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Original Research Paper

Pathology

VALUE OF NEUTROPHIL TO LYMPHOCYTE RATIO AND PLATELET TO LYMPHOCYTE RATIO IN THE DIAGNOSIS OF OVARIAN NEOPLASM IN YOUNG ADULT FEMALE.

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ABSTRACT

Background: Ovarian tumors at a young age are rare and reported to be 2% of all the cases seen. Relationship between poor prognosis of ovarian malignancies and changes in complete blood count parameter have been proposed previously.

Objective: To determine the association among neutrophil to- lymphocyte ratio (NLR), Platelet –to-lymphocyte ratio (PLR), and ovarian tumour in young female adult.

Method:A retrospective and prospective study was performed on 73 young females with ovarian masses. Two groups were constituted with respect to the clinical and histopathologicalresults.Group 1, constitute Non neoplastic patients (n=45); and Group 2, neoplastic patients (n=28). The main parameters recorded from the hospital database and patients' files were age, haemoglobin, haematocrit, white blood cell count, absolute neutrophil, lymphocyte, platelet counts, and postoperative histopathology result.

Result: The Mean age of the patients in group 1 was 24.56±3.55, and in group 2 was 23.61±3.79. Abdominal pain was the most common presentation. Most common lesion in group 1 was Follicular cyst (55.33%) followed by Corpus luteal cyst (1.11%). Benign cystic teratoma (42.9%) was the most common neoplastic ovarian mass.

Haemoglobin, Platelet count, neutrophil to lymphocyte ratio (NLR) and Platelet to lymphocyte ratio (PLR) were highly Significant in neoplastic lesion group than the non-neoplastic group.(p<.001)

Conclusion: Significant Value of NLR and PLR may predict ovarian neoplasm in young females and can be used for discrimination to cancer from pathologically normal patients even in primary setups.

KEYWORDS : young female adult, neutrophil to lymphocyte ratio, platelet to lymphocyte ratio, histopathological diagnosis.

INTRODUCTION

Although Ovarian masses are less common at a young age, they are the most common indication of gynaecological surgery in this population. The exact prevalence of ovarian mass in the young female is unknown. Ovarian lesions are divided into non-neoplastic and neoplastic entities according to the World Health Organization (WHO) criteria[1].

Benign ovarian cysts may occur at any phase of life but they are most common during childbearing age and constitute approximately 90% of ovarian tumour[2]. Functional Cyst, ovarian torsion, and benign neoplasm are the most common ovarian neoplasm in young adolescents[3]. Ovarian neoplasms are supposed to occur at a rate of approximately 2.6 in 100,000 girls per year[4]. Most of the ovarian tumors in young girls are asymptomatic and are very difficult to detect until they are advanced in stage or size. Most ovarian tumors occurring in a young female are diagnosed incidentally through imaging studies and on physical examination[5].

CT and MRI are reserved for challenging cases[6]. The management of such cases is exceedingly imperative to maintain the patient's reproductive and menstrual capabilities. In an attempt to better estimate the patients' outcomes, many prognostic factors have been investigated. Recently numerous studies focusing on inflammatory markers including white blood cells (WBC) and platelets have been published[7-9]. Elevated absolute neutrophil count[10], platelets count[11-12], absolute lymphocyte count, neutrophil to lymphocyte ratio (NLR)[13], or platelets to lymphocyte ratio [14]were reported in epithelial ovarian cancer. PLR has potential clinical value in predicting advanced stage disease and suboptimal surgery and is a better prognostic indicator for the survival of epithelial cell cancer as compared to thrombocytosis.

The response of the patient to cancer has been found to be related to cytokines released from neutrophils and platelets as well as tumor cells. The elevated number of these markers was observed to have a poor prognosis[15]. Inflammatory processes initiate angiogenesis around the neoplastic area [16]. Neutrophils release cytokines along with leukocytic and other phagocytic mediators that induce damage to cellular DNA, inhibit apoptosis, and promote angiogenesis around neoplastic cells leading to tumor growth, progression, and metastasis[17,18]. Similarly, platelets may release some growth factors like platelet-derived growth factor, transforming growth factor, or Vascular endothelial growth factor which acts as a potent mitogen and may stimulate ovarian tumor

cells proliferation and adhesion to other cells resulting in tumor growth and metastasis[19,20].

In this study, we aim to evaluate the value of NLR and PLR for the diagnosis of ovarian neoplasm in young female adults to prevent unnecessary surgical interventions. This is a simple test that can be easily carried out even in primary set up.

MATERIALS AND METHODS

After an ethical approval for the entire study was obtained from the Local Ethics Committee of the Institution. The study was conducted in the department of pathology of Government Medical College of Srinagar Garhwal, retrospectively for 4 years and prospectively for 2 years to identify young females aged between 10 -30 years and managed in our hospital between January 2012 to Dec 2018. A total of 73 young women were identified from the hospital records. Patients, who had incomplete laboratory data particularly preoperative complete blood count value and operative notes were excluded from the study. Histopathologic results of all cases were evaluated in detail.

Hematological parameters were investigated using an automated hematologyanalyzer. These parameters were hemoglobin, hematocrit, white blood cell count,absolute neutrophil, and lymphocyte count, platelets count. We also calculated neutrophil to lymphocyte ratio (NLR) and platelets to lymphocyte ratio (PLR). NLR was defined as the absolute neutrophil count divided by the absolute lymphocyte count.PLR was defined as the absolute platelets count divided by the absolute lymphocyte count A management decision was made according to physical examination, ultrasound findings, and laboratory parameters. Surgical intervention was made only in those cases where cyst did not resolve or decrease in size after 2-3 months or caused severe symptoms such as the acute abdomen or suspected hemorrhage, torsion and malignancy or became greater.

STATISTICAL ANALYSIS

Means and standard deviation (SD) were calculated for continuous variables. Subject characteristics and demographics were analyzed descriptively. Student T-test was applied for statistical analysis. Statistical analysis was carried out using the statistical package SPSS 21.0 (Demo) for Windows

RESULT

Out of the 73 young female adults with ovarian masses included in the current study, forty-five (61.64%) patients with non-neoplastic masses were classified as group 1, 28 (38.35%) cases with neoplastic masses classified as group 2. The Mean age of the patients in group 1 was 24.56±3.55, and in group 2 was 23.61±3.794 . There was no significant differences fromin age between patients with two groups. Abdominal pain was the most common clinical manifestation among the group.

The Most common nonneoplastic lesions were follicular cyst (55.33%) followed by Corpus luteal cyst (31.11%) in group 1. Only one case of corticostromal hyperplasia, endometriosis, twisted ovarian cyst, ossification ovary was seen in non-neoplastic group. **(Table 1).**Benign cystic teratoma (42.9%) was the most common neoplastic lesion in group 2. Endometroidtumor, Ovarian stromal tumor, Krukenbergtumor seen in one case only.**(Table 2)**

On comparing the hematological parameter between two groups, hemoglobin was significantly higher in patients with neoplastic lesions than patients with the non-neoplastic lesion ($p<.001$). Haematocrit was also significant in the neoplastic group ($p<.005$) Platelet count and neutrophil to lymphocyte ratio (NLR) were significantly higher in patients with neoplastic lesion than non-neoplastic lesion ($p<0.001$).Platelet to lymphocyte ratio (PLR) was highly Significant in neoplastic lesion group than the non-neoplastic group.**(Table 3)**

DISCUSSION:

Ovarian lesions are infrequent lesions at a young age and in this age, neoplasms generally originate from the Germ cell lines[21]. 30% tumor of all ovarian neoplasm occurring during childhood and adolescence are malignant[22]. In accord with findings from other studies, children and adolescents with ovarian mass constitute a very little number of cases in our institution[23,24].

Abdominal pain is the most common symptom in a young female with adnexal masses3. In our study, the most common presentation was a pain in the abdomen which is consistent with other studies.

Ovarian torsion is a rare problem that should be considered in the differential diagnosis of any young female presenting with abdominal pain or adnexal mass[25]. In our study, we found one case of Ovarian torsion.

Several studies reported various prognostic factors to predict the outcome of ovarian neoplasm e.g age, race, stage, cell type, grade, tumor marker, and residual tumor after surgery[26,27]. Except for race, age, and tumor marker, other prognostic factors can be evaluated only during or after surgery from the pathologic feature of cancer[14].

Complete blood count which is one of the basic preoperative laboratory evaluations has recently been integrated into many studies in an attempt to evaluate ovarian neoplasm[13].

In a recent study, the authors found that patients with cancer have increased CRP levels, the presence of neutrophilia, and relative lymphocytopenia secondary to the systemic inflammatory response[28,29]. They said that tumor-associated neutrophil (TANS) promotes the remolding of the extracellular matrix via their enzyme action, which results in the release of basic fibroblast, growth factor, migration of endothelial cells, and dissociation of tumor cells. These events finally result in enhanced angiogenesis, tumor growth, and progression to metastasis[30] .Our findings are consistent with these studies. We found that neutrophilia and lymphocytopenia were highly significant in the neoplastic group.

Negrier et.al, 2002 and Teramukai et.al2009 in their studies found that neutrophilia has been associated with poor survival in patients with metastatic renal cell carcinoma and non-small cell lung cancer[31,32].TravaresMurta et al 2010, suggested frequent association of neutrophilia with recurrence and metastasis in patients with advanced-stage cervical cancer and was the parameter that best predicted disease progression[33].Neutrophilia and lymphopenia were also seen in our studies. The findings of the present study are congruent with the others.

The NLR is assumed as a simple and effective marker of inflammation[34]. High NLR is associated with poor prognosis in a cancer patient. GokhanAcmaz et al 2014, in their study found gradually increasing NLR in patients with the pathologically normal group, hyperplasia, and cancer (1.94, 2.01,2.89 respectively)[35]. The immune response of the host to cancer is lymphocyte dependent can be one of the possible factors to explain this association. Other factors responsible for the explanation are that neutrophil contains and secrete the majority of circulating vascular endothelial growth factor which plays an important role in roles in the progression of cancer[36]. NLR was statistically significant in our study.

Studies suggested that platelets are an independent marker

and revealed that thrombocytosis was associated with advanced disease and inoperable cancer[12] .In the current study the platelet count was highly significant in the neoplastic group. Preoperative thrombocytosis may favor a diagnosis of malignancy in women undergoing surgical evaluation of pelvic mass[37,38]It is associated with poor survival outcome and poor clinicopathologicprognostic factors[16]. Our findings are consistent with these studies.

Previous studies suggested that PLR and NLR could be used as a diagnostic marker for certain gynecologic cancer[39,40]. Raungkaewananee et al, 2012 found that PLR of 200 yielded a good predictive value with diagnosis and prognosis of epithelial cancer. ArifKokcuet. al 2014, in their study found that NLR, platelet count and PLR increased with increasing stage of ovarian cancer[41]. They also suggested that PLR is an independent prognostic factor related to the stage of epithelial cancer. GuhurOzaksitet. al 2015 suggested in their study that a PLR value of more than 140 might be a diagnostic marker in the adolescent with a neoplastic ovarian mass[42]. PLR value in our study was more than 176 and was highly significant.

The present study is aimed to evaluate the value of PLR and NLR in the diagnosis of ovarian neoplasm in a young female. The result of our study was consistent with the mentioned study in ovarian cancers which found that PLR and NLR appeared to be a poor prognostic factor.

Our study has several limitations. A major limitation was the retrospective data collection and large duration which was done to bring the sample size up to a substantial figure. Owing to the low population density of the region taking a longer duration under consideration was imperative. Despite these limitations, our study is significant owing to the fact that overall studies in this special age group are very few in number and our study further contributes to the existing research.

CONCLUSION

The main aim of this study is preoperative evaluation for early diagnosis, to conserve fertility, and maintain reproductive and menstrual capabilities with minimal surgical intervention. Our study suggests that both the parameter NLR and PLR may predict ovarian neoplasm in young females and can be used for discrimination to cancer from pathologically normal patients even in primary setups.

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Table 1- Histopathology result of Non neoplastic ovarian lesions Group I

Name of Lesion	Number (n=45)	Percentage(%)
Follicular cyst	24	53.33
Corpus luteal cyst	14	31.11
Simple cyst	02	4.44
Corticostromal hyperplasia	01	2.22
Endometriosis	01	2.22
Twisted Ovarian cyst	01	2.22
Ossification of ovary	01	2.22
Ovarian pregnency	01	2.22

Table 2 - Histopathology result of neoplastic ovarian lesions Group II

Name of Lesion	Number (n=28)	Percentage(%)
Benign Cystic teratoma	12	42.9
Serous tumor	08	28.6
Fibroma	02	7.1
Granulosa cell tumor	02	7.1
Endometroid	01	3.6
Ovarian stromal tumor	01	3.6
Serous cyst adenoma	01	3.6
Krukenberg	01	3.6

Table 3 : Comparison of the Laboratory Parameters Among the Group

Parameter	Group 1(n=45)	Group 2(n=28)	p values
Age	24.56 ± 3.55	23.61 ± 3.794	NS
HGB	12.70 ± 0.73	12.14 ± .67	<.001
HCT	37.78 ± 2.33	36.15 ± 1.95	<.05
ABS Neut	5.62 ± 0.53	6.24 ± 0.44	<.001
Abs lymph	3.25 ± 0.58	1.97 ± .67	<.001
PLT	217.91 ± 45.99	315.75 ± 35.67	<.001
NLR	1.77 ± 0.28	3.47 ± .97	<.001
PLR	68.96 ± 18.45	176.81 ± 55.02	<.001

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