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Original Research Article

A prospective study of clinical and diagnostic methods of ovarian tumors admitted in a tertiary care hospital and its correlation with histopathology

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ABSTRACT

Background: Aim of the study was to study demographic profile and diagnostic modalities of ovarian tumors and their correlation with histopathological report (HPR).
Methods: Prospective observational study conducted in NSCB medical college, Jabalpur from February 2019 to July 2020 on subjects with ultrasonographically diagnosed ovarian tumors. Relevant history obtained, gynecologic examination, investigations recorded. Subjects followed up to collection of HPR and correlation with histopathology done.
Results: Out of 120 cases of ovarian tumors, 39.16% were malignant and 60.83% were benign ovarian tumors. Out of 80 premenopausal females, majority (78.75%) had benign ovarian masses. Amongst 40 postmenopausal females, 75% of ovarian masses were malignant. CA125 had sensitivity 76.59%, specificity 76.71% and accuracy 76.66% in diagnosing ovarian malignancy. Amongst 4 RMI scores, RMI 1 has the highest sensitivity and specificity 85.10%, 86.30% respectively. Sensitivity, specificity, and accuracy of ultrasound score was 65.21%, 86.30% and 77.5% respectively. Sensitivity and specificity of clinical diagnosis was 83% and 95.89% respectively and ROC analysis showed clinical diagnosis can accurately predict benign and malignant ovarian tumors in 89% cases.
Conclusions: RMI 1 score has the highest sensitivity and specificity in our study. When all 4 methods of diagnosis i.e., RMI Score, ultrasound score, CA125 and clinical diagnosis were compared, clinical diagnosis has highest prediction of malignancy.

Keywords: Ovarian cancer, CA 125, Ultrasound score, RMI score

INTRODUCTION

Ovarian malignancy is the most common gynecological cancer in females after breast and cervical carcinoma and second most common cancer of the female reproductive system and the leading cause of the death from gynecologic malignancy in India as well as worldwide and unfortunately it remains clinically silent until advanced stage.[1,3] Rate of malignancy is up to 60% in postmenopausal women and 24% in premenopausal women.[2]

Indian trend analysis showed a steady increase in the age-standardized incidence rate of ovarian cancer ranging from 0.26% to 2.44% per year.[4] The overall 5-years survival is 45% primarily because of the late stage at diagnosis of the disease.[5] By the time the disease becomes symptomatic, the stage of the cancer would have been stage III or IV

and even aggressive treatment is associated with treatment failure and recurrence.[6] Most of these cancers (>80%) are epithelial in nature and among epithelial tumors, most common variety is serous cystadenocarinoma.[7] This tumor secretes a tumor antigen known as CA 125 which can be used as a marker for screening and follow up of women with ovarian malignancy.[8]

Many scoring systems for prediction of ovarian malignancy include CA 125 values in their tumor prediction algorithms, for example, RMI scoring, ROMA index, OVA1 etc. Novel serum biomarkers for detection of ovarian tumors are HE4, mesothelin, prostasin, kallikreins, lysophosphatidic acid, OVX1 and osteopontin. Aggressive debulking surgery, followed by platinum-based chemotherapy, usually results in clinical remission. But, up to 80 percent of these women will develop a relapse that leads to disease progression and death. Newer treatment modalities are bevasizumab and PARP inhibitors. Histomorphological features with radiological, clinical, and other ancillary investigations including tumor markers hold keys for early diagnosis. The purpose of this study is to study the accuracy of diagnostic modalities for ovarian tumors in central India.

Objectives

Objectives of the study was to study demographic profile, diagnostic modalities of ovarian tumors and their correlation with HPR.

METHODS

The study was prospective observation study. The study conducted at Netaji Subhash Chandra Bose medical college, Jabalpur, Madhya Pradesh, India from February 2019 to July 2020.

Inclusion criteria

All subjects with ultrasonographical diagnosis of ovarian tumors were included.

Exclusion criteria

Pelvic masses other than ovarian tumors, functional, inflammatory, and metaplastic ovarian cyst were excluded.

Procedure

Admitted subjects presenting with ovarian tumors on ultrasonography were evaluated according to relevant history, high risk factors for ovarian tumors and demographic characteristics. Clinical evaluation, gynecological examination, ultrasonography, biochemical profile and other relevant investigations were done for the subjects. Surgical staging was done in cases with operable malignant ovarian tumors. Subjects followed up upto collection of histopathological report.

Ethical approval

Ethical approval taken by institutional ethical committee, Netaji Subhash Chandra Bose medical college, Jabalpur (M.P.)

Statistical analysis

Compiled data was statistically analyses using Chi square test and/or Fischer's exact test to compare 2×2 contingency distribution as appropriate and ROC analysis was performed to predict benign and malignant ovarian tumors. $P<0.05$ was considered statistically significant. All statistical calculations were done with SPSS statistics version 20.0.

RESULTS

Total 120 cases of sonographically confirmed ovarian tumors were studied. The 39.16% were malignant and 60.83% were benign neoplasm (Table 1). Maximum number of cases of benign tumors were in age group 31-40 years and that of malignant ovarian tumors were of 41-50 years age group (Table 1). Present study shows no correlation of ovarian malignancy with parity of females, locality, and regularity of menstrual cycle (Table 1). Out of 80 premenopausal females, majority (78.75%) had benign ovarian masses and only 21.25% had malignant ovarian masses. While amongst 40 postmenopausal females, 75% of the ovarian masses were malignant and 25% were benign (Table 1). With standard cut-off value of 35 U/ml, CA125 had sensitivity of 76.59%, specificity of 76.71%, accuracy of 76.66% and positive predictive value 67.92% in diagnosing ovarian malignancy (Table 2). Sensitivity, specificity and accuracy of ultrasound score with a cut off of 3 was 65.21%, 86.30% and 77.5% respectively (Table 3). In our study, ultrasound diagnosis using gray scale and color doppler has sensitivity and specificity of 80.90% and 87.70% for malignant ovarian tumors respectively (Table 4). Amongst 4 RMI scores, RMI 1 has the highest sensitivity and specificity 85.10%, 86.30% while RMI 2 had comparable specificity 85.30% but lower sensitivity 63.82% than RMI 1, RMI 3 has comparable specificity (83.56%) but less sensitivity (59.57%) and accuracy (74.16%) than RMI 1 score. RMI 4 is least specific (82.19%). The positive predictive value as well as the negative predictive value are highest for RMI1, 80% and 90% respectively thus highest accuracy is of RMI 1 (85.83%) (Table 5). RMI 1 has the highest specificity, sensitivity, positive and negative predictive value (Table 6).

In our study clinical diagnosis with thorough preoperative assessment of patients including bimanual pelvic examination, radiological evaluation and CA 125 measurement has highest ability to predict benign and malignant ovarian tumors when compared with gold standard of diagnosis i.e., histopathologic examination (Figure 1).

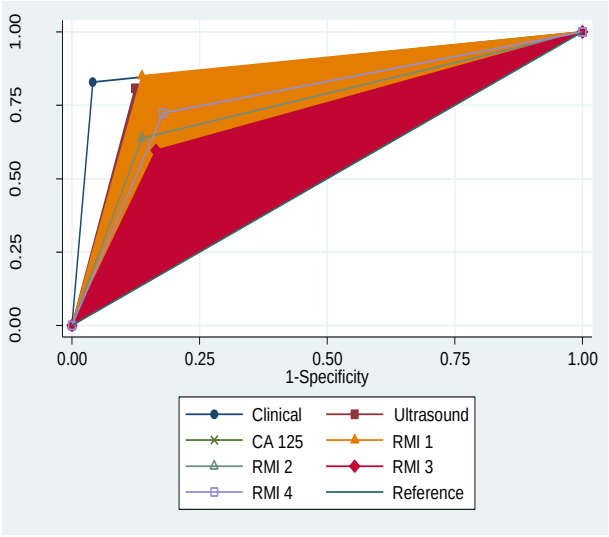

Figure 1: Receiver operating curve (ROC) analysis in prediction of benign and malignant ovarian tumors.

Table 1: Patient characteristics.

Number of patients	Benign (%)	Malignant (%)	P value
	73 (60.83)	47 (39.16)	0.0008
Mean age (Years)	35.5	45.5	<0.0001
Locality	Rural-53 (58.24) Urban-20 (68.96)	Rural-38 (41.75) Urban-9 (31.03)	0.302
Parity	Nulliparous -21 (65.62) Primiparous -9 (65.28) Multiparous -43 (58.10)	Nulliparous -11 (34.37) Primiparous -5 (35.71) Multiparous -31 (41.89)	0.737
Menopausal status at diagnosis	Pre-menopausal -63 (78.75) Post-menopausal -10 (25)	Pre-menopausal -17 (21.25) Post-menopausal -30 (75)	<0.0001

Table 2: Distribution of cases based on serum CA125.

Serum CA 125	Benign, no. (%)	Malignant, no. (%)	Total, no. (%)
<35 u/ml	56 (76.71)	11 (23.40)	67 (55.83)
>35 u/ml	17 (23.28)	36 (76.5)	53 (44.1)
Total	73 (100)	47 (100)	120 (100)

Chi square=32.95; p<0.0001

With standard cut-off value of 35 U/ml, CA125 had sensitivity of 76.59%, specificity of 76.71%, accuracy of 76.66% and positive predictive value 67.92% in diagnosing ovarian malignancy.

Table 3: Distribution of cases based on Lerner's ultrasound score.

Lerner's ultrasound score	Benign, no. (%)	Malignant, no. (%)	Total, no. (%)
<3	63 (86.30)	17 (36.10)	80 (66.66)
>3	10 (13.69)	30 (63.82)	40 (33.33)
Total	73 (100)	47 (100)	120 (100)

Chi square=32.33; p<0.0001

Sensitivity, specificity and accuracy of ultrasound score with a cut off of 3 was 65.21%, 86.30% and 77.5% respectively.

Table 4: Ultrasound diagnosis verses histopathological report for ovarian tumors.

Ultrasound diagnosis (Using Gray scale and color doppler)	Histopathological report		Total
	Benign	**Malignant**	
Benign	64	9	73
Malignant	9	38	47
Total	73	47	120

Chi square=56.344; p<0.0001

In our study, ultrasound diagnosis using gray scale and color doppler has sensitivity and specificity of 80.90% and 87.70% for malignant ovarian tumors respectively.

Table 5: Distribution of cases based on RMI scores.

RMI score	Benign (%)	Malignant (%)	P value
RMI 1 score	<200-63 (86.3) >200-10 (13.6)	<200-7 (14.8) >200-40 (85.10)	<0.0001
RMI 2 score	<200-63 (86.30) >200-10 (13.6)	<200-17 (36.17) >200-30 (63.8)	<0.0001
RMI 3 score	<200-61 (83.56) >200-12 (16.4)	<200-19 (40.42) >200-28 (59.57)	<0.0001
RMI 4 score	<450-60 (82.19) >450-13 (17.80)	<450-12 (25.53) >450-35 (74.46)	<0.0001

Table 6: Statistical parameters of serum CA 125, ultrasound score, RMI 1, RMI 2, RMI 3 and RMI 4 in study population.

Parameters	Sensitivity	Specificity	PPV	NPV	Accuracy
CA 125	76.59	76.71	67.92	83.58	76.66
Ultrasound score	65.21	86.30	75	78.75	77.5
RMI 1	85.10	86.30	80	90	85.83
RMI 2	63.82	85.30	75	78.75	77.5
RMI 3	59.57	83.56	70	76.25	74.16
RMI 4	74.46	82.19	72.91	83.33	79.16

Amongst 4 RMI scores, RMI 1 has the highest sensitivity and specificity 85.10%, 86.30% while RMI 2 had comparable specificity 85.30% but lower sensitivity 63.82% than RMI 1. RMI 3 has comparable specificity (83.56%) but less sensitivity (59.57%) and accuracy (74.16%) than RMI 1 score. RMI 4 is least specific (82.19%). The positive predictive value as well as the negative predictive value are highest for RMI 1, 80% and 90% respectively thus highest accuracy is of RMI 1 (85.83%).

RMI 1 has the highest specificity, sensitivity, positive and negative predictive value.

In our study clinical diagnosis with thorough preoperative assessment of patients including bimanual pelvic examination, radiological evaluation and CA 125 measurement has highest ability to predict benign and malignant ovarian tumors when compared with gold standard of diagnosis i.e., histopathologic examination (Figure 1).

DISCUSSION

Ovarian cancers are one of the malignancies with worst prognosis due to lack of effective screening for early detection. Proper evaluation of ovarian tumors is important because surgical intervention, if possible, can be done in time, thereby decreasing morbidity and mortality of patients. In the present study, out of 120 cases of ovarian tumors, 39.16% were malignant and 60.83% were benign neoplasms. This is comparable to the study done by Mondal et al in which benign tumors were 63.1%, followed by malignant ovarian tumors (29.6%).[9] Study done by Ganga et al and Yogambal et al also found the frequency of benign and malignant tumor to be similar.[11,12]

Age has a strong correlation to ovarian cancer risk and advancing age increased the possibility of malignant transformation. In our study, the mean age of patient with benign ovarian tumor was 40.5 years and for malignant tumor was 45.5 year. This is comparable to findings of Radhamani et al and Bhagde et al but more than the finding of Al Shukri et al.[10,13,14]

Present study shows no correlation of ovarian malignancy with nulliparity or low parity of females which was consistent with the study conducted by Jindal et al.[15]

Out of 80 premenopausal females, 78.75% had benign ovarian masses and only 21.25% had malignant ovarian masses. While amongst 40 postmenopausal females, 75% of the ovarian masses were malignant and 25% were benign. The findings in our study are consistent with Zarchi et al.[16]

The standard cut off values of 35 U/ml was taken for the levels of serum CA 125. Out of total 47 of the malignant cases, 76.5% cases have the values more than standard cut off. While amongst benign cases, 23.28% patients had values more than cut off values. So, that CA125 overall sensitivity of 76.59%, specificity of 76.71%, accuracy of 76.66% and positive predictive value of 67.92%. It is consistent with the study by Radhamani et al which showed a sensitivity of 62.5% and specificity of 84.25% in defining the malignant nature of ovarian neoplasms.[10] Mehboob et al found sensitivity of CA125 in 68% of the cases and specificity in 90%. The diagnostic accuracy was 79% and a positive predictive value of 87%.[17]

Cut off value of ultrasound score taken as 3, 63.82% malignant tumors had score >3 While only 13.69% of benign ovarian disease had a score of more than 3. Sensitivity, specificity and accuracy of ultrasound score in our study was 65.21%, 86.30% and 77.5% respectively. It was consistent with the study of Yelikar et al who concluded the sensitivity and specificity to be 80% and 83.88% respectively, and the diagnostic accuracy of 82.58%.[18]

With cut off value of RMI 1, RMI2, RMI 3 and RMI 4 taken as 200, 200, 200 and 450 respectively, values of RMI1, RMI2, RMI3 and RMI 4 calculated. Amongst these four scores, RMI 1 has the highest sensitivity and specificity 85.10% and 86.30% respectively while RMI 2 had comparable specificity 85.30% but lower sensitivity 63.82% than RMI 1. RMI 3 has comparable specificity (83.56%) but less sensitivity (59.57%) and accuracy (74.16%) than RMI 1 score. RMI 4 is least specific (82.19%). The positive predictive value as well as the negative predictive value are highest for RMI 1, 80% and 90% respectively thus highest accuracy is of RMI 1 (85.83%) This result of our study is consistent with Agrawal et al in which RMI 1 was the most accurate tool for screening purposes with a sensitivity, specificity and accuracy of 89.93%, 86.11% and 85.5% respectively when compared to the gold standard of diagnosis.[19] In the study

by Kumari et al RMI-1 had the highest sensitivity and specificity.[20] It had a sensitivity of 90.9%, specificity 94.4%, PPV 95.2% and NPV 89.5% in RMI 1 and sensitivity of 90.9%, specificity 72.2%, PPV 80% and NPV 86.7% in RMI-2.

Ultrasound has sensitivity and specificity of 80.90% and 87.70% for malignant tumors respectively. Maheshwari et al found sensitivity of 100% and 93.5% for benign and malignant tumors.[21] The corresponding specificities were 93.2% and 98.3% respectively. In the study by Das ultrasonography had a sensitivity of 86.67% and specificity of 95.65% in detecting malignant ovarian masses.[22]

Limitations

Follow up could not be done of these patients because of limited time duration of study. In further studies, we will include the follow up. There was interobserver variability in ultrasound and clinical diagnosis of different patients in study.

CONCLUSION

In our study, clinical diagnosis with thorough preoperative assessment of patients including bimanual pelvic examination, radiological evaluation and Ca125 measurement has highest ability to predict benign and malignant ovarian tumors when compared with gold standard of diagnosis i.e., histopathological examination. Our present study concludes that clinical diagnosis combined with ultrasound findings including color doppler tumor markers and RMI score can be used to detect ovarian malignancy at an early stage and can also determine if patient can be kept on follow up, advised surgery or biopsy if the mass is unresectable and to advise chemotherapy and to detect recurrences.

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