ISSN 2515-8260 Volume 09, Issue 07, 2022

# Original Research Article: Clinical Study On Diagnostic Accuracy Of ROMA (Risk Of Malignancy Algorhithm) Score In Predicting Epithelial Ovarian Cancers For Ovarian Mass

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**ABSTRACT**

**Background:** Ovarian malignant tumors have varied clinical and biologic behaviour. It is the sixth most common cancer among women (Age standaradised incidence rate being 6.6/100,000) and seventh leading cause of cancer deaths globally (age standaradised mortality rate being 4.0/100,00)In India, during the period 2004-2005, proportion of ovarian cancer varied from 1.7% to 8.7% of all female cancers in various population based registries of Indian Council of Medical Research. The proportion of this cancer was 6.0%-7.7% of all cancers among females in Gujarat.

**Objectives:** To Determine Diagnostic accuracy of ROMA Score using HE4 and CA 125 for Epithelial Ovarian Cancer.

**Methodology:** This prospective study using a sample of 50 patients who attends the gynecology out Patient department and Labour room between September 2018 and July 2019 for the evaluation of an ovarian mass. Blood specimens from these patients was obtained during their first assessment for laboratory work up. From the variables collection ROMA was calculated using CA-125 and HE4 results. Boththe receiver operating characteristic (ROC) curve and area under the curve (AUC) was calculated(accordingly), and the most valid cut-offs was determined accordingly. For all statistical comparisons, a p-value < 0.050 was accepted as statistically significant.

**Result:** Thirty-three subjects (66%) had Benign and Seventeen subjects(34%) had Malignant disease.For diagnostic modalities observation of my study is Maximum number of benign cases found by histopathological(66%) and serum CA-125(66%). Maximum number of malignant cases found by USG(48%) and CECT/MRI(48%). Maximum number (54%) of cases were found in 18- 44 age- group.For CA-125, mean and median values were 70.35 and 75 respectively for cases with benign disease and 373.4 and 346.8 respectively for cases with malignant disease. This association was statistically significant ($p<0.05$).For HE-4, mean and median values were 42.28 and 38 respectively for cases with benign disease and 301.17 and 240 respectively for cases with malignant disease. This association was statistically significant ($p<0.05$).For ROMA score, mean and median values were 4% and 3% respectively for cases with benign disease and

56.33% and 50.65% respectively for cases with malignant disease. This association was statistically significant ($p<0.05$).

**Conclusion:**. HE4 and ROMA showed a high specificity, but were less sensitivity than CA-125 and RMI in premenopausal women. However, ROMA is of comparable sensitivity and HE4 has highest specificity as compared to CA125 in postmenopausal women.
**Keywords:** Risk of ovarian malignancy algorithm, Risk of malignancy index, CA-125, HE4, Ovarian cancer,

## INTRODUCTION

Thousands of patients with ovarian tumor or cyst are hospitalized and operated all over the world. According to the National CancerInstitute, USA, 13-21% of women are diagnosed with ovarian cancer (EOC) at various clinical stages [1]. Stratification of pelvic mass cases to high- and low-risk groups is important for several reasons. Firstly, recent research has shown that ovarian cancer patients operated at centers specializing in female malignancies have a greater chance of survival. Secondly, the therapeutic decision in cases of ovarian/ adnexal tumor relies heavily on the correct diagnostication. Whether the tumor is malignant or benign, the surgeon will choose between laparoscopy or laparotomy, abdominal access (midline or transverse), and extent of surgery. Optimal operative cytoreduction by a skilled surgeon combined with correct staging according to FIGO greatly improves distant results of management in ovarian cancer. Modern imaging techniques and fast progress in laboratory tests have enabled a great step forward in diagnostic algorithms[2].

ROMA (Risk of Ovarian Malignancy Algorithm) based on CA125 (Cancer antigen 125) and the novel HE4 marker(Human Epididymis Protein 4. [3,4]has recently emerged as a promising approach to the preoperative categorization of malignancy risk. HE 4 is new marker which was recently proposed for ovarian cancer because of its specificity and high expression in ovarian cancer tissues. The diagnostic performance of ROMA was advocated for the first time by Mooreetal. (2-D), who demonstrated that CA125 combined with HE4 reveals the highest Sensitivity and specificity among nine markers studied.FDA now recommends ROMA in women over 18 years of age with a pelvic tumor or cyst qualified for surgery, emphasizing that ROMA must always be interpreted against clinical and radiology findings. [5]

Currently, several trials are under way using test kits from various manufacturers. The strategy with ROMA, as well as normal ranges, cut-off points, and interpretation await further optimization. This work was undertaken to determine the diagnostic performance of ROMA for preoperative stratification of patients with a pelvic mass using cut-off points determined by us and adopted from literature. Additionally,I studied usefulness of ROMA algorithm due to recent concepts of aetiology of epithelial ovarian malignancies and their categorization to type I and II. I also evaluated the Elecsys HE4 assay from Roche and the Architect i2000 CA125assay from Abbott for calculating ROMA. [6]

**METHODOLOGY** This prospective study was done at the SSG Hospital and Medical College Vadodara,Gujarat using a sample of 50 patients who attends the gynecology out Patient department and Labour room between September 2018 and July 2019 for the evaluation of an ovarian mass.

Minimum 50 pts required to estimate Sensitivity of ROMA score by 82% compare to gold standard HPE with 10% precision & 95% confidence. Based on last year of hospital records we included 50 cases of ovarian tumors in the department. All patients enrolling in the study was completed a written informed consent form in accordance with the Helsinki Declaration.

**Inclusion criteria:** Ovarian tumor, ascites, or elevated CA125. Histopathologic verification obtained.

**Exclusion criteria:**Liver cirrhosis revealed during laparoscopy in patients with ascites and elevated CA125.Tumor found not to involve the ovary.Qualification for follow-up as functional ovarian cyst.Kidney or lung pathology. Elevated Creatinine Levels without kidney Disease

**Study Procedure:**

. Blood specimens from these patients was obtained during their first assessment for laboratory work up. All cases wereundergone surgical intervention at a later stage to obtain Histopathological Diagnosis which wasbe used as the Gold Standard Test. All clinical and laboratory data was collected. The blood samples of the patients were collectedduring their first assessment, before surgical intervention, using standard serum separator tubes (SS T) for different biochemical profiles includingtumor markers. The samples were centrifuged immediately after collection to get the sera and then analyzed. The remaining sera was stored at -$20^0$C. After collecting the required number of specimens, serum HE4 was be measured. Both CA-125 and HE4 assays was done by a two-step immunoassay using the architect i2000 SR Immunoassay Analyzer (Abbott Laboratories, Illinois, US), which uses chemiluminescence microparticle immunoassay technology.All manufacturer recommendation for maintenance,calibration, and internal quality assessment was followed for both assays. Patients were grouped according to age (preandpostmenopausal) and lesion type (benign or malignant). The postmenopausal status was defined as one year or more of amenorrhea or an age of 50 years or more if the woman had undergone a hysterectomy. From the variables collection ROMA was calculated using CA-125 and HE4 results as per the manufacturer's recommendations (Abbott ARCHITECT ci8200; Abbott Laboratories, Illinois, US). This was followed as recommended by Moore et al[7], by calculating a predictive index (PI) for premenopausal and postmenopausal patients separately using equation 1 and 2 as follows:

1) PI for premenopausal women:
   PI = -12.0 + 2.38*lnHE4 + 0.0626*ln(CA-125)
2) PI for postmenopausal women:
   PI = -8.09 + 1.04*lnHE4 + 0.732*ln(CA-125)

The ROMA score was then obtained using the equation:

**ROMA %** = exp PI / (1 + exp PI) × 100%

where Exp PI = ePI

The cut-off value for CA-125 was 35 U/mL as recommended by the manufacturer and the cut-off value for RMI is 200 as proposed by Jacobs et al. [8] The cut-off value for HE4 is 70 pmol/L, and for ROMA for high-risk premenopausal and postmenopausal women is 13.1% and 27.7%, respectively.10 A comparison study was done for the four parameters (CA-125, RMI, HE4, and ROMA) and the validity indicators including Sensitivity, specificity, positive and

negative predictive values (PP V and NPV) and efficiency was calculated. Boththe receiver operating characteristic (ROC) curve and area under the curve (AUC) was calculated(accordingly), and the most valid cut-offs was determined accordingly. For all statistical comparisons, a p-value < 0.050 was accepted as statistically significant. All statistical analysis was done using SPSS Statistics (SPSS Statistics, Chicago, US) version 22.

**Premenopausal patients**

- ROMA value **≥ 7.4%** indicates high risk of finding epithelial ovarian cancer
- ROMA value **< 7.4%** indicates low risk of finding epithelial ovarian cancer

**Postmenopausal patients**

- ROMA value **≥ 25.3%** indicates high risk of finding epithelial ovarian cancer
- ROMA value **< 25.3%** indicates low risk of finding epithelial ovarian cancer

Considering that the ROMA cutoff is different in pre-menopause and post-menopause women, ROMA wasanalyzed first in all patients and then separately in the two subgroups of pre-menopause and post-menopausal patients.

## RESULTS & DISCUSSION

A prospective study was done at the SSG HOSPITAL VADODARA, using a sample of 50 patients who attends the gynecology out Patient department and Labour room between September 2018 and July 2019 to know diagnostic accuracy of ROMA (Risk of Malignancy Algorhithm) Score in Predicting Epithelial Ovarian Cancers for Ovarian Mass

| **PRE-MENOPAUSE** | | **POST-MENOPAUSE** | | **Total** |
|---|---|---|---|---|
| **No** | % | No | % | |
| **30** | 60 | 20 | 40 | 50 |

**Table 1: Type of patients**

Table 1 shows the distribution of subjects by menopausal status. Thirty(60%) subjects were pre-menopausal and Twenty(40%) subjects were post-menopausal.

According to Farah Farzaneh et al[9]. 2014 out of 99 (31.9% ) patients 31 post-menopause patients,22 (22.2%)had malignant masses, and from 68(68.7%) pre-menopausepatients 21 (21.2%)had malignant masses, which was not statistically significant according to their study.

According to Dweep Jindal et al[10]. 2017 Seventy-four (65%) patients were postmenapausal and 35% were regularly menstruating.

According to Sarikapanwilailak et al[11]. out of 328 parientsenrolled 251 (76.5%) were premenopausaland 77 women (23.5%) were postmenopausal

| Age in years | Total | |
|---|---|---|
| | n = 50 | % |
| **18-36** | 14 | 28 |
| **37-54** | 18 | 36 |
| **55-73** | 18 | 36 |

**Table 2: Age Distribution in Cases**

Basu et al[12] reported mean age as 48.8±11.2 years. Another study in India by Mondal et al reported median age of 48 years at diagnosis and maximum incidence of 44.3% in age group of 41-50 years.

An epidemiologic risk prediction model By K li reported median age of EOC in various countries as 52.4 years.

In study by Dweep Jindal et Al[13]. the mean age at diagnosis was 52.1±8.96 years (median=52). The mean age increased in relation to stage of EOC at diagnosis from 44±9.53 years in stage1 to 55.35±9.74 years in stage 4 in present study. Similar findings were reported by Saini et al with mean age of 52.67±8.04 in stage1 to 58.30±8.48 years in stage 4.3 In a limited resource setting, ovarian malignancy screening program may be restricted to age group above 45 years, being high risk.

| **BENIGN** | | **MALIGNANT** | | **Total** |
|---|---|---|---|---|
| **NO.** | % | NO. | % | |
| **33** | 66 | 17 | 34 | 50 |

**Table 3: Distribution of subjects by histopathological (HP) diagnosis**

Table 3 shows distribution of subjects by Histopathological (HP) diagnosis. Thirty-three subjects (66%) had Benign and Seventeen subjects (34%) had Malignant disease.

According to Farah Farzaneh et al[14]. 2014 out of 99 (31.9% ) patients 31 post-menopause patients,22 (22.2%)had malignant masses, and from 68(68.7%) pre-menopausepatients 21 (21.2%)had malignant masses.

According to Richard g. moore et al. 2011 total of 472 patients were evaluated with 383 women diagnosed with benign diseaseand 89 women with a malignancy. The incidence of all cancers was 15% and 10% for ovariancancer.[15]

Richard g. moore et al[16] enrolled 512 women with a pelvic massof which 472 (92.2%) were evaluable and are the focus of this report. Therewere 255 premenopausal patients and 217 postmenopausal patients. Plasma FSH levels wereemployed to determine menopausal status in 36 women, 22 of which had at least aremaining ovary after a prior hysterectomy. The mean age

of all women entered on the trialwas 50.3 years (range: 18 to 89). The mean age for the subgroup of premenopausal womenwas 39.7 years (range: 18 to 56) and for the subgroup of postmenopausal women 62.8 years(range: 44 to 89). Women diagnosed with benign disease made up 81.1% (383) of the cohort(150 postmenopausal and 233 premenopausal), and women diagnosed with a malignancy ora LMP tumor made up 18.9% (89) of the cohort (67 postmenopausal and 22 premenopausal)

| | HP | USG | CECT/MRI | ROMA Score | CA 125 | HE4 |
|---|---|---|---|---|---|---|
| **BENIGN** | 33 | 26 | 26 | 28 | 33 | 29 |
| **MALIGNANT** | 17 | 24 | 24 | 22 | 17 | 21 |

**Table 4: Distribution of subjects by different diagnostic methods**

Table 4 shows distribution of cases by different diagnostic methods. Maximum number of benign cases found by histopathological(66%) and serum CA-125(66%). Maximum number of malignant cases found by USG(48%) and CECT/MRI(48%).

According to Moore RG et al. out of 328 parients enrolled mean age was 41.2±13.0 years; 251 (76.5%) were premenopausaland 77 women (23.5%) were postmenopausal. And About62% of patients had one or more features from ultrasoundfindings. [17]

| Variable | Benign | Malignant | Total | P-Value |
|---|---|---|---|---|
| **Age** | | | | |
| **18-44** | 23 | 4 | 27 | P=0.0027 |
| **45-70** | 10 | 13 | 23 | |
| **Menopausal Status** | | | | |
| **Postmenopausal** | 8 | 12 | 20 | P=0.0042 |
| **Premenopausal** | 25 | 5 | 30 | |
| **CA-125** | | | | |
| **Mean** | 70.35 | 373.4 | 173.38 | P<0.0001 |
| **Median** | 75 | 346.8 | 87.5000 | |
| **Standard Deviation** | 37.75 | 278.28 | 217.3625 | |
| **Minimum** | 12 | 75 | 12 | |
| **Maximum** | 180 | 1095 | 1095 | |
| **HE-4** | | | | |

| | | | | |
|---|---|---|---|---|
| **Mean** | 42.28 | 301.17 | 130.30 | P<0.0001 |
| **Median** | 38 | 240 | 52.50 | |
| **Standard Deviation** | 26.74 | 224.26 | 179.55 | |
| **Minimum** | 5 | 60 | 5 | |
| **Maximum** | 100 | 902 | 902 | |
| **ROMA Score** | | | | |
| **Mean** | 4% | 56.33% | 33.49% | P<0.0001 |
| **Median** | 3% | 50.65% | 25.00% | |
| **Standard Deviation** | 0.056% | 0.30% | 0.35 | |
| **Minimum** | 0.01% | 10.20% | 0.01% | |
| **Maximum** | 23% | 75.80% | 96.90% | |

**Table 5: Distribution of subjects by age, menopausal status, serum CA125, HE-4, ROMA score**

Distribution of cases by Age, menopausal status, serum CA-125, serum HE-4 and ROMA score is shown in Table 5. Maximum number (54%) of cases were found in 18- 44 age- group. The association between age and disease status was found significant with caution ($p<0.05$). 30 (60%) women were premenopausal and 20(40%) were postmenopausal and its association with disease status was statistically significant with caution ($p<0.05$).

For CA-125, mean and median values were 70.35 and 75 respectively for cases with benign disease and 373.4 and 346.8 respectively for cases with malignant disease. This association was statistically significant ($p<0.05$).

For HE-4, mean and median values were 42.28 and 38 respectively for cases with benign disease and 301.17 and 240 respectively for cases with malignant disease. This association was statistically significant ($p<0.05$).

For ROMA score, mean and median values were 4% and 3% respectively for cases with benign disease and 56.33% and 50.65% respectively for cases with malignant disease. This association was statistically significant ($p<0.05$)

| **Variable** | **Benign** | **Malignant** | **Sensitivity** | **Specificity** | **PPV*** | **NPV*** |
|---|---|---|---|---|---|---|
| **Premenopausal** | | | | | | |
| **Roma<7.4%** | 19 | 0 | 76% | 100% | 100% | 45.45% |
| **Roma>7.4%** | 6 | 5 | | | | |
| **Postmenopausal** | | | | | | |
| **Roma<25.3%** | 2 | 0 | 25% | 100% | 100% | 66.67% |
| **Roma>25.3%** | 6 | 12 | | | | |
| **Combined** | | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Low Risk** | 21 | 0 | 47.83% | 100% | 100% | 58.62% |
| **High Risk** | 12 | 17 | | | | |
| **CA-125** | | | | | | |
| **<35** | 6 | 0 | 18.18% | 100% | 100% | 38.64% |
| **>35** | 27 | 17 | | | | |
| **$He_4$** | | | | | | |
| **<70** | 28 | 1 | 84.85% | 94.12% | 96.55% | 76.19% |
| **>70** | 5 | 16 | | | | |

**Table 6: Predictive values of ROMA score, Serum CA-125 levels and Serum $HE_4$ Levels of Benign and Malignant ovarian mass**

* PPV: Positive predictive value, NPV: Negative predictive value

The performance of ROMA score (in pre-menopausal, post-menopausal and in both combined), Serum Ca-125 levels and Serum HE4 Levels in predicting malignancy in this study is presented in Table 6.

In pre-menopausal woman, ROMA had a Sensitivity of 76% (54.87% to 90.64%), a specificity of 100% (47.82% to 100%), a positive predictive value of 100% and negative predictive value of 45.45%.

In post-menopausal woman, ROMA had a Sensitivity of 25% (3.19% to 65.09%), a specificity of 100% (73.54% to 100%), a positive predictive value of 100% and negative predictive value of 66.67%.

In all woman ROMA had a Sensitivity of 47.83% (26.82% to 69.41%), a specificity of 100% (80.49% to 100%), a positive predictive value of 100% and negative predictive value of 58.62%.

Serum CA 125 had a Sensitivity of 18.18% (6.98% to 35.46%), a specificity of 100% (80.49% to 100%), a positive predictive value of 100% and negative predictive value of 38.64%.

Serum HE4 had a Sensitivity of 84.85% (68.10% to 94.89%), a specificity of 94.12% (71.31% to 99.85%), a positive predictive value of 96.55% and negative predictive value of 76.19%.

**ROC Curve Analysis**

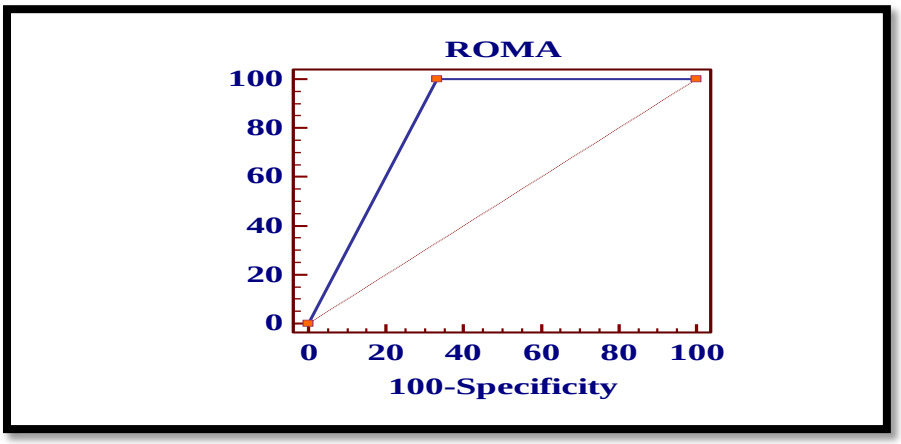

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**Figure 1: Receiver operator Characteristiccurve (ROC) showing relation between Sensitivity and specificity of ROMA score in differentiating between benign and malignant ovarian mass**

| Area under the ROC curve (AUC) | 0.833333 |
|---|---|
| Standard Error | 0.0417 |
| 95% Confidence interval | 0.701075 to 0.923669 |
| z statistic | 8.000 |
| Significance level P (Area=0.5) | <0.0001 |

**Table 7: Analysis of ROC Curve ROMA Score vs Histopathological report**

A Receiver Operating Curve (Figure 5) was plotted. In the table 7 the analysis of ROC curve is given which shows Area under curve 0.83 and it is statistically significant (p<0.001) it means there was 83% chance that ROMA score able to distinguish between positive cases and negative cases, so the diagnostic ability of ROMA score was found good.

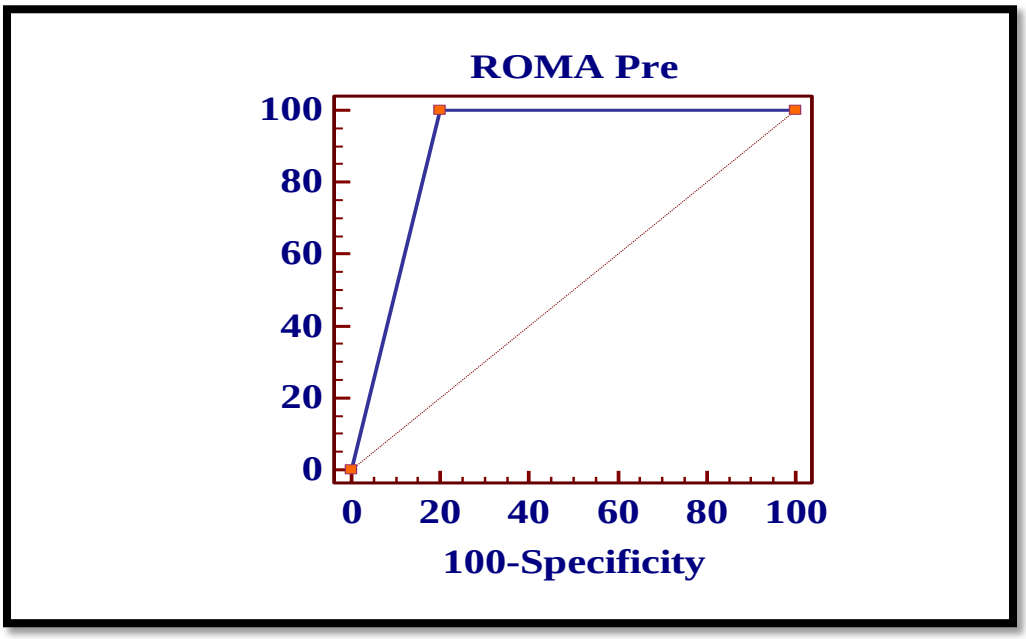


**Figure 2: Receiver operator Characteristic curve (ROC) showing relation between Sensitivity and specificity of ROMA score in differentiating between benign and malignant ovarian mass in Pre-Menopausal Women**

| Area under the ROC curve (AUC) | 0.900000 |
|---|---|
| Standard Error | 0.0408 |
| 95% Confidence interval | 0.734712 to 0.978883 |
| z statistic | 9.798 |
| Significance level P (Area=0.5) | <0.0001 |

**Table 8: Analysis of ROC Curve ROMA Score vs Histopathological report in Pre-Menopausal Women**

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A Receiver Operating Curve (Figure 6) was plotted. In the table 8 the analysis of ROC curve is given which shows Area under curve 0.90 and it is statistically significant (p<0.001) it means there was 90% chance that ROMA score able to distinguish between positive cases and negative cases in Pre-Menopausal Women, so the diagnostic ability of ROMA score was found good.

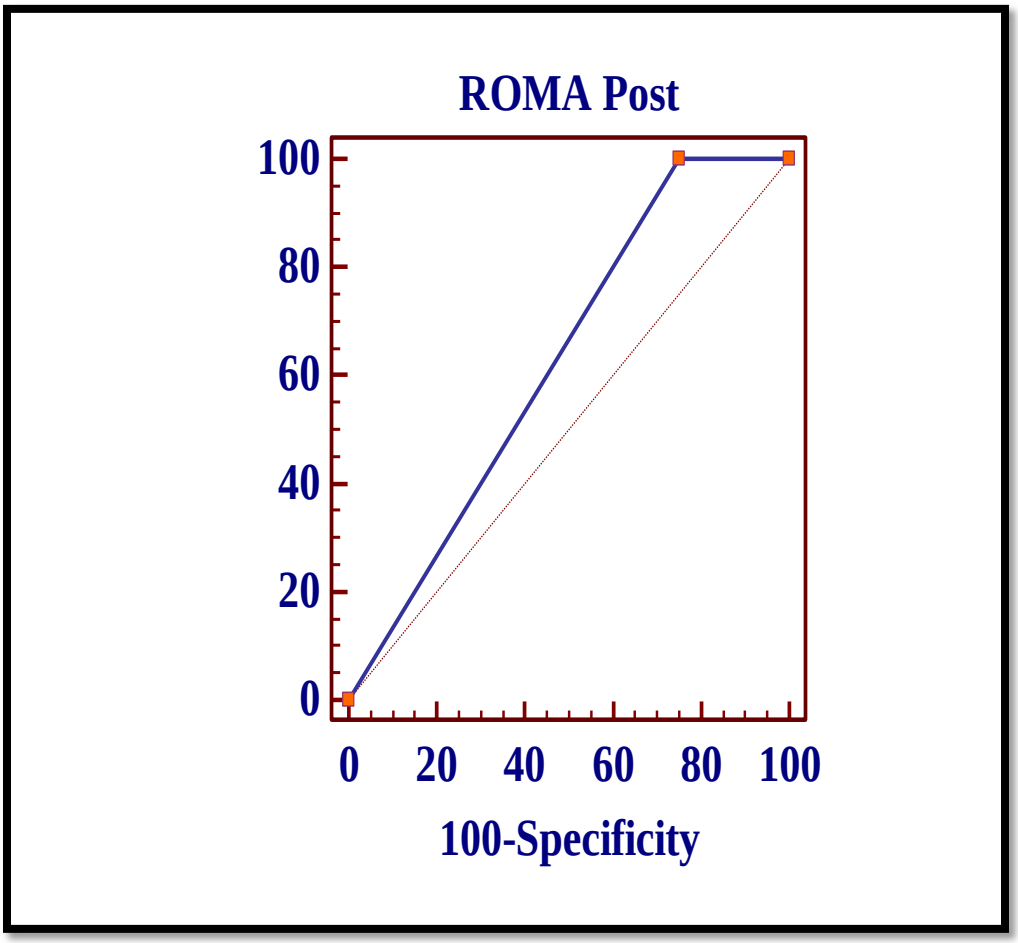


**Figure 3: Receiver operator Characteristic curve (ROC) showing relation between Sensitivity and specificity of ROMA score in differentiating between benign and malignant ovarian mass in Post-Menopausal Women**

| **Area under the ROC curve (AUC)** | **0.625000** |
|---|---|
| **Standard Error** | 0.0818 |
| **95% Confidence interval** | 0.383920 to 0.827724 |
| **z statistic** | 1.528 |
| **Significance level P (Area=0.5)** | 0.1266 |

**Table 9: Analysis of ROC Curve ROMA Score vs Histopathological report in Post-Menopausal Women**

A Receiver Operating Curve (Figure 7) was plotted. In the table 9 the analysis of ROC curve is given which shows Area under curve 0.62 and it is statistically not significant it means there was only 62% chance that ROMA score able to distinguish between positive cases and negative cases in Post-Menopausal Women, so the diagnostic ability of ROMA score was not found good.

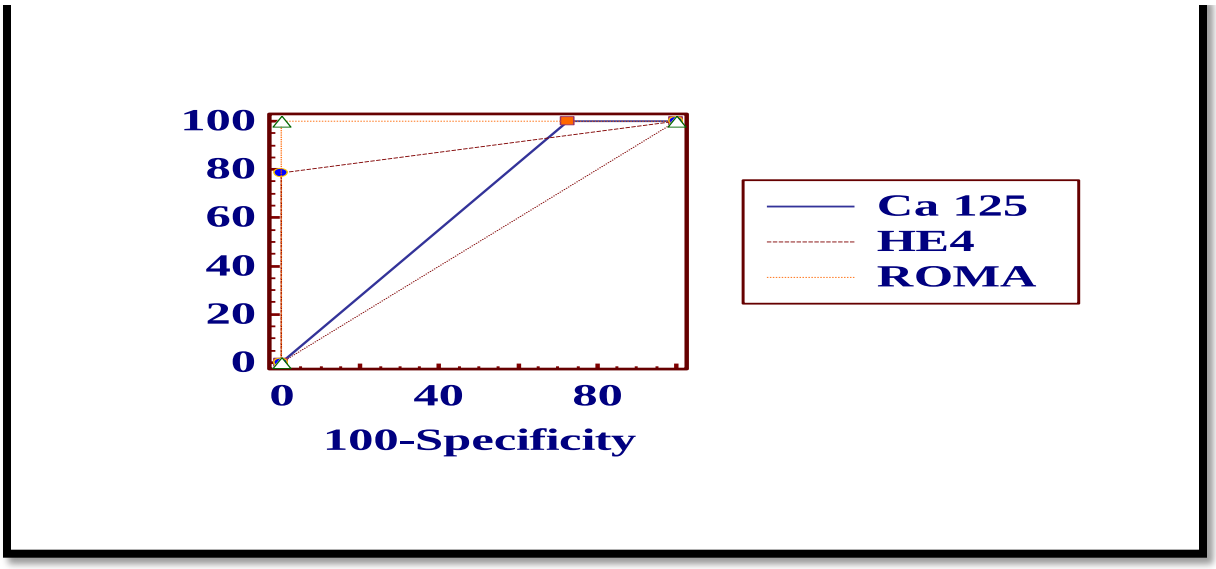


**Figure 4: Comparison of Receiver operator Characteristic curve (ROC) showing relation between Sensitivity and specificity of ROMA score, Serum CA 125 level and Serum HE4 levelin differentiating between benign and malignant ovarian mass**

| | AUC | SE | 95% CI |
|---|---|---|---|
| **CA 125** | 0.636 | 0.0486 | 0.488 to 0.768 |
| **HE4** | 0.893 | 0.0395 | 0.773 to 0.963 |
| **ROMA** | 1.000 | 0.000 | 0.929 to 1.000 |

**Table 10: Analysis of ROC Curve of ROMA score, Serum CA 125 level and Serum HE4 level vs Histopathological report**

A Receiver Operating Curve (Figure 8) was plotted. In the table 11 the analysis of comparison of ROC curve is given which shows Area under curve 0.63, 0.89, 1 of CA 125, HE4 and ROMA score respectively it means there was only 63%, 89% and 100% chance that CA 125, HE4 and ROMA score able to distinguish between positive cases and negative cases, so the diagnostic ability of ROMA score was not found good compared to serum CA125,HE4.

According to HariyonoWinarto et al[18]. Anton C et al[19], his study compared the AUC values among HE4, CA125, RMI and ROMA -In the premenopausal group, HE4 and ROMA had the same AUC value of 85.0% (95%CI: 0.73-0.96), while the postmenopausal group had ROMA for the highest AUC value at 96.9% (95%CI: 0.92-1.00), followed by HE4 (93.9%) and simultaneously CA125 and RMI with a same AUC value at 93,6%. borderline cases were excluded from the analysis, borderline cases were included into the malignant group. Benign vs Malignant analysis of HE4, CA125, RMI and ROMA using modified cutoff values shows a higher specificity and accuracy values than those with standard cutoff values at 85.2%, 75.4%, 80.3%, 86.9% for specificity, and 85.6%, 76.5%, 80.2%, 87.4% for accuracy. From analysis that included borderline cases into malignant group, it can also be seen that modified cutoff values results in higher specificity and accuracy. On the other hand, the use of standard cutoff values results in a higher Sensitivity than the modified one.

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| Ca_125 ~ HE4 | |
|---|---|
| **Difference between areas** | 0.256 |
| **Standard Error** | 0.0626 |
| **95% Confidence Interval** | 0.134 to 0.379 |
| **z statistic** | 4.097 |
| **Significance level** | P < 0.0001 |

| Ca_125 ~ ROMA | |
|---|---|
| **Difference between areas** | 0.364 |
| **Standard Error** | 0.0486 |
| **95% Confidence Interval** | 0.268 to 0.459 |
| **z statistic** | 7.483 |
| **Significance level** | P < 0.0001 |

| HE4 ~ ROMA | |
|---|---|
| **Difference between areas** | 0.107 |
| **Standard Error** | 0.0395 |
| **95% Confidence Interval** | 0.0298 to 0.185 |
| **z statistic** | 2.714 |
| **Significance level** | P = 0.0067 |

**Table 11: Pairwise comparison of ROC curves**

According to Chan KK et Al. AUC for ROMA, HE4, and CA125 were 0.921, 0.855, and 0.919, respectively,for the whole group, 0.944, 0.862 and 0.941 for postmenopausal, and0.818, 0.814, and 0.917 for premenopausal patients. ROMAperformed better in postmenopausal and CA125 in premenopausal[20]

patients. ROMA demonstrated the greatest AUC, irrespectively of menopausal status. Basing on the nonparametric method of DeLong et al[21]. ,They disclosed a significant difference in AUCs between ROMA and HE4 in the whole group (p=0.0036). In postmenopausal patients, significant differences were noted between ROMA and HE4 (p=0.0052) and HE4 and CA125 (p=0.0488).

## CONCLUSION

HE4 and ROMA showed a high specificity, but were less sensitivity than CA-125 and RMI in premenopausal women. However, ROMA is of comparable sensitivity and HE4 has highest specificity as compared to CA125 in postmenopausal women.

## CONFLICT OF INTEREST STATEMENT

Nil

## AUTHOR CONTRIBUTIONS

All authors have equally contributed.

## AUTHORS FUNDING

Nil

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