RISK OF MALIGNANCY INDEX IN EVALUATION OF ADNEXAL MASSES
Basa Akkamamba1, Pothula Padmanalini2, Gurugubelli Sandhya3

1Assistant Professor, Department of Obstetrics and Gynaecology, Rangaraya Medical College.
2Assistant Professor, Department of Obstetrics and Gynaecology, Rangaraya Medical College.
3Postgraduate, Department of Obstetrics and Gynaecology, Rangaraya Medical College.

ABSTRACT

BACKGROUND
The aim of the study is:
1. To evaluate the use of risk of malignancy index in primary evaluation of patients with adnexal masses.
2. To differentiate a benign from malignant ovarian masses, which is a key feature in clinical management and surgical planning in such patients.
3. To correlate histopathologically after surgery and to compare the efficacy of RMI in evaluating adnexal masses.

MATERIALS AND METHODS
This longitudinal prospective study was conducted on 100 women with suspected pelvic mass fitting into the inclusion criteria in the Department of Obstetrics and Gynaecology at Government General Hospital, Rangaraya Medical College, Kakinada, from 2014 to 2016.

RESULTS AND CONCLUSIONS
Out of 100 women in the study in total, 18 were diagnosed as malignant. RMI was >200 in 26 patients. Out of them, 14 are malignant. 4 members in moderate risk are malignant. Preoperative diagnosis is crucial and remains a challenging issue for gynaecologists. RMI alone is better predictor than separately from menopause status, ultrasound score and CA125 leve.

KEYWORDS
RMI, CA125, Menopausal Status, USG Score.


BACKGROUND
Ovarian cancer is second most common cause of death from malignancy in women. The peak incidence of invasive epithelial cancer is at about 60 years of age. About 30% of ovarian neoplasms in postmenopausal women are malignant. Only, 7% of ovarian epithelial tumours in premenopausal patients are frankly malignant. The average age of patient with borderline tumours is approximately 46 years.1,2

A women is risk at birth of having ovarian cancer at some point in her lifetime is 1%-1.5% and that dying from ovarian cancer is almost 0.5%.3

HISTOLOGICAL TYPES OF OVARIAN TUMOURS ARE
Serous, mucinous, endometrioid, clear cell, Brenner, mixed epithelial, undifferentiated, unclassified.

Each type classified into benign, borderline, malignant, germ cell origin, sex cord stromal tumours, lipid cell tumours, sarcomas and small cell carcinomas. Ovarian cancers are broadly classified into epithelial and nonepithelial origin.

NEED FOR TRIAGING IN OVARIAN MALIGNANCIES
One of the most common presentations of ovarian neoplasm is a pelvic mass. The discrimination between benign and malignant tumours is a critical step in clinical assessment. Many women with advanced ovarian carcinoma undergo suboptimal primary surgeries at local hospitals. Therefore, correct preoperative diagnosis is crucial and remains a challenging issue for gynaecologists. This provisional diagnosis is useful in selective referral of relevant patients to specialised oncology centres and is thus helpful in planning for an appropriate surgical treatment. On the other hand, the increased morbidity and mortality due to unnecessary laparotomies performed to determine ovarian cancers at an early stage are a real clinical dilemma.

Appropriate and timely referral to a gynaecology oncologist has proven to increase survival in patients with ovarian cancer. Risk of malignancy index would be valuable for the selective referral of relevant patients to specialised oncology centre.

RISK OF MALIGNANCY INDEX4,5,6
Jacobs developed the Risk of Malignancy Index (RMI) with a sensitivity of 85.4% and a specificity of 96.9% based on menopausal status, ultrasound morphologic features and serum levels of CA125.
RMI was modified by Tingulstad for the first time in 1996 (RMI-2) and for the second time in 1999 (RMI-3). The three versions of RMI were assessed in many prospective and retrospective clinical studies. RMI value of 200 has been proven to be the best for distinction of benign from malignant adnexal masses with high level of sensitivity (51-90%) and specificity (51-97%).

Recently, a fourth RMI was introduced by Yamamoto, which includes tumour size as an additional parameter. Its validity is due to be confirmed in future studies. The aim of the study is to verify the effectiveness of RMI in the discrimination between benign and malignant ovarian tumours, finally its correlation with histopathology.

Risk of Malignancy Index (RMI) = (points for menopausal status) × (points for ultrasound findings) × (serum CA125 in U/mL).

All patients selected will undergo RMI scoring and will be categorised as low risk (RMI <25), moderate risk (RMI 25-200) and high risk (RMI >200). Risk of cancer is 75% when the RMI value is >250. All patients selected and RMI scored will undergo staging laparotomy, appropriate mode of surgery with histopathological examination. This will be correlated to substantiate the efficacy of RMI.

MATERIALS AND METHODS

The study is being conducted on 100 women fitting into the inclusion criteria in the Department of Obstetrics and Gynaecology at Government General Hospital, Rangaraya Medical College, from 2014 to 2016. Study Design- Longitudinal prospective observational study.

Inclusion Criteria
1. All women in premenopausal and postmenopausal age group with suspected pelvic mass.
2. Age group: 15 to 80 years.
3. Women diagnosed with ovarian masses.

Exclusion Criteria
1. Women with inflammatory masses.
2. Pregnancy with ovarian neoplasm.
3. Endometriosis and fallopian carcinoma.

Parameters
1. Menopausal status.
2. Ultrasound findings suggestive of malignancy.
3. Serum CA125 (cancer antigen 125) in U/mL.

Criteria for postmenopausal- Amenorrhoea >1 year or women over 50 years of age with previous hysterectomy.

Ultrasound findings Suggestive of Malignancy
Multiloculated cysts, evidence of solid areas, evidence of metastases, presence of ascites and bilateral lesions.

RMI 2- The ultrasound score is 1 when no or one parameter present in ultrasound; 4 for more than 2 parameters present.

For premenopausal patient, menopausal score is 1 for postmenopausal patient. Menopausal score is 4, size of tumour is not applicable.

After surgery done for this patient, ovarian mass is sent for histopathology; then, we assess risk of malignancy index efficiency, how effectively, it differentiate benign from malignant.

RESULTS

Out of 100 patients studied in above-mentioned period, data regarding age, presenting complaint, obstetric history, menopausal history, ultrasound score, RMI, CT findings, biopsy report were noted and results analysed.

<table>
<thead>
<tr>
<th>CA125 Range (IU/mL)</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0-35</td>
</tr>
<tr>
<td>2</td>
<td>36-100</td>
</tr>
<tr>
<td>3</td>
<td>&gt;100</td>
</tr>
</tbody>
</table>

Distribution of CA125 levels in our study varying among benign and malignant tumours ranging from a minimum value of 2.9 U/mL to a maximum value of 1544.0 U/mL with a mean CA125 level of 62.44 and standard deviation is 174.26 (SD). Sensitivity and specificity of CA125 for >35 U/mL are 68.42%, 76.19%, respectively and for >100 U/mL are 46%, 92%, respectively.

Mean CA125 levels for benign ovarian tumours was 31.79±68.45 U/mL, where for malignant tumours, it was 194.93±145.34 U/mL.

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Menopausal Status</th>
<th>No. of Patients</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Premenopausal</td>
<td>55</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>Postmenopausal</td>
<td>31</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>Post Hysterectomised</td>
<td>14</td>
<td>4</td>
</tr>
</tbody>
</table>

In our study, 55% of patients are premenopausal (score-1), 31% were postmenopausal (score-4) and 14% were hysterectomised (score-4). Out of these, 66.66% of premenopausal cases having malignant tumours and 33.33% of postmenopausal patients having malignant tumours.

Out of 18 malignant cases, 12 cases were premenopausal women and only 6 cases were postmenopausal women. Out of 82 benign ovarian tumours, 43 were premenopausal and 39 were postmenopausal women.

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Ultrasound Score</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>US score 1</td>
<td>72</td>
</tr>
<tr>
<td>2</td>
<td>US score 4</td>
<td>28</td>
</tr>
</tbody>
</table>

For most of the patients (72%), ultrasound score is 1 and 28% patients having US score of 4.
12 cases out 18 malignant cases having USG score of 4 where 6 malignant cases having USG score 1.

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>RMI Score</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&lt;100</td>
<td>63</td>
</tr>
<tr>
<td>2</td>
<td>101-200</td>
<td>11</td>
</tr>
<tr>
<td>3</td>
<td>&gt;200</td>
<td>26</td>
</tr>
</tbody>
</table>

In our present study, overall RMI score ranging from minimum value of 3 to maximum value of 4408 with a mean value of 258.35 and standard deviation was 563.45 (SD).

Mean RMI score in malignant tumours was 869.34±198.42 and mean RMI score in benign cases was 130.22±42.15.

With a cutoff value of 200, true positives were 14, false positives were 8, true negatives were 74 and false negatives were 3. With a sensitivity of 82.35% and specificity of 90.24%, the positive predictive value for the same was 63.63% and negative predictive value was 96.10%.

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Final Diagnosis (Biopsy)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Serous cystadenoma</td>
<td>32</td>
</tr>
<tr>
<td>2</td>
<td>Mucinous cystadenoma</td>
<td>36</td>
</tr>
<tr>
<td>3</td>
<td>Dermoid cysts</td>
<td>4</td>
</tr>
<tr>
<td>4</td>
<td>Adenocarcinoma of ovary and other malignancies</td>
<td>18</td>
</tr>
<tr>
<td>5</td>
<td>Miscellaneous benign tumours</td>
<td>10</td>
</tr>
</tbody>
</table>

Out 100 cases studied, most common tumour diagnosed was mucinous cystadenoma (36%) where the second most common tumour was serous cystadenoma (32%) followed by other tumours like dermoid tumours, fibromas, endodermal sinus tumours. Whereas out of 100 cases, only 18 cases were biopsy proven malignant tumours, rest all were benign tumours.

The mean USG score for benign cases was 1.53±0.13, whereas for malignant cases, it was 3.16±0.23, (p value=<0.0001), which is statistically significant.

The mean CA125 levels for malignant cases was 194.93±145.32, and for benign cases, it was 31.79±68.45 (p value=0.020) and it was statistically significant, so it was reliable marker for diagnosing malignant ovarian tumour, which was the important component of RMI score.

The mean RMI score of benign cases of our study was 130.22±42.14 and of the malignant cases was 869.43±201.16 (p value=0.012). So, RMI is the best scoring system for differentiation of benign and malignant ovarian tumours.

SENSITIVITY, SPECIFICITY AND POSITIVE PREDICTIVE VALUE OF SERUM CA125, ULTRASOUND SCORE, MENOPAUSAL STATUS AND RMI IN THE DIAGNOSIS OF MALIGNANT ADNEXAL MASSES

Sensitivity, specificity and positive predictive value of postmenopausal women in diagnosis of ovarian carcinoma is 40%, 55% and 19.04%, respectively. Ultrasound score in diagnosing malignant ovarian tumours is having sensitivity, specificity and positive predictive value were 70%, 82% and 50%, respectively.

CA125 levels for >35 U/mL was having sensitivity of 68.42% and specificity was 76.19% and positive predictive value was 43.33%. For CA125 levels >100 U/mL. These parameters were 40%, 92% and 57.14%, respectively.

Sensitivity, specificity and positive predictive value for RMI score >100 were 46.4%, 81.41% and 46.42%, respectively. With a cutoff value of RMI score, >200 having sensitivity of 82.35% and specificity of 90.24%. The positive predictive value for the same was 63.63% and negative predictive value was 96.10%.

DISCUSSION

Ovarian cancer is the seventh most common malignancy of female genital tract. Furthermore, it is the fifth mortality cause, since in 70% of cases, it progresses into advanced stage before it is diagnosed (32). There has been recent interest in developing scoring systems to improve the preoperative discrimination between benign and malignant ovarian masses. Most scoring systems have included either tumour markers (Cruickshank et al 1987; Vasilev et al 1988; Einhorn et al 1989; Bast et al 1990) or ultrasonography (Deland et al 1987). No tumour marker has yet been identified, which is unique to ovarian cancer. The tumour marker shown to combine the highest sensitivity and specificity for the disease has been CA125 (Bast et al 1983). Raised serum CA125 levels are also found in association with benign ovarian cysts, endometriosis and pelvic infection in addition to cancers of the endometrium, fallopian tube, breast and colon. Consequently, the accuracy of CA125 measurement in differentiating benign from malignant pelvic pathology is limited (Niloff et al 1984). When combined with pelvic ultrasonography (Gadducci et al 1988) or menopausal status (Vasilev et al 1988), serum CA125 estimation may improve the accuracy of diagnosing ovarian cancer preoperatively.

RMI is a simple scoring system utilising currently available tests. The ultrasound component of the score incorporates features that should be easily seen using transabdominal scanning and increasing numbers of gynaecology departments in the UK have access to serum CA125 estimation. The application of the RMI in clinical practice would provide a rational basis for specialist referral of patients with malignant disease prior to diagnostic surgery. The threshold RMI score used as a trigger for referral could reflect the local facilities. A low score maybe adopted when there is little limitation on referral for specialist care. However, when the availability of specialist care is limited because of distance or resources, a higher RMI score with lower sensitivity, but higher specificity maybe more appropriate.

Our findings are in line with previous studies, which the RMI was found to be effective to classify ovarian masses according to their potential for malignancy. Mean age of presentation in our hospital was 42.46±10.74 years ranging from 15 years to 70 years, which is comparable with a study.
conducted by Camila Campos et al where the mean age was 45.9 years for benign cases and 55.7 years for malignant cases.

We detected that most useful individual criteria of RMI are ultrasound score with sensitivity and a specificity of 70% and 82%, respectively. The mean USG score in our study for benign cases was 1.53±0.13, whereas for malignant cases, it was 3.16±0.23, (p value=<0.0001), which is statistically significant. In a study conducted by Davies et al, mean USG score was 1 in benign cases and score was 3 in malignant cases were comparable with our results.

CA125 is the second most useful individual criteria of RMI to discriminate benign and malignant of ovarian masses with sensitivity and a specificity of 68.42% and 76.19% respectively for values >35 U/mL. In their study, Jung-Woo Park et al reported similar findings. Endometriosis, pelvic inflammatory disease and menstruation can increase CA125 values. Jacobs et al was achieved a sensitivity of 71% and specificity of 75% for CA125 and a sensitivity of 71% and a specificity of 83% for ultrasound score. The mean CA125 levels in our study for malignant cases was 194.93±145.32 and for benign cases, it was 31.79±68.45 (p value = 0.020), Results were comparable with a study conducted by Farah Farzaneh et al. It was reliable marker for diagnosing malignant ovarian tumour, which was the important component of RMI score.

Nonetheless, the most accurate cut-off value for the RMI has been investigated and a value of >200 was found to be best with a sensitivity, a specificity, a Positive Predictive Value (PPV) and a Negative Predictive Value (NPV) of 89-92%, 82-96%, 62-98% and 77-98%, respectively. Supporting this data, we achieved 82.35% of sensitivity and 90.24% of specificity, 63.63% of PPV and 96.10% of NPV when a cut-off value of >200 was used. However, in our study, the best cut-off value for the RMI was 200. So, RMI is the best scoring system for differentiation of benign and malignant ovarian tumours.

CONCLUSION
We researched the predictive role of RMI in clinical approach to adnexal masses. We found that RMI alone is better predictor than separately from menopause status, ultrasound score and CA125 level. Although, utilisation of RMI provides increased diagnostic accuracy in preoperative evaluation of patient with an adnexal mass, new diagnostic tools with higher sensitivity and specificity are needed to discriminate ovarian cancer from benign masses.

REFERENCES