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# Calculation of the Risk of Malignancy Index in Diagnosing Malignant Ovarian Tumours

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## 1. Introduction

Ovarian cancer accounts for 5 to 8 % of all gynaecological malignancies. It has the highest case-fatality ratio of all gynaecological malignancies. A high index of suspicion, better screening modalities and recognition of high risk factors help to detect ovarian malignancy earlier [1]. Risk of malignancy index is able to correctly discriminate between malignant and benign neoplasm of ovary. It is a scoring system which can be introduced easily into clinical practice to facilitate the selection of the patient for primary surgery at an oncological unit .RMI in ovarian malignancy incorporates CA-125, USG and Menopausal status for the accurate pre-operative diagnosis of ovarian cancer. RMI is useful in deciding if an ovarian mass is malignant or benign, screening for suspected pelvic mass, deciding appropriate management protocol and triaging management [2].

*JACOBS RMI SCORE* = USG SCORE X MENOPAUSAL SCORE X CA -125 (U/ml)
USG Score (0 - No risk factor, 1 - One risk factor, 3 - Two - Five risk factors)

High risk factors in ultrasonography include multiloculated cysts, solid areas in tumours, bilateral lesions, ascites and evidence of metastasis. Score of 1for pre-menopausal women and 3 for post-menopausal women.
Score <200 - Low risk (risk of ovarian malignancy is 0.15 times)
Score >200 - High risk (risk of ovarian malignancy is 42 times)
(When 200 is taken as cut -off for RMI , Sensitivity is 85%, Specificity is 97%)

The objective of the prospective cohort study is to screen those patients who are at high risk so that they can be operated by gynaecological oncologist at the specialized centre which will in turn increase the survival rate of the high risk patients. The primary outcome of the study is the sensitivity and specificity of Jacob's RMI in the detection of Ovarian malignancy. Inclusion criteria include all patients with suspected ovarian malignancy visiting the OPD who have given consent to take part in the study. History of bilateral oophorectomy and previous history of malignancy were excluded from the study.

## 2. Methodology

1) Post menopausal women were defined as those with more than one year of amenorrhea or age more than 50 years for women who had their hysterectomy done.
2) All other women who did not meet the above criteria are to be considered pre-menopausal.
3) 100 patients meeting the inclusion and exclusion criteria who consented to take part in the study are to be considered.
4) Detailed Clinical history of the patient to be taken and thorough clinical examination to be done.
5) Ultrasonography (Abdomen and pelvis) to be done to ascertain the High-risk status-multiloculated cysts, solid lesions, ascites, bilateral lesions, and evidence of metastasis.
6) Estimation of CA-125 to be done by fully Automated Bidirectional Interphased Chemiluminiscent Immunoassay.
7) Calculated JACOBS RMI score to be compared with operative surgical staging and histopathological-cytological examination of the biopsy specimen.
8) Data so obtained thereafter will be analyzed using available statistical software.

## 3. Results and Discussion

**Table 1:** Role of CA125 in the Study

| | Pre-menopausal | | Post-menopausal | |
|---|---|---|---|---|
| | Malignant | Benign | Malignant | Benign |
| CA 125 >35 U/mL | 15 (32.60 %) | 11 (20.37 %) | 29 (63.04 %) | 01 (1.85 %) |
| CA 125 <35 U/mL | 02 (4.34 %) | 34 (62.96 %) | 0 | 08 (14.81 %) |

Sensitivity of CA 125 in the pre-menopausal women was 88.23 % and that of the post-menopausal women was 100 %. Specificity of CA 125 in the pre-menopausal women was 75.55 % and that of the post-menopausal women was 88.88 %. The positive predictive value in the pre-menopausal women was 57.69 % and that of the post-menopausal women was 90 %. The negative predictive value in the pre-menopausal women was 94.44 % and that of the post-menopausal women was 100 %.
In 2002, Schutter et al using cut-off value of CA 125 to be 35 IU/ mL; he found a sensitivity of CA 125 to be 81 % and positive value to be 72 %.

In 2003, Stakes et al found CA 125 to be 86 % for risk of ovarian cancer algorithm and specificity of 98 % for CA 125 component of algorithm. Sensitivity and positive predictive value being 83 % and 16 % respectively .The ROC algorithm used the observation that women with ovarian cancer have a rising levels of CA 125 , whereas women without ovarian cancer have static or falling levels , even if the level remain above 30 IU / mL .Because this algorithm analysed the rate of change of CA 125 , women with rising levels are recalled for an ultrasound scan before the level

reaches 30 IU / mL ; this increased the sensitivity and facilitating earlier intervention.

Baron et al in 2005 concluded that the value of CA 125 should be above 135 to achieve 100 % specificity in determining benign from malignant masses [3].

Buys et al in 2005 found a positive predictive value of 4 % for CA 125 alone and 26.5 % for abnormal CA 125 combined with transvaginal sonography [4].

Statistical Analysis revealed that in case of pre-menopausal women Yates corrected Chi-square test value came to be 18.08 and "p" value < 0.0005%. In post-menopausal women Fischer's Exact Two Tailed test gave a "p" value of < 0.0005%. Thus the role of CA 125 in differentiating between benign and malignant ovarian tumour in both the pre and post menopausal women were found to be statistically significant.

**Table 2:** Role of Ultrasonography in the Study

| | Pre-menopausal | | Post-menopausal | |
|---|---|---|---|---|
| USG Score>3 | Malignant | Benign | Malignant | Benign |
| | 17 (36.95 %) | 22 (40.74 %) | 29 (63.04 %) | 06 (11.11 %) |
| USG Score <3 | 0 | 23 (42.59 %) | 0 | 03 (5.55 %) |

Sensitivity of Ultrasonography in the pre-menopausal women was 100 % and that of the post-menopausal women was also 100 %. Specificity of ultrasonography in the pre-menopausal women was 51.11 % and that of the post-menopausal women was 33.33 %. The positive predictive value in the pre-menopausal women was 43.58 % and that of the post-menopausal women was 82.85 %. The negative predictive value in the pre-menopausal women was 100 % and that of the post-menopausal women was also 100 %.

In 1991, the ultrasonographic scoring system by Sassone A. M et al found specificity of 65 % and sensitivity of 89.1 % in discriminating between benign and malignant tumours [5]. They found a positive predictive value of 70 % and negative predictive value of 86.67 % .In 1993, De Priest et al devised a Ultrasonographic scoring system which showed a sensitivity of 88.9 % and specificity of 50 %. Their study showed a positive predictive value of 61.54 % and negative predictive value of 83.3 % [6].In 2003 , Alcazar J L devised a scoring system which showed a sensitivity of 94.4 % , specificity of 95 % , positive predictive value of 94.4 % and a negative predictive value of 95 % [7].

Statistical Analysis revealed that in pre-menopausal women Yates corrected Chi-square test value is 11.71 and "p" value is < 0.0005% which is highly significant. In the post-menopausal age group we did the Fischer Exact Two Tailed test and found that the "p" value to be < 0.05% and thus statistically significant. Thus we can conclude that there is a significant role of ultrasonography while detecting and differentiating ovarian tumour.

**Table 3:** Risk of Malignancy Index (RMI)

| RMI Score > 200 | Pre-menopausal | | Post-menopausal | |
|---|---|---|---|---|
| | Malignant | Benign | Malignant | Benign |
| | 15(32.60 %) | 01(1.85 %) | 29(63.04 %) | 02(3.70 %) |
| RMI Score<200 | 02(4.34 %) | 44(81.48 %) | 0 | 07(12.96 %) |

Sensitivity of RMI in the pre-menopausal women was 88.23 % and that of the post-menopausal women was 100 %. Specificity of RMI in the pre-menopausal women was 97.77 % and that of the post-menopausal women was 77.77 %. The positive predictive value in the pre-menopausal women was 93.75 % and that of the post-menopausal women was 93.54 %. The negative predictive value in the pre-menopausal women was 95.65 % and that of the post-menopausal women was 100 %.

In 1993 De Priest, Shenson D , Fried A et al used a scoring system based on morphology index of the tumour as assessed by ultrasonography and found sensitivity of 88.9 % and specificity of 50 % . Their study showed a positive predictive value of 61.54 % and a negative predictive value of 83.3 % [6]. In 1993, Davies AP, Jacob I, Woolas R et al found that the sensitivity to be 85 % and specificity to be 97 % [8,9]. In 1994, Lerner J P, Timor- Tritsch I E, Federman A, Abramovich G devised a scoring system using transvaginal ultrasonography. The sensitivity was 96.8 % and specificity of 77 %. The positive predictive and negative predictive values were 29.4 % and 99.6 % respectively [10]. In 1998 , Ferrazi E , Zanetta G , Dordoni D , Berlanda N , Mezzopane R , Lissoni AA did a transvaginal ultrasonographic characterization of the ovarian masses using wall thickness, septations, vegetations and echogenic patterns of the ovarian neoplasms. They concluded that differentiation of benign from malignant masses cannot be obtained by sonographic imaging alone[11] .

According to Sassone A M et al devised a scoring system which showed a specificity of 65 % and sensitivity of 89.1 % to distinguish between benign and malignant lesion. They found a positive predictive value of 70 % and a negative predictive value of 86.67 % [5]. Alcazar J L, Meree L T, Laparate C et al devised a scoring system using colour Doppler ultrasonography to differentiate between benign and malignant adnexal mases. This scoring system may yield a total score of 0 to 12. Score of 6 or more was taken as malignant .The sensitivity being 94.4 % and specificity being 95%. They found a positive predictive value of 94.4 % and negative predictive value of 95% [7]. The PLCO trial sponsored by the National Cancer Institute updated its version in 2017 and 2018 and validates the utility of Ca 125 and Ultrasonographic scoring method as adopted in our study. The ratio of surgeries to screen detected cancers was high and most cases were in their late stages. However, the effect of screening on mortality is yet not known [12, 13, 14].

Statistical Analysis revealed that in case of pre-menopausal women Fischer's Exact Two Tailed test gave a "p" value < 0.0005%. In post-menopausal women Fischer's Exact Two Tailed test gave a "p" value of < 0.0005%. Thus the role of Risk of malignancy Index in differentiating between benign and malignant ovarian tumour in both the pre and post

menopausal women were found to be statistically significant.

**Table 4:** Staging of Ovarian Tumours in the Study

| Staging | | Total |
|---|---|---|
| I | A | 1 (2.17 %) |
| | B | 0 |
| | C | 5 (10.86 %) |
| II | A | 0 |
| | B | 0 |
| | C | 0 |
| III | A | 2 (4.34 %) |
| | B | 21(45.65 %) |
| | C | 17(36.95 %) |
| IV | | 0 |
| Total | | 46 ( 100% ) |

## 4. Conclusion

Thus the Study found that the Risk of Malignancy Index in case of Ovarian Malignancy using Jacob's scoring method is very useful. It helps in identifying effectively those patients who require Staging Laparotomy and hence referral to Gynaecologist Oncologist. Thus for every case of Ovarian Cancer the first surgery will be the optimal surgery to begin each fight against this deadly disease.

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