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Impact of Different Platelet Indices in Epithelial Ovarian Cancer

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ABSTRACT

Background: Epithelial ovarian cancer (EOC) remains the most lethal gynecologic malignancy due to its late presentation and high recurrence rate. Despite advances in surgery and chemotherapy, prognosis remains poor, highlighting the need for reliable prognostic biomarkers. Platelet indices, routinely obtained from complete blood counts, have emerged as potential predictors of tumor progression and survival outcomes.

Patient and Method: 140 patients with histopathologically confirmed EOC treated at the Oncology Center, Mansoura University. Baseline clinical, radiological, pathological, and hematological data, including platelet indices [mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT), and platelet-to-lymphocyte ratio (PLR)], were analyzed for associations with clinicopathological features, treatment response, and survival outcomes. Kaplan–Meier survival curves with log-rank tests were used for disease-free survival (DFS).

Results: The mean age at diagnosis was 53.3 years, and most patients were overweight. The majority presented with advanced disease (52.8% in stage III), ascites (70.7%), and omental deposits (47.9%). Elevated PCT, MPV, and PLR were significantly associated with adverse features such as omental deposits and ascites. Thrombocytosis was also correlated with the presence of omental deposits. A low PLR was significantly associated with a reduced risk of recurrence (p=0.042), and the presence of ascites significantly correlated with recurrence (p=0.02). Kaplan–Meier survival analysis demonstrated that altered platelet indices were significantly associated with inferior disease-free survival.

Conclusion: Platelet indices are inexpensive and easily accessible biomarkers that provide valuable prognostic information in EOC. Integrating these parameters into routine clinical evaluation may help stratify patients at higher risk of recurrence and guide treatment planning.

Keywords: Epithelial Ovarian Cancer, Platelet Indices, Thrombocytosis, Prognosis, Survival, Ascites.

INTRODUCTION

Ovarian cancer continues to represent a significant challenge in gynecologic oncology, with its high mortality rate largely attributed to the absence of effective early detection strategies and the aggressive nature of the disease. Globally, it ranks as the eighth most common cancer in women and the fifth leading cause of cancer-related deaths, accounting for nearly 4% of all female cancer mortality[1]. The incidence varies geographically, with higher rates observed in industrialized nations, underscoring the impact of genetic, environmental, and lifestyle factors on disease distribution [2].

Despite advances in surgical techniques and systemic therapy, long-term survival rates remain poor, with a five-year survival ranging between 20% and 40% for advanced disease [3].

Epithelial ovarian cancer (EOC) is the most frequent histological type, comprising over 90% of all ovarian cancers. It is a highly heterogeneous disease that encompasses several subtypes, including high-grade serous carcinoma, endometrioid, clear cell, mucinous, and low-grade serous carcinomas, each with distinctive molecular pathways and clinical behaviors[4].

Among these, high-grade serous carcinoma is the most common, usually diagnosed at an advanced stage due to vague and nonspecific symptoms such as abdominal bloating, pelvic
pain, or early satiety. These clinical challenges contribute to delayed diagnosis, underscoring the urgent need for reliable and accessible biomarkers to aid in prognosis and risk stratification [5].

In recent years, increasing evidence has highlighted the critical role of the tumor microenvironment in disease progression. Within this context, platelets have emerged as key mediators of cancer development and metastasis. Beyond their traditional role in hemostasis, platelets are now recognized as dynamic players in oncogenesis. They interact directly with tumor cells, facilitating immune evasion, angiogenesis, and metastatic spread through the release of pro-inflammatory cytokines, vascular endothelial growth factor (VEGF), and other growth factor. These interactions contribute to a tumor-promoting niche, which supports tumor progression and impairs host immune surveillance [6].

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Platelet indices (PI), which are simple and cost-effective parameters derived from routine complete blood counts, offer an attractive opportunity for prognostic evaluation. The main indices include mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT), and platelet-to-lymphocyte ratio (PLR). Variations in these indices reflect platelet activation and systemic inflammatory status, which are increasingly recognized as critical components of cancer biology. Importantly, these indices are readily available in routine clinical practice, providing an inexpensive tool that could be integrated into patient care[7].

A growing body of literature has investigated the prognostic value of platelet indices in ovarian and other cancers. For instance, abnormal MPV and PDW values have been correlated with tumor burden, chemoresistance, and survival in ovarian cancer patients. Similarly, elevated PLR has been consistently associated with advanced disease and unfavorable outcomes, reflecting the dual contribution of thrombocytosis and lymphopenia in cancer progression. Thrombocytosis itself has been identified as an independent marker of poor prognosis, associated with both advanced stage at presentation and resistance to therapy[8].

Despite these findings, the clinical application of platelet indices in EOC remains underexplored, with some conflicting evidence in the literature. Given their low cost and wide availability, further research is warranted to clarify their role in patient stratification, prognosis, and treatment planning. This study was therefore designed to evaluate the prognostic impact of different platelet indices in a cohort of patients with epithelial ovarian cancer treated at a tertiary oncology center, with particular focus on their association with clinicopathological features and survival outcomes.

AIM OF THE WORK

The aim of this retrospective study was to assess the prognostic role of different platelet indices among ovarian cancer patients who attend Oncology Center, Mansoura University and diagnosed as epithelial ovarian cancer.

PATIENTS AND METHODS

Study Design and Population

This retrospective cohort study was conducted at the Oncology Center, Mansoura University (OCMU), between January 2017 and December 2020. A total of 140 patients with histopathologically confirmed epithelial ovarian cancer (EOC) were included.

Eligibility Criteria

Equal or above eighteen years old, with a histologically proven EOC, available baseline complete blood count (CBC) with platelet indices, and complete follow-up records. Exclusion criteria included other ovarian malignancies (sex cord-stromal tumors, germ cell tumors), double malignancies, pre-existing platelet or hematologic disorders, and incomplete data.

Data Collection

Clinical data included age, body mass index (BMI), menopausal status, presenting symptoms, and presence of ascites. Radiological findings (from CT or MRI abdomen/pelvis and CT chest) documented tumor laterality, ascites, omental caking, peritoneal deposits, and distant metastases. Histopathological features included subtype and staging according to the International Federation of Gynecology and Obstetrics (FIGO) classification [9].

Treatment modalities were recorded, including upfront surgery versus neoadjuvant chemotherapy (NACT) followed by interval cytoreduction, number of chemotherapy cycles, and treatment response. Chemotherapy outcomes were evaluated using the Response Evaluation Criteria in Solid Tumors (RECIST 1.1) [10].

Laboratory data were retrieved from baseline investigations, including liver and kidney function, viral hepatitis screening, serum CA-125, and CBC with platelet indices [mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT), and platelet-to-lymphocyte ratio (PLR)].

Follow-Up and Outcomes

The enrolled patient cohort was subjected to a rigorous, long-term follow-up protocol to monitor for potential disease recurrence. The schedule dictated that follow-up visits were to occur every three months during the initial two years immediately post-treatment, with the frequency subsequently reduced to every six months thereafter. Each visit included a comprehensive assessment comprising a thorough physical examination, quantitative measurement of serum CA-125 levels, and relevant imaging studies to facilitate the early detection of disease progression. Disease-free survival (DFS), which served as a primary survival endpoint, was strictly defined as the time interval commencing from the completion of the initial definitive treatment and concluding at the point of documented disease recurrence. This recurrence was confirmed if established through biochemical (e.g., tumor marker elevation), radiological evidence, or a combination of both diagnostic modalities.

Ethical Considerations

The study protocol was granted approval by the Institutional Review Board (IRB) of Mansoura University. Due to the retrospective design of the investigation, the requirement for informed consent was formally waived. The investigators provided

assurance that the anonymity of all subjects would be rigorously maintained and that their identities would be protected from any unauthorized access. The entire study was conducted in strict adherence to the principles set forth in the Declaration of Helsinki and conformed to all relevant ethical guidelines for clinical research.

Statistical Analysis

All subsequent data analysis procedures were executed utilizing the IBM SPSS Statistics software, version 16. For continuous variables, the data were summarized using the mean ± standard deviation (SD) for those exhibiting a normal distribution, or the median for variables with non-normal distributions. Categorical variables were comprehensively summarized using frequencies and corresponding percentages.

The comparison of categorical variables between distinct groups was conducted using either the Chi-square test or the Fisher's exact test, with the selection governed by the adequacy of the expected frequencies within the contingency tables to ensure statistical validity. A critical aspect of the analysis involved survival estimation, where disease-free survival (DFS) was estimated utilizing the non-parametric Kaplan–Meier method. For all statistical tests performed, a two-sided P-value of <0.05 was prospectively established as the definitive threshold for defining statistical significance.

Platelet indices

Thrombocytosis was defined as platelet count >450 ×10^9/L. PLR was calculated as absolute platelet count divided by absolute lymphocyte count; the PLR cutoff was set at the cohort mean (PLR = X). MPV, PDW and PCT were recorded from the baseline CBC.

RESULTS

Baseline Clinical and Radiological Presentation

A total of 140 patients with epithelial ovarian cancer were included in the study. The mean age at diagnosis was 53.3 years. Abdominal pain was the most frequent presenting symptom (73.6%). Radiologically, bilateral adnexal masses were present in 46.4% of patient. Omental deposits were identified in 47.9% of cases, and ascites was present in 70.7%. Most women were overweight. Most patients manifested advanced disease (FIGO stage III in 52.8%). Among those with distant spread, pleural effusion was the most common metastatic finding, present in 55% Table 1.

Table 1. Baseline Clinical and Radiological Characteristics of the Study Cohort

Variable	n (%)
Mean age (years)	53.3 ± SD
BMI >25	111 (79.3)
Abdominal pain	103 (73.6)
Abdominal enlargement	43 (30.7)
Adnexal masses	
– Bilateral	65 (46.4)
– Left	61 (43.6)
– Right	14 (10.0)
Omental deposits	67 (47.9)
Ascites	99 (70.7)
Stage III (FIGO)	74 (52.8)
Pleural effusion (metastatic cases)	22 (55.0)

BMI (Boby Mass Index)

FIGO (The International Federation of Gynecology and Obstetrics). Most patients presented with advanced disease and unfavorable features such as ascites and omental deposits, reflecting the aggressive nature of EOC.

Surgery, Chemotherapy, and Pathological Outcomes

Of the cohort, 43.6% underwent upfront surgery, while 56.4% received neoadjuvant chemotherapy (NACT). Among those evaluable for response, 78.2% achieved complete or partial remission. One patient died before evaluation Table 2.

Table 2. Treatment Modalities and Response Outcomes (n = 140)

Variable	n (%)
Upfront surgery	61 (43.6)
Neoadjuvant chemotherapy	79 (56.4)
Median NACT cycles	4
Completed 6 cycles	34.6%
Response*	
– Complete/Partial remission	61 (78.2)
– Stable disease	11 (14.1)
– Progressive disease	6 (7.7)

*Excludes 1 patient who died before evaluation.

Most patients required neoadjuvant therapy, with a high overall response rate, although a minority demonstrated treatment resistance.

Platelet Indices and Clinicopathological Features

Elevated PLR and thrombocytosis were significantly associated with omental deposits. PLR was also strongly correlated with the presence of ascites, indicating its relationship with aggressive disease Table 3.

Table 3. PLR and Platelet Count in Relation to Clinicopathological Features

Feature	PLR below mean n (%)	PLR above mean n (%)	p-value	Normal platelets n (%)	Thrombocytosis n (%)	p-value
Omental deposits	57 (64.8)	31 (35.2)	0.0001	63 (55.3)	51 (44.7)	0.03
No omental deposits	16 (30.8)	36 (69.2)		7 (30.4)	16 (69.6)	
Ascites	35 (39.8)	53 (60.2)	0.0001	37 (32.5)	77 (67.5)	0.06
No ascites	6 (11.5)	46 (88.5)		3 (13.0)	20 (87.0)	

Platelet Indices and Treatment Response

Platelet indices (PDW, MPV, PCT, PLR) were not significantly associated with chemotherapy response, indicating their limited predictive value for short-term treatment outcomes Table 4.

Table 4. Platelet Indices and Chemotherapy Response (CR/PR vs. SD/PD)

Index	Below mean n (%)	Above mean n (%)	p-value
PDW	35 (62.5)	21 (37.5)	0.11
MPV	30 (61.2)	19 (38.8)	0.98
PCT	21 (42.0)	29 (58.0)	0.78
PLR	29 (47.5)	32 (52.5)	0.64
NACT cycles ≤3	14 (23.0)		0.58
NACT cycles >3	47 (77.0)		

Platelet Indices and Recurrence

Low PLR was significantly associated with reduced recurrence, confirming its prognostic role. Neither PCT nor thrombocytosis showed significant associations with recurrence risk Table 5.

Table 5. Recurrence According to Platelet Indices (excluding metastases at presentation and PD)

Variable	No Recurrence n (%)	Recurrence n (%)	p-value
PCT below mean	30 (61.2)	19 (38.8)	0.96
PCT above mean	21 (61.8)	13 (38.2)	
Normal PCT	6 (12.2)	5 (14.7)	0.89
Increased PCT	25 (51.0)	18 (52.9)	
Decreased PCT	18 (36.7)	11 (32.4)	
PLR below mean	41 (73.2)	23 (53.5)	0.042
PLR above mean	15 (26.8)	20 (46.5)	
Normal platelets	50 (92.6)	36 (83.7)	0.17
Thrombocytosis	4 (7.4)	7 (16.3)	

Survival Analysis

Kaplan–Meier analysis demonstrated that higher PCT, PLR, and platelet count were significantly associated with shorter disease-free survival Table 6.

Table 6. Disease-Free Survival by Platelet Indices (Kaplan–Meier Analysis)

Platelet Index	Effect on DFS
PCT	High PCT → shorter DFS
PLR	High PLR → shorter DFS
Platelet count	Thrombocytosis → shorter DFS

Platelet indices demonstrated significant prognostic value for disease-free survival, suggesting their role as accessible predictors of long-term outcomes in EOC.

DISCUSSION

Epithelial ovarian cancer (EOC) remains a major challenge in gynecologic oncology due to its frequent late presentation and poor survival outcomes[11].

In this study, we evaluated the prognostic significance of platelet indices, which are inexpensive and routinely available laboratory parameters, among 140 women diagnosed with EOC. Our findings demonstrated that elevated plateletcrit (PCT), mean platelet volume (MPV), and platelet-to-lymphocyte ratio (PLR) were significantly associated with aggressive disease features such as omental deposits and ascites. Thrombocytosis also correlated with omental involvement, while a lower PLR was protective against recurrence. Furthermore, Kaplan–Meier analysis showed that abnormal platelet indices were associated with inferior disease-free survival (DFS).

The strong association between altered platelet indices and adverse clinical features supports the concept that platelets actively contribute to tumor progression. Platelets are known to promote cancer development through multiple mechanisms, including stimulation of angiogenesis, protection of circulating tumor cells from immune surveillance, and facilitation of metastatic niche formation. Platelet-derived growth factors and cytokines such as VEGF, PDGF, and TGF-β contribute to tumor proliferation and invasion by enhancing stromal support and vascular remodeling[12,13]. These mechanisms may explain why elevated PCT, MPV, and PLR in our cohort were linked to the presence of ascites and omental deposits, features that are indicative of tumor spread.

Our results align with those of **Kemal *et al.*** who reported that increased MPV levels were associated with

EOC progression and could serve as a biomarker for monitoring disease activity[7].

Similarly, **Ma *et al.*** found that thrombocytosis and altered platelet parameters were associated with chemoresistance and poor prognosis in ovarian cancer patients[8]. Consistent with these studies, we found thrombocytosis significantly correlated with omental involvement, further reinforcing its role as a negative prognostic marker.

The prognostic value of PLR has been highlighted in several studies. **Raungkaewmanee *et al.*** demonstrated that elevated PLR predicted poor outcomes in EOC and was associated with advanced stage and suboptimal debulking[14]. Likewise, **Chon *et al.*** reported that elevated PLR independently predicted worse survival in advanced EOC [15]. Our findings support this evidence, showing that higher PLR was significantly associated with recurrence and inferior DFS, while lower PLR appeared protective. This relationship may reflect the dual effect of elevated platelets and reduced lymphocytes: thrombocytosis enhances tumor aggressiveness, whereas lymphopenia reflects impaired host immunity, together contributing to poorer survival outcomes.

Interestingly, platelet indices did not correlate with immediate chemotherapy response in our study. This observation suggests that while platelet indices reflect underlying tumor biology and host inflammatory status, they may not influence short-term sensitivity to chemotherapy. Instead, their prognostic value appears to be stronger for recurrence and survival outcomes, as supported by previous work from **Nakao *et al.*** and **Okunade *et al.*** who both reported thrombocytosis as an independent predictor of recurrence and reduced overall survival in ovarian cancer[12,13].

The mechanisms linking platelet activation to recurrence and survival are multifaceted. Activated platelets release microparticles and growth factors that promote epithelial-mesenchymal transition (EMT), angiogenesis, and metastasis[2]. Moreover, platelets sequester chemotherapeutic drugs, potentially reducing their efficacy, and contribute to a pro-thrombotic state that favors tumor progression. This may explain the persistent association between abnormal platelet indices and recurrence despite no significant correlation with initial chemotherapy response.

Our findings are also in agreement with meta-analyses such as that by **Zhu *et al.*** [16] who showed that systemic inflammatory markers including PLR and neutrophil-to-lymphocyte ratio (NLR) were robust prognostic indicators in ovarian cancer[14]. In contrast, some variability exists in the literature, particularly regarding PDW, where conflicting evidence has been reported. For example, **Qin *et al.*** [17] demonstrated that higher PDW was associated with unfavorable prognosis, whereas our data did not show a significant correlation between PDW and outcomes[12]. These discrepancies may be due to differences in patient populations, tumor stage distribution, and cutoff values used across studies.

Taken together, our study reinforces the growing body of evidence that platelet indices can serve as prognostic biomarkers in ovarian cancer. Their accessibility and low cost make them particularly attractive for use in resource-limited settings. Although not predictive of short-term chemotherapy response, these indices may help identify patients at higher risk of recurrence and poor survival who could benefit from closer monitoring or more aggressive therapeutic approaches.

CONCLUSION

The plateletcrit (PCT) score, mean platelet volume (MPV) score, and platelet-to-lymphocyte ratio (PLR) were all found to be significantly associated with the presence of omental deposits and ascites in patients diagnosed with epithelial ovarian cancer. Furthermore, there was a significant association detected between thrombocytosis and omental deposits. Conversely, a low PLR was significantly associated with a lower rate of disease recurrence.

LIMITATIONS

This study is retrospective and single-center which introduces potential selection and information bias. Cutoffs were derived from the study cohort and require external validation. Residual confounding by variables not captured in the dataset (e.g., comorbidities, medication such as antiplatelet agents) is possible. Future prospective studies and external validation cohorts are recommended to confirm these findings.

RECOMMENDATION

Our study's findings warrant the recommendation for future investigations with a larger patient sample size to accurately assess the association between various platelet indices and the clinico-pathological features of epithelial ovarian cancer, as well as their predictive value for the risk of recurrence.

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