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Risk of malignancy index (RMI) for prediction of malignancy in women with adnexal masses

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ABSTRACT

Ovarian cancer is predominantly cancer in the perimenopausal and post-menopausal age group. A definitive biomarker has not been identified for malignant ovarian cancer and histopathology remains the diagnostic gold standard for this. Risk of Malignancy Index (RMI) in predicting malignant pelvic masses includes serum CA125 level, menopausal status, and ultra-sonographic findings. The risk of malignancy index (RMI) was evaluated in the women presented with adnexal masses for its accuracy in predicting the malignancy. This was a retrospective study which included 120 women who presented with adnexal mass in a tertiary hospital. RMI scoring was done based on CA125 levels, ultrasound findings and postmenopausal status and RMI was correlated with the histopathological findings. Out of 120 subjects, 74.1% of subjects were proved to have malignant tumors. RMI in predicting malignancy showed a sensitivity of 88.76%, a specificity of 45.37%, a positive predictive value of 81.63%, a negative predictive value of 66.67% and an accuracy of RMI found to be 82.5%. The RMI is found to be a simple, cost-effective and reliable tool in predicting malignancy in women presenting with adnexal masses that helps in timely referral to a gynaecological oncology center for better management and survival. RMI scoring can be used as it is a better tool for analysing multiple parameters of the tumour.

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INTRODUCTION

Ovarian cancer is predominantly cancer in the perimenopausal and postmenopausal age group constituting the seventh most common cancer (prevalence 295,400 cases) and the eighth leading cause of cancer deaths (184,800 cases) among women worldwide [1]. In India, following cervix and breast cancer, ovarian cancer is the third leading cancer among women. The incidence rate of ovarian cancer widely varies between 5.4 and 8.0 per 100,000 populations in different parts of India [2]. According to the National centre for disease informatics and research, the number of new ovarian cancer cases in the year 2015 in India are 45231 and it is expected to increase to 59276 in the year 2050. Among all gynaecological malignancies, ovarian cancer has the worst prognosis with an overall 5-year survival rate of 45% [3]. This is because of its asymptomatic nature in the early stages and most patients have widespread disease at the time of diagnosis. Ovarian cancer is the seventh most common cancer in the US and the fifth most common cause of death from malignancy in women. There is a 1-1.5% of lifetime risk of developing ovarian cancer and a 0.5%

risk of dying from cancer [4]. Treatment for ovarian cancer usually involves chemotherapy and surgery, and sometimes radiotherapy. For patients with advanced ovarian disease, a combination of surgical cytoreduction with a chemotherapy regimen is preferred. The discrimination between benign and malignant adnexal masses is necessary for further surgical planning and clinical management in such patients. Early identification of malignancy and referral to an oncologist can facilitate accurate staging and optimal cytoreductive treatment, enhancing patient survival. Definitive biomarker has not been identified for malignant ovarian cancer and histopathology remains the diagnostic gold standard for this. Risk of Malignancy Index (RMI) in predicting malignant pelvic masses includes serum CA125 level, menopausal status, and ultrasonographic findings. The present study evaluated how RMI can accurately predict the risk of malignant ovarian tumour. [5]

MATERIALS AND METHODS

Retrospective study was done on the women presented or referred to the gynaecology department for the evaluation and management of an adnexal mass. All clinical and laboratory data were collected using the hospital information system. Measurement of serum CA-125 and ultrasound were performed.

The CA-125 assay was performed by an immunoassay chemiluminescent microparticle technology. Ultrasound scoring was done by trained radiologists. From the variables collected, the RMI was calculated with the following equation:

$$RMI = U \times M \times serum\, CA - 125$$

Where U is the total ultrasound score, M is the menopausal status and the CA-125 value in U/ml. The ultrasound score includes the characteristics looking for the presence of bilateral lesions, multilocular lesions, solid areas, ascites, and intra-abdominal metastasis. One score was given for each ultrasound characteristic feature and the total ultrasound score was calculated as a total ultrasound score of one given for none or one ultrasound feature and a U-score of three was given for two or more ultrasound features. The menopausal status score was given as one for premenopausal and three in case of postmenopausal women. At last, the value of serum CA-125 was directly substituted into the above formula.

The recommended cut-off value for CA-125 was 35 U/ml used internationally. RMI cut-off score of 200 was recommended by Jacobs *et al* to relatively achieve high levels of sensitivity and specificity.

The mean and standard deviation (SD) were calculated by SPSS Statistics. The different groups were compared for the differences in the means of each parameter using a non-parametric *t*-test, Kruskal-Wallis test, and Mann-Whitney U test. The results were classified based on the result of the histopathology report versus the cut-offs used for CA-125 and RMI for each parameter. The indicators (sensitivity, specificity, positive predictive value, negative predictive value and efficiency) for RMI were compared to the histopathology findings and analysed.

RESULTS AND DISCUSSION

This was a retrospective study involving 120 women who attended a gynaecology clinic in a tertiary centre with adnexal masses. Demographic data showed that the mean age of the subjects was 52.01$\pm$12.13 years ranging from 22 to 82 years.

Out of 120 women, 72 of them were in the postmenopausal group and the rest 48 were in the premenopausal group.83.5% of them were multiparous women and the rest 16.5% were nulliparous.

The mean ovarian tumour size was 9.7$\pm$5.58cm detected by imaging modality.

CA125 levels ranged from 18.4 to 9100 U/mL with a mean of 585.63 and a Standard deviation of 1000.662

Histopathological data showed that out of 120 women with adnexal masses, 89 were confirmed to have a malignant ovarian tumour, 2 to have a borderline tumour and 29 women to have benign ovarian pathology.

The data obtained were enumerated in Table 1 based on the histopathology study.

The RMI score was calculated and found that the mean was 3362 with a standard deviation of 5034. 90 women were found to have RMI value $\geq$200 out of which 79 were found to have a malignant tumour, 2 were found to have borderline ovarian pathology and 9 were found to have benign ovarian pathology. Out of 30 women whose RMI score was <200, 10 were found to have a histopathological diagnosis of malignant ovarian tumour and 20 were found to have benign pathology.

Based on the above data, the sensitivity of RMI in predicting malignant disease was calculated as 88.76% with a 95% confidence interval (C.I) ranging from 80.31to 94.48% and the specificity was calculated to be 64.52% with the confidence interval from 45.37 to 80.77%.

Table 1: Demographic data and RMI score classified according to histopathology of adnexal masses illustrated as numbers of subjects and percentage (in brackets)

Parameters	Benign ovarian pathology	Borderline ovarian tumour	Malignant tumour	Total
Age <40 years	27(22.5%)	0	15(12.5%)	42(35%)
Age 40-50 years	2(1.66%)	2(1.66%)	22(18.33)	26(21.66)
Age >50 years	0	0	52(43.33%)	52(43.33%)
Premenopausal women	29(24.1)	2(1.66%)	17(14.1%)	48(40%)
Postmenopausal women	0	0	72(60%)	72(60%)
RMI score <200	20(16.6%)	0	10(8.3%)	30(25%)
RMI score ≥200	9(7.5%)	2(1.66%)	79(65.8%)	90(75%)

The positive and negative likelihood ratio was 2.50 and 0.17 respectively. The positive predictive value was 87.78% with the C.I 81.63 to 92.07 and the negative predictive value was 66.67% with C.I 51.34 to 79.13%.

The accuracy of the RMI scoring in the present study was found to be 82.5% with a confidence interval between 74.5% and 88.83%. Jacob *et al* reported a sensitivity of 85.4% and specificity of 96.9% [6]. The RMI cut-offs for malignancy prediction in many studies reported a range from 25 to 250 [7]. A study with a higher RMI cut-off of 238 was used for the screening and reported a specificity of 96.2%, a sensitivity of 89.5%, a positive predictive value of 77.3%, and a negative predictive value of 98.4% [8]. A study, with an RMI cut-off of 450, reported a sensitivity of 75% and specificity of 91% [9]. In multiple clinical studies, sensitivity for predicting ovarian malignancy has ranged from 71% [10] to 88% [11]. The present study obtained a sensitivity of 88.76% and specificity of 64.2% with the cut off of 200 and the positive predictive value of 87.78% and negative predictive value of 66.67%. Compared to the above tests, the present study showed high sensitivity and low specificity. A study showed that specificity could be increased by modifying the threshold level for malignancy using RMI cutoff as 250. [12]

CONCLUSION

The present study obtained high sensitivity and high positive predictive values compared to previous studies and more sample size may be needed to further prove this conflict. Risk of Malignancy Index is a useful tool for the identification of malignant disease and useful in further management and timely referral to gynaecological oncology centres. It's a simple and cost-effective tool in developing nations. With this data and results, RMI scoring can be used as it is a better tool for analysing multiple parameters of the tumour.

Conflict of Interest

The authors declare that they have no conflict of interest.

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