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Neutrophil Lymphocytes Ratio (NLR) of One-Step and Multi-Step Procedure for Hirschsprung Disease Patients At Arifin Achmad General Hospital

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ABSTRACT

Hirschsprung disease (HD) is a congenital anomaly due to intestinal aganglionosis starting from the internal anal sphincter and spreading to the proximal area with varies extension of the segment. Definitive treatment for this abnormality is to perform surgery to remove the aganglionic bowel and can be carried out in one-step and multi-step procedure. In the process of wound healing after surgery, it involves inflammatory mediators as a marker of whether there is a stress response from the endocrine system such as neutrophil-lymphocyte ratio (NLR). This study aims to compare NLR as an inflammatory biomarker in one-step and multi-step procedure of hirschsprung disease patients at Arifin Achmad Hospital. The design of this study was cross-sectional using medical records and using total sampling for number of samples. Age, gender, and method of surgery were evaluated by univariate and bivariate to determine whether there were statistical differences. Seven HD patient taken from Mei-October at Arifin Achmad Hospital taken for evaluated. The results showed that the most samples were in < 1-month-old (42.9%) and male (71,4%) for gender. The average number of NLR was in 7.33 after one-step procedure and 2.77 for multi-step procedure. This number of NLR both not statistically different neither for the post-operative examination nor the comparison between procedure.

Keywords: Hirschsprung, Multi-stage , NLR, One-stage

Congenital abnormalities are defined as a condition in which abnormalities in function or structure are found at birth.[1] Data found that as many as 8 million births worldwide have congenital abnormalities.[2] Indonesia has a quite high number of these abnormalities among Southeast Asian countries. Based on data of the Ministry of Health in Indonesia, the prevalence of infants with congenital abnormalities was 59.3 per 1000 births. This case give score 18.1% of cause of infant mortality in infant aged 7-28 days and 1.4% in infant aged 0-6 days.[3]

Hirschprung Disease (HD) is one of the congenital abnormalities that occurs due to the absence of neural ganglion cells in the myenteric Auerbach plexus and the submucosal Meissner plexus of some intestinal tracts. The aganglionic segment begins distal to the internal anal sphincter and extends proximally with varying lengths.[4] The prevalence of this birth defect in Indonesia is 1 in every 5000 births.[5] Manifestations of HD can be vary according to the extent of the aganglionic segment and age. In neonates, it is usually characterized by delayed passage of meconium > 48 hours, abdominal distension, and vomiting of bile.[4,6]

Surgical is the definitive therapy of this abnormalities. Reconstruct the intestinal tract and remove the aganglionic part then connected right to the top of anus, so that normal sphincter function can maintained.[7,8] There are two types of surgical method usually use in HD, which are one-step procedure (OS) and Multi-step procedure (MS). The OS procedure taken to HD patients under 6 months, who did not show symptoms of enterocolitis, performed with the pull through technique. While The MS procedure done by making a colostomy in the proximal of aganglionic bowel with laparotomy before the definitive one.[8,9]

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Both procedure mention before bear with postoperative wound healing process. The inflammatory mediators including lymphocytes are involved as a marker of stress response. Physiological stress due to certain disorders or disease can be described by neutrophil-lymphocyte ratio (NLR). [10] NLR is one of the markers of immune response that occurs, and can be seen from an increase in neutrophils and a simultaneous decrease in lymphocytes in circulation. NLR is a parameter that is simple, responsive, inexpensive and easy to abtain.[11,12] Therefore, the objective of this study was to evaluate the NLR value as an inflammatory parameter in the postoperative healing process.

METHODS

Research design

This research was an analytic observational design with cross-sectional study to know NLR in pre and post operative procedure in HD patient. This research took place from May to October 2022. The population of this study were patients with a diagnosis of Hirschsprung disease at the surgical department of Arifin Ahmad Hospital. The inclusion criteria in this study was hirschsprung disease patients who underwent surgical management, either one-step or multi-step surgery. While, the exclusion criteria were the presence of a focus of infection before surgery, and patients with additional congenital abnormalities. The study will take a total sampling of the entire population that meets the inclusion criteria. The research has been approved an ethical review by the Medical and Health Research Ethics Unit, Faculty of Medicine, University of Riau number B/155/UN19.5.1.1.8/UEPKK/2022

Data collection

Routine blood examination with diff count method from leukocytes test was used to determine the number of neutrophils, and lymphochytes, that use to get the value of NLR. Blood test. Blood sampling was done 24 hours before surgery and within the next 24 hours after surgery to describe the pre-op and post-op conditions. Data in the form of gender, age, and operative method were obtained from the patient's medical record.

Procedure

The data that has been obtained is then processed manually and presented descriptively in the form of frequency distribution tables to compare the NLR based on age, gender, and surgical technic.

Statistical analysis

Univariate analysis of categorical data is presented in the form of proportions and statistical analysis was carried out to see the comparison of NLR in the two operating methods using the Mann-Whitney test on SPSS 16.00.

RESULT

From May to October 2022, seven patients met the inclusion criteria. Four of them (57%) were operated on by the one-step method and three patients (43%) were operated on by the multi-step method. Based on age the operative procedure were done, the most number is in < 1.m.o (43%), and then 28% for age 1 m.o – 6 m.o and 29% in >12 m.o of age. While more than half sample were a male (71%). (figure 1 and table 1)

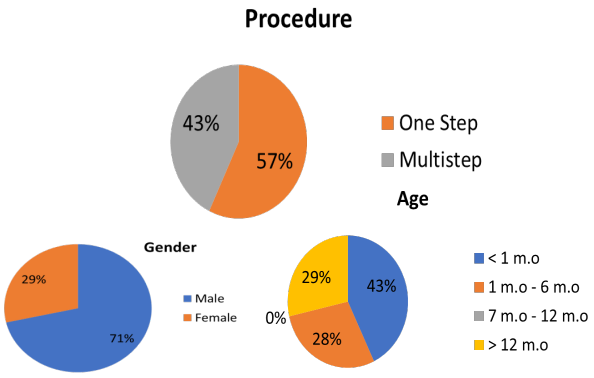

Figure 1. Demographic data of the sample

Table 1. Characterisrics patient HD in Arifin Ahmad General Hospital Mei-October 2022 (n=7)

Characteristics	n	Percentage (%)
Age		
< 1 Month Old	3	43
1-6 Month Old	2	28,5
7 Month Old – 1 Years Old	0	0
>1 Years Old	2	28,5
Gender		
Male	5	71
Female	2	29
Operative Procedure		
One step	4	57
Multi Step	3	43

The average number of NLR was in 7.33 after ones-tep procedure and 2.77 for multi-step procedure. This number of NLR both not statistically different neither for the post-operative examination nor the comparison between procedure. It can be the lack of sample and the possibility of not distributed data, so that is difficult to do a statistical assessment. (figure 2 and table 2)

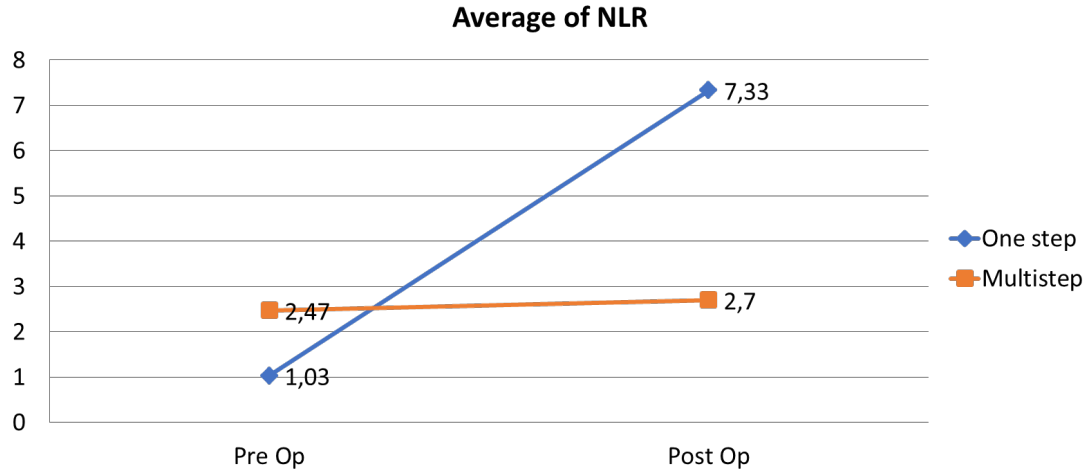

Figure 2. Average of NLR

Table 2. NLR of patient HD in Arifin Ahmad General Hospital Mei-October 2022 (n=7)

Operative Procedure	Average pre op NLR	Average post op NLR	p
One Step	1,03	2,7	0.439
Multi Step	2,47	7,33	0.221

DISCUSSION

Study has investigated that laparoscopic surgery, a less invasive procedure, caused minimal changes in the immune response (type-1/type-2 T-helper cell balance) compared to conventional approaches.[13,14] NLR which is a ratio that represents the best expression of the close functional relationship between the two basic immunocompetent leukocyte populations (neutrophils for innate and lymphocytes for adaptive) is one of the reliable parameters to see the state of immune response in the body.[15,16,17] In this study, we compare two procedure of surgery in HD patient with pull-through procedure as one step, which in this case is likened to a less

invasive surgical procedure, and pull-through plus colonostomy as multistep procedure as the conventional one. The value of NLR that we get, is not significant different statistically from the two procedures nor the postoperative increase of each procedure in this study, makes NLR can not be a parameter yet to predict the value of inflammatory state that occurs in this case.

Wasko *et al*. (2017) indicated that post-operative NLR showed faster changing kinetics than C-reactive protein in response to surgical trauma, This makes NLR a good candidate for being a marker value for whether there will be an excessive inflammatory state after a surgical procedure. However, our data did not illustrate a significant increase in NLR in either the one-step (p=0.439) or multi-step (p=0.221) operating procedures. Zahorec *et al* (2021 find the value of the elevation of neutrophils and decline in lymphocyte count or NLR, know as critical illnesses condition such as septic shock, hemorrhagic shock, multiple trauma, and acute pancreatitis. The NLR value in this case describes the systemic state rather than the inflammatory state of the site of injury at the time of post operation. A much larger series is required to determine the role of NLR as an independent predictor in this kind of study.

Of note, the present study has some limitations. First, this study was a retrospective and single-center study with limited sample. Second, there is a lack of standardized management of postoperative hematology examinations, only relying on routine blood tests within 24 hours postoperatively, there was no definite time which may affect the NLR value.

CONCLUSION

The number of NLR both not statistically different neither for the post-operative examination nor the comparison between procedure

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