



ROLE AND EFFICACY OF SERUM CA-125 IN THE DIAGNOSIS OF MALIGNANCY IN ADNEXAL MASS WITH HISTOPATHOLOGICAL CORRELATION

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ABSTRACT

BACKGROUND: To identify the efficacy of serum CA-125 levels in the diagnosis of malignancy in adnexal mass and its correlation with histo-pathological reports.

METHODS: This is hospital based observational study for a period of 1 year which included 133 patients of adnexal mass attending the OPD who required admission and operative intervention. Following surgery specimens were sent for histopathological examination and the reports were correlated with CA 125 levels.

RESULT: Out of 33 malignant tumors, 25 (75.75%) had serum CA125 >35 U/ml, whereas out of the 100 benign tumors , only 33 (33%) had serum CA125 >35 U/ml ; these benign mass mainly belonged to the epithelial cell tumor group and inflammatory tubo-ovarian mass. Out of the 33 malignant tumors, only 8 (24.24%) had serum CA125 <35 U/ml, these include endodermal sinus tumor , dysgerminoma, granulosa cell tumor and immature teratoma. The mean and median values for serum CA 125 in the subjects with malignant disease were 235.99 and 112.0 respectively, the corresponding values in the subjects with benign disease were 31.93 and 21.63 respectively. The association between was statistically significant at a p value of <0.001. Serum CA 125 had an area of 0.838, SE of 0.065 and Asymptomatic 95% CI of 0.711 to 0.964.

CONCLUSION: Serum CA 125 level is effective in differentiating between benign and malignant adnexal mass since it has CA-125 levels have good sensitivity and specificity, but it is increased in few benign condition also. Hence it can be used as biochemical marker in differentiating malignancy from benign tumors.

Keyword: Adnexal mass, CA 125, Histopathology

1.INTRODUCTION

Ovarian cancer remains a leading cause of gynecological cancer-related mortality worldwide, with a significant proportion of cases diagnosed at an advanced stage. The detection of adnexal masses poses a significant diagnostic challenge, as they may represent a range of benign and malignant conditions. Accurate diagnosis is crucial, as it directly impacts treatment outcomes and patient prognosis. However, the evaluation of adnexal masses is often complicated by the lack of specific symptoms and the limitations of imaging modalities.

Serum CA 125, a glycoprotein biomarker, has been extensively investigated as a diagnostic tool for ovarian cancer. While its utility in monitoring disease recurrence and response to treatment is well

established, the role of serum CA 125 in the diagnosis of malignancy in adnexal masses remains an area of ongoing debate. Several studies have reported varying degrees of sensitivity and specificity for serum CA 125 in detecting ovarian cancer, highlighting the need for further investigation.

The interpretation of serum CA 125 levels is also complicated by the presence of non-neoplastic conditions that may elevate CA 125 levels, such as endometriosis, pregnancy, and pelvic inflammatory disease. Furthermore, CA 125 levels may not be elevated in all cases of ovarian cancer, particularly in early-stage disease or in tumors of non-epithelial origin.

This study aims to investigate the efficacy of serum CA 125 as a diagnostic biomarker for malignancy in adnexal masses, with a focus on histopathological correlation. By examining the relationship between serum CA 125 levels and histopathological findings, this research seeks to contribute to the development of more accurate and effective diagnostic strategies for ovarian cancer. Ultimately, this study aims to provide valuable insights into the utility of serum CA 125 in the diagnostic workup of adnexal masses and to inform the development of evidence-based guidelines for the evaluation and management of ovarian cancer.

2. METHODS

This observational study was conducted on patients with an adnexal masses admitted for surgical management IPD from July 2018 to June 2019 for a total period of 1 year in department of Obstetrics and gynaecology , B.R.D. Medical college Gorakhpur.

Inclusion criteria -All consenting women who have an ovarian mass on presentation were recruited in this study and they were recruited in cohort and was operated and got histopathology reporting done.

Exclusion criteria – Patients with abdominal mass managed conservatively, Ectopic Pregnancy and patient diagnosed with malignant mass who are already on treatment for malignancy.

Detailed history, presenting complaints and menstrual history were obtained. Complete general physical examination with gynecological examination were performed and provisional diagnosis was made. To evaluate the adnexal mass further , ultrasonography consisting of transabdominal ultrasound and transvaginal ultrasound were done where sonographic findings regarding size of adnexal mass, laterality, locularity, solid elements, hemorrhage, presence of ascites, evidence of metastasis. Color doppler was added in suspicious cases of malignancy and doppler studies with pulsatility index (PI) and resistance index (RI) were assessed and ultrasound scoring was made.

Standard laboratory tests consisting of complete haemogram, blood sugar level, liver function test, renal function test and Serum CA 125 done in every case. Laparotomy or Laparoscopy was performed and specimen was sent for histopathological examination and reports were correlated with pre operative clinical, imaging finding and RMI score.

3.OBSERVATION

A total of 133 patients of various age group who presented with an adnexal mass in Gynaecology OPD of BRD Medical college, Gorakhpur for prediction of benign or malignant nature of lesion by calculating the RMI Scores, and the verification of diagnosis was done by histopathological examination of the tissue obtained after laparotomy.

Table 1:Distribution of adnexal mass

Nature of tumor	Number	percentage
Malignant	33	24.8%
Benign	100	75.2%
Total	133	100.0%

Out of the total of 133 patients, 33(24.8) patients had malignant adnexal mass and 100(75.2%) patients had benign adnexal mass.

Table -2 :Distribution of malignant mass based on histopathology

Histopathological type	Number	Percentage
1.Epithelial cell tumors	24	72.72
Serous cystadenocarcinoma	11	33.33
Mucinous cystadenocarcinoma	7	21.21
Endometrioid cystadenocarcinoma	3	9.09
Clear cell adenocarcinoma	3	9.09
2.Sex-cord stromal tumors	9	27.27
Immature teratoma	2	6.06
Endodermal sinus tumor	2	6.06
Dysgerminoma	3	9.09
Granulosa cell tumor	2	6.06
Total	33	100

Out of 33 malignant tumors in our study, majority (72.72%) were epithelial cell ovarian carcinoma. Out of these serous cystadenocarcinoma was the most common (33.33%) and clear cell carcinoma was the least common (9.09%). Sex cord stromal tumors were 9 in number, thus constituted 27.27% of all the malignant mass ,among these dysgerminoma was the most common (9.09%) and granulosa cell tumor was the least common (6.06%).

Table -3:Distribution of benign mass based on histopathology

Histopathological type	Number	Percentage
1.Non –Neoplastic	27	27
Endometrioma	9	9
Follicular cyst	11	11
Tubercular TO Mass	3	3
Corpus luteal cyst	4	4
Hydrosalpinx,TO-abscess(non tubercular)	5	5
2.Neoplastic	73	73
Serous cystadenoma	32	32
Mucinous cystadenoma	24	24
Fibroma	5	5
Thecoma	4	4
Dermoid tumor	8	8
Total	100	100

Out of the 100 benign mass, majority were of epithelial cell type 73% . Among these, serous cystadenoma was the most common 44% (32/73) followed by Mucinous cystadenoma 33% (24/73).Among the non neoplastic tumours, follicular cyst is the most common.

Table 4:Distribution of malignant and benign mass according to cut-off level of serum CA125

Serum CA125	Malignant(n=33)		Benign(n=100)		Total(n=133)	
	No.	%	No.	%	No.	%
>35 U/ml	25	75.75	33	33	58.75	43
<35 U/ml	8	24.24	67	67	75.24	56

Out of 33 malignant tumors, 25 (75.75%) had serum CA125 >35 U/ml, whereas out of the 100 benign tumors, only 33 (33%) had serum CA125 >35 U/ml; these benign mass mainly belonged to the epithelial cell tumor group, and inflammatory tuboovarian mass. Out of the 33 malignant tumors, only 8 (24.24%) had serum CA125 <35 U/ml. These included endodermal sinus tumor, dysgerminoma, granulosa cell tumor and immature teratoma.

Table 5: Comparative screening efficacy of CA 125 and RMI.

Variable		Malignant (n=33)		Benign (n=100)		Total (n=133)	
		No	%	No.	%	No.	%
Serum CA 125 cut of level	<35	25	75.75%	33	33%	58	43%
	>35	8	24.24%	67	67%	75	56%
	>200	28	84.84%	5	5%	33	24.82%

Out of the 33 malignant tumors, only 8 (24.24%) had serum CA125 <35 U/ml.

Table 6: Distribution of levels of serum CA 125 in malignant and benign tumors

Serum CA 125	Malignant	Benign	P value
Mean	235.99	31.93	<0.001
Grouped median	112.0	21.67	
Minimum	12.0	3.9	
Maximum	1100.0	200.0	
Std.Deviation	322.26	33.31	

The mean and median values for serum CA 125 in the subjects with malignant disease were 235.99 and 112.0 respectively, the corresponding values in the subjects with benign disease were 31.93 and 21.63 respectively. The association between was statistically significant at a p value of <0.001.

Table 7:

Test result variable	Area under curve	Std Error ^a	Asymptomatic ^b	Asymptomatic 95% confidence interval	
				Lower bound	Upper bound
CA 125	0.838	0.065	0.000	0.711	0.964

Serum CA 125 had an area of 0.838, SE of 0.065 and Asymptomatic 95% CI of 0.711 to 0.964.

The test result variables serum has atleast one tie between the positive actual state group and negative actual state group. Statistics may be biased because of

a. Under the non parametric assumption

b. Null hypothesis :true area=0.5

Table 8: Association of CA-125 in between Benign and Malignant

	Benign		Malignant		T	p-Value
	Mean	±SD	Mean	±SD		
CA-125 U/ML	28.45	31.37	174.57	287.58	-4.75	<0.001

The table presents a comparison of CA-125 levels between benign and malignant cases, the mean CA-125 level is 28.45 U/mL (±31.37) in benign cases and 174.57 U/mL (±287.58) in malignant cases. The t-value for CA-125 is -4.75, also with a p-value of less than 0.001, indicating a statistically significant difference between the two groups.

4. Discussion

1. Out of the total of 133 patients, 33(24.8) patients had malignant adnexal mass and 100(75.2%) patients had benign adnexal mass.

2. Out of 33 malignant tumors in our study, majority (72.72%) were epithelial cell ovarian carcinoma. Out of these serous cystadenocarcinoma was the most common (33.33%) and clear cell carcinoma was the least common (9.09%). Sex cord stromal tumors were 9 in number, thus constituted 27.27% of all the malignant mass, among these dysgerminoma was the most common (9.09%) and granulosa cell tumor was the least common (6.06%).

Wentzensen N et al is under conclusion that the heterogeneous associations of risk factors with ovarian cancer subtypes emphasize the importance of conducting etiologic studies by ovarian cancer subtypes. Most established risk factors were more strongly associated with nonserous carcinomas, which demonstrate challenges for risk prediction of serous cancers, the most fatal subtype.¹

Ayhan A et al based on his study came to conclusion that the high levels of tumor markers, especially for CA 125 and CA 19-9, may indicate the larger tumor size. The elevation of serum CA 125 may suggest serous tumors, while the high level of serum CA 19-9 and CEA may indicate mucinous borderline ovarian tumors.²

Milojkovic et al based on his study, Preoperative determination of CA 125 is a very useful method to discriminate between benign and malignant masses in the pelvis.³

3. Out of the 100 benign mass, majority were of epithelial cell type 73%. Among these, serous cystadenoma was the most common 44% (32/73) followed by Mucinous cystadenoma 33% (24/73). Among the non-neoplastic tumours, follicular cyst is the most common.

Hasholzner U et al got result regarding histological types of ovarian carcinomas, we found a sensitivity of 50% for CA 125 II and CASA, 36% for CA 72-4 and 33% for CYFRA 21-1 in serous ovarian cancer (n = 53), 21% for CA 125 II and CASA, 36% for CYFRA 21-1 and 43% for CA 72-4 for mucinous ovarian cancer (n = 27). Serous ovarian carcinomas were classified by higher FIGO-stages than mucinous ovarian carcinomas. Additional sensitivities were found at the time of primary diagnosis for the combination of CA 125 II and CA 72-4 and in serous ovarian cancer for CA 125 II and CASA. According to our results, at the time of primary diagnosis the combined determination of CA 125 II and CA 72-4 is useful. If both are negative, determination of CASA can be helpful. For follow-up care and control of efficacy of treatment the preoperative positive or leading marker is sufficient.⁴

Poncelet C et al concluded that Serum tumor marker assays modified both preoperative assessment and surgical management of borderline ovarian tumors.⁵

4. Out of 33 malignant tumors, 25 (75.75%) had serum CA125 >35 U/ml, whereas out of the 100 benign tumors, only 33 (33%) had serum CA125 >35 U/ml; these benign mass mainly belonged to the epithelial cell tumor group, and inflammatory tubo-ovarian mass. Out of the 33 malignant tumors, only 8 (24.24%) had serum CA125 <35 U/ml. These included endodermal sinus tumor, dysgerminoma, granulosa cell tumor and immature teratoma.

Engelen MJ says If one chooses to use serum markers in follow-up of mucinous borderline ovarian tumors CA 19-9 should be included. Measurement of serum tumor markers in the follow-up of patients with borderline ovarian tumors may lead to earlier detection of recurrence in only a very small proportion of patients, while the clinical value of earlier detection of recurrence remains to be established.⁶

5. Out of the 33 malignant tumors, only 8 (24.24%) had serum CA125 <35 U/ml.

Behnamfar F based on his analysis concluded that CA-125 marker, along with other ultrasound findings, can be more accurate in identifying the malignancy of the adnexal tumor.⁷

According to McDonald et al study, Patients with solid or complex ovarian tumors and an elevated serum CA 125 level (greater than 35 units/mL) are at high risk of ovarian malignancy.⁸

Oehler MK et al says, CA 125 and CASA have similar characteristics in preoperative diagnosis and postoperative follow-up. In clinical situations with inconclusive or negative CA 125 serum values CASA is helpful to improve management of patients with advanced ovarian cancer.⁹

6. The mean and median values for serum CA 125 in the subjects with malignant disease were 235.99 and 112.0 respectively, the corresponding values in the subjects with benign disease were

31.93 and 21.63 respectively. The association between was statistically significant at a p value of <0.001.

Sehoul J et al researched and came to conclusion that the combination of CA-125 and CASA can improve the detection of patients with suspected ovarian cancer.¹⁰

Khoiwal K et al concluded that both Ca-125, as well as RMI scoring, are important diagnostic tools. RMI scoring has a better overall diagnostic performance than Ca-125 in predicting malignancy.¹¹

7. Serum CA 125 had an area of 0.838, SE of 0.065 and Asymptomatic 95% CI of 0.711 to 0.964. The test result variables serum has atleast one tie between the positive actual state group and negative actual state group. Statistics may be biased because of

a. Under the non parametric assumption

b. Null hypothesis :true area=0.5

Rossi AC et al came to conclusion that Preoperative CA 125 correlated well with FIGO stage but not with age, grade, residual disease after primary surgery, relapse and disease free interval.¹²

Zeimet AG et al results suggest that the best predictive value (positive and negative) was obtained if CA-125 is assigned a relatively high cut-off value (65 U/ml) in conjunction with a low cut-off level (3.2 U/ml or 4 U/ml) for TAG-72. In the present study, at threshold values of 65 U/ml respectively, a sensitivity of 86%, a specificity of 83% and a positive and negative predictive value of 85% were obtained. In mucinous carcinomas of the ovary, however, the additional TAG-72 determination did not lead to a better predictive power than did CA-125 measurement alone.¹³

Bozkurt M et al in his research says that CA-125 and CA15-3 serum levels were statistically significant to distinguish between benign and malignant ovarian tumors, CA 19-9, CEA, and AFP were not significant. The different test combinations did not contribute to the diagnostic accuracy.¹⁴

5.Limitation

As this was a single center, hospital based study and it does not represent an entire population and as our sample size was relatively small, our results may have less statistical power and it is difficult to draw a definite conclusion.

6.Source of funding

None

7.Conflict of interest

The author declared no conflict of interest

8.Ethical approval

All procedures followed were in accordance with the institutional ethics committee for human research,

9.References

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