ORIGINAL RESEARCH

Comparison of Neutrophil Lymphocyte Ratio and Platelet Lymphocyte Ratio levels in ovarian cyst among epithelial ovarian cancer patients at RSUP H. Adam Malik Medan, Indonesia

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ABSTRACT

Objective: To assess Neutrophil Lymphocyte Ratio (NLR) and Platelet Lymphocyte Ratio (PLR) as independent prognostic markers in epithelial ovarian cancer patients at RSUP H. Adam Malik Medan, Indonesia, considering the disease's common occurrence and typically late-stage diagnosis with a poor prognosis due to inflammatory processes implicated in malignancy mechanisms.
Materials and Methods: A comparative case-control study was conducted at the Department of Obstetrics and Gynecology, RSUP H. Adam Malik Medan, from December 2019 to February 2020. The study included 40 patients each diagnosed with ovarian cysts and epithelial ovarian cancer. Bivariate analysis was conducted using independent T-test for normally distributed data and the Mann-Whitney test for non-normally distributed data. Significance was established at $p < 0.05$.
Results: The median NLR in the ovarian cancer group was 2.45 (1.06 to 38.44) and in the ovarian cysts group was 2.34 (1.44 to 3.78). Median PLR levels in ovarian cancer were 12813.94 (3178.08 to 19040.0) and in ovarian cysts were 11138.15 (5026.18 to 22839.51). Statistical analysis revealed no significant difference in NLR and PLR levels between ovarian cancer and ovarian cysts ($p > 0.05$).
Conclusion: NLR and PLR levels demonstrated no significant difference between ovarian cancer and ovarian cyst patients at RSUP H. Adam Malik Medan, Indonesia. However, NLR and PLR can still serve as valuable markers for identifying malignant processes in patients suspected of malignancy.

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Highlights:

1. Neutrophil Lymphocyte Ratio (NLR) and Platelet Lymphocyte Ratio (PLR) have potential as independent prognostic markers for ovarian cancer.
2. This research was to evaluate NLR and PLR levels in ovarian cysts with epithelial ovarian cancer patients at RSUP H. Adam Malik Medan, Indonesia.

INTRODUCTION

Ovarian cancer ranks 6th and 10th among all cancers, constituting the most prevalent malignancy with 13,310 (7.1%) new cases in 2018, as per GLOBOCAN data.[1] The majority of diagnoses occur at advanced stages (stages 3 and 4), yielding a discouraging 5-year survival of 40%. Early detection significantly improves prognosis, raising the 5-year survival rate to approximately 90%.[2,3]

Inflammation and immunology intricately influence cancer development and metastasis. The Neutrophil Lymphocyte Ratio (NLR) and Platelet Lymphocyte Ratio (PLR) serve as indicators of systemic and immunological inflammation.[4] These parameters, reflecting the systemic inflammatory response, emerge as independent prognostic markers for adverse clinical outcomes in ovarian cancer.[5,6]

Williams et al. (2014) demonstrated that elevated NLR levels correlate with advanced disease stages, moderate to poor histological and pathological differentiation, and an unfavorable prognosis.[7] Previous studies underscore the diagnostic utility of NLR (2.25) and PLR (128.08) in benign ovarian cysts, contrasting with NLR (3.54) and PLR (198.87) values for ovarian cancer.[8] Additionally, Miao et al. emphasized the association between elevated NLR levels and more severe progression-free survival (PFS).[9] In a study by Chen et al., the ovarian cancer group exhibited significantly higher platelet counts and PLR compared to the endometriosis group. Platelet count and PLR emerge as valuable parameters for detecting ovarian cancer. These findings collectively underscore the important role of NLR and PLR in assessing ovarian cancer prognosis and potential diagnostic applications.[10,11]

In view of conflicting findings from various studies regarding the Neutrophil Lymphocyte Ratio (NLR) and Platelet Lymphocyte Ratio (PLR) in individuals with ovarian cancer and ovarian cysts, correlations with prognosis and disease trajectory have been subjects of debate. Therefore, we attempted to investigate the NLR and PLR cut-off values in ovarian cancer and ovarian cyst patients. This study aimed to ascertain the potential utility of these parameters as independent predictive diagnostics for malignancies.

MATERIALS AND METHODS

This comparative case-control study, undertaken at the Department of Obstetrics and Gynecology, RSUP H. Adam Malik Medan, from December 2019 to February 2020, involved 40 patients diagnosed with ovarian cysts and epithelial ovarian cancer at the Department of Gynecology-Oncology, RSUP H. Adam Malik Medan.

Inclusion criteria comprised histopathologically confirmed ovarian cyst patients with pertinent medical records at RSUP H. Adam Malik Medan and histopathologically confirmed epithelial ovarian cancer patients with corresponding medical records at the same institution. Exclusion criteria encompassed patients with concurrent oncological diseases, those with coexisting conditions such as heart valve disorders, viral infections, autoimmune disorders, and blood disorders potentially affecting neutrophil, lymphocyte, and platelet values. Additionally, patients lacking routine preoperative blood laboratory data and complete operating reports, as well as those with concurrent gynecological diseases, were excluded.

Histopathological data from ovarian cysts and epithelial ovarian cancer patients were retrieved from anatomic pathology records. Anthropometric details, including height and weight, were extracted from medical records. Complete blood count, patient age, parity history, Neutrophil Lymphocyte Ratio (NLR), and Platelet Lymphocyte Ratio (PLR) data were collected from the medical records. Ethical approval for this study was obtained from the Health Research Ethics Committee of the Faculty of Medicine, Universitas Sumatera Utara, Indonesia.

Statistical analysis

Univariate and multivariate statistical analyses were conducted to evaluate the frequency distribution of study sample characteristics, including age, parity, neutrophils, platelets, and lymphocytes. The Kolmogorov-Smirnov normality test was employed to assess the normality of data distribution. Bivariate analysis utilized the independent T-test for normally distributed data and the Mann-Whitney test for non-normally distributed data. A significance level of <0.05 was applied to all results, which were presented in tabulated format.

RESULTS AND DISCUSSION

Among patients with ovarian cancer, 31 patients (77.5%) aged 18-49 years, and 9 patients (22.5%) were 50 years old. Regarding patients with ovarian cysts, 29 patients (72.5%) aged 18-49 years, 10 patients (25.0%) were 50 years old, and 1 individual (2.5%) aged <18 years. In terms of menopausal status, the majority of the patients not in menopause experienced ovarian cancer, with 33 patients (82.5%) and 34 patients (84.6%) in each respective group.

Table 1. Research patient characteristics

Characteristics		Ovarian cancer		Ovarian cyst		p value
Age (years old)	<18	0	0.0%	1	2.5%	
	18-49	31	77.5%	29	72.5%	0.571
	≥50	9	22.5%	10	25.0%	
Menopause Status	Yes	7	17.5%	6	15.4%	0.800
	No	33	82.5%	34	84.6%	
Parity	Primiparous	5	12.5%	8	20.5%	
	Secundi-Multiparous	14	35.0%	8	20.5%	0.300
	Grand multiparous	21	52.5%	24	59.0%	

Table 2. Differences in mean levels of NLR and PLR in ovarian cancer and ovarian cysts patients

		Mean	SD	Median	Min	Max	P value*
NLR	Ovarian Cancer	5.27	8.39	2.45	1.06	38.44	0.351
	Ovarian Cyst	2.38	0.48	2.34	1.44	3.78	
PLR	Ovarian Cancer	20881.74	31973.82	12813.94	3178.08	190400.0	0.285
	Ovarian Cyst	11894.29	4814.34	11138.15	5026.18	22839.51	

* Mann Whitney Test

In terms of parity, 21 patients (52.5%) with ovarian cancer were grand multiparous, while in the ovarian cysts group, 24 patients (59.0%) had a history of grand multiparity. No significant differences were observed in age, menopausal status, or parity between patients with ovarian cancer and those with ovarian cysts (p >0.05).

The median NLR in the ovarian cancer group was 2.45 (1.06 – 38.44), and in the ovarian cysts group, it was 2.34 (1.44 – 3.78). The median PLR in the ovarian cancer group was 12813.94 (3178.08 – 19040.0), and in the ovarian cysts group, it was 11138.15 (5026.18 – 22839.51). Statistical analysis revealed no significant differences in NLR and PLR levels between patients with ovarian cancer and those with ovarian cysts (p >0.05).

Regarding age distribution, patients with ovarian cancer were predominantly aged 18-49 years (77.5%), followed by those aged 50 years (22.5%). Similarly, the ovarian cysts group was dominated by patients aged 18-49 years (72.5%), with 2.5% aged <18 years and 25.0% aged 50 years. The analysis indicated no significant differences in age distribution between the ovarian cancer and ovarian cysts groups, different from the results of previous studies. For example, Nurlailiyani's research reported that from 82 ovarian cancer patients, only 1.2% of the patients aged <20 years, followed by 12.2% aged 20-34 years, 37.8% aged 35-50 years, and the largest age group (48.8%) comprised individuals over 50 years. The mean age at diagnosis for women with ovarian cancer was 63 years, highlighting age as a major risk and prognosis factor, with worse outcomes in elderly patients.[12]

In this research, it was also found that 33 (82.5%) patients with ovarian cancer had not experienced menopause, and ovarian cyst patients who have not experienced menopause were as many as 34 people (84.6%). Each year, over 23,000 cases of epithelial ovarian cancer are reported in the United States, with a median age at diagnosis being 63 years old.[13] Although post-menopausal women account for more than two-thirds of ovarian cancer incidences, the majority of established risk factors arise predominantly when women are in their twenties or thirties. According to one study, menopausal age is negatively connected to the development of ovarian cancer. These studies suggest that menopause at a later age is associated with an increased risk of ovarian cancer.[14]

The majority of postmenopausal ovarian cancer patients are between the ages of 60 and 64 worldwide; with the median age upon diagnosis in developed countries is 63 years old. According to the research by Shen et al, 38% of women diagnosed with epithelial ovarian cancer and 76% of women diagnosed with borderline epithelial ovarian cancer were diagnosed before menopause, implying that the age at diagnosis of ovarian cancer in Chinese (Asian) women is younger than in Caucasians. Therefore, it is crucial to study if Asian women's younger age at diagnosis could explain their poor clinical prognosis.[15-17]

Tumor-associated inflammation is thought to have a key role in carcinogenesis and tumor progression. In clinical practice, assessing tumor inflammatory response is simpler and less expensive. The immune system's function in disease remission or progression has been studied, and hematological markers such as leukocytes have been postulated as diagnostic and prognostic criteria in a variety of malignancies. The NLR has been suggested as simple index of systemic inflammatory response in patients with cancer. NLR and PLR are considered as predictive factors in survival of ovarian cancer patients. In addition, preoperative NLR and PLR can help differentiate malignant ovarian masses from benign ovarian masses.[18]

In this research, mean NLR value for ovarian cancer group was 5.27, the median was 2.45 and SD was 8.39 and mean NLR value for ovarian cysts group was 2.38, median was 2.34 and SD was 0.48. The statistical test result showed the p value of this comparison was 0.351. Based on this result, NLR levels did not differ statistically between ovarian cancer and ovarian cyst patients ($p > 0.05$).

In this research, mean PLR value for ovarian cancer group was 20881.74, the median was 12813.94 and SD was 31973.82 compared to Mean PLR value for ovarian cysts group was 11894.29, median was 11138.15 and SD was 4814.34. The statistical test results result showed the p value of this comparison was 0.285. Based on this result, there was no statistically significant difference in PLR levels between ovarian cancer patients and ovarian cysts patients ($p > 0.05$).

In this study, we analyzed the calculation of NLR and PLR as markers of inflammation in epithelial ovarian cancer and ovarian cysts patients. Statistical studies on each level of NLR and PLR revealed no statistically significant correlation between NLR and PLR levels and the prevalence of epithelial ovarian cancer and ovarian cysts ($p > 0.05$). However, mean and median NLR values of subjects with ovarian cancer had higher values (5.27 and 2.45) than subjects with ovarian cysts which could have clinical significance (2.38 and 2.34).

However, this was not in accordance with the study conducted by Yildirim (2015).[8] It was found that individuals with ovarian cancer had significantly elevated NLR and PLR levels ($p < 0.05$ and $p < 0.001$). According to a multivariate analysis, greater NLR and PLR levels predicted ovarian cancer at a cut-off value of 3.35, with 55% sensitivity and 81% specificity for NLR (95% CI: 0.544-0.752, $p < 0.05$) and cut-off value of 572.9, with 100% sensitivity and 0.38% specificity for PLR (95% CI: 0.192-0.381, $p=0.001$). According to the findings of the study, preoperative NLR and PLR readings could detect ovarian cancer in patients with adnexal masses.[19]

In another study, 316 patients with benign adnexal masses and 253 patients with malignant adnexal masses underwent surgical treatment. Contrary to our findings, this study revealed higher values of NLR, PLR, neutrophil count, CA-125, and platelets in malignant cases compared to benign cases ($p < 0.01$). These elevated biomarker values suggest potential use in early-stage detection of ovarian malignancy, thereby enhancing treatment options and improving survival rates.[20] While our study did not observe a significant difference in PLR values between ovarian cancer and ovarian cyst patients, the overall PLR values for ovarian cancer were higher than those for ovarian cysts patients.

Nevertheless, this study was not without limitations. The case-control design within a retrospective framework posed challenges in determining external variables due to technical constraints and insufficient information on numerous risk factors. Additionally, the single-center nature of this study, conducted at RSUP H. Adam Malik Medan, a national referral hospital, introduced variations in patient characteristics, including undetected comorbidities upon admission. Statistical associations between mean NLR and PLR levels in ovarian cancer and ovarian cyst patients could not be conclusively established due to limited sample size, research factors, and the relatively short study duration.[20] Despite these limitations, the significance of this study lies in being the first to explore differences in mean NLR and PLR levels between patients with epithelial ovarian cancer and ovarian cysts, providing a foundational basis for future investigations.

CONCLUSION

While no statistical difference was found in Neutrophil Lymphocyte Ratio (NLR) and Platelet Lymphocyte Ratio (PLR) levels between ovarian cancer and ovarian cyst patients at RSUP H. Adam Malik Medan, Indonesia, the persistent correlation of NLR and PLR with inflammatory process in malignancy mechanisms highlights their clinical relevance. The absence of statistical difference does not deny the benefit of NLR and PLR levels in suspected malignancy cases. Future studies should prioritize larger, more homogenous samples for enhanced outcomes and deeper insights into the clinical implications of NLR and PLR in ovarian pathologies.

DISCLOSURES

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Conflict of interest

There are no conflicts of interest among the authors.

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Author Contribution

All authors participated to all aspects of this study, including preparation, data collection and analysis, drafting, and approval for publishing.

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