include old traumatic wounds with retained devitalized tissue and those that involve existing clinical infection or perforated viscera. This definition suggests that the organisms causing post operative infection were present in the operative field before the operation.

Estimated Risk of Infection
- Clean wounds 1–5%
- Clean–contaminated wounds 3–11%
- Contaminated wounds 10–17%
- Dirty or infected wounds > 27%

**OBJECTIVE OF THE STUDY**
This study was conducted to determine whether the post operative Neutrophil-Lymphocyte Ratio can be a predictor of the outcome of elective surgery in clean and clean contaminated categories operation in Pediatric Surgery patients at Moewardi Hospital Surakarta.

**RESEARCH METHODOLOGY**
This was an analytical observational quantitative study using a prospective cohort study approach. The subjects in this study were Pediatric Surgery patients aged 1 month to 18 years who had elective surgery in clean and clean contaminated operation categories. 6 hours after surgery, differential counting was performed on their blood examination, then we followed up the outcome of elective post operative treatment, whether improvement or deterioration of the condition, seen from the patient's medical record data. Samples were separated into 2 groups, namely NLR ≤ 5 and NLR ≥ 5. Then we proceed with making a 2x2 cross tabulation to get the value of sensitivity and specificity, it considered good if the value was >80%. The p value < 0.05 was considered significant.

**RESULT**
1. Univariate Analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Outcome Improvement Condition (without complication)</th>
<th>Deterioration Condition (with complication)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Improvement</td>
<td>Deterioration</td>
<td></td>
</tr>
<tr>
<td>&lt;1 y.o</td>
<td>15 (44.1%)</td>
<td>8 (47.1%)</td>
<td>23 (45.1%)</td>
</tr>
<tr>
<td>1 y.o - &lt;5 y.o</td>
<td>16 (47.1%)</td>
<td>5 (29.4%)</td>
<td>21 (41.2%)</td>
</tr>
<tr>
<td>≥5 y.o</td>
<td>3 (8.8%)</td>
<td>4 (23.5%)</td>
<td>7 (13.7%)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boy</td>
<td>25 (73.5%)</td>
<td>7 (41.2%)</td>
<td>32 (62.7%)</td>
</tr>
<tr>
<td>Girl</td>
<td>9 (26.5%)</td>
<td>10 (58.8%)</td>
<td>19 (37.3%)</td>
</tr>
<tr>
<td>RNL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤5</td>
<td>25 (73.5%)</td>
<td>5 (29.4%)</td>
<td>30 (58.8%)</td>
</tr>
<tr>
<td>&gt;5</td>
<td>9 (26.5%)</td>
<td>12 (70.6%)</td>
<td>21 (41.2%)</td>
</tr>
</tbody>
</table>

The table above explained that the age of the 34 patients who experienced improvement were mostly aged 1 year to <5 years, i.e. there were 16 patients (47.1%), while the age of the 17 patients who did not experience improvement/ worsen condition occurred mostly with age ≤1 years there were 8 patients (47.1%).
The gender of the 34 patients who experienced improvement were mostly male, namely 25 patients (73.5%), while of the 17 patients who experienced worsening, most of them were female, namely there were 10 patients (58.8%).

The RNL (Neutrophil Lymphocyte Ratio) of 34 patients who experienced improvement condition (without complication) were mostly with RNL <5, namely 25 patients (73.5%), while of the 17 patients who had worsened condition (with complication) most with RNL>5, there were 12 patients (70.6%).

### 2. Bivariate and Multivariate Analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Bivariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1 y.o</td>
<td>Ref.</td>
<td>0.586 (0.156-2.195)</td>
</tr>
<tr>
<td>1 y.o sd</td>
<td></td>
<td>2.500 (0.445-14.037)</td>
</tr>
<tr>
<td>≥5 y.o</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boy</td>
<td>Ref.</td>
<td>3.968 (1.160-13.579)</td>
</tr>
<tr>
<td>Girl</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RNL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤5</td>
<td>Ref.</td>
<td>6.667 (1.832-24.264)</td>
</tr>
<tr>
<td>&gt;5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

In the bivariate analysis the variables that were not significantly related to the outcome of pediatric surgery patients who had elective surgery were clean and clean contaminated categories (clean and clean contaminated), namely the age variable from 1 year to <5 years (OR=0.586; 95%CI=0.156-2.195; p=0.428 and age ≥5 years (OR=2500; 95%CI=0.445-14.037;p=0.298). The variable that was significantly associated with postoperative outcome was gender (OR=3.966; 95%CI=1.160-13.579; p=0.028), where female patients were 3.966 times more likely to have an outcome without improvement compared to male patients. and RNL (OR=6.666; 95%CI=1.832-24.264; p=0.004) where patients with RNL>5 were 6,666 times more at risk of no improvement in outcome compared to RNL<5.

Based on the description above, it can be seen that RNL can be used as a predictor of outcome for pediatric surgical patients who have undergone elective surgery in clean and clean contaminated categories, because both bivariate and multivariate analysis, RNL remains a variable related to outcome and is not affected by confounding variables of age and gender.

### 3. Sensitivity & Specificity RNL

Results of Cross Tabulation between NLR and Outcome of Surgical Patients Children aged 1 month-18 years who had elective surgery performed clean and clean contaminated categories

<table>
<thead>
<tr>
<th>RNL</th>
<th>Improvement (complication)</th>
<th>Condition</th>
<th>Outcome (without Deterioration complication)</th>
<th>Condition</th>
<th>Total</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤5</td>
<td>25</td>
<td>5</td>
<td>30</td>
<td>0.00</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>&gt;5</td>
<td>9</td>
<td>12</td>
<td>21</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>34</td>
<td>17</td>
<td>51</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Sensitivity = \( \frac{a}{a+c} \)

Specificity = \( \frac{d}{b+d} \)

Prevalence Ratio = \( \frac{a}{a+b} : \frac{c}{c+d} \)

The RNL of 34 patients who experienced improvement were mostly with RNL <5, namely 25 patients (73.5%), while of the 17 patients who had worsened most of them with RNL >5, there were 12 patients (70.6%). The result of sensitivity is 0.735, and specificity is 0.706 and prevalence ratio is 1.716. The results of the chi square test obtained a value of p = 0.003 (p <0.05) which means that there is a significant...
relationship between RNL and outcome of pediatric surgical patients aged 1 month-≤18 years who have had elective surgery, where normal NLR tends to give positive results without complication (improvement outcomes).

DISCUSSION

The neutrophil-lymphocyte ratio is the ratio of different and complementary pathways of the immunological system, which integrates the role of neutrophils responsible for non-specific inflammatory reactions and lymphopenia, which are markers of severe physiological stress and poor body condition. This neutrophil-lymphocyte ratio represents two important and predictive pathways of the immunological system compared to only one parameter.5

In this study, blood tests were taken 6 hours postoperatively to obtain laboratory values for neutrophils and lymphocytes. In inflammatory conditions, there is an increase in the number of neutrophils (neutrophilia), accompanied by a decrease in the number of lymphocytes (lymphocytopenia). The state of neutrophilia occurs due to demargination, delayed apoptosis, and increased stimulation of G-CSF stem cells, causing an increase in the number of neutrophils. On the other hand, lymphocytopenia occurs when there is a marginalization and redistribution of lymphocytes to the lymphatic system and accelerates apoptosis.6

Systemic inflammation in critically ill patients is part of the disease process. This inflammatory process affects the total number of leukocytes, especially the number of neutrophils, lymphocytes, and monocytes. These leukocytes have an important role in the systemic inflammatory response, for example in severe infection, trauma, or shock. The immune response to endotoxin was found by increasing the number of neutrophils and decreasing the number of lymphocytes.1 Saliciccioli et al (2015)7 used the neutrophil-lymphocyte ratio as a physiological marker of mortality. An increase in the neutrophil lymphocyte ratio can also identify patients with a low physiological response to survival from inflammatory disorders and concomitantly reduce survival rates.

The value of the neutrophil to lymphocyte ratio differs between sexes at the same age. The ratio of neutrophil to lymphocyte in women was higher in the age group <50 years compared to the male sex. This is related to the cortisol response to physical stress in women which is higher than in men. However, in the age group > 50 years, the neutrophil to lymphocyte ratio in males is higher than in females. This occurs because of changes in hematopoiesis at different levels of estrogen during menopause. Sex hormones represented by estrogen and progesterone can increase the recruitment of neutrophils from the bone marrow significantly in women aged >40 years. A decrease in the number of neutrophils in postmenopausal women with a relatively unchanged lymphocyte count results in a decrease in the value of the neutrophil to lymphocyte ratio (Gwak, M. S. et al., 2007).

This is consistent with the results in this study where the variables that were significantly related to postoperative outcomes were gender, where patients with female sex were 3,968 times more at risk of worsening outcomes compared to men, and RNL where patients with RNL>5 were more at risk. 6,667 times worsened outcome compared with RNL < 5.

The multivariate analysis that followed in this study analyzed that gender was significantly related to outcome, where female patients were 4,755 times more at risk of worsening outcomes compared to men. RNL of patients in which RNL >5 had a 7,165 times greater risk of adverse outcome compared with RNL<5.

Based on the explanation above, it can be concluded that the Neutrophil Lymphocyte Ratio can be one of the predictors of elective postoperative conditions in the clean and clean contaminated category in Pediatric Surgery patients at dr Moewardi hospital.

CONCLUSION

There is a significant relationship between RNL and outcome of pediatric surgery patients aged 1 month-≤18 years who have undergone elective surgery in clean and clean contaminated categories, where normal NLR tends to provide improved outcomes (without complications).

REFERENCES

the normal value of the neutrophil-to-lymphocyte ratio?.
