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RESEARCH ARTICLE

Evaluation of risk of malignancy index in the preoperative assessment of ovarian tumors compared with histopathology

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ABSTRACT

Background: Ovarian cancer is the second most common gynaecological cancer in India. Risk of malignancy index (RMI) is reliable to predict whether an adnexal mass is benign or malignant. **Methods:** The present prospective cohort study was conducted in patients who were admitted in Department of Obstetrics and Gynecology, Government general hospital, Guntur. Patients with ovarian mass detected by clinical or ultrasonography (USG) was considered as Inclusion criteria. On the other hand, premenopausal women with Simple cyst <2 cm, extra ovarian masses and inoperable ovarian masses were excluded. **Results:** The present study included 88 patients with ovarian masses who met with eligibility criteria were diagnosed and operated. After excluding one case with ectopic pregnancy and two cases of mesenteric cysts, the final sample analyzed was 85 patients. In the current study, 75.3% cases were benign and 24.7% were malignant. RMI 3 had sensitivity, specificity, PPV, NPV and diagnostic accuracy of 80.95%, 93.75%, 80.98%, 93.75% and 90.6% respectively. **Conclusion:** In this study RMI3 was found to be more sensitive and specific than CA 125 and USG when used individually in distinguishing benign and malignant ovarian tumors RMI is a simple index which can be used in daily gynecological practice applicable in low resource setting even in covid pandemic in suspicious and high risk cases so as to identify malignancy in ovarian tumors at an early stage requiring staging laparotomy and appropriate referral to a gynecologic oncologist.

Keywords: Ovarian tumour, USG, CA 125, menopause.

Ovarian cancer is the second most common gynaecological cancer in India and fourth leading cause of mortality due to malignancies in woman with incidence varying between 54 and 80 per one million population in different parts of the country [1]. The high mortality rate in ovarian malignancy is mainly due to delay in disease detection. Preoperative imaging plays an important role in assessing the extent of the disease and guides in surgical decision making and operative planning. Achievement of optimal cytoreduction (single most important prognostic criteria) and disease treatment is possible only when detected in an early stage. Various screening tests for ovarian cancer includes pelvic examination, tumor markers (CA-125), transabdominal sonography (TAS), transvaginal sonography (TVS) with colour doppler, computed tomography (CT) scan and magnetic resonance imaging (MRI). Multimodality screening using sequential CA-125 measurement and ultrasound technique achieve high specificity and promising sensitivity in screening ovarian cancer.

Although, several investigation procedures are available for diagnosing ovarian tumors, but none of them have shown significantly better performance in distinguishing malignant tumors. The development of a mathematical formula using a logistic model, incorporating menopausal status, serum levels of a glycoprotein (CA 125) and ultrasound findings in a score system have been described in the literature in the form of a malignancy index RMI 1 by 1990, Jacobs et al [2].

Ultrasonographic scoring of ovarian mass was considered mainly depends on features such as existence of ascites, intra abdominal metastasis, solid areas, multilocular cyst and

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bilateral lesion. One point for each above features was considered for examination. Ultrasound score (U) of 0 yielded U=0, a score of 1 yielded U=1, and a score of >=2 yielded U = 3. Premenopausal status (M) = 1 and postmenopausal status yielded M = 3. The serum level of CA 125 was applied directly to the calculation. RMI=UxMxCA125. Tingulstad, et al [3] developed their version of the RMI in 1996, and it is known as RMI 2. RMI2 = UxMxCA125; a total USG score of 0 or 1 yielded U=1 and a score of >=2 yielded U = 4. Premenopausal status yielded M = 1 and postmenopausal status yielded M = 4. The serum level of CA 125 was applied directly to the calculation. In1999, Tingulstad et al [4] modified the RMI, which is termed RMI 3. RMI3 = UxMxCA125; a total USG score of 0 or 1 yielded U = 1 and a score of >= 2 yielded U = 3. Premenopausal status yielded M = 1 and postmenopausal status yielded M = 3. The serum CA 125 level was applied directly to the calculation. In 2009, Yamamoto, et al [5] added the parameter of the tumor size score (S) to the RMI and have termed it the RMI 4.

RMI 4 = U x M x CA 125, where a total US score of 0 or 1 yielded U = 1 and a score of >= 2 yielded U = 2. Premenopausal status yielded M = 1 and postmenopausal status yielded M = 4. A tumor size (single greatest diameter) of < 7 cm yielded S = 1 and >= 7 cm yielded S = 2. The serum level of CA 125 was applied directly to the calculation.

Materials and methods

The present prospective cohort study was conducted in patients who were admitted in Department of Obstetrics and Gynecology, Government general hospital, Guntur medical college, Guntur during the period of September 2020 to March 2022. All patients presenting with adnexal mass was considered as major eligibility criteria of selection. Patients with ovarian mass detected by clinical or ultrasonography (USG) was considered as Inclusion criteria. On the other hand, premenopausal women with simple cyst <2 cm, extra ovarian masses (found in USG, histopathological examination) and inoperable ovarian masses were considered as exclusion criteria. All the general and gynecological examinations were performed after obtaining written consent from the patients and their health history was noted. Subjects then underwent a transvaginal or transabdominal ultrasound scan, regular investigations and specific investigations such as USG, CA 125 with cutoff value of 35 U/ml were performed. RMI was calculated for all test cases according to RMI 3 and a score of > 200 is considered for the diagnosis of malignant ovarian neoplasm as recommended by Jacobs et al [2]. Laparotomy was performed in all feasible cases and the corresponding findings were noted. Specimens were removed and allowed for detailed histopathological examination. Later, the obtained results of clinical examination, investigations and RMI were correlated with operative findings and histopathological examination report. Sensitivity, specificity and positive predictive value of individual investigations, RMI in distinguishing benign and malignant tumors were calculated, followed by their comparison was done taking histopathology as a standard reference. Tumors were classified according to WHO definitions [6]. Data was entered in MS EXCEL spread sheet and analyzed using SPSS version 24.

Results

The present study included 88 patients with ovarian masses who met with eligibility criteria were diagnosed and operated at Guntur medical college, Guntur, Andhra Pradesh, India. After excluding one case with ectopic pregnancy and two cases of mesenteric cysts, the final sample analyzed was 85 patients.

Table 1: Age wise distribution of cases

Age	Benign	Malignant	Total
<40 years	34	8	42 (49.4%)
41-59 years	24	9	33 (38.8%)
> 60 years	6	4	10 (11.7%)
Total	64	21	85

Table 1 showed the average age of the patients with benign and malignant tumors was about 41.3 years and 43.4 years correspondingly. Table also showed that the patients with age below 40 years exhibited ovarian tumors of about 49.4% (42/85), among which benign, malignant tumor constitutes about 40% (34/85) and 9.4% (8/85) respectively. On the other hand, patients with age between 41 to 59 years showed the total cases of about 38.8% (33/85), out of which benign were comparatively higher (28.2% (24/85)) than malignant (10.6% (9/85)). Similarly, patients with age above 60 years constituting total cases of about 11.7% (10/85), of which 7% (6/85) are benign and 4.7% (4/85) malignant tumor.

Table 2: Distribution of cases according to symptoms

Symptoms	Benign	Malignant	Total
Pain	48	17	65 (76.4%)
Mass P/A	22	9	31 (47.6%)
Menstrual disorder	4	1	5 (5.8%)
Abdominal distension	3	4	7 (8.2%)
Loss of weight/ appetite	2	2	4 (4.7%)
Pressure Symptoms	1	2	3 (3.5%)
SOB	0	1	1 (1.2%)

Table 2 represented the most common presentation in our study which was pain abdomen 76.4% (65/85) among which benign and malignant constitutes 56.4% (48/85) and 20%

(17/85) respectively. Additionally, it was found that the mass per abdomen was about 47.6% (31/85) among which 25.8% (22/85) were benign and 10.5% (9/85) were malignant.

Table 3: Role of CA 125

CA 125 level	Premenopausal (N = 51)		Post menopausal (N=34)		Total
	Malignant	Benign	malignant	Benign	
CA125 > 35	8	5	9	3	25
CA 125 < 35	1	37	3	19	60
Total	9	42	12	22	

Table 4: Role of ultrasonography

USG score	Premenopausal		Postmenopausal		Total
	Malignant	Benign	Malignant	Benign	
USG score >3	3	3	4	1	11
USG score <3	6	39	8	21	74

Table 5: Histopathological findings

Sl no	HPE Diagnosis	N	%
Benign			
a. Surface epithelial tumors			
1	Mucinous cystadenoma	23	27
2	Mucinous cystadenofibroma	3	3.5
3	Serous cystadenoma	28	32.9
4	Papillary serous cystadenofibroma	4	4.7
b. Sex cord stromal tumours			
5	Ovarian fibroma	2	2.3
6	Sclerosing stromal tumor	1	1.2
c. Germ cell tumor			
7	Dermoid cyst	3	3.5
	Total	64	75.3
Malignant			
a.Surface epithelial tumors			
1	Serous cystadenocarcinoma	6	7
2	Mucinous cystadenocarcinoma	5	5.5
3	Borderline serous tumor	1	1.2
4	Borderline mucinous tumour	2	2.3
5	Endometroid carcinoma (seromucinous sub type)	1	1.2
6	Clear cell carcinoma	1	1.2
b. Sex cord stromal tumor			
7	Granulosa cell tumour	1	1.2
c. Germ cell tumor			
8	Immature teratoma	1	1.2
d. Secondaries			
9	Krukenberg tumor	1	1.2
	Total	21	24.7
	Total (Benign+Malignant)	85	

Table 3 showed that premenopausal patients predominate in this study with 60% (51/85). It is also found that about 49.4% (42/85) were benign and 10.5% (9/85) were malignant. On the other hand, 40% (34/85) of patients were in post menopausal group, which constitutes about 25.8% (22/85) of benign and 14.1% (12/85) malignant cases. In premenopausal age group, most of the ovarian masses were benign compared to malignant disease. In this study, 25 cases were found to exhibit CA125 >35, in which malignant tumors (17 cases) were greater than benign (8 cases). In contrast, 60 cases have shown CA 125 <35 in which benign tumors (56 cases) were greater than malignant tumors (4 cases).

Table 4 showed that 74 cases exhibited an ultrasound score <3, among which benign tumors (60 cases) were found to be higher than those of malignant tumors (14 cases). However, 11 cases have shown an ultrasound score >3 in which malignant tumors (7 cases) were greater than benign tumors (4 cases).

Table 5 showed the study among of 85 cases, in which most common encountered tumors was serous cystadenoma 32.9% (28/85) followed by mucinous cystadenoma 27% (23/85), serous cystadenocarcinama 7% (6/85), mucinous cystadenocarcinama 5.5% (5/85). Additionally, this study showed that malignant tumors constitute 24.7% (21/85) and benign tumors 75.3% (64/85). The surface epithelial tumors were the commonest constituting 87% (74/85) followed by germ cell tumors 4.7% (4/85) and sex cord stromal tumors 4.7% (4/85).

Table 6: Diagnostic efficacy of RMI score for malignancy

RMI	Benign	Malignant	Total
>200	4(4.7%)	17(20%)	21(24.7%)
<200	60(70.5%)	4(4.7%)	64(75.2%)
Total	64(75.2%)	21(24.7%)	85(100%)

Table 7 : Comparison of parameter's sensitivity, specificity, PPV,NPV, diagnostic accuracy

Parameters	Sensitivity	Specificity	PPV	NPV	Diagnostic accuracy
Menopause	54.14%	65.62%	35.31%	82.35%	63.53%
USG	33.34%	93.75%	63.63%	81.1%	78.82%
CA-125	80.95%	87.5%	68%	93.34%	85.88%
RMI	80.95%	93.75%	80.98%	93.75%	90.6%

Table 6 showed that the total number of cases with RMI score above and below 200 were 21 (24.7%) and 64 (75.2%), respectively. Majority of cases with RMI score >200 were malignant (17/21) where as with RMI score <200 were benign (60/64). RMI 3 with cut-off point 200 have exhibited a sensitivity, specificity, PPV, NPV and accuracy values of 80.95%, 93.75%, 80.98%, 93.75% and 90.6% respectively.

Discussion

The estimation of malignancy risk in patients with ovarian tumors is to improve survival of patients with early ovarian cancer. The most effective diagnostic tool should be accurate, easy to perform, and cheap. Furthermore, it should be helpful to prioritize treatment for high risk patients and in deciding the extent, time of surgery for low risk patients. Survival rate in ovarian cancer patients is primarily related to the stage of disease during diagnosis. Five year survival was reported over 90 percent for women with stage 1 disease. However, this number drops to about 75 to 80 percent for regional disease and 25 percent for those with distant metastases. Despite the good prognosis associated with early stage disease, overall five year survival in women with ovarian cancer is less than 45 percent [7]. This poor survival rate is due to the spread of cancer beyond the ovary at the time of clinical detection in 75 percent of patients.

The present study was conducted to compare the sensitivity and specificity indices of various investigations performed to distinguish benign and malignant ovarian tumors. Also, this work aims, to identify malignancy at an earlier stage to increase 5 year survival rates and decrease mortality due to ovarian malignancies. In the present study 85 women with ovarian tumor admitted in Gynecology OPD were considered and their disease symptoms, menopausal status was taken. Later, the patients were subjected to various routine and special investigations like CA 125, USG. RMI was calculated for all cases. Out of 85 cases, 64 women had benign ovarian tumors and 21 women had malignant ovarian tumors as identified by histopathology.

In the current study, total 85 cases were studied out of which 75.3% were benign and 24.7% were malignant. The incidence rates were comparable to the results obtained in research work done by Vora and Bhargava et al [8]. They studied 330 cases, and 81% of them were benign and 19% were malignant tumours. The average age of patients with ovarian mass in our study was 41.3 years for benign and 43.4 years for malignant disease which is consistent with study done by Parker et al [9] in which 33.1 years for benign and 44.6 years for malignant disease. On the other hand, the most common presentation in our study was pain abdomen 76.4% followed by mass per abdomen 47.6%, and the results are in agreement with Rao PS et al [10]. In this study, it was observed that the patients with CA 125>35 IU/ml showed 68% malignant and 32% benign tumors. Data seems to be in agreement with earlier report from Santhosh Kumar Dora et al study [11] which showed that 69% were malignant and 32% were benign among cases with CA125 >35IU/ml. Additionally, the sensitivity, specificity, PPV, and NPV percentage for CA125 were found to be 80.95%, 87.5%, 68% and 93.34%, respectively. Diagnostic accuracy of CA125 was found to be 85.88%. These findings are comparable to results obtained from AI Mushali et al [12]. In this study, an ultrasound score had sensitivity, specificity, PPV and NPV percentage of about 33.34%, 93.75%, 63.63%, 81.1% and 78.82%, correspondingly. Most common benign tumor in our study was serous cystadenoma followed by mucinous cystadenoma. These findings are comparable to previous studies done by Rao PS et al, Manjunath AP et al, and Watcharada Moolthiya et al [10,13,14]. In current study, RMI >200 in 80.9% of malignant tumors and 6% of benign tumors were found which is comparable to AI Musalhi et al study [12] where RMI >200 in 57% of malignant tumors and 18% of benign tumors. In present study RMI 3 had sensitivity, specificity, PPV, NPV and diagnostic accuracy of 80.95%, 93.75%, 80.98%, 93.75% and 90.6% respectively. The findings are comparable to earlier studies of Ma et al [15], which showed that RMI >200 had sensitivity, specificity, PPV, NPV of 87.3%, 84.4%, 82% and 89% correspondingly.

Conclusion

Ovarian cancer survival rates are much lower than other cancers that affect women survival rates vary depending on the stage of diagnosis. Women diagnosed at an early stage have a much higher five year survival rate than those diagnosed at a later stage. In this study RMI was found to be more sensitive and specific than CA 125 and USG when used individually in distinguishing benign and malignant ovarian tumors. CT is not a cost effective method when compared with that of RMI as screening method in early identification of malignant ovarian tumors. RMI is a simple index which can be used in daily gynecological practice in suspicious and high risk cases so as to identify malignancy in ovarian tumors at an early stage requiring staging laparotomy and appropriate referral to a gynecologic oncologist, so that 5 year survival rate can be improved. RMI is still simple and applicable in low resource setting even in covid pandemic.

Conflict of interest: None. **Disclaimer:** Nil.

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