The Accuracy of Glutaminase (GLS) and Ca-125 Protein Levels in Diagnosing Presurgical Epithelial Type of Ovarian Cancer

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KEYWORDS

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CA-125
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ABSTRACT:

Background: Ovarian cancer remains one of the leading causes of gynecologic cancer-related mortality, with epithelial-type ovarian carcinoma being the most common subtype. Accurate preoperative diagnosis is crucial for determining appropriate treatment strategies. While CA-125 is widely used as a tumor marker for ovarian cancer, its specificity and sensitivity remain limited. Recent studies suggest that glutaminase (GLS) may play a role in tumor metabolism, making it a potential biomarker for ovarian carcinoma diagnosis.

Objective: This study aims to evaluate the diagnostic accuracy of GLS and CA-125 protein levels in distinguishing preoperative epithelial-type ovarian carcinoma from non-epithelial ovarian tumors in patients at Dr. Wahidin Sudirohusodo Hospital Makassar and its network hospitals.

Results: The mean CA-125 and GLS levels in epithelial-type ovarian carcinoma patients were 540.61 ± 860.45 and 6.30 ± 1.91, respectively. At a cut-off of 259.6, CA-125 demonstrated a sensitivity of 44.44% and a specificity of 42.86%. Meanwhile, GLS with a cut-off of 5.675 exhibited a slightly better sensitivity and specificity at 53.09% and 57.41%, respectively. Despite this, both biomarkers showed inadequate significance in differentiating epithelial-type ovarian carcinoma from non-epithelial ovarian carcinoma.

Conclusion: CA-125 and GLS levels alone do not provide sufficient diagnostic accuracy for preoperative differentiation of epithelial-type ovarian carcinoma. Further research is needed to explore their combined use with other biomarkers or imaging techniques to enhance diagnostic precision.

1. Introduction

In developed countries such as the United States, ovarian carcinoma accounts for 5% of total cancer cases in women. There were an estimated 21,290 new cases with 14,180 deaths [1]. Death from this disease occurs in one woman every 44 minutes, while the risk of progression is one in 68 women . In Indonesia, based on data from the Indonesian Society of Gynecologic Oncology in 2020, there were 354 cases of ovarian cancer, making it the second most common gynecological cancer [2]. Data from the Carcinoma Registry of the Division of Gynecological Oncology, Department of Obstetrics and Gynecology, Faculty of Medicine, Hasanuddin University in 2019 shows that ovarian carcinoma is the second most common case (37%) after cervical carcinoma (57%), with 58% of cases in the advanced stage [3].

Various methods can be used to help predict the diagnosis of ovarian carcinoma before surgery. Thorough examination through anamnesis, physical examination, measurement of tumor markers, and imaging are commonly used approaches [4]. This step is crucial to determine the next therapy plan. If the results of the examination show a suspicion of ovarian carcinoma, the type of operation will be determined [5]. Surgery can be in the form of surgical staging for the early stage or debulking for the advanced stage. A tumor marker that is often used in preoperative diagnosis is CA-125. which increases in more than 80% of women with ovarian carcinoma [6].

CA-125, also known as Mucin 16 (MUC16), is a glycoprotein that is expressed in various cell types and has an important role in various diseases, especially carcinoma. MUC16 is the most commonly expressed antigen in ovarian carcinoma. In the case of ovarian carcinoma, MUC16 interacts with Natural Killer (NK) cells, resulting in immunosuppressive conditions in the body [7]. Increased

expression of CA-125 in carcinoma cells triggers activation of Epidermal Growth Factor Receptor (EGFR), which further increases Akt expression via the Phosphatydilinositol 3 Kinase/Protein kinase B (PI3K/Akt) signaling pathway [8].

CA-125 has been used as an initial screening tool for ovarian carcinoma, helping to differentiate between benign and malignant tumors, as well as monitoring response to therapy. In addition, CA-125 levels have also been studied as a predictor of the success of cytoresorption operations. A meta-analysis study showed that CA-125 levels above 500 IU/ml are a risk factor for suboptimal citorduction surgery [9]. It is reported that CA-125 is increased in more than 80% of women with ovarian carcinoma. The sensitivity of CA-125 is only around 50% in stage I ovarian carcinoma and 80% in advanced stage. On the other hand, several recent studies state that potential biomarker candidates are biomarkers that are involved in the tumor metabolism process [10].

Glucose is an important substance as a fuel source for almost all body cells, including carcinoma cells. To be able to supply energy in the form of ATP, glucose goes through a series of processes, namely glycolysis, Krebs cycle and oxidative phosphorylation [11]. Carcinoma cells have a tendency to metabolize glucose through the aerobic glycolysis process rather than through the oxidative phosphorylation process to obtain ATP. Glutamine increases glucose absorption in carcinoma cells. Glutamine is also associated with increased intracellular ATP levels [12]. ATP production decreases drastically if inhibition is carried out in the glycolysis and glutaminolysis processes. Difference in glutamine requirements between carcinoma cells with a high rate of invasion compared to ovarian carcinoma cells with a low rate of invasion [13].

Protein Glutaminase (GLS) catalyzes the hydrolysis of L-glutamine into L-glutamate which is involved in oxidation within mitochondria. In a state of glutamine deficiency, the expression of Glutaminase (GLS) will increase and in the state of glutamine increases, the expression of the protein Glutaminase (GLS) will decrease [14]. Glutaminase (GLS) expression is regulated in the cell cycle and its expression increases in the S phase and decreases as it progresses into the G2/M phase. CA-125 and Glutaminase (GLS) levels can increase sensitivity, specificity and accuracy in predicting the optimal citorduction surgery in advanced epithelial ovarian carcinoma [14].

The PI3K/Akt signaling pathway is an intracellular effector pathway found in tyrosine kinase receptors including EGFR, Insulin-like growth factor-I (IGF-I) and insulin receptors. Loss of tumor suppressor inhibitor pathways of PI3K and Phosphatase and Tensin Homologous (PTEN) can increase PI3K signaling which can lead to the onset of carcinoma [15]. In carcinoma cells, Akt can induce glucose transport. If Akt activation is not controlled due to disruption of the PIK3/Akt signaling pathway, glutamine expression will be overexpressed followed by increased glucose absorption as seen in carcinoma [16].

2. Objectives

Analyzing the accuracy of glutaminase protein (GLS) and CA-125 levels in diagnosing preoperative epithelial-type ovarian carcinoma at Dr. Wahidin Sudirohusodo Hospital Makassar and Network Hospitals. Analyzing the sensitivity and specificity of Glutaminase (GLS) protein in diagnosing preoperative epithelial-type ovarian carcinoma at Dr. Wahidin Sudirohusodo Hospital Makassar and Network Hospitals. Analyzing the sensitivity and specificity of CA-125 protein in diagnosing preoperative epithelial-type ovarian carcinoma at Dr. Wahidin Sudirohusodo Hospital Makassar and Network Hospitals. To analyze the comparison of accuracy, sensitivity, and specificity of Glutaminase protein (GLS) with CA-125 protein in diagnosing preoperative epithelial-type ovarian carcinoma at Dr. Wahidin Sudirohusodo Hospital Makassar and Network Hospitals.

3. Methods

This study is an observational analytical study with a cross sectional design that aims to analyze the accuracy of glutaminase protein (GLS) and CA-125 levels in diagnosing preoperative epithelial-type ovarian carcinoma at Dr. Wahidin Sudirohusodo Hospital, Makassar. The purpose of the study was achieved through observation of cases assisted by supporting examinations, but without any empirical

intervention. Observational research is research in which the researcher only makes observations without intervening on the research subject. Analytics is a study that explores how and why health phenomena occur. The population in this study was all patients with pre-operative epithelial ovarian carcinoma at Dr. Wahidin Sudirohusodo Makassar Hospital, Ibnu Sina Hospital, and UNHAS Hospital. The research sample is a population that meets the inclusion criteria and exclusion criteria from the population reached by the consecutive sampling method with a minimum sample calculated based on the minimum sample formula. The data taken is extracted into the form of research and analyzed using a computer.

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4. Results

This study involved as many as 88 samples consisting of 81 samples with epithelial ovarian carcinoma and 7 samples without epithelial ovarian carcinoma. This study aims to analyze the accuracy of glutaminase protein (GLS) and CA-125 levels in diagnosing preoperative epithelial-type ovarian carcinoma at Dr. Wahidin Sudirohusodo Hospital Makassar and Network Hospitals.

Table 1. Characteristics of the research sample

Variable	N=88	Epithelial-type ovarian carcinoma		p-value
		Yes (n=81)	No (n=7)	
Age (years)				
Mean ± SD	44.56 ± 13.95	44.25 ± 14.23	48.14 ± 10.14	
Median	47.00	47.00	51.00	0.481a
Range (min-max)	14.00 – 82.00	14.00 – 82.00	30.00 – 59.00	
Parity				
0	36 (40.9%)	34 (42.0%)	2 (28.6%)	
1	15 (17.0%)	14 (17.3%)	1 (14.3%)	0.814b
2	15 (17.0%)	13 (16.0%)	2 (28.6%)	
≥ 3	22 (25.0%)	20 (24.7%)	2 (28.6%)	
IMT				
Mean ± SD	23.38 ± 4.34	11.45 p.m. ± 4.21 p.m.	22.59 ± 5.91	
Median	22.90	22.94	20.81	0.621A
Range (min-max)	14.57 – 38.71	15.60 – 38.71	14.57 – 31.11	
PA Results				
Serosa	27 (30.7%)	26 (32.1%)	1 (14.3%)	
Mucinous	41 (46.6%)	41 (50.6%)	0 (0.0%)	
Endometriod	6 (6.8%)	6 (7.4%)	0 (0.0%)	**0.000c***
Clear cell	4 (4.5%)	4 (4.9%)	0 (0.0%)	
Other	10 (11.4%)	4 (4.9%)	6 (85.7%)	

T-independent test, [b.] Chi-square test, [c.] Fisher Test Exact*significant (p<0.05)

Table 1. the distribution of samples with a comparative test of whether the sample has epithelial-type ovarian carcinoma or not. In the overall sample, 88 samples had an average age of 44.56 years with a standard deviation of 13.95, while in 81 samples with epithelial ovarian carcinoma had an average age of 44.25 years with a standard deviation of 14.23, in addition, 7 samples that did not have epithelial ovarian carcinoma had an average age of 48.14 with a standard deviation of 10.14. The overall half-life value of the sample was 47 years, while in the sample with epithelial type ovarian carcinoma it was 47 years and the sample without epithelial type ovarian carcinoma was 51 years. The minimum overall age of the sample is 14 years while the maximum is 82 years. The results of the comparison test showed a p-value of 0.481 which was greater than 0.05, which showed

that there was no significant difference in age between the samples with epithelium-type ovarian carcinoma and those without.

The results of the parity variable showed that as a whole, most of the samples had a parity of 0 as many as 36 samples (40.9%), while in the samples that experienced epithelial type ovarian carcinoma, most of them had a parity of 0 as many as 34 samples (42%). In addition, in samples that did not have epithelial type ovarian carcinoma, most of them had a parity of 0, 2, and more than or equal to 3 as many as 2 samples each (28.6%). The results of the comparison test showed a p-value of 0.814 which was greater than 0.05, which showed that there was no significant difference in parity in the samples with and without epithelial-type ovarian carcinoma.

The results of the BMI variable showed that the average BMI value for all samples was 23.38 with a standard deviation of 4.34. In addition, the median value of BMI in all samples was 22.90 with a minimum value of 14.57 and a maximum of 38.71. In samples that experienced epithelial-type ovarian carcinoma, the average had a BMI value of 23.35 with a standard deviation of 4.21. In addition, the median BMI value in all samples was 22.94 with a minimum value of 15.60 and a maximum of 38.71. Meanwhile, in samples that did not experience epithelial ovarian carcinoma, the average had a BMI value of 22.59 with a standard deviation of 5.91. In addition, the median value of BMI in all samples was 20.81 with a minimum value of 14.57 and a maximum of 31.11. The results of the comparison test showed a p-value of 0.621 which was greater than 0.05, which showed that there was no significant difference in BMI between samples with epithelial-type ovarian carcinoma and non-epithelial-type.

The results in the PA variable showed that most of the samples experienced a Mucinos incidence of 41 samples (46.6%). In the samples that had epithelial type ovarian carcinoma, most of them had PA results in the Mucinos category as many as 41 samples (50.6%), while in the samples that did not have epithelial type ovarian carcinoma, most of them had PA results in other categories as many as 6 samples (85.7%). The results of the chi square test showed a p-value of 0.000 which was smaller than 0.05, this showed that there was a relationship between PA results and the incidence of epithelial-type ovarian carcinoma.

Table 2. Comparison of GLS and CA-125 against epithelium-type ovarian carcinoma

Variable	N=88	Epithelial-type ovarian carcinoma		p-value
		Yes (n=81)	No (n=7)	
GLS				
Mean ± SD	6.27 ± 1.87	6.30 ± 1.91	5.92 ± 1.31	
Median	5.84	5.87	5.74	0.787
Range (min-max)	3.30 – 11.69	3.30 – 11.69	4.07 – 8.18	
CA-125				
Mean ± SD	565.58 ± 932.70	540.61 ± 860.45	854.45 ± 1623.80	0.982
Median	213.50	210.10	293.35	
Range (min-max)	5.19 – 5185.10	5.19 – 5185.10	18.23 – 4519.10	

Mann-Whitney test, *significant (p<0.05)

The data presented in Table 2. results of the GLS variable showed an average value of 6.27 with a standard deviation of 1.87, a median value of 5.84 with a minimum value of 3.30 and a maximum of 11.69. In the samples that experienced epithelial type ovarian carcinoma, the average value was 6.30 with a standard deviation of 1.91, the median value obtained was 5.87 with a minimum value of 3.30 and a maximum of 11.69, while the sample that did not experience epithelial ovarian carcinoma showed an average value of 5.92 with a standard deviation of 1.31, the median value obtained was

5.74 with a minimum value of 4.07 and a maximum of 8.18. This showed that the average GLS value in samples with epithelium-type ovarian carcinoma was greater than that of those without. The results of the comparison test showed a p-value of 0.787 which was greater than 0.05, which showed that there was no significant difference in GLS values in samples with and without epithelium-type ovarian carcinoma.

The results on the CA-125 variable showed an average value of 565.58 with a standard deviation of 932.70, a median value of 213.50 with a minimum value of 5.19 and a maximum of 5185.10. In the samples that experienced epithelial type ovarian carcinoma, the average value was 540.61 with a standard deviation of 860.45, the median value obtained was 210.10 with a minimum value of 5.19 and a maximum of 5185.10, while the sample that did not experience epithelial ovarian carcinoma showed an average value of 854.45 with a standard deviation of 1623.80, the median value obtained was 293.35 with a minimum value of 18.23 and a maximum of 4519. 10. This shows that the average CA-125 value in samples with epithelium-type ovarian carcinoma is smaller than that of those without. The results of the comparison test showed a p-value of 0.982 which was greater than 0.05, this showed that there was no significant difference in CA-125 values in samples with and without epithelial-type ovarian carcinoma.

Table 3. Comparison of GLS and CA-125 diagnostic models in epithelium-type ovarian carcinoma

Variable	*Cut off*	*Sensitivity*	*Specificity*	*Accuracy*	*Positive predictive value*	*Negative predictive value*	*p-value*
GLS	5.765	53.09%	57.14%	53.41%	93.48%	9.52%	0.603
CA-125	259.6	44.44%	42.86%	44.32%	90%	6.25%	0.517

Chi-square test, *significant (p<0.05)

The data presented in Table 3 the test results for the GLS and CA-125 diagnostic models in epithelial-type ovarian carcinoma. It was shown that the sensitivity value of the GLS model was 53.09%, with specificity of 57.14%, and accuracy of 53.41%. The p-value of the GLS variable was 0.603 which indicates that the GLS variable has an insignificant diagnostic model. In addition, on the test results for the CA-125 diagnostic model. It was shown that the sensitivity value of the CA-125 model was 44.44%, with a specificity of 42.86%, and an accuracy of 44.32%. The p-value of the CA-125 variable is 0.517 which indicates that the CA-125 variable has an insignificant diagnostic model. In comparison of diagnostic models, it is shown that GLS is better compared to CA-125 in sensitivity, specifity, and accuracy.

Table 4. Comparative Test Results of CA-125 and GLS Based on the patient's stage level

Stadium	N	CA-125			GLS		
		Mean	SD	p-value	Mean	SD	p-value
IA	18	347,903	375,265		6,349	2,132	
IB	10	519,195	790,439		6,066	1,617	
IC	2	72,550	38,820		5,660	1,202	
IC1	5	217,380	158,599		6,890	2,786	
IC2	4	390,735	241,890		5,670	2,020	
IC3	1	44,000	.	0,189	7,330	.	0,320
IIA	7	1035,400	1517,075		5,904	1,885	
IIB	6	1413,533	1712,064		6,733	1,411	
IIC	1	109,500	.		4,350	.	
IIIA	1	101,600	.		8,180	.	
IIIB	8	1214,617	1701,688		5,156	0,938	

IIIC	13	387,640	345,252	7,403	2,143
IVB	2	307,220	266,324	7,585	1,279
Other	10	416,704	697,033	5,410	1,124

Kruskal Wallis Comparative Test, *significant (p<0.05)

The data presented in Table 4 it shows the comparative test of CA-125 values at each stage. In stage IA, the average CA-125 score is 347.903 with a standard deviation of 375.265. Stage IB has an average CA-125 score of 519.195 with a standard deviation of 790.439. At the IC stage, the average CA-125 score was recorded at 72,550 with a standard deviation of 38,820. For the IC1 stage, the average value of CA-125 is 217,380 with a standard deviation of 158,599. Stage IC2 has an average CA-125 value of 390,735 with a standard deviation of 241,890, while in the IC3 substage, the average value of CA-125 is 44,000 without a standard deviation. In stage IIA, the average value of CA-125 was 1,035,400 with a standard deviation of 1,517,075. Stage IIB has an average CA-125 value of 1,413,533 with a standard deviation of 1,712,064. In stage IIIC, the average value of CA-125 is 109,500, while in stage IIIA, the average value is 101,600. In stage IIIB, the average CA-125 value is 1,214,617 with a standard deviation of 1,701,688. Stage IIIC has an average score of 387,640 with a standard deviation of 345,252, while stage IVB has an average score of 207,220 with a standard deviation of 266,324.

Finally, in other groups, the average value of CA-125 was recorded at 416.704 with a standard deviation of 697.033. The test results using the wallis crucial test showed a p-value of 0.189 (p-value > 0.05), which means that there was no significant difference in the CA-125 value at each stage. Based on table 7, it shows a comparative test of GLS values at each stage. In stage IA, the average GLS score is 6.349 with a standard deviation of 2.132. Stage IB has an average GLS score of 6.066 with a standard deviation of 1.617. In the IC stage, the average GLS value was recorded at 5.560 with a standard deviation of 1.202. For the IC1 stage, the average value of GLS is 6.890 with a standard deviation of 2.786. Stage IC2 has an average GLS value of 5.670 with a standard deviation of 2.020, while in the IC3 substage, the average GLS value is 7.330 without a standard deviation.

The results in stage IIA, the average GLS value was 5.904 with a standard deviation of 1.885. Stage IIB has an average GLS value of 6.733 with a standard deviation of 1.411. At the IIC stage, the average GLS value is 4.350, with no standard deviation recorded. At stage IIIA, the average GLS value is 8,180. Stage IIIB has an average GLS value of 5.156 with a standard deviation of 0.938. In stage IIIC, the average GLS score is 7.403 with a standard deviation of 2.143, while stage IVB has an average score of 7.585 with a standard deviation of 1.279. Finally, in other groups, the average GLS score was recorded at 5.410 with a standard deviation of 1.124. The test results using the Kruskal-Wallis test showed a p-value of 0.320 (p-value > 0.05), which means that there was no significant difference in the GLS value at each stage.

Table 5. Results of the test on the relationship between CA-125 and GLS with the patient's ovarian mass

		Ovarian mass
CA-125	Correlation Coefficient	-0,111
	Sig. (2-tailed)	0,305
	N	88
GLS	Correlation Coefficient	0,219
	Sig. (2-tailed)	0,041*
	N	88

Spearman Correlation Test, *significant (p<0.05)

The data presented in Table 5 it shows the results of the correlation test using the spearman rank correlation test. The correlation value between CA-125 and Ovarian Mass, the correlation coefficient obtained was -0.111, with a p-value of 0.305 (p-value > 0.05). Based on the value of the correlation coefficient, this relationship is classified as very weak. This showed that there was no significant relationship between CA-125 value and ovarian mass due to the smaller p-value compared to 0.05. The value of the relationship between GLS and ovarian mass, the correlation coefficient obtained was 0.219, with a p-value of 0.041 (p-value < 0.05). Based on the value of the correlation coefficient, this relationship is relatively weak. This shows that there is a significant positive relationship between the GLS value and ovarian mass because the p-value is smaller compared to 0.05. The larger the ovarian mass, the higher the GLS value.

5. Discussion

This study involved a total of 88 samples consisting of 81 samples of epithelial ovarian carcinoma and 7 samples of non-epithelial ovarian carcinoma. In this study, it was found that the average age of patients with epithelial ovarian carcinoma was 44.25 ± 14.23 years. These findings are supported by another study that found that 65.11% of patients with epithelial-type ovarian carcinoma are aged 40-59 years [17]. Different results were found in another study that found that epithelial-type ovarian carcinoma was most common in women aged >55 years with an incidence of 60.1% while at the age of <55 years reached 39.9% . Another study also found that the average age of patients with epithelial ovarian carcinoma was 54.5 years [18].

In general, the average age of women diagnosed with ovarian carcinoma is 50-59 years, and the number increases at >65 years. Recent studies show that ovarian carcinoma diagnoses are increasing in women <50 years of age. Age is a risk factor for ovarian carcinoma and usually occurs before or after menopause, with the average age when diagnosed approaching 60 years old [19]. In this study, most patients with epithelial ovarian carcinoma were nullipara women, which was at 40.9%. These results are also supported by other studies that found that nullipara condition is a risk factor for epithelial type ovarian carcinoma while multipara status provides a protective effect on the incidence of epithelial type ovarian carcinoma. Parity lowers the risk of all subtypes of epithelial ovarian carcinoma in women <55 years of age. The risk reduction is about 70% in clear cell carcinoma and 40%-50% in other subtypes [20]. A possible explanation for the reduced risk in parous women is that during pregnancy and lactation conditions there is a disruption of the ovulation pro-inflammatory environment that has taken place continuously, by modifying the hormonal environment or through the mechanism of clearing pre-malignant cells from the ovaries. In this study, the average body mass index of epithelial ovarian carcinoma patients was 23.45 ± 4.21 kg/m2. These findings can be compared to found that 62.72% of patients had BMI within normal limits [21]. Another study also found that 34.7% of epithelium-type ovarian carcinoma patients had a normal BMI, 32.3% had an overweight BMI and another 33.1% were obese. In previous studies, it was found that an increase in BMI in the 5 years prior to diagnosis was associated with an increased risk of death in patients with epithelial-type ovarian carcinoma (HR= 1.17; 95% CI 1.07-1.28; p=0.0007) [22].

Several interrelated mechanisms involving hormonal pathways have been reported to explain the possible role of obesity on the survival of carcinoma. These include effects on insulin resistance and insulin-like growth factor-I as well as increased aromatization of androstenedion to estradiol on peripheral adipocytes, thereby increasing the bioavailability of sex steroids and adrenal and ovarian androgen secretion [23]. Higher circulating estrogen levels can stimulate estrogen buildup around the ovaries, resulting in ovarian carcinoma and resulting in faster metastatic tissue growth. Obesity is also known to induce chronic inflammation and interfere with immune function. There is also a direct link between obesity and C-reactive protein (CRP), a marker of systemic inflammation. At the same time, higher serum CRP levels have been shown to be an independent predictor for lower ovarian carcinoma survival [24]. Overall, the hormonal and metabolic changes associated with increased adipocyte tissue trigger progressive genetic instability, tumor growth, tumor development, and metastasis. In addition,

since obesity is a strong predictor of dose deficits, it is possible that obese patients receiving suboptimal doses of chemotherapy may contribute to lower survival in early-stage cases [25].

In this study, most of the histopathological types of epithelium-type ovarian carcinoma are mucinous types, which is at 50.6%. Serosa histopathology types were found as much as 32.1%, endometrioids as much as 7.4%, clear cells as much as 4.9% and other types as much as 4.9%. Similar results were also found in a study conducted in Indonesia which found that the most frequent type was mucinous carcinoma at 25.5% [26]. United States which found that the most common type of histopathology was serous carcinoma, which was in 54.4% of the samples. Different results were also found in the European female population which found that the most common type of histopathology was the serous carcinoma type in 52.8% of the samples [27]. In the study, it was also found that the mucinous carcinoma type was found as much as 14.17%, the endometrioid type as much as 13.95%, the clear cell type as much as 5.27% and other types as much as 13.73% [28].

In this study, it was found that the average GLS level of epithelium-type ovarian carcinoma patients was 6.30 ± 1.91. The average GLS level in ovarian carcinoma patients was 17.37±12,156 μg/mL [29]. In this study, there was no significant difference in GLS levels between patients with epithelial-type ovarian carcinoma and non-epithelium-type ovarian carcinoma. Tumor growth is characterized by specific metabolic changes. Increased proliferation of tumor cells requires changes in metabolic function to support their proliferation. In addition to high glucose needs, tumors also depend on glutamine, which is a source of bioenergy for carcinoma cells to proliferate [30].

6. Conclusion

The average levels of CA-125 and GLS in patients with epithelial-type ovarian carcinoma were 540.61 ± 860.45 and 6.30 ± 1.91, respectively. CA-125, with a cut-off value of 259.6, demonstrated a sensitivity of 44.44% and a specificity of 42.86%. Meanwhile, GLS, with a cut-off value of 5.675, exhibited slightly better sensitivity and specificity, at 53.09% and 57.41%, respectively. However, both CA-125 and GLS levels showed an insufficient level of significance in distinguishing epithelial-type ovarian carcinoma from non-epithelial-type ovarian carcinoma.

7. Conflict of Interest

The authors declare no conflicts of interest regarding the publication of this literature review. No financial, institutional, or personal relationships influenced the research, analysis, or conclusions presented in this manuscript.

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