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## Original Research Article

# Clinicopathological significance of preoperative thrombocytosis in patients with epithelial ovarian cancer

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## ABSTRACT

**Background:** Reactive thrombocytosis is reported in a variety of solid tumors. A few studies have documented preoperative thrombocytosis in ovarian cancer.

**Methods:** This was a cross-sectional study conducted in the Department of Gynaecological Oncology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, during January to December 2019. A total of 94 patients with epithelial ovarian cancer between 18-70 years of age who underwent primary surgical treatment were included in this study. Chi-square tests were done to see the significance of differences between the two groups where  $p < 0.05$  considered as the level of significance with 95% CI.

**Results:** The mean age was  $45.39 \pm 13.23$  years in the thrombocytosis and  $48.98 \pm 15.46$  years in without thrombocytosis group with a range of 18 to 70 years ( $p = 0.231$ ). The difference in education and occupation were statistically significant ( $p < 0.05$ ) between the two groups. The mean Hb% was  $10.02 \pm 1.47$  (gm/dl) in thrombocytosis and  $11.15 \pm 1.52$  (gm/dl) without thrombocytosis group. The difference was statistically significant ( $p < 0.001$ ) between two groups. The study showed that 30 (75.0%) patient's serum CA-125 was  $> 500$  in the thrombocytosis group and 9 (16.7%) in the without thrombocytosis group ( $p = 0.001$ ), OR=15.0, 95.0% CI=4.92 to 47.72,  $p = 0.001$ . Optimal cytoreduction between two groups were observed statistically significant ( $p = 0.004$ ), OR=3.49, 95.0% CI=1.33 to 9.28. The difference of grade of tumor observed statistically significant between the groups ( $p = 0.022$ ). The 11 (27.5%) patients had lymph node metastasis in thrombocytosis group and 6 (11.1%) in without thrombocytosis, OR=3.03, 95.0% CI=0.91 to 10.48,  $p = 0.022$ . The OR of developing lymph node metastasis was 3.03 times higher in the thrombocytosis group.

**Conclusions:** Thrombocytosis was commonly detected in preoperative evaluation of women diagnosed with epithelial ovarian cancer. Anemia, higher serum CA-125 level  $> 500$ , sub-optimal cytoreduction, advanced stage disease, higher grade tumor, and lymphnode metastasis were significantly more frequent in patients with thrombocytosis.

**Keywords:** Epithelial ovarian cancer, Thrombocytosis, CA-125

## INTRODUCTION

Ovarian cancer is a rapidly progressive and lethal disease. It is the 5th leading cause of cancer death among women in the world.<sup>1</sup> Due to difficulties in early detection, diagnosis, and treatment, the overall survival (OS) of patients with ovarian cancer is poor.<sup>2</sup> According to Globocan 2020, ovarian cancer is responsible for 314000 new cases and 207000 cancer deaths that occurred globally in 2020.<sup>3</sup> Ovarian cancer lacks a detectable pre-invasive stage that can be reliably evaluated by screening on a population level.<sup>4</sup> Despite dramatic improvements in cytoreductive surgery and platinum-based chemotherapy that have revolutionized the management of OC patients, the clinical outcome of OC remains unsatisfactory.<sup>5</sup> Over 75% of patients are diagnosed in the advanced stages (stages III and IV) and the 5-year survival rate is less than 30%.<sup>6</sup>

Thrombocytosis is defined as an elevated platelet counts above  $400 \times 10^9/L$ .<sup>7</sup> The association of thrombocytosis with malignancies has been known for more than 100 years, reported by Reiss in 1872 initially. Many solid tumors such as lung, colon, gastric, pancreatic and renal cell carcinoma have been detected accompanied by thrombocytosis.<sup>8-10</sup> Gynaecological malignancies also shown to be associated with thrombocytosis were endometrial, vulvar, and cervical cancer.<sup>11-13</sup> Internal scholars have reported platelet count increased may be the first symptom of carcinoma without any clinical character.<sup>14</sup> Platelets are associated with cancer progression, invasion, and metastasis.<sup>17</sup> Platelets release some growth factors i.e. platelet-derived growth factor, platelet factor 4, transforming growth factor $\beta$ , vascular endothelial growth factor, and thrombospondin, which function as a potent mitogen or adhesive glycoprotein for different cell types including the ovarian surface epithelium.<sup>4</sup> These growth factors can stimulate ovarian tumor cells proliferation and adhesion to other cells leading to tumor growth and metastases, respectively.<sup>16</sup> Using an orthotopic mouse model of ovarian cancer, platelet transfusion resulted in increased tumor growth, and platelets were demonstrated to protect cancer cells from apoptosis.<sup>17</sup> The persistent paracrine cycle in which platelets promote tumor cell proliferation and sustain cancer cell viability may influence cancer progression.<sup>18</sup> Additionally, paraneoplastic thrombocytosis has recently been implicated in playing a causal factor in the poor prognosis of EOC.<sup>19</sup> The rate of pre-operative thrombocytosis in epithelial ovarian cancer has been reported to range from 31-42%.<sup>15</sup>

Approximately 90% of ovarian cancer are of epithelial origin. Known prognostic factors for EOC include age, stage, histological type, grade, and optimal cytoreduction.<sup>20</sup> Various molecular markers have been proposed for early diagnosis and prognosis of ovarian cancer, but most are not ready to be included as a part of the routine diagnostic algorithm, because they still lack sensitivity and specificity. CA-125 is the most useful and studied molecular marker in detecting epithelial ovarian

cancer. New studies have shown that inflammatory markers and blood cells may have a relationship with epithelial ovarian cancer. Serologic measurements including carbohydrate antigen (CA-125), hemoglobin and platelet levels have emerged as potential pre-operative predictors of outcome. With this background, this study was performed to determine the number of thrombocytosis in patients with epithelial ovarian cancer and to evaluate its significance with clinical and pathological prognostic factors such as CA-125, presence of ascites, optimal cytoreduction, lymphnode metastasis, histology, stage of the disease and grade of the tumor.<sup>21</sup>

## Objective

### General objective

The general objective was to observe the clinicopathological significance of preoperative thrombocytosis in patients with epithelial ovarian cancer.

### Specific objectives

Specific objectives were to measure total platelet count and CA-125 in study population, also to assess the level of ascites, optimal cytoreduction, histological type, stage, grade, and lymphnode metastasis in patients with and without thrombocytosis and to compare these clinicopathological factors between two groups.

## METHODS

A cross-sectional comparative study was conducted in the department of gynaecological oncology, Bangabandhu Sheikh Mujib medical university, Dhaka, from January to December 2019. A total of 94 patients with epithelial ovarian cancer between 18-70 years of age who underwent primary surgical treatment were included in this study. After recruitment, pre-operative complete blood count and CA-125 were done in every patient 7 days before surgery. Complete surgical staging and cytoreductive surgery were performed when the frozen section biopsy report was positive for malignancy. The histopathology report was reviewed prospectively. Histopathologically confirmed epithelial ovarian cancer was included in this study. All clinical information including the presence of ascites, optimal cytoreduction, stage of the disease, grade and histology of the tumor, lymphnode metastasis were abstracted in the data collection sheet. Patients were grouped into two according to the presence or absence of thrombocytosis. The purposive sampling method was used in this study. Informed written consent was taken from those who agree to participate. Ethical committee clearance was obtained from the institution. A thorough clinical examination was done of all the subjects. For continuous variables, distributions were expressed by mean and standard deviation. Mean comparisons between two groups were done by unpaired t-test. For qualitative variables, distributions were expressed by frequency and percentages. Chi-square tests were done to see the

significance of differences between two groups. Odds ratio (OR) and 95% confidence interval were also estimated for the outcome. The statistical analysis was performed using the SPSS software version 22.0. There was minimum physical, psychological, social, and legal risk during the collection of blood and physical examinations, and confidentiality was maintained.

### Inclusion criteria

Histologically confirmed case of epithelial ovarian cancer between 18 to 70 years of age. Patients who had given consent to participate in the study were included in the study.

### Exclusion criteria

Patients with H/O acute inflammatory disease, autoimmune disorders, myeloproliferative disorders, recurrent malignancies, splenectomy, patients undergoing neoadjuvant chemotherapy, and patients who did not give consent to participate in the study were excluded.

## RESULTS

It was observed that there were no significant differences between two groups in terms of age, marital status, socioeconomic status, parity, and menopausal status. The difference in education and occupation were statistically significant ( $p < 0.05$ ) between two groups (Table 1).

In this study, (62.5%) of patients had Hb% 8-10 (g/dl) in thrombocytosis and (31.5%) without thrombocytosis. The mean Hb% was  $10.02 \pm 1.47$  (g/dl) in thrombocytosis and  $11.15 \pm 1.52$  (g/dl) without thrombocytosis. The difference was statistically significant ( $p < 0.05$ ) between 2 groups (Table 2).

The study showed that 30 (75.0%) patient's serum CA-125 was  $>500$  in thrombocytosis group and 9 (16.7%) in without thrombocytosis group. Serum CA-125  $>500$  had

significantly ( $p < 0.05$ ) increased risk 15.0 times to develop thrombocytosis with (95.0% C.I. 4.92 to 47.72) (Table 3).

Table 4 shows 11 (27.5%) patients had grade 1, followed by 10 (25%) grade 2, 19 (47.5%) grade 3 ascites in Thrombocytosis group while in without Thrombocytosis group had 11 (20.4%) grade 1, followed by 11 (20.4%) grade 2, and 32 (59.3%) grade 3 ascites ( $p = 0.466$ ). The difference was not statistically significant ( $p < 0.05$ ) between two groups.

It was observed that 21 (52.5%) patients had sub-optimal cytorreduction ( $\geq 1$  cm) in thrombocytosis group and 13 (24.1%) in without thrombocytosis group. The OR of sub-optimal cytorreduction was 3.49 (95.0% CI=1.33 to 9.28) times higher in thrombocytosis group. The difference was statistically significant ( $p < 0.05$ ) between two groups (Table 5).

It was observed that 25 (62.5%) patients were in stage III/IV in the thrombocytosis group and 12 (22.2%) in without thrombocytosis group. The difference between advance stage (III and IV) and early stage (I and II) were statistically significant ( $p < 0.05$ ) between two groups (Table 6).

Table 7 shows 14 (35.0%) patients had grade-1 tumor, in Thrombocytosis group, followed by 21 (52.5%), grade-2 and 5 (12.5%), grade-3 while in without Thrombocytosis group, 25 (46.3%) had grade-1 tumor followed by 14 (25.9%), grade-2 and 15 (27.8%), grade-3. The difference of grade of tumor observed statistically significant between two groups ( $p = 0.022$ ).

Table 8 shows 11 (27.5%) patients had lymphnode metastasis in thrombocytosis group and 6 (11.1%) in without thrombocytosis. The OR of developing lymphnode metastasis was 3.03 times higher in the thrombocytosis group. The difference was statistically significant ( $p < 0.05$ ) between two groups.

**Table 1: Socio-demographic characteristics of the study population, (n=94).**

Socio-demographic characteristics, (N)	Thrombocytosis (PLT $>400 \times 10^9/l$ ), n=40 (%)	Without thrombocytosis (PLT $\leq 400 \times 10^9/l$ ), n=54 (%)	P value
<b>Age (years)</b>			
$\leq 30$ (22)	6 (15)	16 (29.6)	
31-40 (14)	7 (17.5)	7 (13)	
41-50 (21)	5 (12.5)	16 (29.6)	
51-60 (29)	17 (42.5)	12 (22.2)	
61-70 (8)	5 (12.5)	3 (5.6)	
Mean $\pm$ SD (47.19 $\pm$ 14.34)	45.39 $\pm$ 13.23	48.98 $\pm$ 15.46	<sup>a</sup> 0.231 <sup>ns</sup>
Range (min-max) (18-70)	18-70	18-70	
<b>Education</b>			
Nil (29)	13 (32.5)	16 (29.6)	
Primary (29)	15 (37.5)	14 (25.9)	
SSC (17)	5 (12.5)	12 (22.2)	
HSC (10)	7 (17.5)	3 (5.6)	<sup>b</sup> 0.017 <sup>s</sup>
Graduate (9)	0 (0)	9 (16.7)	

Continued.

Socio-demographic characteristics, (N)	Thrombocytosis (PLT>400×10 <sup>9</sup> /l), n=40 (%)	Without thrombocytosis (PLT≤400×10 <sup>9</sup> /l), n=54 (%)	P value
Marital status			
Yes (83)	37 (92.5)	46 (85.2)	b0.275 <sup>ns</sup>
No (11)	3 (7.5)	8 (14.8)	
Socio economic status			
Low income (45)	22 (55)	23 (42.6)	b0.284 <sup>ns</sup>
Lower middle (36)	14 (35)	22 (40.7)	
Upper middle (13)	4 (10)	9 (16.7)	
Occupation			
Housewife (75)	36 (90)	39 (72.2)	b0.034 <sup>s</sup>
Day labour (2)	2 (5)	0 (0)	
Service holder (5)	1 (2.5)	4 (7.4)	
Students (12)	1 (2.5)	11(20.4)	
Parity			
Nuliparous (17)	2 (5)	15 (27.8)	b0.057 <sup>ns</sup>
Multiparous (77)	38 (95)	39 (72.2)	
Menopausal status			
Yes (42)	18 (45)	24 (44.4)	b0.853 <sup>ns</sup>
No (52)	22 (55)	30 (55.6)	

PLT=Platelet count, s=significant, ns=not significant, <sup>a</sup>p value reached from Unpaired t-test, <sup>b</sup>p value reached from the Chi-square test.

**Table 2: Distribution of the study patients by Hb%, (n=94).**

Hemoglobin, (gm/dl) (N)	Thrombocytosis (PLT>400×10 <sup>9</sup> /l), n=40 (%)	Without thrombocytosis (PLT≤400×10 <sup>9</sup> /l), n=54 (%)	P value
10-12 (51)	14 (35)	37 (68.5)	0.001 <sup>s</sup>
8-10 (42)	25 (62.5)	17 (31.5)	
<8 (1)	1 (2.5)	0 (0)	
Mean±SD (10.58±1.49)	10.02±1.47	11.15±1.52	

PLT=Platelet count, s=significant, p value reached from unpaired t-test.

**Table 3: Distribution of the study patients by serum CA-125, (n=94).**

Serum CA-125, (N)	Thrombocytosis (PLT>400×10 <sup>9</sup> /l), n=40 (%)	Without thrombocytosis (PLT≤400×10 <sup>9</sup> /l), n=54 (%)	OR (95% CI)	P value
>500 (39)	30 (75)	9 (16.7)	15 (4.92-47.72)	0.001 <sup>s</sup>
≤500 (55)	10 (25)	45 (83.3)		

PLT= Platelet count, s=significant, p value reached from the Chi-square test.

**Table 4: Distribution of the study patients by ascites volume, (n=94).**

Ascites volume, (N)	Thrombocytosis (PLT>400×10 <sup>9</sup> /l), n=40 (%)	Without thrombocytosis (PLT≤400×10 <sup>9</sup> /l), n=54 (%)	P value
Grade 1 (22)	11 (27.5)	11 (20.4)	0.466 <sup>ns</sup>
Grade 2 (21)	10 (25)	11 (20.4)	
Grade 3 (51)	19 (47.5)	32 (59.3)	

PLT=Platelet count, Ns=not significant, p value reached from the Chi-square test.

**Table 5: Distribution of the study patients by optimal cytoreduction, (n=94).**

Optimal cytoreduction, (N)	Thrombocytosis (PLT>400×10 <sup>9</sup> /l), n=40 (%)	Without thrombocytosis (PLT≤400×10 <sup>9</sup> /l), n=54 (%)	OR (95% CI)	P value
Sub-optimal (≥1 cm) (34)	21 (52.5)	13 (24.1)	3.49 (1.33-9.28)	0.004 <sup>s</sup>
Optimal (<1 cm) (60)	19 (47.5)	41 (75.9)		

PLT=Platelet count. s=significant, p value reached from the Chi-square test

**Table 6: Distribution of the study patients by stage of the tumor, (n=94).**

Stage of the tumor, (N)	Thrombocytosis (PLT>400×10 <sup>9</sup> /l), n=40 (%)	Without thrombocytosis (PLT≤400×10 <sup>9</sup> /l), n=54 (%)	P value
<b>I/ II (57)</b>	15 (37.5)	42 (77.8)	0.001 <sup>s</sup>
<b>III/ IV (37)</b>	25 (62.5)	12 (22.2)	0.001 <sup>s</sup>

PLT=Platelet count, s=significant, p value reached from the Chi-square test.

**Table 7: Distribution of the study patients by grade of the tumor, (n=94).**

Grade of tumor, (N)	Thrombocytosis (PLT>400×10 <sup>9</sup> /l), n=40 (%)	Without thrombocytosis (PLT≤400×10 <sup>9</sup> /l), n=54 (%)	P value
<b>Grade 1 (39)</b>	14 (35)	25 (46.3)	0.022 <sup>s</sup>
<b>Grade 2-3 (35)</b>	21 (52.5)	14 (25.9)	
<b>Unknown (20)</b>	5 (12.5)	15 (27.8)	

PLT=Platelet count, s=not significant, p value reached from the Chi-square test.

**Table 8: Distribution of the study patients by lymph node metastasis of the tumor, (n=94).**

Lymphnode metastasis, (N)	Thrombocytosis (PLT>400×10 <sup>9</sup> /l), n=40 (%)	Without thrombocytosis (PLT≤400×10 <sup>9</sup> /l), n=54 (%)	OR (95%CI)	P value
<b>Yes (17)</b>	11 (27.5)	6 (11.1)	3.03 (0.91-10.48)	0.029 <sup>s</sup>
<b>No (77)</b>	29 (72.5)	48 (88.9)		

PLT=Platelet count, s=significant, p value reached from Chi-square test.

## DISCUSSION

Thrombocytosis (platelet count, >400×10<sup>9</sup>/l) has been demonstrated in approximately one-third of malignancies at the time of diagnosis.<sup>22,23</sup> Preoperative thrombocytosis has been described to be of prognostic value in gynaecologic cancers such as cervical cancer.<sup>24</sup> Ovarian cancer, appearing as intra-abdominal wide spreading, has the highest fatality among gynaecologic malignancies. However, data related to the prognostic significance of thrombocytosis in patients with epithelial ovarian cancer (EOC) is still limited. This cross-sectional comparative study was carried out to measure Hb%, total platelet count and CA-125 in the study population and also to assess the level of ascites, optimal cytoreduction, stage, grade and lymphnode metastasis in patient with thrombocytosis and without thrombocytosis.

It was observed that almost half (42.5%) of patients belonged to age 51-60 years in the thrombocytosis and 12 (22.2%) without thrombocytosis group. The mean age was 45.39±13.23 years in thrombocytosis and 48.98±15.46 years in without thrombocytosis group with a range from 18 to 70 years. The difference was not statistically significant (p>0.05) between the two groups. Liang and Zhang study found the mean ages were 47.6±11.2 years in the early-stage epithelial ovarian cancer group, 49.8±10.2 years in the advanced-stage epithelial ovarian cancer group.<sup>25</sup> On the other hand, Ma et al study found the mean age was 59.66±6.08 years in the thrombocytosis and 58.12±7.33 years in the without thrombocytosis group, which is higher than the present study.<sup>26</sup> Similarly higher mean age was also observed by other authors.<sup>21,16,7</sup> The higher mean age and age range mentioned by the above authors may be due to geographical variations, racial, and

ethnic differences, and genetic causes that may have a significant influence on Epithelial Ovarian Cancer in their study subjects. The present study showed more than one-third (37.5%) of the study population having primary education in thrombocytosis and 14 (25.9%) without thrombocytosis group. More than half (55.0%) of patients' socio-economic status were low income in the thrombocytosis group and 23 (42.6%) in the without thrombocytosis group. The majority (92.5%) of patients were married in thrombocytosis and 46 (85.2%) in without thrombocytosis. Thirty-six (90.0%) patients were housewives in thrombocytosis and 39 (72.2%) were in without thrombocytosis group. Most of the (95%) patients were multiparous in thrombocytosis and 39 (72.2%) were in without thrombocytosis group. Almost half of 18 (45%) patients were menopausal in thrombocytosis and 24 (44.4%) in without thrombocytosis group. The difference in education and occupation were statistically significant (p<0.05) between two groups. There were no significant differences between two groups in terms of age, marital status, socioeconomic status, parity, and menopausal status. Chen et al study found 61.3% of their study patients were diagnosed in the postmenopausal age, which is comparable to the current study.<sup>21</sup>

In this present study, it was observed that 62.5% of patients had Hb% 8-10 (gm/dl) in thrombocytosis and 31.5% in the without thrombocytosis group. The mean Hb% was 10.02±1.47 (g/dl) in thrombocytosis and 11.15±1.52 (gm/dl) in without thrombocytosis group. The mean Hb% was significantly (p<0.05) lower in the thrombocytosis group. Ma et al found that mean hemoglobin was 130.15±12.26 g/l in thrombocytosis and 135.07±16.20 g/l in without thrombocytosis group, which is lower in thrombocytosis group.<sup>26</sup> Allensworth et al and Crasta et al



showed that pre-operative thrombocytosis was associated with lower Hb levels. The above-mentioned findings support the present study.<sup>15,27</sup>

In this current study, it was observed that 75.0% of patients' serum CA-125 was >500 in thrombocytosis group and 16.7% in without thrombocytosis group. The odds ratio (OR) of developing thrombocytosis with serum CA-125>500 was 15 (95% CI=4.92 to 47.72) times significantly higher than that in patients with CA-125<500. Zhou et al (2018) aimed to explore that thrombocytosis was significantly correlated with higher serum CA-125 level (OR=1.68, 95% CI=1.33- 2.12,  $p<0.001$ ).<sup>28</sup> Ramu and Sinha et al and Chen et al also found the positive co-relation of thrombocytosis with a higher level of serum CA-125.<sup>21,29</sup> Similarly, patients with thrombocytosis were found to have statistically greater elevations of preoperative CA-125 levels, observed by Lee et al. (2011), which closely resembled the present study.<sup>30</sup> Gungor et al study found that mean CA-125 was  $1543.2\pm37.4$  U/ml in thrombocytosis and  $978.1\pm26.7$  U/ml in without thrombocytosis group.<sup>7</sup>

In current study, 47.5% of the patient's ascites volume was in grade 3 in thrombocytosis group and 59.3% in without thrombocytosis group. Grade 2 ascites were found in 25% and 20.4% of thrombocytosis and without thrombocytosis groups respectively. Grade 1 ascites was found in 27.5% of patients in thrombocytosis and 20.4% in those without thrombocytosis group. Ascites volume was not significantly ( $p>0.05$ ) associated with thrombocytosis in my study. Allensworth et al study found a significantly ( $p<0.05$ ) greater volume of ascites in patients with thrombocytosis group.<sup>15</sup>

In this current study, 52.5% of patients had sub-optimal cytoreduction ( $\geq 1$  cm) in the thrombocytosis group and 24.1% in without thrombocytosis group. The risk of achieving sub-optimal cytoreduction ( $\geq 1$  cm) was significantly ( $p<0.05$ ) 3.49 times higher in thrombocytosis group with 95% CI=1.33 to 9.28%. Zhou et al study found residual tumor mass positively correlated with thrombocytosis (OR=3.07, 95% CI=1.46-6.47,  $p=0.003$ ).<sup>28</sup> Ma et al. (2014) study found that epithelial ovarian cancer patients with thrombocytosis have a greater likelihood of suboptimal cytoreduction ( $p<0.05$ ) in thrombocytosis group.<sup>26</sup> Crasta et al and Gungor et al study identified thrombocytosis as a prognostic factor in EOC.<sup>27,7</sup> Gungor et al study demonstrated that 66.1% of patients had optimal cytoreduction in thrombocytosis and 61.3% in the without thrombocytosis group.<sup>7</sup> Li et al study reported that suboptimal cytoreduction was achieved in 46.3% of patients in the thrombocytosis and 2.8% without thrombocytosis group ( $p<0.05$ ). The above findings closely resembled the present study.<sup>31</sup>

Regarding the stage of the tumor in this present study, 62.5% of patients were in stage III/ IV disease in the thrombocytosis group and 22.2% in the without thrombocytosis group. The difference between two group

were statistically significant ( $p<0.05$ ). Zhou et al demonstrated that thrombocytosis was positively correlated with the FIGO stage (OR=2.71, 95% CI=1.88-3.90,  $p<0.001$ ).<sup>28</sup> Cozzi et al identified a significant association was found with a higher stage of disease ( $p=0.038$ ).<sup>4</sup> Slabuszewska-Jozwiak et al study identified that thrombocytosis was more frequently found in stage III and IV disease. Ma et al and Digikila et al also found a significant association between thrombocytosis with advanced stage disease.<sup>17,26,32</sup> Digikila et al reported that in the thrombocytosis group, 71.8% of patients were found with stage III disease and 28.2% with stage IV disease.<sup>17</sup> In Liang and Zhang study, thrombocytosis was found in 40 patients, out of which 17.5% of the early stage (stage I and stage II) and 52.0% of the advanced stage (stage III and stage IV).<sup>25</sup> Gungor et al study observed 66.9% and 45.2% had tumor stage III/IV in the thrombocytosis group and without thrombocytosis group respectively, which was significantly higher in the thrombocytosis group which is similar to the present study.<sup>7</sup>

In present study, 52.5% of patients were in grades 2-3 in the thrombocytosis group and 25.9% in the without thrombocytosis group. Grade 2-3 was significantly ( $p<0.05$ ) higher in the thrombocytosis group. Similarly, Cozzi et al, Slabuszewska-Jozwiak et al study identified a significant association between higher-grade tumors with thrombocytosis ( $p<0.05$ ).<sup>4,32</sup> In Ma et al study, grade 1 was present in 11.3% of thrombocytosis and 24.8% in the without thrombocytosis group, grade 2 was 37.7% in thrombocytosis and 38.7% without thrombocytosis group. Grade 3 was 50.9% in thrombocytosis and 36.5% in the without thrombocytosis group. Grade 3 was significantly ( $p<0.05$ ) higher in the thrombocytosis group.<sup>26</sup> In another study, Gungor et al showed that EOC patients with thrombocytosis were found to have a significantly higher grade. Tumor grade 2/3 was present in 77.4% of patients in thrombocytosis and 51.8% of patients without thrombocytosis group, which was also significantly ( $p<0.05$ ) higher in the thrombocytosis group, which is similar to the present study.<sup>7</sup>

Present study showed that, 27.5% of patients had lymph node metastasis in thrombocytosis group and 11.1% in the without thrombocytosis group. The risk of developing lymphnode metastasis was 3.03 times higher in the thrombocytosis group with 95.0% CI=0.91 to 10.48%. Similarly, Chen et al study observed that patients with thrombocytosis had statistically more frequent lymph node metastases, which is consistent with the current study.<sup>21</sup>

### Limitations

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community. The major limitation of this study was the lack of follow-up of this patient to find out the progression-free survival (PFS) and overall survival (OS) of EOC patients due to time constrain.

## CONCLUSION

This study concluded that thrombocytosis is a frequent finding in patients with epithelial ovarian cancer. Patients with thrombocytosis were found to have statistically greater elevation of pre-operative serum CA-125 level, low Hb%, sub-optimal cytoreduction, advanced stage disease, higher grade tumor, and more frequent lymphnode metastasis. So, platelet count can be used as a marker besides CA-125 to predict the prognosis of EOC.

## Recommendations

Molecular studies investigating the expression of platelet secretory factors should be done required to elucidate the differences in clinical outcomes and findings to validate the importance of platelet count. Moreover, further studies should be conducted involving a large sample size and multiple centers.

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