C-reactive protein as a diagnostic marker for ovarian carcinoma

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ABSTRACT

Ovarian carcinoma is a leading cause of death in gynecological cancers, making early detection crucial for improving survival rates. C-reactive protein (CRP) has shown promise as a cost-effective biomarker to distinguish ovarian carcinoma from benign ovarian masses. Elevated CRP levels are associated with an increased risk of ovarian cancer. This cross-sectional study included 87 patients: 59 with ovarian carcinoma and 28 with ovarian cysts. The aim was to evaluate CRP as a diagnostic marker to improve early detection and clinical management of ovarian carcinoma. CRP levels were measured using the enzyme-linked immunosorbent assay method. Statistical analysis was conducted to assess the differences in CRP levels between the ovarian carcinoma group and the ovarian cyst group. All statistical analyses were performed using the Statistical Program for Social Sciences (IBM SPSS 24, IL, USA). Most subjects in the study were 50 years old or younger (69%) and had ovarian carcinoma (67.8%). Age over 50 [odds ratio (OR) 5.71, p=0.01] and menopausal status (OR 4.72, p=0.01) were significant risk factors for ovarian carcinoma. No significant difference in CRP levels was found between ovarian carcinoma and ovarian cyst patients (p=0.23). Based on the results, CRP cannot be used as an effective predictor to differentiate ovarian carcinoma from ovarian cysts.

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Introduction

Ovarian carcinoma is the leading cause of death from gynecological cancers globally, largely due to its asymptomatic nature in its early stages, which leads to late diagnosis in most cases.[1] Risk factors include age, family history of ovarian or breast cancer, and mutations in *BRCA1* and *BRCA2* genes, which significantly increase the likelihood of developing ovarian carcinoma.[2] Due to its high mortality rate, early-stage detection is crucial, as it significantly improves patient outcomes and survival rates. Identifying reliable biomarkers for early diagnosis can help differentiate ovarian carcinoma from benign ovarian masses, improving prognosis.[3,4]

C-reactive protein (CRP) is an inflammation marker that has shown potential in distinguishing ovarian carcinoma from benign ovarian masses. CRP levels above 10 mg/L are associated with a higher risk of ovarian cancer, particularly mucinous and endometrioid carcinoma subtypes.[1,5] This marker is advantageous because it is easily measurable through routine blood tests, providing a cost-effective option for screening high-risk individuals.[6-8]

Materials and Methods

Subjects and data collections

This is a cross-sectional study involving 87 patients: 59 patients with ovarian carcinoma and 28 patients with ovarian cysts. CRP levels were measured using the enzyme-linked immunosorbent assay method. Statistical analysis was con-

ducted to assess the differences in CRP levels between the ovarian carcinoma group and the ovarian cyst group. All statistical analyses were performed using the Statistical Program for Social Sciences (IBM SPSS 24, Chicago, IL, USA). This study was approved by the Research Ethics Commission of the Faculty of Medicine, Hasanuddin University (No: 550/UN4.6.4.5.31/PP36/2023).

Statistical analysis

Baseline data (age, parity, menopausal status, and use of hormonal contraception) were descriptively summarized and analyzed with Chi-square. Bivariate analysis between CRP level and type of mass was analyzed using the Mann-Whittney test. Significant values were determined at $p<0.05$. All statistical analyses were performed using the Statistical Program for Social Sciences (IBM SPSS 24, Chicago, IL, USA).

Results

The majority of subjects in the study were 50 years old or younger (69%), and most had ovarian carcinoma (67.8%) (Table 1). Age above 50 years [odds ratio (OR) 5.71 (1.54-21.08), p=0.01] and menopausal status [OR 4.72 4.72 (1.46-15.33), p=0.01] were both significant risk factors for ovarian carcinoma (Table 2). There was no statistically significant difference in CRP levels between patients with ovarian carcinoma and those with ovarian cysts (p=0.23) (Table 3).

Discussion

Age is a significant factor influencing the incidence of ovarian carcinoma. This phenomenon is intricately linked to cellular senescence, inflammation resulting from alterations in the peritoneal environment, and immunosenescence. These conditions collectively contribute to various derangements in cellular mitosis, differentiation, and growth due to inflammation. The primary drivers of cellular senescence are DNA damage or the accumulation of reactive oxygen species, which serve as critical triggers for cellular aging.[9-12]

Parity was not identified as a significant factor in this study. Increased parity is associated with a reduced risk of ovarian carcinoma, though this relationship remains ambiguous and is specific to certain histological subtypes. Reproductive factors have been implicated in the etiology of ovarian carcinoma, wherein higher parity tends to lower the risk of ovarian carcinoma, particularly of the epithelial subtype.[13-15]

Table 1. Subjects' characteristics.

Variable	Mean (SD)	n (%)
Age	43.32 (14.55)	-
>50 years old	-	27 (31.00)
≤50 years old	-	60 (69.00)
Parity		
Nullipara	-	24 (27.60)
Para	-	63 (72.40)
Mass type		
Ovarian cyst	-	28 (32.20)
Ovarian carcinoma	-	59 (67.80)
Menopausal status		
Menopausal	-	27 (31.00)
Not yet	-	60 (69.00)
History of hormonal contraception		
Yes	-	27 (31.00)
No	-	60 (69.00)
CRP (mg/dL)	1.52 (0.34)	-

SD, standard deviation; CRP, C-reactive protein.

Table 2. Risk factors of ovarian carcinoma.

Variable	Ovarian carcinoma n (%)	Ovarian cyst n (%)	OR CI 95%	p
Age				
>50 years old24 (88.90)	3 (11.10)	5.71 (1.54-21.08)	0.01a*	
≤50 years old	35 (58.30)	25 (41.70)		
Parity				
Nullipara	15 (65.20)	8 (34.80)	0.85 (0.31-2.33)	0.80a
Para	44 (68.80)	20 (31.30)		
Hormonal contraception				
Yes	15 (55.60)	12 (44.40)	0.46 (0.18-1.18)	0.13a
No	44 (73.30)	16 (26.70)		
Menopausal status				
Menopausal	26 (86.70)	4 (13.30)	4.72 (1.46-15.33)	0.01a*
Not yet	33 (57.90)	24 (42.10)		

OR, odds ratio; CI, confidence interval; aChi-square test, *significant.

Table 3. Bivariate analysis of C-reactive protein among ovarian carcinoma and ovarian cyst.

Variable	Ovarian carcinoma Mean (SD)	Ovarian cyst Mean (SD)	p
CRP (mg/dL)	1.50 (0.33)	1.55 (0.38)	0.23a

SD, standard deviation; CRP, C-reactive protein; aMann Whittney test.

Pregnancy induces significant alterations in metabolic and hormonal states, potentially explaining the differential incidence of carcinoma between multiparous and nulliparous women. Furthermore, infertility has been linked to an elevated risk of ovarian carcinoma.[16-18]

Hormonal contraceptives were not found to be significantly associated with the incidence of ovarian carcinoma. Previous studies suggested that contraceptive use lowers the occurrence of ovarian carcinoma by manipulating the menstrual cycle to prolong the resting phase. The protective effect of hormonal contraceptives has been shown to persist even after cessation of use.[19,20]

Menopausal status emerged as a significant risk factor for ovarian cancer. This is attributed to the cessation of ovum growth, which leads to subsequent mitotic activation and abnormal differentiation of the estrogen-receptor-rich ovarian epithelium due to hormonal influences.[21-23] The associated inflammation arises from processes like inflammaging, cellular senescence, and immunosenescence.[24-26]

CRP is not a significant marker for distinguishing between cancerous and non-cancerous populations. This is due to several factors, one of which is that CRP is an acute-phase protein; hence, during chronic inflammation, its concentration tends to decrease, and it ceases to be produced by the liver. The CRP signaling pathway is primarily activated in response to interleukin-6, which occurs in response to tissue damage through damage-associated molecular pattern recognition. In carcinoma, however, the inflammatory response is more closely associated with mitotic and differentiation signaling activity, which means CRP concentration is not significantly impacted. Previous studies have indicated that CRP is only influential within specific populations and cannot differentiate between malignancy and cysts in the general population presenting with ovarian masses. This limitation is related to the pathophysiology of CRP elevation, which is more prominent in acute and tissue damage conditions rather than the chronic inflammatory states typical of cancer.[1,5,27]

Conclusions

In conclusion, age above 50 years and menopausal status were identified as significant risk factors for ovarian carcinoma. However, CRP levels were not significantly different between ovarian carcinoma and ovarian cyst patients, suggesting CRP may not be a reliable marker for differentiating between these conditions. Further research is needed to identify more effective biomarkers for early detection.

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