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Study on the accuracy of CA-125 combined with Transvaginal Ultrasound for presurgical Diagnosis of Endometriosis

Kritika Thapa [1], **Suniti Rawal**[1], **Anamika Jha**[2]

[1]Department of Obstetrics and Gynecology, Tribhuwan University Teaching Hospital, Kathmandu, Nepal
[2]Department of Radiology, Tribhuwan University Teaching Hospital, Kathmandu, Nepal

ABSTRACT

Introduction: Endometriosis is a gynecological condition often diagnosed surgically. Non-invasive tools such as CA125 and transvaginal sonography (TVS) may improve early detection.

Methods: This descriptive observational study was conducted from April 2017 to October 2018. A total of 77 women with a clinical diagnosis of endometriosis underwent evaluation using serum CA125 and TVS. Surgical and histopathological findings were used as the gold standard. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated.

Results: A total of 85 patients were initially included; however, eight were excluded because they did not meet the inclusion criteria. The mean age of the participants was 35.5 years. Dysmenorrhea was the most common symptom, followed by deep-seated lower abdominal pain. When the cutoff of CA125 was taken as 35 IU/ml, sensitivity, specificity, PPV, and NPV were 98.6%,0%,90.8%, and 0% respectively, with an accuracy of 89.6%. ROC curve determined the cut-off point of 55 IU/ml for CA125 with a PPV of 95.7%. Endometriosis was present in 90.9% cases during surgery and was proven histopathologically in 80.5%. A combination of CA125 and endometrioma in TVS had a sensitivity of 80% with an accuracy of 80%.

Conclusion: The combined use of CA125 and TVS improves preoperative diagnostic accuracy for endometriosis and may reduce reliance on invasive procedures. Thus, these can be used for initial assessment to avoid diagnostic delay and enable the clinician to plan appropriate surgical treatment.

Keywords: CA125, Endometriosis, Transvaginal sonography

INTRODUCTION

Endometriosis is a clinical and pathological entity characterized by the presence and growth of endometrial glands and stroma outside the uterine cavity.[1] It impacts around 6-10% of women of reproductive age group.[2]

Patients present with symptoms like dysmenorrhea, dyspareunia, deep-seated lower abdominal pain, dyschezia, and subfertility. Similar symptoms are seen in irritable bowel syndrome, pelvic inflammatory disease, and others, creating a diagnostic challenge.[3,4]

Bimanual pelvic examination(BPE) may reveal tender uterosacral ligaments, cul-de-sac nodularity, induration of the rectovaginal septum, fixed retroverted uterus, adnexal masses, and pelvic tenderness.[5,6]

Laparoscopy is the gold standard for definitive diagnosis, involving visualisation of lesions followed by histological confirmation by a pathologist.[7] While accurate, it is invasive, costly, requires an experienced surgeon, and is associated with risks and complications. Consequently, there has been increasing interest in non-invasive alternatives.

Corresponding Author:
Dr Kritika Thapa
Email: creeteeca@gmail.com

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Investigations for diagnosis include biochemical markers and imaging modalities. Biochemical markers include Cancer Antigen (CA125), Vascular Endothelial Growth Factor (VEGF), Tumour Necrosis Factor(TNF)-alpha, CRP, Interleukin(IL)-6, and cytokines.[8] Levels of CA125 are significantly higher in women with moderate or severe endometriosis.[9]

TVS is an essential diagnostic tool that is readily available, safe, inexpensive, and noninvasive.[10] CT scans and MRIs can provide additional and confirmatory information in the assessment of endometriosis. Still, they are not recommended as primary diagnostic tools due to their high cost and limited access.[11, 12]

Guerriero et al. reported improved sensitivity for diagnosing endometriomas when both were combined, though specificity was limited.[10] Similarly, Mol et al. and Hirsch et al., through meta-analyses, concluded that CA-125 is inadequate on its own but may strengthen diagnostic accuracy when paired with imaging. [13,14] Bazot et al. further emphasized the central role of TVS, while noting that biomarkers can add value in preoperative assessment.[15]

Despite these findings, little is known about the diagnostic performance of this combined strategy in resource-constrained environments, where reliance on non-invasive methods is significant.

The present study aimed to evaluate the diagnostic accuracy of serum CA-125 in combination with transvaginal sonography for the presurgical diagnosis of endometriosis, using surgical and histopathological findings as the reference standard.

METHODS

A descriptive observational study was conducted over 18 months, from 1st Baisakh 2074 to 31st Asoj 2075 (14th April 2017 to 17th October 2018) in the Department of Obstetrics and Gynecology and the Department

of Radiology.

All patients admitted for laparotomy/TAH with BSO (Total Abdominal Hysterectomy and bilateral salpingoophorectomy) with preoperative diagnosis of endometriosis were included. A non-probability sampling technique was used. Sample size was calculated using the formula $N = z^2*pq/e^2$, where N = Required sample size, z = A constant value 1.96 for a confidence interval 95% p = Prevalence of endometriosis in the hospital P=28(Prevalence of endometriosis in the previous year was 28 cases) q =1-p e =Allowable error (an error margin of 10% was taken). Substituting all the values, the sample size of 77 was calculated.

Exclusion criteria included pelvic inflammatory disease, previous surgery for endometriosis, large fibroids or ovarian tumors, no history of contact, gynecological cancer, and anatomical anomalies precluding TVS.

After informed consent, each patient underwent structured history-taking, clinical pelvic examination, serum CA125 measurement, and TVS. In the BPE, uterine mobility, fixed retroverted uterus, adnexal masses, Pouch Of Douglas(POD)nodularity, and tenderness were assessed. CA-125 was measured at the biochemistry lab. A cutoff value of 35 IU/mL was initially used, followed by ROC analysis to determine an optimal threshold. TVS was conducted using a Medison Accuvix A30 machine by a single radiologist in the Department of Radiology. Features evaluated included ovarian cysts, uterine retroversion, POD obliteration, probe tenderness, and nodules.

Intraoperative findings served as the gold standard. Specimens were analyzed histologically for the presence of endometrial glands and stroma.

SPSS was used for data analysis. Sensitivity, specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV), and accuracy were calculated. Receiver Operating Characteristic (ROC) curves were used to determine optimal CA125 cutoffs. The agreement between BPE and TVS was assessed using Cohen's Kappa.

RESULTS

During the study period, a total of 77 cases with a preoperative diagnosis of endometriosis who underwent surgery and met the inclusion criteria were enrolled. The total Cases studied were 85; however, eight were excluded as 4 had a history of previous laparotomy for endometriosis, two each had huge fibroids, and no history of sexual contact.

The mean age of participants was 35.35 years (range 21–58). Among 77 patients,49(63.6%) patients had Dysmenorrhea, 43(55.8%)had Deep-seated lower abdominal pain,17(22.1%)had Infertility, 15(19.5%) had Dyspareunia, and 10(13%) had Dyschezia.

On BPE about 15(19.5%) patient had generalized tenderness ,40(51.9%) had fixed retroverted uterus, 20(26%) had uterine motion tenderness and 55(71.4%) had enlarged ovaries. Adnexal tenderness was present in 10(13%) patients, and a fixed adnexal mass was present in 18(23.4%). Twenty-three patients (29.9%) had fullness in POD,13(16.9%) had a mass felt in POD,15(19.5%) had nodularity in POD, and 11(14.3%) had local tenderness. The Mean CA125 was 85.9 IU/ml (range 26–404).

Table 1: Diagnostic Performance of CA125 at Two Cutoffs

CA125 cutoff (IU/ml)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
≥ 35	98.6	0	90.8	0
≥ 55 (ROC-based)	64.3	71.4	95.7	16.7

Receiver Operating Characteristics Curve was used for the detection of the cut-off point for CA125. The cut-off value for CA125 was 55 IU, with the area under the curve being 0.728(figure 1).

When the cutoff for CA125 was set at 35 IU/ml, sensitivity was 98.6%, specificity was 0%, PPV was 90.8%, NPV was 0%, and accuracy was 89.6%. About 90.8% had endometriosis intraoperatively with CA125 ≥ 35IU/ml(Table 1).

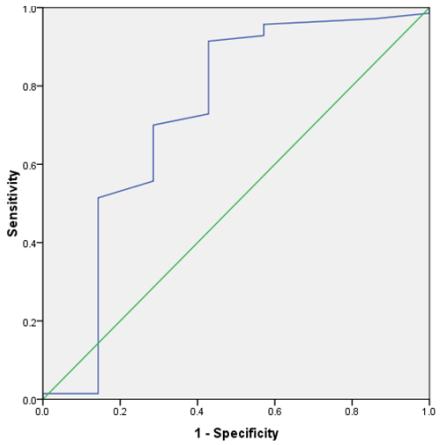

Figure 1: ROC Curve of CA125

When CA125 was used with a cutoff of 55 IU/ml, sensitivity was 64.3%, specificity 71.4%, PPV 95.7%, NPV 16.7%, and accuracy 64.9%. When CA125 levels were≥ 55 IU/ml, sensitivity and specificity were similar, with an accuracy of 64.9%(Table 1).

Table 2: Transvaginal Sonography (TVS) Findings(n=77)

Sonographic Feature	n	%
Endometrioma detected	64	83.1
Retroverted uterus	32	41.6
Obliteration of the pouch of Douglas (POD)	15	19.5
POD Nodules	7	9.1
Ovarian Fixity	16	20.8

Out of 77 patients 83.1% had endometrioma. A retroverted uterus was present in 41.6% patients, and nodules in POD in 9.1% of the cases. Fifteen patients (19.5%) had obliterated POD, 33.8% had probe tenderness, and 20.8% had fixed ovaries. Mobile ovaries were present in 75.3% patients. In 3.39% no ovaries were visualized (Table 2).

About 89% had the presence of endometriosis during TVS, which was also present during surgery.There was no intraoperative endometrioma when the TVS did not show positive results. The sensitivity of the test is 81.4%, the accuracy of 74% and the specificity and NPV are nil. The sensitivity of TVS for a retroverted uterus is 44.4%, with a higher specificity of 85.7% and a PPV of 96.90%. Seven patients had nodules on POD TVS, which were also present at surgery. The specificity of the test was 100% with a high PPV. TVS's finding of obliterated POD had a sensitivity of 20% with a specificity of 85.7%. True positive cases were 14 out of 77, and true negatives were 6. Probe tenderness during TVS had low sensitivity but high specificity. The test's accuracy was 40.3%.

Table 3: Confirmation of Endometriosis (n=77)

Finding	n	%
During Surgery	70	90.9
Histopathologically confirmed endometriosis	62	80.5

Endometriosis was present in 90.9% during surgery. Sixty-two patients (80.5%) had the presence of endometriosis during histopathological examination(Table 3). Fifteen patients (19.5%) had other pathologies, including 8 with hemorrhagic cysts, four corpus luteal cysts, 1each with papillary carcinoma of the ovary, mucinous cystadenocarcinoma, and borderline ovarian tumor.

Patients with endometrioma on TVS and CA-125 levels ≥ 35 IU/ml were

correlated with the operative findings. With a combination of CA125 and endometrioma in TVS, sensitivity was 80% with an accuracy of 80%; however, the NPV and specificity were 0. There were 56 patients (88.9%) who had endometrioma with a CA125 value ≥ 35IU/ml and the presence of endometriosis during surgery. The combination had an accuracy of 80%.

The combination correctly identifies endometriosis preoperatively (sensitivity = 80%) and is reliable, as it detects endometriosis when present (PPV = 88.9%). But the exclusion of endometriosis cannot be made based on CA125 and TVS findings (specificity and NPV: 0).

DISCUSSION

Diagnosis and treatment of endometriosis are among the most common indications for laparoscopic surgery today, as the disease occurs in reproductive-age women and leads to pelvic pain and/or infertility. Laparoscopic diagnosis carries the risks of bladder, bowel, and significant blood vessel damage, infection, and adhesion formation. It is also expensive and imposes a substantial economic burden on the health service and on the patient. Using a non-invasive method is a major priority in endometriosis research.[16]

This study supports the use of CA125 and TVS as complementary tools in the diagnosis of endometriosis, with particular utility in resource-constrained settings where laparoscopy may be unavailable or delayed.

Clinical presentation of endometriosis is highly diverse; none of the presenting signs or symptoms is pathognomonic for this disease. The overlap in symptoms with other gynecologic conditions (e.g., primary dysmenorrhea, adenomyosis, pelvic adhesions, ovarian cysts, pelvic inflammatory disease)[17] and chronic pain syndromes (e.g., irritable bowel, interstitial cystitis/painful bladder, fibromyalgia, musculoskeletal disorders) is an important facet in identifying endometriosis.

In the present study, patients included were aged 21 to 58 years, with a mean age of 35.35 years. The age group of patients is similar to the study by Bazot et al,[5] which included 92 women, with ages ranging from 20 to 51 years (median, 31.8 years), and Hudelist et al, in which 200 women were with an age range of 16 to 45 years, with a median of 33 years.[15]

In the present study, 4 (5.19%) patients were asymptomatic, 31 (40.25%) patients presented with a single symptom, 26 patients (33.76 %) had two symptoms, 13 patients (16.8%) presented with three symptoms, and the remaining 4% presented with more than three symptoms. Dysmenorrhea was the most common symptom, followed by deep-seated lower abdominal pain, dyspareunia, dyschezia, and infertility.

In the present study, the combined use of serum CA-125 and transvaginal sonography (TVS) yielded a sensitivity of 80% and an overall accuracy of 80% for presurgical diagnosis of endometriosis. The positive predictive value was high (88.9%), indicating that the combination helps confirm the disease. However, the low specificity and negative predictive value suggest that the absence of these markers cannot reliably exclude the condition.

Our findings align with earlier reports emphasizing the importance of multimodal diagnostic strategies. Guerriero et al. demonstrated that combining CA-125 with TVS improved sensitivity for detecting ovarian endometriomas, although specificity remained modest.[10] Hudelist et al. reported excellent diagnostic performance when clinical pelvic examination was combined with TVS, underscoring the general principle that multiple diagnostic tools together outperform single modalities.5 Similarly, Bazot and colleagues highlighted the high diagnostic yield of TVS for deep infiltrating endometriosis, supporting the central role of ultrasound imaging.[15]

The limited performance of CA-125 alone in our study is consistent with prior meta-analyses, which concluded that this biomarker has insufficient sensitivity and specificity for use in isolation.[13,14] The improvement in diagnostic accuracy observed when CA-125 was combined with TVS, therefore, reflects the complementary strengths of biochemical and imaging assessments.

Certain sonographic signs, such as ovarian fixity, probe tenderness, or obliteration of the pouch of Douglas, were also noted in our patients. These features, however, are not specific to endometriosis and may occur in other pelvic disorders, including ovarian neoplasms, pelvic inflammatory disease, or adhesions from prior surgery.[18,19,20] Thus, while helpful, they should not be interpreted as diagnostic markers on their own.

Methodological variations may explain differences between our results and those reported in other studies. For instance, Hudelist et al.[5] used laparoscopy with histology as the reference standard. They included a larger sample size, whereas our study relied on laparotomy/TAH findings because laparoscopy was not available at our center. Additionally, our study was limited to patients already suspected of having endometriosis, which may have inflated sensitivity and PPV but reduced specificity. Operator variability in TVS and inter-surgeon differences in intraoperative assessment may also contribute to disparities across studies.

Overall, our findings suggest that while CA-125 and TVS individually have limitations, their combined use provides a practical, non-invasive approach for confirming endometriosis before surgery. This strategy may be beneficial in settings with limited access to laparoscopy, enabling earlier clinical decision-making and more effective surgical planning.

CONCLUSION

The combination of serum CA125 and TVS offers a reliable, non-invasive diagnostic alternative for preoperative identification of endometriosis. While not suitable for ruling out disease, this dual approach facilitates early clinical decision-making, reduces reliance on invasive procedures, and improves patient counseling.

DECLARATION

Acknowledgement

None.

Author Contribution

KT was involved in the Concept of research, Design of research, Literature Search, Data Collection, Data Analysis, Data Interpretation. SR was involved in the Concept of research, drafting, and reviewing of the manuscript; AJ was involved in Drafting and reviewing the manuscript.

Ethical Approval

Research Department TUTH; IRC Ref:369(6-11-E)/073/074.

Data Availability Statement

The data that support the findings of the study are available with the corresponding author.

Consent/Assent

Informed written consent was obtained from the all the participants before data collection

Conflicts of Interest

NO conflict of interest

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NO funds for research

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