Value of NLR in The Patient With Ovarian Tumor in H. Adam Malik General Hospital Medan 2017-2018

Darus MG, Edianto D, Tala MR, Tobing JL, Halim B, Yaznil MR

Department of Obstetrics and Gynecology
Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia.

Abstract : To know the value of NRL in patients with ovarian tumor in Adam Malik General Hospital year 2017- 2018. This study is a descriptive analytic research with cross sectional approach which assesses NLR ovarian tumor patients at H. Adam Malik General Hospital Medan in 2017-2018. Data taken from the medical records department of H. Adam Malik General Hospital used total sampling method. All supporting data such as antopometry, data on a complete blood count, patient age, and history of parity, stage, histopathology, CA-125 were collected and analyzed. Statistic Data were analyzed using independent t-test and One-Way Anova for multivariate analysis. A p value less than 0.05 is applied to each statistical test as significant. Of the study subjects, the majority of patients who come to the department of H Adam Malik with the diagnosis of ovarian cancer aged <50 years with a total sample of 146 people, with parity varying by group multipara found as a group the most, by 88 people and most of the cancer patients ovarim stage III with the number 67. In histopathological characteristics found patients who come to the department of H. Adam Malik General Hospital is a malignant ovarian tumors with adenocarcinoma. NLR value is based on the highest common life characteristics at age over 50 years of age ≥ 4.64, save raw 1.34, P 0001, the value of NLR parity highest encountered in secundipara with value 4.54, 1.19 standard deviations, P = 0188, in histopathology highest NLR value found in mucinous adenocarcinoma of 4.64, standard deviations. There is a relationship between the increase in the value of NLR on-stage ovarian cancer. The high-stage ovarian cancer will increasing value of NLR.

I. INTRODUCTION

Today many studies have shown that inflammation plays an important role in the various stages of the disease perkembagan especially malignancies, including initiation, promotion, malignant conversion, invasion, and metastasis. Systemic inflammation is associated with poor prognosis in most cancers. The prognostic value of markers of systemic inflammatory response has been a concern, and various blood-based parameters which reflect the status of systemic inflammation that has been extensively explored as a biomarker in various kanker.[1]

The ratio of neutrophil-to-lymphocyte (NLR) is a biomarker that is easily obtained and calculated based on the examination of routine hematological profile. NLR has previously been shown to predict treatment outcomes in oncology patients and has been tested in a number of malignancies, including lung, ovarian and breast. The preoperative NLR has proven to be a prognostic factor in patients undergoing colorectal cancer resection. The mechanisms underlying the relationship NLR ratio is high and adverse outcomes in cancer patients is still poorly understood. One potential mechanism underlying the prognostic impact of NLR is a close relationship with inflammation.

In recent studies, NLR was identified as an important prognostic biomarker in a variety of tumors. NLR easily obtained from routine blood tests at no extra cost. And NLR changes can be easily detected in ovarian cancer treatment process. Therefore, NLR is a promising predictor in individualized treatment and more attention is given to detect NLR role in the prognosis of ovarian cancer. Several retrospective studies conducted to determine the effect of NLR against ovarian cancer prognosis, but the results contradictive. 3,4

Of several other studies that have been done, there is some controversy over the value of NLR in patients Ca. Ovarian cysts and endometriosis correlated to the prognosis and course of the disease the patient. From this phenomenon, researchers interested in comparing the value of the cut-off neutrophil-lymphocyte ratio between patients Ca. Ovarian cysts and endometriosis. That way we will get a clearer picture of the disease so that the expected clinical Issuer will be able to predict the prognosis and course of the disease better.

II. MATERIALS AND METHOD

This research is descriptive analytic research with cross sectional approach which assesses NLR patients with ovarian tumors, Previous investigators will seek medical record women who develop ovarian tumors and then look for a complete blood lab results that have been done. This study was conducted using medical record of patients in the department. H. Adam Malik. The study population was patients with ovarian tumors Medical Record-gynecologic oncology clinic at Dr. H. Adam Malik during the period January 2017 - December 2018. Inclusion criteria were the medical records of patients with ovarian tumors who come to the clinic-gynecologic oncology in the department of human rights during the period January 2017 - December 2018 with the exclusion criteria Medical Record is not complete and patients with a history chronic illness diagnosed before or during ovarian tumors, the sample size in this study was calculated by total sampling. This research was conducted with the approval of the Ethics Committee of the Faculty of Medicine, University of North Sumatra. Do the recording of history, physical examination, and laboratory has been performed on a patient. is recording absolute value of the ratio of neutrophils, lymphocytes absolute, histopathology, Stadium, CA-125 from the woman who became the study sample, the data are collected and then analyzed statistically. The results of this study are presented in frequency distribution table. To assess the frequency distribution characteristics of the study sample based on age, parity and BMI, absolute neutrophil, lymphocyte absolute, Histopathology, Stadium, performed univariate and multivariate statistical analysis. To assess the normality of the data distribution is done

kolomogov-Smirnov test for normality, for the bivariate analysis used independent T test, whereas multivariate analysis used to test one way annove. This study uses a 95% confidence level.

III. Results and Discussion

The study found the distribution of samples of this study were the most by age was <50 years as many as 146 people, by the parity is multipara many as 88 people, based on the stage of the cancer is found most common with stage III by the number 67 followed by stage II as many as 57 people attended stage I as much as 54.

Table 1. Characteristics of Research Subjects

Variables	N	%
Age		
<50	146	53.9
≥ 50	125	46.1
Parity		
nulliparous	70	25.83
primiparas	43	15.87
Sekundipara	42	15:50
multiparas	88	32.47
Grandemultipara	28	10:33
Histopathology		
Mucinous adenocarcinoma Ovari	77	28.41
Adenocarcinoma serosum Ovari	94	34.69
dysgerminomas	7	2:58
Granulosa Cell Tumor	6	2:21
Giant Cell Tumor	1	0:37
Kistadenoma mucinous	32	11.81
Kistadenoma serosum	18	6.64
Dermoid cysts	10	3.69
endometriosis	26	9:59
Stadium		
I	54	29.19
II	57	30.81
III	67	36.22
IV	7	3.78

By histopathology, malignant tumors found serosum adenocarcinoma were 94 people while in the benign tumor was found as many as 32 people are cystadenomas mucinous. It was found that very high levels of NLR with a mean value of 5.66. whereas parity encountered highest NLR found in sekundipara 4.54.

On histopathological tissue examination NLR value successively obtained the highest value at 4.57 mucinous adenocarcinoma, and adenocarcinoma serosum 4.57.

Table 2. NLR distribution based on characteristics

	NLR		
Variables	mean	median	SD
Age			
<50	3:45	3.76	0.84
≥ 50	4.64	3.99	1:34
Parity			
nulliparous	4:16	3.69	1.60
primiparas	3.68	3:59	0:56
sekundipara	4:54	4:54	1:19
multiparas	4:27	4:21	1:25
grandemultipara	3.74	3.63	0.89

Histopathology			
mucinous adenocarcinoma	4.64	4:37	1:24
adenocarcinoma serosum	4:57	4:38	1:09
Granulosa cell tumors	3:46	3:43	0:32
Dysgerminoma	3.77	3.73	0.75
Giant cell tumor	3.63	3.63	0:00
Kistadenoma mucinous	2.73	2.62	0.61
Kistadenoma serosum	2.71	2:52	0.66
Dermoid cysts	2.67	2.61	0.63
cysts Endometriosis	3:50	3:18	0.86
Stadium			
I	3:47	3:49	0:43
II	4:02	4:01	0.5
III	4.84	4.64	0.81
IV	5.66	5.79	0.89

Table 3. Age distribution of the NLR

	NLR			P
Age	mean	median	SD	
<50	3:45	3.76	0.84	0001 *
≥ 50	4.64	3.99	1:34	

** T Test Independent*

Based on Table 3 NLR value found at the age of 50 years is 4.64 with standard deviations 1:34 and a median of 3.99. based on statistical tests to test T dindependent found value P 0001

Table 4. Distribution parity against NLR

	NLR			P
Parity	mean	median	SD	
nulliparous	4:16	3.69	1.60	
primiparas	3.68	3:59	0:56	
sekundipara	4:54	4:54	1:19	0188 *
multiparas	4:27	4:21	1:25	
Grandemultipara	3.74	3.63	0.89	

** One way ANOVA test*

In Table 4.4 is found on the highest value NLR NLR sekundipara with a value of 4:54, 1:19 and standard deviations with a P value of 0118 which showed no significant difference in the value of the parity patient NLR.

Table 5. Against Malignant Tumors distribution NLR

	NLR			P
variables	mean	median	SD	
Malignant tumor				
mucinous adenocarcinoma	4.64	4:37	1:24	
adenocarcinoma serosum	4:57	4:38	1:09	0043 *
Granulosa cell tumors	3:46	3:43	0:32	
Dysgerminoma	3.77	3.73	0.75	
Giant cell tumor	3.63	3.63	0:00	

** One Way Annova Test*

In Table 5 NLR highest values were found in mucinous adenocarcinoma of 4.64 with standard deviations 1:24 and a P value of 0.0043, this indicates the difference between the value of the NLR in malignant ovarian tumor histopathology.

Table 6. Distribution of benign tumors of the NLR

variables	NLR			P
	mean	median	SD	
Benign tumor				
Kistadenoma mucinous	2.73	2.62	0.61	
Kistadenoma serosum	2.71	2:52	0.66	0001 *
Dermoid cysts	2.67	2.61	0.63	
cysts Endometriosis	3:50	3:18	0.86	

** One Way Annova Test*

In Table 6 NLR highest value encountered in cysts endometriosis with 3:50 values and standard deviations 0.86 with a P value of 0.001, it mnunjukka presence of a significant difference between the value based on the value NLR NLR benign tumors

Table 7. Neutrophil-Lymphocyte Ratio Distribution Based Stadium

variables	NLR			P
	mean	median	SD	
Stadium				
I	3:47	3:49	0:43	
II	4:02	4:01	0.5	0001 *
III	4.84	4.64	0.81	
IV	5.66	5.79	0.89	

** One Way Annova Test*

Based on Table 7 shows that the value of the highest NLR stage IV malignant ovarian tumors with NLR values of 5.6, 0.89 standard deviations with a P value of 0.001, this indicates a significant difference between the value of the NLR in malignant ovarian tumors based on the stage..

Table 8. Comparison of NLR and Ca-125 in benign and malignant tumors

Parameter	Benign Ovarian Tumors			Malignant Ovarian Tumors			P
	mean	median	SD	mean	median	SD	
NLR	2,94	2.80	0.78	4.56	4.38	1.12	0001
Ca-125	87.91	96,00	40.73	254.28	261.00	64.09	0001

Based on Table 8 it can be seen that the NLR in benign tumors with mean 2.94, median 2.80, standard deviation of 0.78. In malignant tumors with a mean value of 4.56 and a median value of 4.38 standard deviation scores 1:12 with the results of the statistical test p = 0.001. In Ca-125 benign tumors are the mean value of 87.91, 96.00 and the median standard deviation 40.73. In malignant tumors with a mean value of 261.00 254.28 median value, standard deviation of 64.09 with the results of the statistical test P = 0.001

IV. Discussion

Ovarian cancer is often fatal because it is not found in its early stages. Therefore, the study of incentives for early detection sangatbanyak do. Microarrays are ideally positioned to provide data on a potential biomarker for early detection, and indeed, a number of such genes have been identified. Because the ultimate goal is a non-invasive test.

The relationship between inflammation and cancer development has attracted much attention of researchers for decades terakhir.5 been proven that hematologic markers of systemic inflammation (including C-reactive protein, albumin, neutrophils, and so on) may help predict clinical parameters in patients with various types of kanker.6 among these predictors, NLR is a hematological laboratory markers that can be easily repeated and widely available in routine clinical practice. Neutrophils have been considered the primary source of circulating VEGF, which plays an important role in angiogenesis-related tumor.41 addition, neutrophils can increase the production of inflammatory cytokines such as tumor necrosis factor, interleukin 1, interleukin 6, and therefore provides a microenvironment that is beneficial for survival and tumor proliferation.[7] Conversely, lymphocytes exert an important role in cancer-specific immune responses.8 It has been shown that increased lymphocyte infiltration in tumor tissue is associated with a good prognosis.[9]

From the research, it can be seen that the distribution of this sample that is most by age was <45 years as many as 152 people, by the parity is multipara many as 88 people, based on the stage of the cancer is found most common with stage IV with the number 58 followed by stage I were 51 people attended the stadium 3 as many as 41 people. By histopathology, malignant tumors found serosum adenocarcinoma were 94 people while in the benign tumor was found as many as 32 people are cystadenomas mucinous.

Cho et al investigated the diagnostic value NLR in epithelial ovarian cancer cases and found that preoperative NLR in ovarian cancer patients (median, 6.02) was significantly higher than in patients with benign ovarian tumors (mean, 2.57), benign gynecological disease (mean, 2.55) and healthy controls (mean, 1.98) (P <0.001). In addition, they reported sensitivity and specificity in detecting ovarian cancer NLR was 66.1% (95% CI: 59.52 to 72.68%) and 82.7% (95% CI: 79.02 to 86.38%) (the cut-off, 2.60) .[10]

It was found the value NLR of 5.67 and a P value of 0.001. This shows that the higher the level of severity of the disease, there will be an increase in NLR, whereas parity is found that the levels of the highest levels of NLR found on sekundipara 4.54. On histopathological tissue examination NLR value successively obtained the highest scores on mucinous adenocarcinoma of 4.64 with standard deviations 1:24 and a P value of 0.0043, this indicates the difference between the value of the NLR in malignant ovarian tumor histopathology , Williams et al have confirmed further that the NLR higher levels associated with different clinical characteristics (including levels and higher levels of tumor, presence of ascites, and so on) and disruption of prognosis in cancer patients 519 ovarium.[11]

It can be seen that the NLR in benign tumors with mean 2.94, median 2.80, standard deviation of 0.78. In malignant tumors with a mean value of 4.56 and a median value of 4.38 standard deviation scores 1:12 with the results of the statistical test p = 0.001. In Ca-125 benign tumors are the mean value of 87.91, 96.00 and the median standard deviation 40.73. In malignant tumors with a mean value of 261.00 254.28 median value, standard deviation of 64.09 with the results of the statistical test P = 0.001. The results of this study have shown that the majority of patients with ovarian tumors coined the neutrophil-lymphocyte ratio values were increased in line with other studies that have shown the average value of the neutrophil-lymphocyte ratio as one of the prognostic value of the severity of ovarian cancer. The value range can be petimbangan to be a prognostic value for future research.

As more biomarkers discovered and validated, future studies will focus on the use of a combination of serum tumor markers. Although NLR can not provide all the information necessary for optimal diagnosis of ovarian cancer, our results suggest that this study could be used to complement CA125 examination, especially in the early stages of ovarian cancer. In addition, NLR can be calculated from the data that is already available on a regular basis and do not require additional spending.

There are several possible reasons to explain the relationship between the increase in NLR and poor prognosis. Host immune response against the tumor depends on lymphocytes. Patients with increased limfositopenia NLR has a relative and, as a result, can show lymphocyte-mediated immune response that worse towards malignancy, thus worsening their prognosis and increase the potential for tumor relapse. Alternatively, circulating neutrophils has been shown to contain and emit the majority of circulating VEGF, a pro-angiogenic factors are considered to play an integral role in tumor progression.

The analysis in our study showed that increasing age, FIGO stage advanced stage, and an increase in the value of the NLR at primary diagnosis is a prognostic indicator for ovarian cancer. The survival of patients depending on tumor stage and age, but also influenced by the value of the NLR, suggesting that the immune system plays an important role in monitoring ovarian cancer imunosurvei. Therefore we believe that the recovery immunocompetence and nutritional status may be helpful in improving the prognosis of patients with ovarian cancer. The ability to successfully predict poor prognosis in patients with ovarian cancer who use NLR will be valuable in directing the pre- and postoperative therapy to improve prognosis.

The prognostic significance of preoperative serum CA125 levels remain controversial in the literature. Although some publications describing the relationship between levels of serum CA125 and tumor histology and stage only a few studies that show the relationship with prognosis CA125 in epithelial ovarian cancer. Paramasivam et al. reported preoperative serum CA125 more than 30 U / mL were significantly associated with impaired survival (Hazard Ratio = 2.40 [95% CI:1.26 to 4.59]; P = 0.028) in stage I epithelial ovarian cancer.

In conclusion, we have documented changes in the NLR in some women with ovarian cancer. Many patients with ovarian cancer have a significantly increased NLR indicating that NLR measurement can be part of the routine diagnosis of early stage ovarian cancer. In addition, patients with high NLR at the time of diagnosis had overall survival rates were significantly worse. NLR measurement prior to surgery in these patients may provide a simple method to identify patients with a worse prognosis and aid in guiding the treatment effectively.

V. Conclusion

Based on this study it was found that the majority of patients who come to H Adam Malik Hospital with the diagnosis of ovarian cancer aged <50 years with a total sample of 146 people.

The majority of patients with ovarian cancer diagnosis who came to the department Adam Malik has varied parity with multipara group found as the largest group, totaling 88 people. Based on this study, the majority of patients who come to the department of H Adam Malik is ovarim cancer patients with stage III by the number of 67 people. In histopathological characteristics found patients who come to the department of H Adam Malik is a malignant ovarian tumors with adenocarcinoma serosum as many as 94 people. NLR value is based on the highest common life characteristics at age over 50 years of age ≥ 4.64, save raw 1.34, P 0.001. NLR value parity highest encountered in sekundipara with a value of 4.54, 1.19 standard deviations, P 0188. NLR histopathologically highest value found in mucinous adenocarcinoma of 4.64, 1.24 standard deviations, P 0.043. Based on the stage, NLR highest value encountered in stage IV of 5.66, 0.89 standard deviations, P 0001

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