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The Diagnostic Accuracy of Hematologic Parameters, Neutrophil-Lymphocyte Ratio and Platelet-Lymphocyte Ratio, in Malignant and Benign Epithelial Neoplasms of the Ovary in Philippine General Hospital Service Patients

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ABSTRACT

Background and Objectives. Early detection of ovarian neoplasms confer a better outcome and prognosis for patients. Although newer diagnostic modalities have been recently developed, the availability and accessibility of complete blood count parameters specifically, neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) make it a convenient and cost-effective marker to aid as a pre-operative predictor of epithelial ovarian neoplasms. We aim to determine the significance and relationship of preoperative NLR and PLR in predicting a diagnosis of malignant surface epithelial ovarian tumor.

Methodology. We gathered surgical pathology reports and complete blood count parameters of service patients with benign and malignant surface epithelial ovarian neoplasms. Diagnostic accuracy of NLR and PLR was determined by using receiver operating curve (ROC) plots. Optimal cutoff points were set using the Youden index.

Results. We have included 351 cases of ovarian surface epithelial neoplasms, 209 of which were benign and 142 of which were malignant. The ROC curve for PLR had an area under curve (AUC) of 0.6629 [0.6043, 0.7215]. The optimal cut-off point of was set at 195.99 with the maximal Youden index of 0.295 [9.193, 0.396]. The corresponding sensitivity of this test to determine malignancy at this point was 56.5% [47.8, 64.6] while the specificity was at 73.2% [66.7, 79.1]. The ROC curve for NLR had an AUC of 0.6616 [0.6051, 0.7180]. The optimal cut-off point of was set at 2.60 with the maximal Youden index of 0.316 [0.219, 0.413]. The corresponding sensitivity of this test to determine malignancy at this point was 76.1% [68.2, 82.8] while the specificity was at 55.5% [48.5, 62.4].

Conclusion. The utility of CBC parameters such as PLR and NLR are cost-effective tools which may have some diagnostic value but, they cannot be used as a stand-alone predictor of malignancy and must be correlated with other clinical, laboratory and radiologic studies.

Key words: ovarian neoplasms, blood cell count, lymphocytes, neutrophils, blood platelets

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INTRODUCTION

According to the Philippine Cancer Society, ovarian cancer ranks as the 10th most common site of cancer in both sexes combined and 5th most common cancer in women. Approximately 90% of these ovarian malignancies are surface epithelial tumors. Among them are mucinous, serous, endometrioid, clear cell and Brenner carcinomas.[1] These neoplasms primarily present as a mass that is usually discovered at a much later time in the course of illness, with approximately 66% having metastasis outside of the pelvis at the time of diagnosis. This late detection contributes to a more severe morbidity and poorer outcome.[2-4] Although early detection is still the best approach to ovarian neoplasms, this may be clinically challenging because patients may present with non-specific signs and symptoms in the early stages of disease.

Histopathologic diagnosis remains definitive of tumor nature. The preoperative impression guides surgical technique and intraoperative staging. For equivocal cases,

intraoperative consultation (frozen section) may be done. Clinical data and history may give suspicion towards a benign or malignant diagnosis such as age, family history and sonographic findings among others. Tumor markers have been utilized and no marker has been used as frequently as CA-125.[4] However, like all tumor markers, CA-125 is not wholly sensitive and specific, with variable results depending on menopausal status. Tumors outside the gynecologic tract and other inflammatory states may give elevated CA-125 values.[5]

The search for improved diagnostic modalities for ovarian neoplasms continues. Studies have demonstrated the importance of the inflammatory response in the development of cancer and its progression. Inflammatory cells play a key role in the tumorigenesis. Complete blood count (CBC) parameters and their relationship with cancers have been studied over the years. This affordable and accessible test is included in all admitting and preoperative work ups, making it a convenient marker, specifically, platelet-lymphocyte ratio (PLR) and neutrophil-lymphocyte ratio (NLR). The theory behind the use of NLR is backed up by the pathophysiology of systemic inflammation. Inflammation increases the risk and progression of malignancies and is known to play an important role in tumorigenesis, among them include initiation, promotion, malignant conversion, invasion, and metastasis.[6] The rationale on the use of PLR, on the other hand, is due to previous studies indicating that in tumor and host tissues, increase production of thrombopoietic cytokines, mainly interleukin 6, leads to paraneoplastic thrombocytosis which eventually results in tumor growth and progression.[7] The degree of immune response inherent in solid tumors, represents the body's overall retortion to the tumor such that progression is associated with systemic inflammation.[8-9] Conversely, chronic inflammation is one of the contributors to oncogenesis.[10] It has also been demonstrated that there is a significant rise in inflammatory markers in different cancers. CBC parameters in inflammation have been the subject of recent studies about cancers in various organ system, even in prognostication.[11-14] Of particular interest is the recent hypothesis that a microenvironment and subsequent remodeling and transformation of the epithelial cells by proinflammatory cytokines initiate the development of epithelial ovarian cancers.[15] Since chronic inflammation plays a significant role in the pathogenesis of ovarian cancers, systemic inflammatory response markers such as neutrophil-lymphocyte and platelet-lymphocyte ratio have been evaluated and advocated because of its simplicity, accessibility and cost-effectiveness.

The relationship between neutrophils and oncogenesis has been the subject of recent studies in that neutrophilia, tumor-infiltrating neutrophils and elevated NLR has been associated with poor clinical outcomes, most notably in renal cell carcinoma, melanoma, colorectal cancer, hepatocellular carcinoma, cholangiocarcinoma, glioblastoma, gastrointestinal stromal tumors, gastric, esophageal, lung, ovarian and head and neck cancer.[14] In a study comparing neutrophil and NLR in patients with ovarian carcinoma, NLR was shown to have a significantly higher value in predicting tumor recurrence and disease-specific survival.[16] Another study done in South Korea compared NLR among patients with epithelial ovarian cancers versus patients with benign epithelial ovarian tumors and healthy controls. They have found out that the preoperative NLR was significantly higher in subjects with ovarian cancer than those with a benign tumor. They have also utilized their finding using Cox multivariate analysis, to demonstrate that NLR positivity (above the 2.60 cut-off), age and late stage (Stage III or IV) are independent poor prognostic factors with NLR being having the highest predictive power.[17] With regards to using NLR as a prognostic factor for the stage of disease, progression-free survival (PFS) and overall survival (OS), several studies have found a relationship between advance stage disease, decreased overall survival and even adverse surgical and platinum-based therapy resistance with increasing NLR.[18-20] Like NLR, the use of PLR as a prognostic factor for malignant epithelial tumors shows that increased PLR levels are associated with advanced-stage disease, poor response to chemotherapy, and poor surgical outcome.[17,19]

General Objective

To determine the significance and relationship of preoperative NLR and PLR in predicting a diagnosis of malignant surface epithelial ovarian tumor.

Specific Objectives

1. To compare patient factors such as age, size of tumor and CBC parameters in the benign and malignant ovarian epithelial tumors.
2. To compare the values of NLR of post-operatively diagnosed benign ovarian epithelial tumors versus the values of NLR of post-operatively diagnosed malignant ovarian epithelial tumors.
3. To correlate and compare the values of PLR of post-operatively diagnosed benign ovarian epithelial tumors versus the values of PLR of post-operatively diagnosed malignant ovarian epithelial tumors.
4. To determine the sensitivity and specificity of PLR and NLR at generated cut-off points from the Receiver Operating Characteristics (ROC) curve.
5. To analyze the difference in PLR and NLR between patients with malignant ovarian epithelial tumors and those with benign ovarian epithelial tumors and to determine whether this difference can be of clinical utility to the surgeons.

METHODOLOGY

Data Collection

The Philippine General Hospital, a governmental tertiary and national university hospital, receives referrals for subspecialty care. Service patients, mostly those diagnosed with adnexal tumors, commonly ovarian, are referred to the Gynecologic Oncology out-patient for surgical intervention. Surgically removed tissues from these patients are sent for routine histopathologic evaluation; sometimes for intraoperative consultation (frozen section) depending on the case. The section of Surgical Pathology under the Department of Laboratories receives the specimens and assigns them to the pathology resident for gross examination and initial histopathologic evaluation. Afterwards, the case is shown to a consultant pathologist wherein the final diagnosis will be rendered.

The study was cross-sectional by design and involves patients diagnosed with epithelial ovarian neoplasms in Philippine General Hospital service patients for the year 2015 and 2016. The histopathologic reports indicating the patient's diagnosis are obtained from the Section of Surgical Pathology organ file records.

The study included 351 cases of women, ages 11 to 83 years old, assessed preoperatively with an adnexal mass, surgically managed by Gynecologic Oncology physicians, and diagnosed with an epithelial ovarian neoplasm by the consultant pathologist. The study population is further divided into benign (209 patients) and malignant (142 patients) groups. Patients with a benign ovarian tumor served as the control group (group I), while those with a malignant diagnosis belong to the disease group (group II). Patients with a borderline diagnosis fell under group I because it is considered that their clinical course behaves more similarly to a benign condition rather than a malignancy. We also excluded patients with other primary or concurrent neoplastic malignant lesions of the female genital tract (e.g., uterine or cervical) or elsewhere (e.g., colonic tumors). In the event of a benign tumor in one ovary and a diagnosis of malignancy in the other, we have included this patient and her data in malignancy group. We also recorded additional patient information in the surgical pathology report such as age, size of tumor and laterality.

Simultaneously, patient CBC records were retrieved in the Laboratory Information System (LIS). The CBC parameters recorded includes red blood cell (RBC) and white blood cell (WBC) count, hemoglobin, hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), platelet count and the differential counts of WBC (lymphocyte, neutrophil, monocyte, eosinophil and basophil). Patients without CBC records have been excluded from the study as well as patients with platelet counts values written as "clumps." The date of the surgery was determined, and we have only used CBC results that have been done preoperatively and would not exceed a month before the surgery.

Statistical Analysis

CBC parameters were organized via Microsoft Excel. The neutrophil and lymphocyte counts were computed in absolute values from their percentages based on the WBC count. The NLR was obtained by dividing the neutrophil count with the lymphocyte count. Likewise, the PLR was obtained by dividing the platelet count with the lymphocyte count. Mann-Whitney U test was done to determine whether there is a significant difference in the variables (age, ovarian size, CBC parameters, NLR and PLR) between the benign and malignant groups.

To determine the diagnostic accuracy of the PLR and NLR in determining malignancy, their values were plotted in the Receiver Operating Characteristics (ROC) curve. The ROC curve plots the true positive rate (TPR) against the false positive rate (FPR) and corresponding Area Under the Curve (AUC) has been determined. The cut point with maximal Youden index was reported as the optimal cut-off point. Youden index is a statistic defined as the sum of the sensitivity and specificity minus one, with a maximum value equal to one, which denotes a perfect test, and a minimum value equal to zero, which denotes the test has no diagnostic value. It is used when sensitivity and specificity are diagnostically equally important or desirable. The data and ROC curve were tested and generated using Stata version 17.1.

Ethical Considerations

Ethical review and approval were sought and was done through the University of the Philippines Manila Research Ethics Board (UPMREB). All surgical pathology reports and CBC results were deidentified and given a numerical code to ensure anonymity of the patients.

Limitations of the Study

The sample population included service patients for the year 2015 and 2016. This excluded patients from the pay services where histopathology reports were not arranged in the organ filing system. Also, other patient information outside of the histopathology report and CBC were not included in the study. Therefore, any comorbidities and medical conditions were unknown to us.

RESULTS

Characteristics of Benign and Malignant Groups

We have included in this study 351 cases of ovarian surface epithelial neoplasms. We have used the data of 209 benign and 142 malignant cases. We have 194 diagnosed cases of epithelial ovarian neoplasms in 2015 and 202 cases in 2016. There was an increase in cases from 2015 to 2016 in the benign and malignant groups by 11% and 22%, respectively. Figure 1 shows the distribution of benign and malignant patients according to year.

Mucinous tumors, specifically mucinous adenoma and mucinous adenocarcinoma, was the most common diagnosis comprising 47% (increased to 70%, including the borderline mucinous tumors) and 40% of the benign and malignant groups, respectively. This was followed by the serous tumors, serous adenoma and serous adenocarcinoma comprising 29% (increased to 30% including

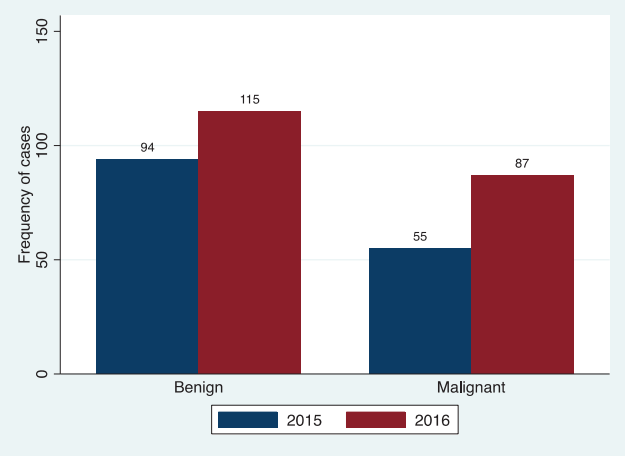

Figure 1. Distribution of benign and malignant cases in 2015 and 2016.

the borderline serous tumors) and 28% of the benign and malignant groups, respectively. The distribution of the benign and malignant diagnoses is shown on Figure 2.

Age, size of the mass and CBC parameters between the benign and malignant group were compared based on the median, interquartile range and p-value using Mann-Whitney U test. The summary of these findings is shown on Tables 1 to 3. There was significantly higher median/mean rank of the following variables among the malignant ovarian tumor group than the benign ovarian tumor group: age, RDW, platelet count, WBC count, absolute neutrophil count, PLR and NLR. On the other hand, there was significantly lower median/mean rank of the following variables among the malignant ovarian tumor group than the benign ovarian tumor group: hemoglobin, MCV, MCH, MCHC, absolute lymphocyte count and lymphocyte differential count. For the following variables, there was no sufficient evidence to conclude that they have significant median/mean rank differences between the benign and malignant ovarian tumor groups: tumor size, RBC count, hematocrit, monocyte differential count and basophil differential count.

The ROC Curve of PLR and NLR

The ROC curve for PLR had an AUC of 0.6629 [0.6043, 0.7215]. The optimal cut-off point was set at 195.99 with the maximal Youden index of 0.295 [9.193, 0.396]. The corresponding sensitivity of this test to determine malignancy at this point was 56.5% [47.8, 64.6], while the specificity was at 73.2% [66.7, 79.1]. Figure 3 shows the PLR values on the ROC curve; plotted as the x-axis being the true positive rate (sensitivity) and y-axis as the false positive rate (1-specificity).

The ROC curve for NLR had an AUC of 0.6616 [0.6051, 0.7180]. The optimal cut-off point was set at 2.60 with the maximal Youden index of 0.316 [0.219, 0.413]. The corresponding sensitivity of this test to determine malignancy at this point was 76.1% [68.2, 82.8], while the specificity was at 55.5% [48.5, 62.4]. Figure 4 shows the NLR values on the ROC curve; plotted as the x-axis being the true positive rate (sensitivity) and y-axis as the false positive rate (1-specificity).

Figure 5 shows a comparison between the ROC curves of PLR and NLR, it showed the seemingly inverse relationship the two variables had with each other, that while NLR had greater sensitivity, PLR had greater specificity. Table 4 summarizes the ROC curve analysis.

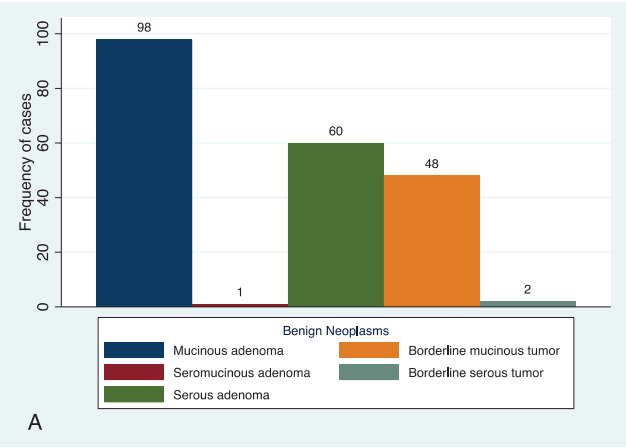

Figure 2. Distribution of **(A)** benign ovarian tumors and **(B)** malignant ovarian tumors according to specific diagnosis.

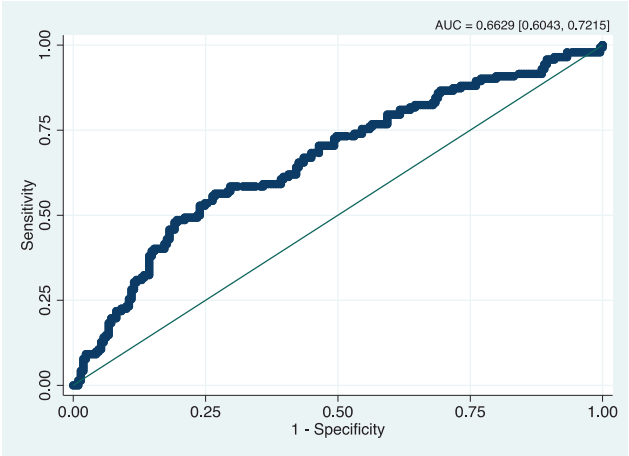

Figure 3. ROC curve for PLR with an AUC of 0.6629 [0.6043, 0.7215]. The optimal cut-point is 1.99 based on the Youden index of 0.295 [0.193, 0.396]. This cut-point has sensitivity of 56.3% [47.8, 64.6] and specificity of 73.2% [66.7, 79.1].

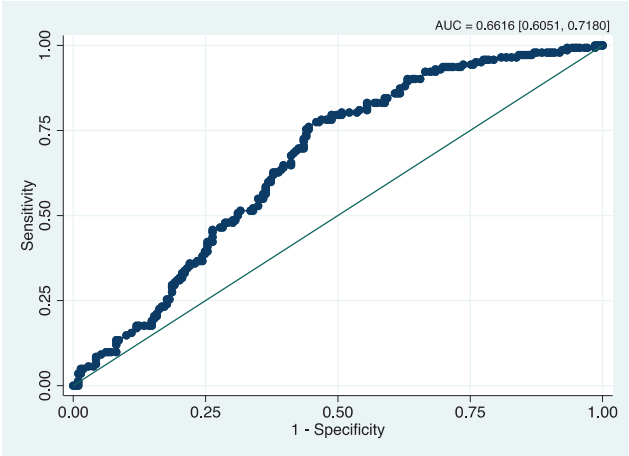

Figure 4. ROC for NLR with an AUC of 0.6616 [0.6051, 0.7180]. The optimal cut-point is 2.60 based on the Youden index of 0.316 [0.219, 0.413]. This cut-point has sensitivity of 76.1% [68.2, 82.8] and specificity of 55.5% [48.5, 62.4].

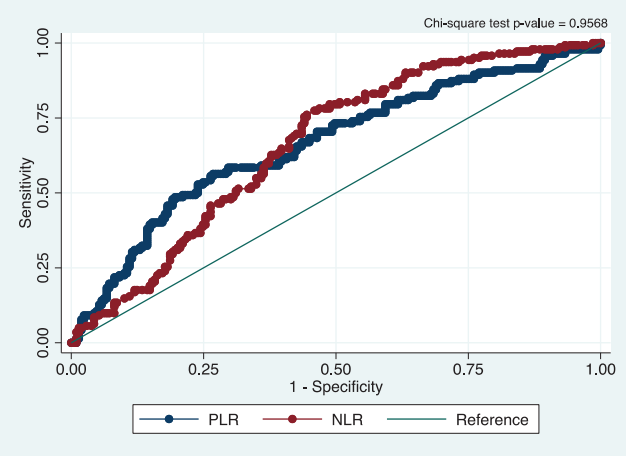

Figure 5. ROC curves of PLR and NLR have no sufficient evidence of significant differences in AUC (p-value = 0.9568).

DISCUSSION

ROC Curve Analysis

Our findings do not stray from data in other studies as demonstrated in a systematic review by Prodromidou et al., that included 18 studies, using PLR and NLR to detect and assess prognosis (in progression-free survival and overall survival). This study mentions that majority of the studies had relatively similar cut-off values denoting applicability of these biomarkers. However, actual efficacy remains relatively small ranging between 55% to 80%.[18]

Ozaksit et al., evaluated PLR as a diagnostic test to differentiate adnexal tumors between neoplastic and non-neoplastic in adolescent patients. PLR was used in conjunction with the size of the mass, CA-125 and mean platelet volume. With a PLR cut-off value at 140, they found that the sensitivity and specificity of PLR in diagnosing neoplastic tumors is 65.7% and 57.6%, respectively.[21] Further studies by Polat et al., Yildrim et al. and Bakakak et al. also used ROC analysis to differentiate malignant tumors from the benign tumors with their cut-off points set at 2.47, 3.35 and 3.47 respectively.[22-24] Their NLR sensitivity ranged from 55% to 68.8% while specificity ranged from 54.1% to 81%. The above studies also found that PLR was a significant predictor of malignancy. Their PLR cut-off values were at 144.3, 572.9 and 161.13 respectively. Yildrim et al., set their cut-off point at 100% sensitivity in exchange for a poor 0.38% specificity. The NLR sensitivity of Polat et. al and Bakakak et al., were 54% and 66.7%, respectively and the specificity was at 59% and 77.9%, respectively. Compared to the three reported studies, we report a higher NLR sensitivity. Although we are uncertain as to the exact reason for this striking difference, we can hypothesize that patients who sought consult at our institution may have already been in the higher stage of their disease at the time of admission and surgery.

Clinical Use of PLR and NLR

We reiterate that CBC and its parameters were never done to diagnose malignancy outright but is only meant to give the clinician a very initial suspicion of malignant condition. Being the most common first line diagnostic test, like most screening methods, increasing sensitivity is better. Among the two, NLR has a higher sensitivity at the set cut-off point. Values above a particular cut-off point indicate the level of sensitivity and specificity at which the diagnosis would most likely be a malignancy. Conversely, when we maximize sensitivity to 95%, the cut-off for NLR would be about 1.64-1.65. Consequently, our specificity would drop to 22-24% but clinicians may be interested at this point with detection of any possibility of a malignancy. If we were to give PLR the same 95% sensitivity, the cut-off would be along 85-86 and in exchange for a decreased specificity of 10-11%. Surely, a highly sensitive test casts a wider net and thus leads to an overdiagnosis of malignancy. But we intended that this data be interpreted in a way that PLR

Table 1. Clinicopathologic characteristics of the post-operatively diagnosed ovarian epithelial tumor patients in the Philippine General Hospital in the years 2015-2016

Variable	Benign		Malignant		*p*-value*
	Median	IQR	Median	IQR	
Age, years	38.5	27	49	16	<0.0001
Ovarian tumor size, cm	16	11	16	9	0.5669
Complete blood count					
RBC count, 10^6/uL	4.35	0.67	4.33	0.65	0.4286
Hemoglobin, g/dL	124	19	116.5	19	<0.0001
Hematocrit, %	38	5	37	5	0.0559
Mean corpuscular volume, fL	86.8	6.4	85.6	8.1	0.0484
Mean corpuscular hemoglobin, pg	28.7	2.8	27.6	3.4	<0.0001
Mean corpuscular hemoglobin concentration, g/dL	328	19	317	25	<0.0001
Red cell distribution width, %	13.4	1.5	14.55	2.9	<0.0001
Platelet count, 10^9/uL	295	109	364.5	193	<0.0001
WBC count, 10^3/uL	8.62	4.37	10.325	5.67	0.0001
Absolute neutrophil count, 10^3/uL	5.26	4.26	7.63	5.31	<0.0001
Absolute lymphocyte count, 10^3/uL	2	0.96	1.84	0.97	0.0099
Differential count					
Neutrophil, %	63	20	73	16	<0.0001
Lymphocyte, %	26	17	18.5	14	<0.0001
Monocyte, %	5	2	5	2	0.2747
Eosinophil, %	2	3	2	2	0.0273
Basophil, %	0	1	0	1	0.8913
Platelet – lymphocyte ratio	143.16	95.23	206.7	167.91	<0.0001
Neutrophil – lymphocyte ratio	2.41	2.98	3.82	4.18	<0.0001

*Mann Whitney U test

Table 2. Comparison of the Median and Interquartile Range Between Group I (Benign) Service Patients in the Philippine General Hospital for the year 2015 and 2016

Variable	Borderline Mucinous		Borderline Serous		Mucinous Adenoma		Serous Adenoma	
	Median	IQR	Median	IQR	Median	IQR	Median	IQR
Age (years)	43	25.5	53	22	35	26	39	27
Size (cm)	20.5	7.25	16.5	1	16	10	9.5	10.5
RBC (x10^6 cells/uL)	4.275	0.71	4.445	0.89	4.36	0.61	4.39	0.705
WBC (x10^3 cells/uL)	9.425	4.615	10.89	6.46	7.59	3.99	9.19	5.445
Hemoglobin (g/dL)	118.5	20.5	125	16	124	16	125	20
HCT (%)	0.365	0.05	0.38	0.06	0.38	0.05	0.38	0.05
MCV (fL)	85.25	8.9	86.35	4.7	87.65	5.6	86.15	5.95
MCH (pg)	28.2	3.3	28.25	1.9	28.8	2.7	28.9	2.5
MCHC (g/dL)	322	24.5	327	4	328	16	330.5	14.5
RDW (%)	13.95	1.95	13.3	0	13.25	1.5	13.5	1.9
PLT (x10^9 cells/uL)	327	122	329	104	290.5	98	287.5	103
Neutrophl	0.685	0.185	0.605	0.05	0.59	0.21	0.675	0.23
Lymphocyte	0.21	0.155	0.28	0.02	0.28	0.17	0.245	0.195
Monocyte	0.05	0.02	0.05	0.02	0.06	0.03	0.05	0.02
Eosinophil	0.02	0.03	0.065	0.05	0.03	0.04	0.02	0.025
Basophil	0.01	0.01	0	0	0	0.01	0	0.01
PLR	180.425	156.55	113.485	40.89	135.355	78.31	137.71	111.23
NLR	3.285	3.675	2.165	0.33	2.075	2.25	2.75	4.88

Table 3. Comparison of the Median and Interquartile Range Between Group II (Malignant) Service Patients in the Philippine General Hospital for the year 2015 and 2016

Variable	Mucinous Adenocarcinoma		Serous Adenocarcinoma		Clear Cell Carcinoma		Endometrioid Carcinoma	
	Median	IQR	Median	IQR	Median	IQR	Median	IQR
Age (years)	49	18	44.5	18.5	51	15	52	7
Size (cm)	20	6	11	5.5	17	6	13	8
RBC (x10^6 cells/uL)	4.36	0.67	4.31	0.645	4.28	0.83	4.05	0.69
WBC (x10^9 cells/uL)	9.06	4.26	10.33	5.885	10.61	6.83	12.51	8.17
Hemoglobin (g/dL)	120	20	118.5	19	107	32	112	21
HCT (%)	0.37	0.06	0.365	0.055	0.35	0.08	0.36	0.05
MCV (fL)	86.5	5.8	85.45	9.65	83.8	8.2	85	10.4
MCH (pg)	27.8	2.6	27.65	4.4	26.6	4.1	27.5	2.3
MCHC (g/dL)	317	20	318	30.5	304	25	319	22
RDW (%)	14.2	1.9	14.85	3.7	14.6	1.8	15	2.9
PLT (x10^9 cells/uL)	352	156	362.5	171	432	281	399	210
Neutrophil	0.7	0.14	0.735	0.17	0.77	0.15	0.78	0.15
Lymphocyte	0.22	0.11	0.185	0.145	0.13	0.15	0.15	0.12
Monocyte	0.06	0.03	0.06	0.01	0.04	0.02	0.04	0.02
Eosinophil	0.02	0.03	0.015	0.02	0.01	0.02	0.01	0.02
Basophil	0	0.01	0.01	0.01	0	0.01	0	0.01
PLR	198.53	145.83	181.335	172.02	260.43	201.94	224.09	109.87
NLR	3.23	2.87	3.82	4.02	5.92	9.58	5.2	4.31

Table 4. Summary of ROC Analysis: Cut-off point, Sensitivity, Specificity and AUC

	AUC	Cut-off point	Youden Index	Sensitivity	Specificity
PLR	0.6629 [0.6043, 0.7215]	195.99	0.295 [9.193, 0.396]	56.5% [47.8, 64.6]	73.2% [66.7, 79.1]
NLR	0.6616 [0.6051, 0.7180]	2.60	0.316 [0.219, 0.413]	76.1% [68.2, 82.8]	55.5% [48.5, 62.4]

and NLR would only alert the clinician and stress the need for ordering more specific tests.

An AUC of 0.66 for both PLR and NLR is useful for as a screening tool and because they are not intended to be used in isolation. In practice, risk of malignancy indices (RMI) comprised of CA-125, menopausal status and ultrasonographic findings are used to improve diagnostic performance.[25] It is not uncommon that studies include other tumor markers, specifically CA-125, to increase diagnostic accuracy. They have seen that this further increased diagnostic ability, particularly in the early stages of disease.[23] A study evaluated the use of NLR, as well as tumor markers CA-125 and CA-19-9, in predicting a benign and borderline versus malignant mucinous ovarian tumor for patients intraoperatively diagnosed as a borderline mucinous tumor. The WBC count, neutrophil and NLR appear to be significantly higher in the malignant group. Comparing the definitive diagnosis of the frozen section, they found out that CA-19-9 and NLR has the highest sensitivity in diagnosing a malignant mucinous tumor with an 81% and 78% sensitivity, respectively.[25] Pairing PLR and NLR values to these RMI achieves greater diagnostic accuracy.[26,27] The added convenience from the readily accessible PLR and NLR makes it a good and flexible screening tool. Furthermore, intraoperative histopathologic consultation or frozen section may still be done and will always be an option for tumors that remain equivocal despite all these factors.

CONCLUSION AND RECOMMENDATIONS

Early detection of ovarian malignancies is a deterrent to a fatal course and poor prognosis. Hence, any novel biomarkers have gained much attention in research. The utility of CBC parameters such as PLR and NLR have some diagnostic value but at present, they cannot be entirely independent of other clinical, laboratory and radiologic signs indicative of malignancy. The CBC parameters are indeed important cost-effective tools but may still be affected by unaccounted variables and pathologies outside our ovarian neoplasms. Studying PLR and NLR further, albeit in a more specific and controlled sample such as in menopausal women or those with early-stage disease may help limit and determine the exact value of PLR and NLR. We recommend further evaluation of NLR and PLR against other currently used diagnostic modalities such as CA-125, International Federation of Gynecology and Obstetrics (FIGO) staging and imaging studies to compare its acceptability as a prognostic marker. Studies regarding determination of cut-off values may also be done to determine an acceptable level of sensitivity and specificity for NLR and PLR.

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STATEMENT OF AUTHORSHIP

All authors fulfilled the ICMJE authorship criteria.

AUTHOR DISCLOSURE

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