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ORIGINAL RESEARCH

Clinicopathological and Immunohistochemical Profile of Malignant Surface Epithelial Ovarian Tumors

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ABSTRACT

Background: 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. Generally ovarian tumors occur in perimenopausal and post-menopausal women, infrequently in children also. The risk of developing an ovarian malignancy peak in fifth decade of life. Aim and Objectives: To Study and characterize the ovarian tumors based on gross and histopathological features. To compare the frequency of benign and malignant neoplasms of the ovary with other studies.

Materials and Methods: This study is a prospective study. The cases were obtained from Department of Pathology, at a tertiary care hospital in Alappuzha over a period of 1 year. 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 ovarian tumors (2014).

Results: A total of 80 SEOT ovarian tumors were studied. Of these ovarian tumors, 42 were benign, 11 were borderline and 27 were malignant. Right sided tumors of ovary 48 (60%) were more common than the left sided tumors 25(31%). 07(09%) cases were bilateral. The commonest epithelial tumors were serous 64 cases (75 %), 16 mucinous (25%), remaining are not presented on my study period. Serous tumors formed the majority of ovarian neoplasms in the study. There was a total of 64 serous tumors, constituting about 75%.

Conclusion: 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.

Keywords: Immunohistochemical Profile, Ovarian Tumors, Ki-67.

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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, specialized 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 3rdcommonest cause of death due to malignancies of female genital tract in the western world. In India, ovarian tumors account for 80% of all the gynaecological malignancies.[5]
Generally ovarian tumors occur in perimenopausal and post-menopausal women, 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.[6]
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.[6] 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.[7]
Serum HCG, Serum CA125, Serum alpha fetoprotein, placental alkaline phosphatase and lactate dehydrogenase are useful tumor markers, but their accessibility to the practicing pathologist for rural based poor population remains very limited even today.[8]
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.[9]

Aim and Objectives:
To Study and characterize the ovarian tumors based on gross and histopathological features.
To compare the frequency of benign and malignant neoplasms of the ovary with other studies.

MATERIALS & METHODS
This study is a prospective study. The cases were obtained from the Department of Pathology, at a tertiary care hospital in Alappuzha from June 2017 to May 2018.
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 ovarian tumors (2014).

RESULTS
A total of 80 SEOT ovarian tumors were studied. Of these ovarian tumors, 42 were benign, 11 were borderline and 27 were malignant.
The age range of the tumors diagnosed varied from 22 to 71 years, with a peak incidence in 4th and 5thdecade of life. Maximum benign cases were seen between 30-40 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 1:Showing the age Wise Distribution of Ovarian Neoplasms in the Present Study

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%

Table 2: Showing the Distribution of Tumors in Parous Women

Type of tumors	Unmarried	Married	
		Nulliparous	Parous
Benign	02	08	32
Borderline	-	-	11
Malignant	01	01	25

Table 3: Clinical Presentation of Patients

Clinical	Benign	Boderline	Malignant
Presentation			
Mass per abdomen	34	3	27
Associated pain abdomen/ back pain	47	3	20
DUB	5	-	-
Amenorrhoea	4	-	2
Postmenopausal bleeding	10	1	9
Urinary symptoms	7	-	-
Loss of weight	4	-	2
Ascites	1	-	8

The most common clinical presentation was pain in abdomen, seen in 47 cases (26.5%) followed by mass per abdomen in 34 cases (17%).

Table4: Showing Presentation of Tumours.

Side of ovaryinvolved	Number of cases	Percentage
Right	48	60%
Left	25	31%
Bilateral	07	09%

Right sided tumors of ovary 48 (60%) were more common than the left sided tumors 25(31%). 07(09%) cases were bilateral.

Table 5: Showing the Size Range of the Ovarian Neoplasms in the Present Study

Size (cm)	Number of cases	Percentage
≤5	03	3.7%
6-10	40	50.1%
11-19	33	41.2%
≥20	04	05%
Total	80	100%

There was a wide size range 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 6: Showing Consistency of Benign, Borderline and Malignant Tumors in Present Study

Consistency	Benign	Borderline	Malignant	Total	Percentage
Cystic	38	07	08	53	66.2%
Solid and cystic	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 ovarian tumors and the incidence of different histologic types noted.

Table-7: Number of Cases and Percentage Distribution of Various Types of Surface Epithelial Tumours (n=80)

Histological type	Benign	Borderline	Malignant	Total
Serous	38(53.1%)	07(10.9%)	23(35.9%)	64(75%)
Mucinous	08(50%)	04(25%)	04(25%)	16(25%)
Endometrioid				00
Clear cell				00
Transitional cell				00
Seromucinous				00

The commonest epithelial tumors were serous 64 cases (75 %), 16 mucinous (25%), remaining are not presented on my study period.

Table 8: Showing Distribution of Surface Epithelial Tumors

Type of surface epithelialtumor	No of cases	Percentage
Serous Cystadenoma	30	37.5 %
Serous cystadeno fibroma	04	5%
Borderline serous Tumor	07	8%
Serous cystadenocarcinomalow grade	15	18%
Serous cystadenocarcinomahigh 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	%
T Total number of surface epithelial tumors	80	100 %

Serous tumors formed the majority of ovarian neoplasms in the study. There were a total of 64 serous tumors, constituting about75%.

Table 9: Showing Distribution of Serous Tumors

Type	No. of cases	Percentage
Serous cystadenoma	30	45.5%
Borderline serous tumor	07	10.9%
Serous cystadenocarcinoma	23	35.9%
Serous cystadenofibroma	04	8.5%
Total	64	100%

Table 10: Distribution of Mucinous Tumors

Tumor type	No. of cases	Percentage
Mucinous cystadenoma	08	50%
Borderline mucinoustumor	04	25%
Mucinous cystadenocarcinoma	04	25%
Total	16	100%

Grossly, the largest tumor measured 30x20 cm, which was also the largest tumor encountered in the present study.

The benign tumors were cystic while borderline and malignant ones were partly solid and partly cystic containing mucinous fluid.

Five cases of borderline mucinous were diagnosed in tumor with papillary projections lined by atypical cells up to one- two cell thickness and no stromal invasion was seen.

Malignant tumours showed complex papillary pattern with pleomorphic mucinous cells. Areas of necrosis and stromal invasion were seen.

Table 11: 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%)

DISCUSSION

Ovarian neoplasms are one of the most fascinating tumors in women in terms of their histogenesis, clinical behavior and malignant potentiality. They account for a disproportionate number of fatal cancers, being responsible for almost half of the deaths from cancers of the female genital tract.

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%).[10] But this is slightly lower than other more recent studies like Swamy et al who had 71% benign tumors in their series.[11]

This variation could be due to the fact that the hospitals from which data was collected for this study (MNJ) is a tertiary level specialized hospital for cancer and hence majority of patients coming there are malignant. This selection bias may have inflated the number of malignant cases and reduced the benign ones.

30.5% of tumors in this study are malignant. This was comparable to studies like and Swamy et al (25%) and Jha et al (16%).[11,12]

This study showed a slightly lower percentage of malignant ovarian tumors (30.5%) but this was similar to the study done by Verma and Bhatia. [10] The study done by Jha et al recorded the least percentage of malignant cases (16.1%).[12]

The percentage of borderline tumors in this study was 17.5 % which was comparable to the study done by Gupta et al (4.1).[13]

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).[12] In contrast Swamy et al reported a bilaterality rate of 29% in benign tumors.[11] 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.[11,12]

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),[12] to 71% (Pilli et al).[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 most of the studies that compared the results with. (Jha et al, Swamy et al, Ganga Pilli et al, Tyagi et al. etc.).

Serous cystadenoma comprised 59 cases (29.5%) in this study while Ganga Pilli et al reported 31.2% and Tyagi et al reported 39.5%.[14,15]

In present study, the expression of ER was 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] This may support the role of estrogen in oncogenesis.

In our study, the expression of PR was 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%). This probably indicates the protective effect of progesterone in the Development of ovarian 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%. 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%) and benign (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 sylvia et al.in overall cases.[16]

PR positivity more in benign and borderline compared to malignant this is similar to sylvia et al.[16] P53 expression is more in malignant (66.6%) as compared to silvia et al he has 41%.

CONCLUSION

Benign are the most common, of these surface epithelial tumors are the commonest, affects mainly reproductive age group. 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.

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