



## STUDY OF CORRELATION OF SERUM CA-125 LEVELS AND SEVERITY OF DISEASE IN CASES OF EXTRA OVARIAN ENDOMETRIOSIS.

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### ABSTRACT

**Introduction:** Extraovarian endometriosis is difficult to diagnosis as generally missed on ultrasound. The study evaluates the role of CA-125 in diagnosing extra-ovarian endometriosis when ovarian endometrioma is not present on ultrasound. **AIMS:** To study the correlation of serum CA-125 levels and severity of extra-ovarian endometriosis on laparoscopy when ovarian endometrioma is not present. **MATERIAL AND METHODS:** The study was a prospective study done for a period of 1 year in all patients with symptoms suggestive of endometriosis and ultrasound showing no ovarian endometrioma. Serum CA-125 levels assessments were done pre-op and were correlated with findings with extra-ovarian endometriosis on laparoscopy. The patients were divided in two groups (on the basis of CA-125 levels <35 U/ML and >35 U/ML). The following parameter were compared in these two groups: Age, BMI, symptoms, signs, presence of DIE, r-ASRM staging and score. **RESULTS:** No correlation between CA-125U/ML levels and age, BMI, was found. No correlation between symptoms and CA-125 levels and symptoms suggestive of endometriosis. The correlation between restricted mobility and presence of uterosacral nodule on clinical examination was significantly correlated with CA125 >35U/ML. Adenomyosis in (26%) and fibroid (34%) was found in association with endometriosis. About two third subjects with levels > 35 U/ML were in Stage 3 and stage 4 of the r-ASRM classification. The presence of dense adhesions and POD obliteration was also correlated with higher CA125 >35 U/ML. **CONCLUSION:** CA-125 levels >35U/ML were associated with stage 3 and stage 4, presence of DIE, dense adhesions in patients where symptoms are suggestive of endometriosis and ultrasound showing no ovarian endometrioma hence CA-125 levels can be used to judge the severity of extra ovarian endometriosis in patients with symptoms suggestive of endometriosis.

### KEYWORDS :

#### INTRODUCTION:

Endometriosis is a progressive disease defined as presence of the endometrial glands and stroma outside the uterus. (1) The prevalence of endometriosis in the general population is estimated to be 10% (2). Endometriosis is of three types: Peritoneal, superficial endometriosis, ovarian endometrioma and deep infiltrating endometriosis (DIE). DIE is the disease that extends more than 5 mm under the peritoneal surface and such lesions are easier to palpate than being visible to the naked eye. (3) 70% present with pelvic pain, 80% with dysmenorrhea, 44% with dyspareunia and 15 to 20% with infertility. (4). Tender nodularity in the cul-de-sac and the uterosacral has approximately 85% sensitivity and 50% specificity as a clinical criterion of deeply infiltrating endometriosis. (5) The gold standard for the diagnosis of endometriosis is direct visualization of ectopic endometrial lesions under laparoscopy. Endometriosis is classified into four stages as per revised American Society for Reproductive Medicine classification 1996 (I-minimal, II-mild, III-moderate, IV-severe) depending on location, extent and depth of endometriosis implants, presence and severity of adhesions, POD obliteration and presence and size of ovarian endometriomas. (6) A score of 1-15 indicates minimal or mild endometriosis and a score of 16-40 indicates moderate and a score >40 indicates severe disease. Non-invasive modalities to diagnose these extraovarian endometriosis is MRI and certain biochemical markers like CA-125. (7) The present study was done with the aim of studying the correlation of serum CA-125 levels and laparoscopic findings in women where symptoms are suggestive of endometriosis and ultrasound shows no evidence of endometrioma.

#### MATERIAL AND METHODS:

The study was conducted at a Multispecialty tertiary care hospital where laparoscopic surgeries are routinely performed in urban women of reproductive age group with symptoms of endometriosis. It was a prospective observational study done for 1 year. Total 450 laparoscopic surgeries were performed over a span of 1 year at the institute. CA-125 was done in all patients with symptoms suggestive of endometriosis (dyspareunia, chronic pelvic pain, dysmenorrhea, abnormal uterine bleeding and infertility) and ultrasound showing no ovarian endometrioma. Patients with laparoscopic confirmed extra-ovarian endometriosis were included in the study. A total of 50 such patients were included. Patients were divided into 2 groups according to CA-125 preoperative levels (<35 U/ML and >35U/ML) and following parameters were compared between the two groups: age,

BMI, clinical signs (restricted uterine mobility, uterosacral nodule) and symptoms of endometriosis, r-ASM score and stage.

**Statistical Analysis:** Qualitative data was represented in form of frequency and percentage. Association between qualitative variables was assessed by Chi-Square test with Continuity Correction for all 2 X 2 tables and Fisher's exact test for all 2 X 2 tables where p-value of Chi-Square test was not valid due to small counts. Quantitative data was represented using Mean  $\pm$  SD. Analysis of Quantitative data between the two groups was done using unpaired t-test. Co-relation between CA-125 and r-ASM score, was computed via spearman co-relation test. P value < 0.05 was considered as statistically significant

#### Results:

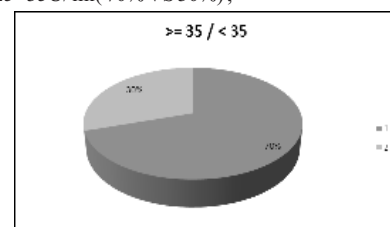
The result of the study shows that out of the 50 patients, 35 presented with CA-125 >35U/ML and 15 with CA125 <35U/ML. (70% VS 30%). Endometriosis was associated 26% with fibroid and 34% with adenomyosis.

**Table 1 (Comparison of various variables by pre-op CA-125 levels.**

Variables	Pre op CA-125 U/ML	Mean	P value
Age	>35	37.46	0.6 (Not significant)
	<35	36.87	
BMI	>35	23.37	0.9 (Not significant)
	<35	23.3	

No correlation was found between age, BMI and CA-125 levels. The mean age of presentation was 37 years and BMI was 23.

In the study of 50 patients, 35 presented with CA125  $\geq$  35U/ml and 15 with CA125 <35U/ml (70% VS 30%),



**Figure 1**

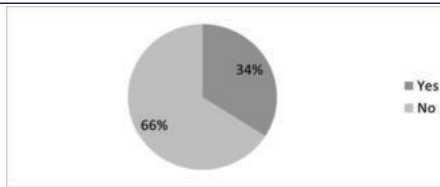


Figure 2: Association of endometriosis with fibroid

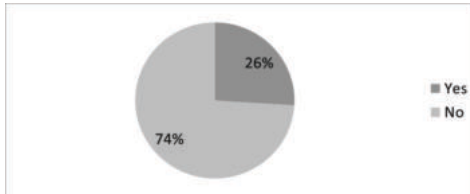


Figure 3: Association of endometriosis with adenomyosis

Table 2: Correlation between symptoms of endometriosis and CA-125 values

SYMPTOMS	Pre op CA-125 LEVEL(U/ML)		P value
Dysmenorrhea	>35	<35	
present	20 (83.3%)	4 (16.7%)	0.095
absent	15 (57.7%)	11(42.3)	(Not significant)
Chronic pelvic pain			
present	17 (77%)	5(23%)	0.222
absent	18(64%)	10 (36%)	(Not significant)
Dyspareunia			
present	1 (50%)	1(50%)	0.514
absent	34 (70.8%)	14(29.2%)	(Not significant)
Infertility			
present	4 (50%)	4 (50%)	0.220
absent	31 (73.8)	11(26.2%)	(Not significant)
Abnormal uterine bleeding			
present	7 (63.6%)	4(36.4%)	0.713
absent	28 (71.8%)	11 (28.2%)	(Not significant)

With regards to CA-125 levels and symptoms of endometriosis (dysmenorrhea, chronic pelvic pain, infertility, dyspareunia and abnormal uterine bleeding) no correlation was found. Hence symptoms are not correlated with CA-125 levels

Table 3: Correlation between clinical findings and CA125 levels

Clinical Finding	Pre op CA-125 level U/ML		P value
	>35	<35	
Uterosacral nodule			
present	10(100%)	0 (0%)	0.022 (Significant)
absent	25 (62.5%)	15(37.5%)	
Restricted mobility of uterus			
present	13(92.9%)	1 (7.1%)	0.0391 (Significant)
absent	22(61.1%)	14(38.9%)	

The presence of uterosacral nodule and restricted mobility of uterus were correlated with higher CA-125 levels and showed positive correlation as evident in the table above.

Table 4: Correlation between Lap Findings (Adhesions, superficial endometrial implants and pod obliteration, deep endometriosis)

Lap Findings	Pre op CA-125 Levels(U/ML)		P value
Superficial endometrial implants	>35	<35	
present	27 (67.5%)	13 (32.5%)	0.702
Absent	8 (80%)	2 (20%)	(Not significant)
Type of adhesion			
Dense	28 (96.6%)	1 ( 3.4%)	0.0015
Flimsy	5 (55.6%)	4 (44.4%)	(Significant)
No adhesion	2 (16.7%)	10( 83.3%)	
POD obliteration			
Complete	18 (94.5%)	1(5.3%)	0.00152
Partial	3(100%)	0 (0%)	(Significant)
No obliteration	14 ( 50%)	14(50)	
Deep endometriosis			
present	18 (90%)	2(10%)	0.012
absent	17(56.7%)	13 (43.3%)	(Significant)

The laparoscopic finding showed that presence of dense adhesions and pouch of Douglas obliteration and presence showed significant correlation with CA-125 levels more than 35 U/ML.

Table 5 Correlation of r-ASRM staging and preop CA-125 levels

r AS RM stage	Preop CA-125(U/ML)		P value
Stage	>35	<35	
Stage 1	1(8.3%)	11 (91.7%)	
Stage 2	11(78.6%)	3(21.4%)	
Stage 3	5(100%)	0 (0%)	
Stage 4	18(94.7%)	1(5.3%)	(0.00000397) (Significant)

The CA-125 levels>35 U/ML were correlated with stage 3 and 4 endometriosis.

**Discussion:**

In the study, mean age and BMI of study subjects was 37.5 ± 4.8 years and 21.1 ± 2.9 Kg/m2 with no significant difference between two groups (p> 0.05). In a similar study by Zomer MT et al. no difference between the groups was observed with respect to median age (34.5 vs. 35.4 years; p=0.2) and median BMI (24 versus 24 kg/ m2; p=0.5). (8,9) . 34% associated with fibroid and 26 % with adenomyosis and endometriosis has been found to be associated with the two. Most common symptom observed was dysmenorrhea (48%) followed by chronic pelvic pain (44%) abnormal uterine bleeding (22%), infertility (16%), dyspareunia (4%). No difference was observed between two groups based on symptoms (p> 0.05). Most common clinical finding observed were restricted mobility of uterus (28%) and utero-sacral nodules which were also present in 28% of cases and both were statistically correlated with CA-125 levels. Tender nodularity in the cul de sac and along the uterosacrals has approximately 85% sensitivity and 50% specificity as a clinical criterion for deeply infiltrating endometriosis and previous studies show ultrasound involvement of uterosacral as a marker of ureteral involvement. (10). At the time of laparoscopy, endometriosis was found to be stage 1 in 74%, stage 2 in 28%, stage 3 in 17% and stage 4 in 41%. In the study described over 90% of subjects with CA-125 levels of < 35 U/ ml were in r-ASRM stage I and II subjects while about two third subjects with levels above 35 U/ ml were in stage III and IV. The association of CA-125 levels with increasing severity and staging of endometriosis was found to be statistically significant (p< 0.05) and such similar results were obtained by Runa et al. (11). We also observed that deep infiltrating endometrial lesions were significantly associated with higher CA-125 levels. (50% VS 18.8%).

P. R. Koninckx studied the role of CA-125 in management of endometriosis and concluded that CA-125 can be used to diagnose deeply infiltrating endometriosis which are the more severe forms and are clinically easily missed. (13) . The importance of the findings of this study concerns the correlation between preoperative high levels of CA-125 (> 35 U/ mL) and the presence of DIE when preoperative

imaging study does not identify ovarian endometriosis and symptoms are suggestive of endometriosis. Given these findings, CA-125 level can be suggested in the preoperative assessment of women with suspected extra ovarian endometriosis.

## CONCLUSION

The result of the study shows in patients presenting with symptoms of endometriosis without an ovarian endometrioma, where CA-125 levels >35 U/mL, laparoscopy discloses more severe spectrum of the disease as demonstrated by higher r-ASRM stage and score, the presence of DIE, adhesions and pouch of Douglas obliteration. Hence CA-125 can be considered as a marker to judge severity pre-operatively and employ multidisciplinary approach in the management of such cases.

Limitation of the study: The small no of subjects could be the limitation. More study is needed in this regard.

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No conflict of interest

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