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Clinicopathological and Immunohistochemical Profile of Malignant Surface Epithelial Ovarian Tumors

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Abstract

INTRODUCTION: The ovaries are important organs for reproduction. Ovarian neoplasms have become increasingly important not only because of large variety of neoplastic entities but more because they have gradually increased mortality rate in female genital cancers. The role of IHC is now employed not only for diagnosis but also for other Parameters including prognosis, staging, prediction of response to therapy and for the selection oftherapeutic agents.

Materials and Methods: This is a prospective study conducted in the Department of Pathology at Fakir Mohan Medical College and hospital, Balasore and S.C.B.Medical College and Hospital, Cuttack, Odisha from March 2019 to February 2020. The gross specimen received were fixed in 10 % formalin for 24hours and from every specimen multiple sections were taken from representative site for histological examination. The number of blocks varied from four to eight in number. Sections were processed in paraffin, which were cut at five microns thickness. Sections were stained with conventional hematoxylin and eosin stain.

RESULTS: The age range of the tumors diagnosed varied from 22 to 71 years, with a peak incidence in 4^{th} and 5^{th} decade of life. Maximum benign cases were seen between30-40 years. Maximum number of malignant tumors were seen between 40-60 years. Youngest patient was 22 years old, oldest was 71 years old. The maximum number of tumors were seen in the 30-40 years. There was a wide range of size variation in ovarian neoplasms in the present study. It ranged from 3x2cm to 30x20cm. Majority of them 40(50.1%) were in the size range of 6-10cm, followed by 33(41.2%) in the size range of 11-19 cm. Serous tumors formed the majority of ovarian neoplasms in the study. There wasa total of 64 serous tumors, constituting about 75%.

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CONCLUSION: The role of IHC is now employed not only for diagnosis but also for other Parameters including prognosis, staging, prediction of response to therapy and for the selection oftherapeutic agents.

Keywords: Immunohistochemical, Malignant, Ovarian Tumors

INTRODUCTION

The ovaries are important organs for reproduction. The ovaries are paired pelvic organs located on the sides of the uterus close to the lateral pelvic wall, behind the broad ligament and anterior to the rectum. [1]

The ovary is complex in its embryology, histology, steroidogenesis and has potential to develop malignancy. The ovarian tumors are not a single entity but a complex wide spectrum of neoplasms involving variety of histologic tissues ranging from epithelial tissues, connective tissues, specialised hormone secreting cells to germinal or embryonal cells. [2]

The main function of the ovaries is to produce ova to implant after fertilization in the endometrium, the preparation of which is co-ordinated afresh each time by ovarian hormones. It also functions as an endocrine gland in the development of secondary sexual characters as well as their maintenance. Thus, the ovary is always in a dynamic state. [3]

Ovarian neoplasms have become increasingly important not only because of large variety of neoplastic entities but more because they have gradually increased mortality rate in female genital cancers. [4] Ovarian cancers account for 25% of the all gynaecological malignancies and 3rd commonest cause of death due to malignancies of female genital tract in the western world. [4] In India, ovarian tumors account for 80% of all the gynaecological malignancies. [5]

The ovary, after the uterus and cervix, is the second common site for the development of gynaecological malignancy and prognosis remains poor About 75% of the tumors are benign and 25% are malignant. [6]

Generally ovarian tumors occur in perimenopausal and post-menopausalwomen, infrequently in children also. The risk of developing an ovarian malignancy peaks in fifth decade of life. Ovarian tumors in adolescents and children are not frequently encountered in the clinical practice. The rarity of the condition, asymptomatic nature in earlier stage, variation in clinical presentation and unawareness among girls and parents sometimes makes diagnosis delayed and difficult. [7]

Risk factors for ovarian cancer are much less clear than for other genital tumors, but nulliparity, family history and heritable mutation play a role in the tumor development. Women between 40 to 59 years of age who have taken oral contraceptives or undergone tubal ligation have a reduced risk of developing a cancer. [8]

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Serum HCG, Serum CA125, Serum alpha fetoprotein, placental alkaline phosphatise and lactate dehydrogenase are useful tumor markers, but their accessibility to the practising pathologist for rural based poor population remains verylimited even today. [9] Screening for ovarian epithelial cancer can be improved by measurement of additional tumor markers such as ovarian cancer antigen OVx, and Ca 15-3, and numerous other antigens and by combination of tumor marker measurement and Doppler colour flow ultrasonography & transvaginal ultrasonography. [10]

Materials and Methods:

This is a prospective study conducted in the Department of Pathology at Fakir Mohan Medical College and Hospital, Balasore,and S.C.B.Medical College and Hospital, Cuttack,Odisha from March 2019 to February 2020.

The gross specimen received were fixed in 10 % formalin for 24hours and from every specimen multiple sections were taken from representative site for histological examination. The number of blocks varied from four to eight in number. Sections were processed in paraffin, which were cut at five microns thickness. Sections were stained with conventional hematoxylin and eosin stain The lesions were classified and studied as per the WHO classification of ovariantumors (2014).

Fixation for light microscopy: All the specimens obtained were fixed in buffered 10% formalin. Fixation time was 12-24 hrs, and then processed.

Eosin – Preparation: 1 gm of eosin powder dissolved in 100 ml of distilled water. A large crystal of thymol or 0.25 ml of 400/o formaldehyde is added to each 100 ml of stock to prevent the growth of mould·

IMMUNOHISTOCHEMISTRY

Immunohistochemical staining of ER and PR was done using peroxidase–antiperoxidase method according to the protocol described by DAKO.ER- Monoclonal Rabbit, Clone- EP 1

RESULTS

Table-1: Age Wise Distribution of Ovarian Neoplasms

Age	Benign	Percent	Borderline	Percent	Malignant	Percent
Up to 20	00	00%	00	00%	00	00%
21-30	06	14.2%	02	18.18%	00	00%
31-40	32	76.1%	01	9.0%	02	07%
41-50	02	4.7%	06	54.5%	07	25.7%
51-60	01	2.6%	01	9.0%	16	59.2%
61-70	01	2.6%	01	9.0%	02	07%
71-80	00	00%	00	00%	00	00%
TOTAL	42	51.55%	11	17.95%	27	30.45%

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The age range of the tumors diagnosed varied from 22 to 71 years, with a peak incidence in 4th and 5th decade of life. Maximum benign cases were seen between30-40 years. Maximum number of malignant tumors were seen between 40-60 years. Youngest patient was 22 years old, oldest was 71 years old. The maximum number of tumors were seen in the 30-40 years.

Table-2: SHOWING PRESENTATION OF TUMOURS

Side of ovary involved	Number of cases	Percentage
Right	48	**60%**
Left	25	**31%**
Bilateral	07	**09%**

There was a wide range of size variation in ovarian neoplasms in the present study. It ranged from 3x2cm to 30x20cm. Majority of them 40(50.1%) were in the size range of 6-10cm, followed by 33(41.2%) in the size range of 11-19cm.

Table-3: Showing Consistency of Benign, Borderline andMalignant Tumors

Consistency	Benign	Borderline	Malignant	Total	Percentage
Cystic	38	07	08	53	66.2%
Solid andcystic	04	02	16	22	27.5 %
Solid	-	02	03	05	6.2 %
Total	42	**11**	**27**	**80**	**100%**

The tumors were classified according to WHO histologic classification of ovariantumors and the incidence of different histologic types noted.

Table–4: Showing Distribution of Surface Epithelial Tumors

Type of surface epithelial tumor	No of cases	Percentage
Serous Cystadenoma	30	37.5 %
Serous cystadeno fibroma	04	5%
Borderline serous Tumor	07	8%
Serous cystadenocarcinoma low grade	15	18%
Serous cystadenocarcinoma high grade	08	10%
Mucinous Cystadenoma	08	10%
Borderline Mucinous tumor	04	5%
Mucinous cystadenocarcinoma	04	5 %
Brenner Tumor	00	%
Endometroid Tumor	00	%
un differentiated carcinoma	00	%

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Total number of surface epithelial tumors	80	100 %

Serous tumors formed the majority of ovarian neoplasms in the study. There werea total of 64 serous tumors, constituting about 75%.

Table 5: Expression of IHC Markers in Benign, Borderline, and Malignant

SEOT	ER (%)	PR (%)	p53 (%)	Ki-67 (%)
Benign (*n*=42)	21(50%)	33(68.5%)	18(42%)	11(26.7%)
Borderline (*n*=11)	07(66.6%)	06(54.5%)	07(66.6%)	09(81.3%)
Malignant (*n*=27)	23(81%)	12(44%)	22(81%)	24(88.8%)

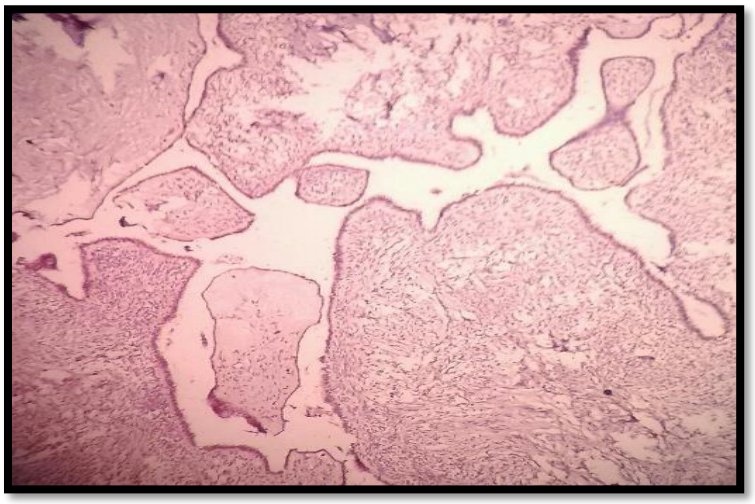

Fig-1;ER POSTIVE (40X) SEROUS BENIGN CYSTADENOMAS

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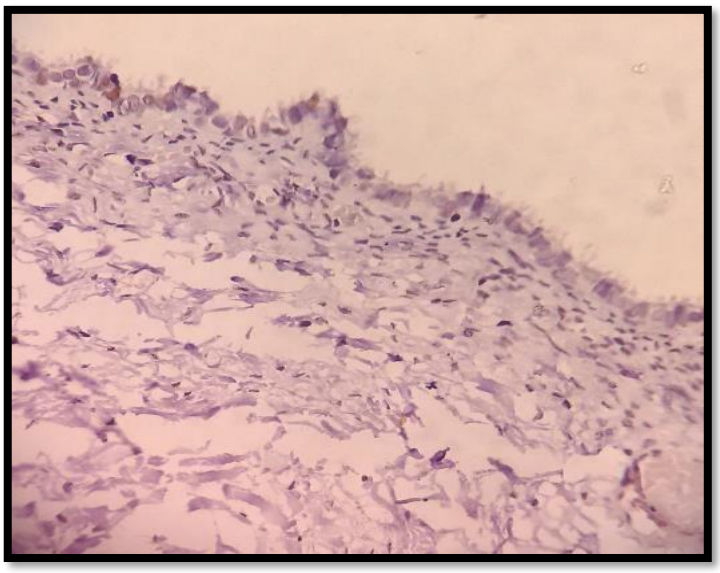

Fig-2; P 53 FOCAL POSITVE (40X) IN BORDERLINE CYSTADENOMA

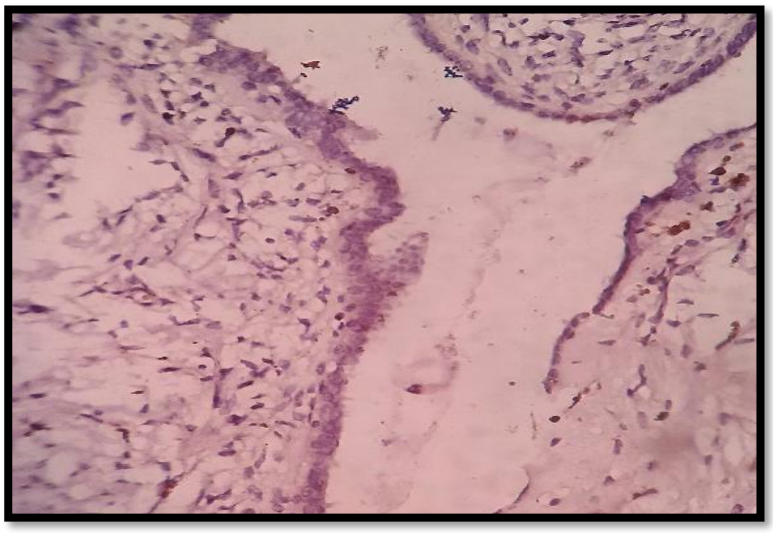

Fig-3; Ki67 FOCAL POSITIVE (40X) IN BENIGN SEROUS CYSTADENOMA

DISCUSSION

In present study, peak incidence of SEOTs is seen in the age group of 30 to 40. This is in similar to the studies like that done by Jha et al (2008) in which the majority of patients were in the 31 to 40 age group. [11]

The current study results had shown that 51.5%of patients were benign. This compares well with older studies like the one published by Verma and Bhatia (66.99%).[12] But this is slightly lower than other more recent studies like Swamy et al who had 71% benign tumors in their series. [13] This variation could be due to the fact that one of the hospitals from which data was collected for this study (MNJ) is a tertiary level specialised hospital for cancer and hence

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majority of patients coming there are malignant. This selection bias may have inflated the number of malignant cases and reduced the benign ones.

Most of the benign tumors in this study were unilateral with only 12% cases showing bilateral tumor involvement. This is comparable to findings of study done by Jha et al (93.34% unilateral). [11] In contrast Swamy et al reported a bilaterality rate of 29% in benign tumors. [13] In malignant tumors that were noted a bilaterality rate of just 7.5% compared to Swamy et al who reported a bilaterality rate of 50% and Jha et al in which 42% of the malignant tumors were bilateral. [13,11]

In the present series, as in all the other studies, it was found that surface epithelial tumors to be the most common tumors ranging from 56% (Jha et al) to 71% (Pilli et al). [11, 14] In this series there were 80 ovarian neoplasms. The relative percentage of various histological subtypes of ovarian tumors in this study was comparable to mostof the studies that compared the results with Tyagi et al. [15]

Serous cystadenoma comprised 59 cases (29.5%) in this study while Ganga Pilli etal reported 31.2% and Tyagi et al reported 39.5%.[15]

In present study, the expression of ER was detected more in malignant tumors (81%) than borderline (66.6%) and benign (50%). This is parallel to study done by sylvia *et al* in malignant (88%), in borderline (60.2%), in benign (40.5%).[16]

In our study, the expression of PR was noticed more in benign (62.4%)than borderline(50%) and Malignant tumors (54%). Buchynska et al PR expression is more in benign (58%), in borderline (48%), in malignant (40%).[17] This probably indicates the protective effect of progesterone in the Development ofovarian carcinomas.

Gursan *et al*. demonstrated that the mean ki-67 li in benign tumors was 24.9% in borderline tumors, it was 68.8%; in malignant tumors, it was 85.8%.[18]When compared with the benign tumors, ki-67 li was found to be significantly increased in the malignant tumors.

In the case of serous tumors, ER was expressed in all high and Low-grade tumors. The expression of PR was more in low-grade tumors than high- grade ones. P53 expression was seen in all high-grade tumors and low- grade tumor. The ki-67 li was more in high-grade tumors than low-grade tumors. The expression of ER was more in malignant tumors (23/27, 81%) than borderline (07/11, 66%) andbenign (21/42, 50%). The expression of PR was more in benign (33/42, 68.19%) than borderline (6/11, 54.5%) and malignant tumors (12/27, 44.25%). The expression of p53 was less in benign (18/42, 42%) than borderline (7/11, 66.6%)and malignant tumors (22/27, 81%). The expression of ki-67 was more in malignant (24/27, 88.8%) than borderline(09/11, 81.33%)and benign tumors (11/42, 26.1%).

In present study ER positivity more in malignant tumors (75%) as compared to Borderline (66.6%) and malignant (30%).this is similar to Silvian et al. in overall cases. PR positivity

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more in benign and borderline compared to malignant this is similar to Silvian et al. P53 expression is more in malignant (66.6%) as compared to Silvian et al he has41%.[19]

CONCLUSION

As compared to ER the expression of PR was more in benign than borderline and malignant tumors. p53 was expressed more often in malignant tumors followed by borderline and benign tumors. The mean ki-67 labeling index was the highest in malignant followed by borderline and benign tumors. Ki-67 index was higher in tumors with adverse prognostic factors. Hence, it Would Help in prognostication and differentiation of the three-morphological type. P53 were expressed only in malignant tumors suggesting their carcinogenic role and help in the differentiation of borderline and malignant tumors. The findings of this study indicate that IHC marker report of ER, PR status and Ki-67 If included in each pathology report will pave the way for better Understanding of Biological behavior and modify treatment strategies in Malignant Surface Epithelial Tumors of Ovary.

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