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Research Article

Evaluation of the validity of risk malignancy index in clinically diagnosed ovarian masses and to compare it with the validity of individual constituent parameter of risk malignancy index

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ABSTRACT

Background: Pre-operative knowledge regarding the nature of ovarian mass is necessary in order to plan surgery. Risk malignancy index (RMI) is a simple scoring system based on three factors serum CA 125, USG score & menopausal status. The RMI was interpreted as 1) score > 250 = high risk, 2) 25-250 =intermediate risk, 3) score <25 = low risk. The objective of the study was, 1) to evaluate risk malignancy index (RMI) in pre-operatively clinically diagnosed ovarian mass, 2) to compare the validity of individual parameter in RMI i.e. menopausal status, serum CA 125 & USG score with validity of RMI as a comprehensive index .
Methods: This was an observational study conducted at department of obstetrics and gynaecology, GMCH Aurangabad from October 2012 to 2014 with sample size of 102 cases with clinical diagnosis of ovarian mass admitted for laparotomy. The validity of RMI and validity of individual parameter was calculated and compared.
Results: RMI showed better sensitivity of 85.71%, specificity of 85.07% and ppv of 75%, npv of 91.93% and accuracy of 82.29% as compared to validity of individual parameters.
Conclusions: RMI is simple, valuable & highly reliable in pre-operative differentiation of malignant & benign lesion. Simplicity and applicability of this method in the primary evaluation of patients with pelvic masses makes it a good option in daily clinical gynaecological practice.

Keywords: USG, RMI, serum CA 125, Ovarian mass

INTRODUCTION

Ovarian cancer is one of the leading cause of mortality due to female genital tract malignancy.[1] Ovarian cancer has emerged as one of the most common malignancy affecting Indian women. The annual percentage of increase in age standardized incidence rates ranged from 0.7% to 2.4%.[2] Gynaecological cancers have increased in India and are estimated to be around 182,602 by the year 2020 constituting about 30% of the total cancers among women in India. Ovarian cancer contributes about 19.8% of the total cases.[3]

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

Pre-operative knowledge regarding the nature of ovarian mass is necessary so as to plan surgery. There is a significant difference in management of a malignant tumour which may require radical surgery, chemotherapy, counselling regarding the disease

prognosis and costs involved. On the other hand benign adnexal mass may simply be managed with cystectomy or laparotomy. This is adequate to signify the importance of pre-operative determination of the nature of adnexal mass for optimal and appropriate primary treatment.

Various combined methods of evaluating the risk of ovarian cancer have been proposed.[4] The scoring methods based on menopausal status, ultrasonographic examination and serum CA-125 yield much better results than the earlier mentioned individual parameters. Risk of Malignancy Index (RMI) is calculated with a simplified regression equation obtained from the product of menopausal status score (M), ultrasonographic score (U) and absolute value of serum CA-1255. RMI was originally developed by Jacobs et al at 1990. It is known as RMI-1 and that developed by Tingulstad et al with slight modification in score value of menopausal status and ultrasound score is RMI-2.[5] It was modified to RMI-3 in 1999.[6]

RMI is a simple scoring system which can be applied in less specialized centres. In many studies, cut off value of Risk of malignancy index was taken as 200 but according to RCOG guidelines,[7] the cut off level is 250 for predicting malignancy since higher cut off level increased the detection rate of true negative cases.

Keeping this in mind, we have considered cut off level 250 for predicting malignancy in present study.[7-9] This study was aimed to assess the validity of RMI in clinically diagnosed ovarian masses in pre-operative women & comparing it with the validity of individual constituent parameter of RMI.

METHODS

This was an observational study conducted at department of obstetrics and gynaecology, GMCH Aurangabad from October 2012 to 2014 with sample size of 102 cases with clinical diagnosis of ovarian mass admitted for laparotomy.

Inclusion criteria

1. Women with clinically restricted ovarian mass of any age group.
2. For premenopausal women, criteria for ovarian masses are its size more than 8 cm and for postmenopausal women size more than 5 cm.
3. Post-menopausal status defined as more than 1 year of amenorrhea or, women who underwent hysterectomy.

Exclusion criteria

1. Women having ovarian tumor with other condition like endometriosis, fibroid, pregnancy, PID, women in menstruating phase and associated with concurrent malignancy.
2. Patients who were unfit for major surgery, inoperable cases, previous major pelvic surgery.
3. Intra-operatively, any other mass than ovary was also excluded from study.

Total 102 women with clinically diagnosed as ovarian mass who were admitted for laparotomy in a tertiary care hospital, after fulfilling the inclusion and exclusion criteria were studied. Detailed clinical history was taken pertaining to their age, parity, socioeconomic status along with symptoms. Clinical examination was done. USG (abdomen + pelvis) performed with full bladder technique with 3-5 MHz probe frequency.

Ultrasound scoring

Ultrasound score (U) was based on one point for each of the following,

1. Bilateral lesion
2. Multilocular cyst or septation
3. Evidence of solid areas
4. Evidence of metastasis
5. Presence of ascites

For RMI USG Score,

U = 0 for ultrasound point of 0
U = 1 for ultrasound point of 1
U = 3 for ultrasound point of 2 OR >2

Ultrasound scoring were recent ones done within two weeks prior to laparotomy.

Serum CA-125 level estimation

Peripheral venous blood sample (5 ml) was drawn from each patient, prior to surgery for the estimation of serum CA-125 level. Serum CA-125 level was determined by radioimmunoassay (MINIVEDAS CA-125 MACHINE). SERUM CA 125 >200 IU/ml in premenopausal & >35 IU/ml in postmenopausal women were considered together as high risk of ovarian malignancy.[10,11]

Menopausal Scoring (M)

For premenopausal woman score 1 was given, for post-menopausal woman score 3 was given. RMI calculated for each subject by multiplying USG score, menopausal score and Serum CA125 level value.

$$RMI = U \times M \times \text{Serum CA-125 level}^{12}$$

Operative findings during laparotomy of all cases were obtained. It was made sure that the operated specimen or tissue was immersed in formalin solution and sent for histopathological examination; ascitic fluid or peritoneal washing was sent for cytological examination in a sterile syringe immediately. The cytological and histopathological examinations were all done in,

department of Pathology. Histopathological diagnosis was considered as gold standard for defining outcome.

Interpretation of risk malignancy index (RMI)

If the score < 25, it was considered as low risk,
If the score 25-250, it was considered as, moderate risk &
If the score > 250, it was considered as high risk.

Statistical analysis was done with appropriate test at the end of the study.[7] Results of RMI were validated against histopathologically confirmed lesions.

RESULTS

Table 1 shows baseline characteristics of study group.

Table 1: Baseline characteristics.

Characteristics	Distribution
Mean age	34.6 years
Mean parity	2
Socioeconomic status (Kuppuswami scale)	
Class I	7.8%
Class II	9.8%
Class III	24.51%
Class IV	41.17%
Class V	6.66%

Table 2: Distribution of cases according to USG score, menopausal status, serum CA 125 levels and RMI.

Variable	Total number of ovarian masses (n=102)	% Of ovarian masses n=100
USG score		
0	6	5.8
1	57	55.88
3	39	38.2
Serum CA 125 in IU /ml		
CA-125> cut off	40	39.22
CA-125< cut off	62	60.78
Menopausal status		
Postmenopausal	40	39.22
Premenopausal	62	60.88
RMI		
<25	38	37.25
25-250	24	23.52
>250	40	39.21

38.2% women having USG score >3, 60.88% women were postm enopausal & 39.22% cases having CA125 above cut off level, 39.21% cases having RMI >250.

Table 3: Co-relation of RMI and its individual parameter with histopathology.

Variables		Histopathology		
		Malignant N=35	Benign N=67	Total
USG score	USG score>3	28	11	39
	*USG score 0 or 1	7	56	63
CA-125	CA-125>cut off	28	12	40
	CA-125<cut off	7	55	62
Menopausal Status	Postmenopausal	21	19	40
	Premenopausal	14	48	62
RMI	RMI>250	30	10	40
	**RMI<250	5	57	62

*For statistical calculation purpose USG score 0 & 1 combined together.
**For statistical analysis purpose, The RMI score (25-250)i.e. intermediate group was merge with group whose RMI was <25 i.e. Low risk group.

Table 4: Comparison of validity of RMI and validity of its individual parameter.

Statistical parameter	Sensitivity	Specificity	PPV	NPV	Accuracy
USG score	80	83.88	71.79	88.88	82.58
Serum CA-125 Level	80	82.08	70.00	88.78	81.08
Menopausal Status	71.64	60.00	77.41	47.50	67.64
RMI	85.71	85.07	75.00	91.93	82.29

In cases RMI >250, 30 were confirmed as malignancy. In cases USG score 0 or 1, 56 were found to be benign. In cases serum CA125 above cut off level, 28 were found to be malignant. In postmenopausal women, 19 cases were found to be malignant

Sensitivity of menopausal status is 71.64% & specificity of 60.00%.
Sensitivity of Serum CA-125 was 80.00% & specificity of 82.08%.
Sensitivity of USG score was 80.00% & specificity of 83.88%.
Sensitivity of RMI is 85.71% & specificity of 85.07%.

DISCUSSION

Risk of malignancy index is the integration of serum CA-125, menopausal status and USG findings. In the present study, the cut off level of RMI is taken as 250.This scoring was more closer to Zinatossadat Bouzari et al,[13] who used 265 as cut off .In the present study sensitivity, specificity, PPV & NPV of RMI was found to be 85.71%, 85.07%, 75%, 91.93% respectively. Similar statistical significance was observed by Ismail Kestane et al[14] and Zinatossadat Bouzari et al.[13]

In the present study, out of 102 clinically diagnosed ovarian masses, 7 cases were noted with lower RMI (i.e.<250) which turned out to be malignant on histopathology. This gave the false negative rate of 11.11%. It was also noted that in these 7 cases, Serum CA 125 was within normal range. This could be explained on the basis of histopathology of individual cases. Out of these seven cases, three cases were of mucinous cystadenocarcinomas & two were dysgerminomas, one was immature teratoma & one case of sex cord stromal tumor (steroidal cell tumor). This could be because of serum CA-125 has limited role in recognizing mucinous cystadenocarcinomas. Similar findings were noted by Ismail Kestane et al.[14] Immuno histochemical studies have demonstrated Serum CA-125 expression to be a feature of cells derived from embryonal coelomic epithelium and mullerian duct.[15] Serum CA-125 levels usually rise in epithelial tumors whereas levels may not increase in non-epithelial tumor like dysgerminoma, immature teratoma , sex cord stromal tumor.

In the present study, USG score 0 was seen in 5.8% cases which resulted into RMI zero in those cases. Hence USG score 0 was major factor to contribute to more false negative results in RMI. This USG score 0 was excluded by Taherah Ashrafgangooei et al,[16] M.A. Suuiqing et al,[17] Ismail Kestane et al[14] so as to decrease the false negative results. These authors included the USG score 1 & 3 only to calculate the RMI.

In the present study, menopausal status had a sensitivity of 60% & specificity of 71.64%. Hence menopausal status could be a weak constituent of RMI. Taherah Ashrafgangooei et al[16] had shown higher specificity of 93.18% .This discrepancy in the present study was due to the proportion of sample size which included a larger number of pre-menapausal women as compared to post-menopausal (86.3%).

Comprehensive index overcomes the false positive result obtained when using a single parameter like menopausal status or serum CA-125 or USG alone. RMI also increases the sensitivity & specificity in the pre-operative diagnosis of ovarian mass.

If patients with ovarian cancers are diagnosed at early stage (I or II), the cure rate could be as high as 80-90% and the mortality rate could decrease up to 50%. Hence, this method of diagnosis is of great importance for prediction of the prognosis. Selective referral of patients with high risk of malignancy to specialized oncology centers is of paramount importance. The primary cytoreductive surgery has a great role in deciding the prognosis of ovarian cancers.

CONCLUSIONS

RMI is simple, valuable, highly reliable & clinically applicable scoring system, in pre-operative evaluation of ovarian mass. RMI is very useful in differentiating malignant from benign lesion.

The present study demonstrates that the validity of RMI is higher as compared to validity of individual parameters and hence, has a better discriminating power to diagnose malignancy.

Simplicity and applicability of the method in the primary evaluation of patients with pelvic masses, makes it a good option in daily clinical gynaecological practice.

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REFERENCES

1. Spencer JA. A multidisciplinary approach to ovarian cancer at diagnosis. The British J Radiol. 2005;78(2005):S95-102.rmi 17.
2. Murthy NS, Shalini S, Suman G, Pruthvish S, Mathew A. Changing trends in incidence of ovarian cancer - the Indian scenario. Asian Pac J Cancer Prev. 2009;10(6):1025-30.
3. Takiar R, Nadayil D, Nandakumar A. Projections of cancer cases in India (2010-2030) by cancer groups. Asian Pacific J Cancer Prev. 11:1045-104. rmi21.
4. Cruickshank DJ, Fullerton WT, Klcper A. The clinical significance of pre-operative serum CA-125 in ovarian cancer. Br J Obstet Gynecol. 1987;94:692-95.

5. Jacobs I, Oram D, Fairbanks J, Turner J, Crost C, Grudzinskas JG. A risk of malignancy index incorporating CA-125, ultrasound and menopausal status for the accurate pre-operative diagnosis of ovarian cancer. Br J Obstet Gynecol. 1990;97:922-92.
6. Zalel Y, Tepper R, Altaras M, Beyth Y. Transvaginal sonographic measurements of postmenopausal ovarian volumes as a possible detection of ovarian neoplasia. Acta Obstet Gynecol Scand. 1996;75:668-71.
7. RCOG Guideline No. 34 October 2003, Reviewed 2010.
8. Hartge P, Hayes R, Reding D, Sherman ME, Prorok P, Schiffman M et al. Complex ovarian cysts in postmenopausal women are not associated with ovarian cancer risk factors: preliminary data from the prostate, lung, colon, and ovarian cancer screening trial. Am J Obstet Gynecol. 2000;183:1232-7.
9. Barber HR, Graber EA. The PMPO syndrome (postmenopausal palpable ovary syndrome). Obstet Gynecol. 1971;38:921-3.
10. Lippincott Williams & Wilkins. The American College of Obstetricians and Gynecologists (ACOG). 2015;105(1).
11. ACOG Committee Opinion: number 280, December 2002. The role of the generalist obstetrician-gynecologist in the early detection of ovarian cancer. Obstet Gynecol. 2002;100:1413-6.
12. Tingulstad S, Hagen B, Skjeldestad FE, Onsrud M, Kiserud T, Halvorsen et al. Evaluation of risk of malignancy index based upon serum CA-125, ultrasound score and menopausal status in the pre-operative diagnosis of pelvis masses. Br J Obstet Gynaecol. 1996;103:826-31.
13. Bouzari Z, Yazdani S, Ahmadi MH, Barat S, Kelagar ZS, Kutenaie MJ et al. Comparison of three malignancy risk indices and CA-125 in the preoperative evaluation of patients with pelvic masses. BMC Res Notes. 2011;4:206.
14. Kestane I, Senol T, Kahramanoglu I, Kestane D. The use of risk of malignancy index for adnexal masses. Gynecol Obstet. 2014;4:226.
15. Kabawat SE, Bast RC, Welch WR, Knapp RC, Calvin RB. Immunopathologic characterization of a monoclonal antibody that recognizes common surface antigens of human ovarian tumours of serous, endometrioid and dear cell types. Am J Clin Pathol. 1983;79:98-104.
16. Tahereh A, Mahdieh R. Risk of malignancy index in preoperative evaluation of pelvic masses. Asian Pac J Cancer Prev. 2011;12:1727-30.
17. Shuiqing Ma, Keng S, Jinglie LA. Risk of malignancy index in pre-operative diagnosis of ovarian cancer. Chin Med J. 2003;116(3):396-9.

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