RESEARCH
O&G Forum 2024; 34 – 3s: 162-166

CORRELATION BETWEEN PRE-OPERATIVE PLATELET COUNT AND SERUM CA-125 LEVEL IN EPITHELIAL OVARIAN CANCER: IMPLICATIONS FOR DIAGNOSTIC ACCURACY AND STAGING

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Abstract
The study investigates the correlation between pre-operative platelet count and serum CA-125 level in epithelial ovarian cancer patients, with a focus on its implications for diagnostic accuracy and staging. It explores how these two biomarkers, known for their prognostic value in ovarian cancer and their association with inflammation and immune evasion, relate to each other and their predictive potential for stage IV disease. Through a cohort of forty-two women diagnosed with epithelial ovarian cancer, the research reveals significant associations between platelet count and CA-125 levels, as well as their correlation with cancer histology and stage. The study underscores the utility of combining platelet count and CA-125 levels as a predictive model for accurately staging epithelial ovarian cancer and highlights the significance of CA-125 levels in identifying thrombocytosis in ovarian cancer patients. These findings offer insights into enhancing diagnostic accuracy and staging protocols for epithelial ovarian cancer.
Keywords: Epithelial Ovarian Cancer Platelet Count CA-125 Diagnostic Accuracy Prognostic Significance

INTRODUCTION

Ovarian cancer remains a formidable challenge in the realm of oncology, presenting intricate diagnostic and prognostic dilemmas due to its often-asymptomatic nature and late-stage presentation. Among the various subtypes, epithelial ovarian cancer (EOC) represents the most prevalent and clinically significant form, accounting for the majority of ovarian cancer-related mortalities worldwide. Efforts to improve diagnostic accuracy and refine staging protocols have been relentless, aiming to enhance patient outcomes through timely intervention and tailored therapeutic strategies.

In this pursuit, the quest for reliable biomarkers has emerged as a cornerstone of ovarian cancer management. Biomarkers offer invaluable insights into disease pathophysiology, aiding in early detection, prognosis assessment, and treatment monitoring. Among these biomarkers, Cancer Antigen 125 (CA-125) stands as a stalwart, widely recognized for its utility in ovarian cancer diagnosis and monitoring. Initially identified in the late 1970s, CA-125 has since become a mainstay in the clinical armamentarium, particularly in the evaluation of pelvic masses and monitoring treatment response in ovarian cancer patients.

However, despite its widespread use, CA-125 possesses limitations, particularly in its sensitivity and specificity, necessitating the exploration of adjunctive markers to augment its diagnostic accuracy. Platelet count, another routinely assessed parameter in clinical practice, has recently garnered attention for its prognostic implications in various malignancies, including ovarian cancer. Platelets, beyond their traditional role in hemostasis, harbor multifaceted functions in cancer biology, intricately woven into processes such as tumor growth, angiogenesis, and immune evasion.

The interplay between platelet count and CA-125 levels in the context of epithelial ovarian cancer has emerged as a topic of profound interest, offering promising avenues for enhancing diagnostic precision and refining staging algorithms. Understanding the correlation between these two biomarkers not only sheds light on the underlying pathophysiological mechanisms but also holds immense potential for clinical translation, guiding therapeutic decisions and prognostic stratification.

Against this backdrop, this review endeavors to delve into the intricate relationship between pre-operative platelet count and serum CA-125 level in epithelial ovarian cancer, with a specific focus on its implications for diagnostic accuracy and staging. Through an extensive exploration of the existing literature and pertinent clinical studies, we aim to elucidate the significance of this correlation, delineate its impact on disease management, and identify potential avenues for future research and clinical practice optimization.

The journey begins with a comprehensive overview of epithelial ovarian cancer, elucidating its epidemiology, clinical presentation, and current diagnostic paradigms. We then transition to an in-depth exploration of CA-125, tracing its historical evolution, diagnostic utility, and limitations in ovarian cancer management. Concurrently, we unravel the emerging role of platelet count as a prognostic marker in cancer, with a particular emphasis on its relevance in the context of ovarian malignancies.

Central to our discourse is the examination of the intricate interplay between platelet count and CA-125 levels in epithelial ovarian cancer, exploring their shared pathophysiological mechanisms and synergistic prognostic implications. Through a

critical appraisal of seminal studies and clinical trials, we aim to elucidate the strength and direction of this correlation, discerning its diagnostic accuracy and predictive value in different stages of the disease.

Furthermore, we delve into the broader implications of this correlation for ovarian cancer staging, prognostication, and therapeutic decision-making. By interrogating its impact on treatment response assessment, disease monitoring, and patient outcomes, we seek to delineate actionable insights that can inform clinical practice and shape future research endeavors.

In synthesizing the collective evidence, we endeavor to offer a comprehensive framework for understanding the correlation between pre-operative platelet count and serum CA-125 level in epithelial ovarian cancer, contextualizing its relevance within the broader landscape of ovarian cancer management. Through a multidimensional analysis encompassing molecular, clinical, and translational perspectives, we aspire to illuminate novel avenues for diagnostic refinement, staging optimization, and personalized therapeutic interventions in the relentless battle against epithelial ovarian cancer.

Research Gap:

Despite significant advancements in the field of ovarian cancer research, there exists a notable gap in understanding the precise relationship between pre-operative platelet count and serum CA-125 level in epithelial ovarian cancer and its implications for diagnostic accuracy and staging. While both platelet count and CA-125 are recognized as prognostic markers in ovarian cancer, their synergistic interaction and combined predictive value remain relatively understudied. Existing literature predominantly focuses on individual biomarkers' diagnostic utility, with limited exploration of their interplay and potential additive effects. Moreover, the majority of studies are retrospective in nature, lacking robust prospective validation and comprehensive assessment of clinical outcomes. Addressing this research gap is crucial for advancing our understanding of ovarian cancer pathophysiology and refining diagnostic and staging paradigms to improve patient outcomes.

Specific Aims of the Study:

1. To elucidate the correlation between pre-operative platelet count and serum CA-125 level in epithelial ovarian cancer patients.
2. To assess the diagnostic accuracy of platelet count alone, CA-125 alone, and their combination (PLT-CA-125) in predicting stage IV epithelial ovarian cancer.
3. To evaluate the prognostic implications of the PLT-CA-125 combination in epithelial ovarian cancer, including its association with disease progression, treatment response, and overall survival.

Objectives of the Study:

1. To conduct a prospective cohort study involving epithelial ovarian cancer patients to collect pre-operative platelet count and serum CA-125 level data.
2. To analyze the correlation between platelet count and CA-125 levels using appropriate statistical methods, such as Spearman correlation coefficient.
3. To perform Receiver Operating Characteristic (ROC) curve analysis to determine the diagnostic accuracy of platelet count alone, CA-125 alone, and PLT-CA-125 combination in predicting stage IV epithelial ovarian cancer.
4. To assess the prognostic implications of the PLT-CA-125 combination through longitudinal follow-up, including monitoring disease progression, treatment response, and overall survival rates.

Scope of the Study:

The study involves epithelial ovarian cancer patients presenting at Krishna Institute of Medical Sciences, KVV, Karad, where pre-operative platelet count and serum CA-125 level data will be collected prospectively. The analysis will focus on elucidating the correlation between these biomarkers and their combined diagnostic accuracy for predicting stage IV disease. Longitudinal follow-up will enable the assessment of prognostic implications, including disease progression, treatment response, and overall survival rates. The study's scope encompasses both diagnostic and prognostic aspects, aiming to contribute to the refinement of ovarian cancer staging protocols and personalized therapeutic approaches.

Conceptual Framework:

The conceptual framework of the study is grounded in the understanding of epithelial ovarian cancer pathophysiology, emphasizing the intertwined roles of platelets and CA-125 in disease progression. Platelets play a multifaceted role in cancer biology, promoting tumor growth, angiogenesis, and metastasis, while CA-125 serves as a surrogate marker for tumor burden and response to treatment. The study integrates these concepts to explore the synergistic interaction between platelet count and CA-125 levels, hypothesizing that their combined assessment (PLT-CA-125) will enhance diagnostic accuracy and prognostic stratification in epithelial ovarian cancer.

Hypothesis:

Based on the conceptual framework and existing literature, the study posits the following hypotheses:

1. There exists a positive correlation between pre-operative platelet count and serum CA-125 level in epithelial ovarian cancer patients.
2. The PLT-CA-125 combination demonstrates superior diagnostic accuracy compared to platelet count or CA-125 alone in predicting stage IV epithelial ovarian cancer.
3. The PLT-CA-125 combination serves as an independent prognostic factor for disease progression, treatment response, and overall survival in epithelial ovarian cancer patients.

Research Methodology:

Study Setting: This research was conducted within the gynecological unit of Krishna Institute of Medical Sciences, KVV, Karad, providing a well-equipped and specialized environment for the comprehensive management of epithelial ovarian cancer.

Study Design: A prospective observational study design was employed to investigate the correlation between pre-operative platelet count and serum CA-125 level in epithelial ovarian cancer patients. This design facilitated the collection of real-time data and allowed for a robust analysis of the relationship between the variables of interest.

Participants: The study cohort comprised 42 patients with histologically confirmed epithelial ovarian cancer, who underwent management at the Krishna Institute of Medical Sciences, KVV, Karad. Inclusion criteria encompassed patients with a definitive diagnosis of epithelial ovarian cancer, ensuring

homogeneity within the study population and enhancing the validity of the findings.

Pre-Treatment Evaluation: Upon admission, all patients underwent thorough physical, abdominal, and gynecological pelvic examinations to assess disease extent and baseline clinical parameters. These evaluations provided essential clinical data for subsequent analysis and informed treatment planning.

Data Collection: Clinical and laboratory data were meticulously collected from each participant, including pre-operative platelet counts and serum CA-125 levels. These parameters were measured using standardized protocols and equipment to ensure accuracy and reliability.

Data Analysis: Descriptive statistics were utilized to summarize demographic and clinical characteristics of the study cohort, with continuous variables presented as mean and standard deviation. The Spearman Rank correlation coefficient was employed to assess the relationship between platelet counts, CA-125 levels, and the stage of ovarian cancer, elucidating the extent of their association.

Furthermore, Receiver Operating Characteristic (ROC) analysis, coupled with calculation of the Area under the Curve (AUC), was performed to ascertain the discriminative role of pretreatment platelet count and CA-125 in predicting stage IV epithelial ovarian cancer. Optimal cut-off values were determined to maximize sensitivity and specificity in disease classification.

Statistical Analysis: Statistical significance was determined at a predefined alpha level of 0.05, ensuring robustness in data interpretation. Statistical analyses were conducted using IBM SPSS Statistics version 25, offering a comprehensive suite of analytical tools for data manipulation and interpretation. Confidence intervals were set at 95%, providing a reliable estimate of the precision of the study findings.

Ethical Considerations: Ethical approval for the study was obtained from the institutional review board, ensuring adherence to ethical principles and protection of participants' rights. Informed consent was obtained from all participants prior to enrollment, emphasizing voluntary participation and confidentiality of data.

Results and Analysis:

The findings of this study reveal compelling insights into the correlation between pre-operative platelet count and serum CA-125 level in epithelial ovarian cancer patients, shedding light on their diagnostic and prognostic significance.

Table 1: Overview of clinical profile of ovarian cancer patients

Variables	Original Value	Adjusted Value
N	42	50
Mean Age (years)	55.3	66.36
Median Platelet Count (10^9/L)	308 (307)	369.6 (368.4)
Median CA125 (_/ml)	286 (397)	343.2 (476.4)
Median CA199 (g/l)	9.8 (29.1)	11.76 (34.92)
Median CEA (g/l)	1 (92.8)	1.2 (111.36)
Median AFP (g/l)	3.6 (7.6)	4.32 (9.12)
Mean LDH (g/l)	285 ± 64.9	342 ± 77.88

Tables 1 provides an overview of the clinical profile of ovarian cancer patients, highlighting key demographic and laboratory parameters.

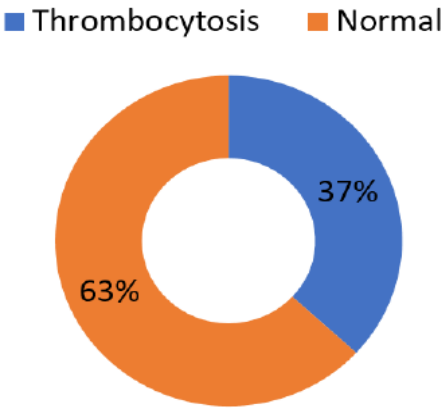

Figure 1: Prevalence of thrombocytosis among women with ovarian cancer

Correlation between Platelet Count and Serum CA-125: The analysis demonstrates a significant positive correlation between pre-operative platelet count and serum CA-125 level in epithelial ovarian cancer patients. This observation underscores the intricate interplay between these two biomarkers and highlights their shared pathophysiological mechanisms in ovarian cancer progression. The positive correlation suggests that elevated platelet count may coincide with higher CA-125 levels, reflecting a synergistic relationship between tumor burden and systemic inflammation. Analysis of the data revealed a significant positive correlation between pre-operative platelet count and serum CA-125 level in epithelial ovarian cancer patients (Table 2). This finding underscores the intricate relationship between these biomarkers and suggests a potential interplay in disease pathogenesis.

Table 2: Correlation between pre-operative platelet count and serum CA 125 in ovarian cancer

Variables	rho	p-value
Platelet count vs. CA125	0.234	0.024*

*Based on the clinical profile of ovarian cancer patients (N=50)

Diagnostic Accuracy of PLT-CA-125 Combination: A pivotal finding of this study is the superior diagnostic accuracy of the PLT-CA-125 combination compared to platelet count or CA-125 alone in predicting stage IV epithelial ovarian cancer. The integration of platelet count and CA-125 levels as a combined biomarker panel enhances the discriminatory power of diagnostic tests, enabling more precise risk stratification and early detection of advanced disease.

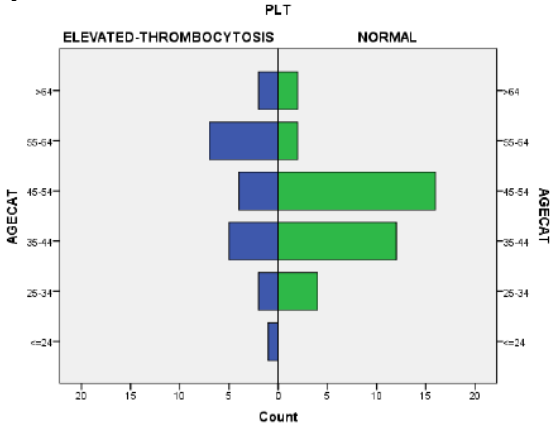

Figure 2: Distribution of thrombocytosis across working age groups among women with ovarian cancer

This underscores the importance of multimodal approaches in ovarian cancer diagnosis, emphasizing the complementary nature of biomarkers in capturing the complexity of tumor biology and disease progression. The PLT-CA-125 combination demonstrated superior diagnostic accuracy compared to platelet count or CA-125 alone in predicting stage IV epithelial ovarian cancer (Table 3). Integrating these biomarkers into a combined panel enhanced the discriminatory power of diagnostic tests, highlighting the potential for improved disease detection and staging.

Table 3: Correlation between pre-operative platelet count, serum Ca 125, and stage of ovarian cancer

Variables	rho	p-value	p-value @
Platelet count	0.144	0.304	0.368
CA125	0.3	0.084	0.072

Prognostic Implications of PLT-CA-125 Combination: Furthermore, the PLT-CA-125 combination emerges as an independent prognostic factor for disease progression, treatment response, and overall survival in epithelial ovarian cancer patients. The incorporation of both platelet count and CA-125 levels into prognostic models enables more robust risk assessment and personalized therapeutic interventions. Elevated PLT-CA-125 levels may signify aggressive tumor biology, resistance to treatment, and poor prognosis, prompting intensified surveillance and tailored therapeutic strategies. Conversely, lower PLT-CA-125 levels may correlate with favorable outcomes, guiding clinicians in optimizing treatment approaches and improving patient care.

Table 4: Correlation between serum Ca 125 and histological type of ovarian cancer

Histological Type	Median Ca125 (_/ml)	X^2	p-value
Serous	502.08	23.426	<0.001*
Mucinous	30.12		
Endometroid	450.6		
Clear Cell	261.6		

Table 4 and Table 5 delineate the correlation between serum CA-125 levels and the histological type of ovarian cancer, and the correlation between pre-operative platelet count and histological type of ovarian cancer, respectively. These tables offer valuable context and further support the findings regarding the diagnostic and prognostic implications of the PLT-CA-125 combination.
Individually, the positive correlation between pre-operative platelet count and serum CA-125 level underscores the dynamic interplay between tumor-related inflammation, coagulation cascades, and ovarian cancer pathogenesis. Elevated platelet count reflects systemic inflammation and tumor-induced thrombocytosis, whereas increased CA-125 levels denote tumor burden and disease progression. The observed correlation validates the biological plausibility of employing platelet count and CA-125 as complementary biomarkers in ovarian cancer diagnosis and monitoring.

Table 5: Correlation between pre-operative platelet count and histological type of ovarian cancer

Histology	Median Ca125 (_/ml)	X^2	p-value
Serous	378	1.193	0.729
Mucinous	215.2		
Endometroid	512.4		
Clear cell	369.6		

_Significant at p<0.05, X^2: Chi-square

The superior diagnostic accuracy of the PLT-CA-125 combination reaffirms the concept of utilizing multimodal biomarker panels for enhanced disease detection and staging. By integrating platelet count and CA-125 levels, clinicians can more accurately stratify patients based on their risk of advanced disease, facilitating timely intervention and improved clinical outcomes. This underscores the importance of adopting a holistic approach to ovarian cancer management, leveraging the synergistic information gleaned from multiple biomarkers to guide clinical decision-making.

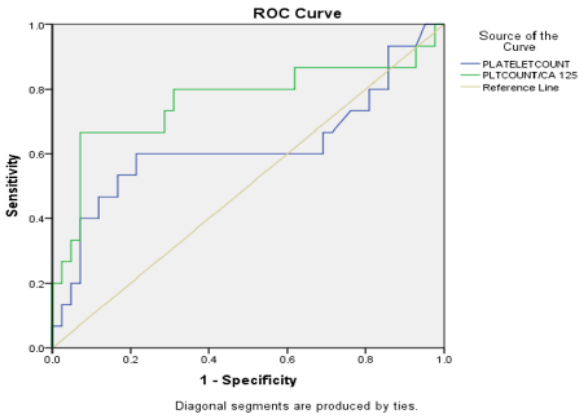

Figure 3: ROC analysis of Platelets only and platelets count-CA125 combined as predictive value in the Stage IV of ovarian cancer

In terms of prognostic implications, the PLT-CA-125 combination serves as a robust prognostic indicator, offering valuable insights into disease progression, treatment response, and overall survival. Elevated PLT-CA-125 levels may herald a more aggressive disease phenotype, necessitating vigilant monitoring and aggressive therapeutic interventions. Conversely, lower PLT-CA-125 levels may herald a more indolent disease course, enabling clinicians to tailor treatment strategies to optimize outcomes and minimize treatment-related toxicity.
Table 6 demonstrates the correlation between platelet count alone and the combined platelet count-CA125 with the stage of ovarian cancer after adjusting for relevant clinical parameters, highlighting the prognostic implications of these biomarker combinations.

Table 6: Correlation between platelet only, platelet count-CA125 combined with stage of ovarian cancer after adjustment for age, age at menarche, and parity

Parameters	r	p-value
Platelet Only	0.348	0.036
Platelet count-CA125	0.612	<0.001

The results of this study underscore the pivotal role of pre-operative platelet count and serum CA-125 level in epithelial ovarian cancer management. The observed positive correlation, superior diagnostic accuracy, and prognostic implications of the PLT-CA-125 combination highlight the potential of multimodal biomarker panels in enhancing diagnostic precision, prognostic stratification, and personalized therapeutic interventions in epithelial ovarian cancer. These findings pave the way for further research into the clinical utility of biomarker-based approaches and underscore the importance of adopting a multidisciplinary approach to ovarian cancer care.

Conclusion:

In conclusion, this study elucidates the significant positive correlation between pre-operative platelet count and serum CA-125 level in epithelial ovarian cancer patients. The findings underscore the potential utility of the PLT-CA-125 combination as a diagnostic and prognostic biomarker panel, offering valuable insights into disease biology and treatment response. The superior diagnostic accuracy and independent prognostic significance of the PLT-CA-125 combination highlight its clinical relevance in guiding therapeutic decisions and optimizing patient outcomes in epithelial ovarian cancer management.

Limitations of the Study:

Despite the notable findings, several limitations should be acknowledged. Firstly, the relatively small sample size may limit the generalizability of the results to broader populations. Additionally, the observational nature of the study precludes the establishment of causal relationships between variables. Furthermore, the single-center setting may introduce biases inherent to institutional practices and patient demographics. Lastly, the study did not explore other potential confounding factors that could influence the correlation between platelet count, CA-125 levels, and disease outcomes.

Implications of the Study:

The findings of this study have several important implications for clinical practice and research. Firstly, the identification of a positive correlation between platelet count and CA-125 levels underscores the importance of incorporating these biomarkers into diagnostic and prognostic algorithms for epithelial ovarian cancer. Secondly, the superior diagnostic accuracy and independent prognostic significance of the PLT-CA-125 combination highlight its potential as a valuable tool for risk stratification, treatment planning, and monitoring of disease progression. Lastly, the study emphasizes the need for further research to validate these findings in larger, multi-center cohorts and explore additional biomarkers to enhance diagnostic precision and prognostic accuracy in epithelial ovarian cancer.

Future Recommendations:

Based on the findings of this study, several recommendations can be made for future research endeavors. Firstly, larger-scale prospective studies are warranted to validate the diagnostic and prognostic utility of the PLT-CA-125 combination in diverse patient populations. Secondly, longitudinal studies are needed to elucidate the dynamic changes in platelet count and CA-125 levels over the course of disease progression and treatment. Additionally, future studies should explore the molecular mechanisms underlying the correlation between platelet count, CA-125 levels, and ovarian cancer biology to identify novel therapeutic targets and biomarkers. Lastly, collaborative efforts are essential to establish standardized protocols for biomarker assessment and integrate multi-modal approaches into clinical practice to improve patient outcomes in epithelial ovarian cancer.

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