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Diagnostic Accuracy of Risk Malignancy Index (RMI) in Diagnosing Ovarian Carcinoma, Confirming the Diagnosis by Histopathology

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ABSTRACT

Objective: To determine the diagnostic accuracy of risk malignancy index (RMI) in early diagnosis of ovarian carcinoma, keeping histopathology as gold standard.
Study Design: Cross-sectional study.
Place and Duration of Study: Department of Obstetrics and Gynecology, Combined Military Hospital, Skardu Pakistan, from Nov 2022 to Nov 2023.
Methodology: A total of 106 patients aged 20-60 years with presence of ovarian mass on ultrasonography were included in the study. Risk malignancy index was calculated, and presence or absence of ovarian carcinoma was noted. All patients then underwent surgery, and specimen was sent for histopathology. RMI findings were compared with histopathology report.
Results: RMI supported the diagnosis of ovarian carcinoma in 62(58.49%) patients. Histopathology findings confirmed ovarian cancer in 64(60.38%) cases. In RMI positive patients, 57 were True Positive and 05 were False Positive. Among the 44 RMI negative patients, 07 were False Negative whereas 37 were True Negative. Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of risk malignancy index (RMI) in early diagnosis of ovarian carcinoma, confirming the diagnosis by histopathology was 89.06%, 88.10%, 91.94%, 84.08% and 88.68% respectively.
Conclusion: This study concluded that diagnostic accuracy of risk malignancy index (RMI) in early diagnosis of ovarian carcinoma is significantly high.

Keywords: Histopathology, Ovarian Carcinoma, Risk Malignancy Index.

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INTRODUCTION

Gynecologic malignancies including the ovarian cancer remain a leading cause of death.[1] More than two-thirds of ovarian cancer cases are diagnosed when the disease has progressed to stage III or IV and has involved the peritoneal cavity or other organs.[2] Symptoms that are associated with ovarian cancer are nonspecific and the association is often not recognized until the disease has advanced. Therefore, recognizing it at an early stage is of utmost importance. However, several features of ovarian cancer complicate its screening. Two-thirds of ovarian cancer cases are diagnosed in women over the age of 55 years.[3] In a study conducted in tertiary care hospital of Hyderabad Sindh, the estimated frequency of ovarian carcinoma among different gynecological malignancies was found to be 45.53%.[4]

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Various combined methods of evaluating the risk of ovarian cancer have been proposed. The scoring methods based on menopausal status, ultrasonographic examination and serum CA-125 yield much better results than the earlier mentioned individual parameters.[5] The diagnostic yield of CA-125, a tumor marker frequently used for ovarian cancer is the most useful noninvasive diagnostic test in women with an adnexal mass. The role of imaging is to detect and characterize adnexal masses, and recognize unusual findings that may suggest atypical pathology.[6] Sonography is the initial imaging study of choice in the evaluation of women with suspected adnexal masses because of its widespread availability, relatively low cost, and high sensitivity in the detection of masses.[7] However, sonography is limited by its decreased specificity for the diagnosis of benign masses and as many as 20% of adnexal masses being classified as indeterminate.[8] Therefore, advanced MR imaging techniques such as Diffusion Weighted Imaging (DWI), Perfusion Weighted Imaging (PWI),

and proton Magnetic Resonance Spectroscopy (1HMRS) have been employed in the differential diagnosis of these lesions.[9]

Risk malignancy index (RMI) is a simple scoring system based on three factors namely serum CA 125, USG score and menopausal status. It is very useful in predicting a malignant ovarian mass. It is also useful in differentiating malignant from benign ovarian mass.[10]

The international literature available on this topic shows a lot of variation in the results. Moreover, no local study is available on this topic, so this study was conducted to determine the diagnostic accuracy of risk malignancy index (RMI) in diagnosing ovarian carcinoma in our setup, keeping histopathology as gold standard. The study aimed to provide basis for easily applicable method of pre-operative evaluation for ovarian mass.

METHODOLOGY

This study was carried out at Department of Obstetrics and Gynecology, Combined Military Hospital, Skardu Pakistan, from November 2022 to November 2023, after the approval of Ethical Committee (Sr. No. 5 Dated Dec 1, 2022). Due to extreme weather conditions and high altitude issue we included all the patients of ovarian carcinoma that reported in our study duration.

Inclusion Criteria: All female patients aged between 20-60 years with presence of ovarian mass for more than 3 months duration confirmed on ultrasonography of any size such as bilateral echo patterns like papillary projections, solid component, septations >3mm, free fluid and metastatic deposits were included in the study.

Exclusion Criteria: Pregnant females, Patients already operated for adnexal mass, Patients with chronic liver disease and chronic renal failure were excluded.

After taking informed consent and menopausal history, ultrasonography was done in each patient for scoring. After this peripheral venous blood sample (5 ml) was drawn from each patient for the estimation of serum CA-125 level. Serum CA-125 level was determined by radioimmunoassay. Pre and post-menopausal status of each patient was noted. Risk of malignancy index was calculated and presence or absence of ovarian carcinoma was calculated. All patients then underwent surgery, and the specimen was sent for histopathology. RMI findings were compared with histopathology report. Data pertaining to age, duration of disease, size of lesion, parity, place of living, CA-125 levels and menopausal status was recorded on a specially designed proforma.

The collected data was analyzed through Statistical Package for Social Sciences (SPSS version 23.0). Age, duration of disease, size of lesion and CA-125 levels were presented as mean and standard deviation. Parity (Primiparous/multiparous), place of living (rural/urban), family h/o ovarian carcinoma (yes/no), menopausal status (pre-menopause/post-menopause) and presence or absence of ovarian carcinoma on RMI and histopathology were presented as frequency and percentage. 2×2 contingency table was used to calculate sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of RMI in diagnosing ovarian carcinoma, taking histopathology as gold standard.

RESULTS

The age range in this study was from 20-60 years with mean age of 40.06±11.68 years. Majority of the patients 70(66.04%) were between 41 to 60 years of age. Mean duration of disease was 6.49±1.48 months. Mean size of lesion was 3.17±1.12 cm (Table-I). The risk malignancy index was calculated, and presence or absence of ovarian carcinoma was noted. RMI supported the diagnosis of ovarian carcinoma in 62(58.49%) patients. Histopathology findings confirmed ovarian cancer in 64(60.38%) cases. In RMI positive patients, 57 were True Positive and 05 were False Positive. Among 44, RMI negative patients, 07 were False Negative whereas 37 were True Negative. Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of risk malignancy index (RMI) in early diagnosis of ovarian carcinoma, confirming the diagnosis by histopathology was 89.06%, 88.10%, 91.94%, 84.08% and 88.68% respectively (Table-II).

DISCUSSION

The findings of this study advocate the diagnostic accuracy of risk malignancy index (RMI) in early diagnosis of ovarian carcinoma. The diagnostic accuracy of RMI is significantly high. The importance of the risk of malignancy index (RMI), as an effective discriminating tool has been widely accepted during the last decade. In most of the cases, ovarian tumours are diagnosed at a later stage since incidence of onset and progression of this tumour makes early diagnosis difficult.[11] The results of our study are in harmony with the studies conducted previously such as Yelikar *et al.*, reported that among their cohort the sensitivity

of RMI in diagnosing ovarian cancer was 83.81%, the specificity was 77.24%, the positive predictive value (PPV) was 47.06%, and the negative predictive value (NPV) was 95.18%. In premenopausal women, the RMI sensitivity was 83.87%, specificity, 80.31%, PPV, 28.89%, and NPV, 98.12%. In postmenopausal women the RMI sensitivity was 83.78%, specificity, 68.18%, PPV, 63.92%, and NPV, 74.71%.[12] In another study conducted in India, RMI showed better sensitivity of 85.71%, specificity of 85.07% and PPV of 75%, NPV of 91.93% and accuracy of 82.29%.[13]

Table-I: Demographic and Clinical Profile of the Patients (n=106)

Parameters	Values
Age (years)	40.06±11.68 years
Age Groups	
20-40 years	36(33.96%)
41-60 years	70(66.04%)
Duration of lesion (months)	6.49±1.48 months
Size of lesion (cm)	3.17±1.12 cm
Parity	
Primiparous	33(31.13%)
Multiparous	73(68.87%)
Family History of Ovarian Cancer	
Yes	42(39.62%)
No	64(60.38%
Menopausal Status	
Pre-menopause	47(44.34%)
Post-menopause	59(55.56%)
Place of Living	
Rural	59(55.56%)
Urban	47(44.34%)

Table-II: Diagnostic Accuracy of Risk Malignancy Index (RMI) keeping by Histopathology as Gold Standard (n=106)

	Positive result on Histopathology	Negative result on Histopathology
Positive on RMI	57 (TP)*	05 (FP)***
Negative on RMI	07 (FN)**	37 (TN)****
Sensitivity:		89.06%
Specificity:		88.10%
Positive Predictive Value (PPV):		91.94%
Negative Predictive Value (NPV):		84.09%
Positive likelihood ratio:		7.48
Negative likelihood ratio:		0.12
Diagnostic Accuracy:		88.68%

**-TP=True positive*
***-FN=False negative*
****-FP=False positive*
*****-TN=True negative*

Age range in our study was from 20-60 years with mean age of 40.06±11.68 years. RMI supported the diagnosis of ovarian carcinoma in 62(58.49%) patients. Histopathology findings confirmed ovarian cancer in 64(60.38%) cases. In another study, the sensitivity of the RMI in diagnosing ovarian cancer was 83.81%; the specificity was 77.24%; the positive predictive value (PPV) was 47.06%, and the negative predictive value (NPV) was 95.18%. In premenopausal women, the RMI sensitivity was 83.87%; specificity, 80.31%; PPV, 28.89%; and NPV, 98.12%. In postmenopausal women the RMI sensitivity was 83.78%; specificity, 68.18%; PPV, 63.92%; and NPV, 74.71%.[14] In another study, RMI showed better sensitivity of 85.71%, specificity of 85.07% and PPV of 75%, NPV of 91.93% and accuracy of 82.29%.[14]

A study in Pakistan by Irshad *et al.,* showed that sensitivity of RMI in diagnosing malignancy is 91.3%, specificity is 76.9%, positive predictive value is 87.5% and negative predictive value is 83.3%[15] which is in alignment with our results. In a study by Van Trappen *et al.,*[16] analysis of 123 patients managed sequentially, using RMI cut off values of ≥25 and <1,000 and then US and MRI provided a sensitivity of 94% and a specificity of 90%.

During 2010, Van Den Akker *et al.,* performed a study on 548 patients, with a mean age of 52 for those with benign lesion and 62 for those with malignant masses. This study involved 415 benign mass (76%), 80 malignant mass (24%), and 53 borderline malignancies (10%). The most common benign and malignant masses were mucinous cystadenoma and serous cystadenocarcinoma, respectively. They calculated one RMI with a cutoff point of 200, at which the sensitivity, specificity, PPV, and NPV were 81%, 85%, 48%, and 96%, respectively.[17] In another study, the sensitivity and specificity of CA-125 at 35kU/L were 76% and 67%, respectively. CA-125 was found to be a relevant predictor of malignancy but the area under the receiver operating characteristic curve for each of the risk of malignancy indices was greater than the area for the CA-125 serum levels alone. Each of the RMIs has a different optimal threshold, however using a threshold of 200, RMI 1 had a sensitivity of 66% and a specificity of 91%; RMI 2 had a sensitivity of 74% and a specificity of 79%; and RMI 3 had a sensitivity of 68% and a specificity of 85%.[18]

Research by Manjunath *et al.,*[19] was done on 152 patients with pelvic masses in which three RMI were checked without considerable difference in calculated parameters and in all RMIs the best cutoff point was at 200. Obeidat *et al.,*[20] performed a study on 100 patients with pelvic masses. The best cutoff point for RMI was determined to be 200, in which the sensitivity, specificity, PPV, and NPV were 90%, 89%, 96%, and

78%, respectively. In another study, 172 patients were included; RMI-3 gave sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) and diagnostic accuracy of 80.7%, 93.1%, 70%, 96% and 91% respectively. For RMI-4 these figures were 76.9%, 93.8%, 71.4%, 95.3%, and 91% respectively. In patients with borderline ovarian masses, RMI-3 gave sensitivity, specificity, PPV, NPV and diagnostic accuracy of 60%, 93.1%, 50%, 95.3% and 83.7% respectively. For RMI-4 these figures were 52.9%, 93.1%, 50%, 93.8%, and 88.5% respectively. Both RMI-3 and RMI-4 are more accurate in predicting malignant rather than borderline adnexal masses.[21]

A study on 302 women with adnexal mass indicated an RMI at a cutoff point of 250 had a sensitivity of 88.2%, a specificity of 74.3%, a PPV of 71.3%, a NPV of 90% for diagnosing invasive lesions.[22] According to the Royal College of Obstetricians and Gynecologists (RCOG) guidelines, applying a cutoff point of 250 provides a sensitivity of 70% and a specificity of 90%.[23] Using the same cutoff value in our study, we observed a sensitivity of 70.5% and specificity of 93.5%, which closely aligns with the guideline-based performance metrics.

CONCLUSION

This study concluded that diagnostic accuracy of risk malignancy index (RMI) in early diagnosis of ovarian carcinoma is high. It has not only improved our ability of differentiating benign and malignant ovarian tumours pre-operatively but also aids the surgeons in decision making. Therefore, we recommend that this simple and easily applicable method should be applied routinely in all suspected cases of ovarian lesions for diagnosing ovarian carcinoma pre-operatively.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

AMA & SSA: Data acquisition, data analysis, critical review, approval of the final version to be published.

JA & SAG: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

UA & MA: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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