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HISTOPATHOLOGICAL STUDY OF OVARIAN NEOPLASMS

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ABSTRACT

Background: Ovarian tumors are the second most common tumor of female genital tract. The Ovarian neoplasm manifest a wide spectrum of clinical, morphological and histological features. Their complex nature, unpredictable behaviour, prognosis and varying therapeutic strategies, necessitates an accurate diagnosis. This study is aimed to record the histopathological spectrum of ovarian neoplasms and study the age wise distribution and frequency of benign and malignant ovarian neoplasms.

Materials and methods: This Study was conducted in Mysore Medical College and Research Institute for a period of 18 months. All the 120 cases of ovarian neoplasms obtained were grossed, processed, examined and categorised. All relevant clinical data of patients analysed from the hospital records.

Results: The total number of ovarian neoplasms studied during study period was 120 cases. The peak age incidence was fifth decade. Among them 102 (85%) cases were benign, 11(9.1%) malignant and 7(5.8%) Borderline tumors. Based on histological type, Surface epithelial tumors accounted for 96(80%), Germ cell tumors were 18(15%) and Sex cord stromal tumors were 6(5%). The most common benign neoplastic encountered was Serous Cystadenoma. In Malignant cases, maximum were Adult Granulosa cell tumor.

Conclusion: Ovarian neoplasms posses wide spectrum of histology. Early detection and surgical intervention prevents the progression of disease. Hence, their recognition is important from the view point of therapy and prognosis. Histopathological examination still remains the gold standard investigation. Hence this study is undertaken, to determine the histopthologica spectrum of ovarian neoplasms.

Keywords: Neoplasm, Serous Cystadenoma, Adult Granulosa cell tumor, Histopathology

INTRODUCTION

Ovarian neoplasms are one of the most serious health problems affecting women worldwide. It is the second most common cancer of the female reproductive system and the leading cause of gynecological cancer death and accounts for about 3% of all female cancers. [1,2]

Ovaries are paired intra-pelvic female reproductive organs that are a common site for both benign and malignant neoplasms in all age groups. The ovary has a peculiar anatomy and physiology, with constant cyclical changes from puberty to menopause, and is made up of several cell types, each of which can give rise to tumours. Ovarian neoplasms inherit a diverse range of histogenesis, clinical behaviour, and histological types due to their complex structure. Younger women are more likely to develop benign tumours, whereas older women are more likely to develop malignant tumours. Postmenopausal women, unmarried women, and married women with low parity are more likely to be affected.[3,4,5]

Ovarian neoplasms have grown in importance not only because of their wide range of histo-morphological patterns, but also because they have a higher mortality rate than other female genital cancers.[3] Early detection of ovarian tumours is difficult for gynaecologists, owing to the fact that symptoms in early disease are vague and non-specific. Although some of the specific tumours have distinguishing characteristics and are hormonally active, the majority are non-functional and symptomless, with non-specific signs until they reach a large size. By the time an ovarian malignancy is diagnosed, approximately two-thirds of them have progressed to a late stage.[5] Because there are no screening tests for ovarian tumours and these tumours cannot be confidently distinguished from one another based on clinical, radiological, or gross characteristics. [6]

The diagnosis of various histological patterns are very important for predicting tumor behaviour and to decide further management of patients.[7]

Ovarian Carcinoma poses a major health problem, especially among Indian women. Every year, 240,000 women worldwide are diagnosed with ovarian cancer, and with a five-year survival rate of less than 45%. It is responsible for 150,00 deaths, making it the seventh most common cancer and the eighth most common cause of cancer death among women.[8]

The disease incidence continues to vary by age and race, with less developed countries showing a higher incidence (approximately 70%). In Europe, the incidence rate of ovarian cancer increased significantly from 4.9 to 6.1/100,000 females between 1982 and 2008. In 2012, the United States (81.8% of all cases), China (14.60% of all cases), and India (11.33% of all cases) had the highest ovarian cancer incidence rates.[9]

Ovarian tumours are one of the most common neoplasms affecting women in India, ranking fourth/fifth among all cancers. They also claim that the age-standardized incidence rate of ovarian neoplasms has increased by 0.26% to 2.44% per year, based on data from various registries.[10]

According to various population-based cancer registers in India, the incidence of ovarian carcinoma (age adjusted for 100,000) ranged from 1.7 to 15.2 from 2012 to 2014.

The incidence of ovarian carcinoma is expected to rise by 55% to 371,000 per year by 2035, while the death rate will rise by 67% to 254,000. According to the World Ovarian Cancer Coalition Atlas 2018, India has the world's second highest ovarian carcinoma incidence/frequency. Pune and Delhi registries had the highest incidence in India.[9]

Histopathological examination still remains the gold standard investigation. Hence this study is undertaken, to determine the histopathological spectrum, age wise distribution and frequency of benign and malignant ovarian neoplasms.

METHODS

This is a prospective study done in Department of Pathology, Mysore Medical College and Research Institute, Mysuru during the period of March 2021 – August 2022(18 months). The ethical approval was obtained from the Institutional ethics committee. The resected specimens were collected from the Department of Pathology. All types of Primary Ovarian tumors were included in the study. Cases of other nonneoplastic ovarian lesions, metastatic tumors and tumor with extensive necrosis, without viable tumor cells were excluded from the study. The detailed clinical history and relevant investigation done, was collected from the patient's case records. In each case the standard protocol

for surgical grossing of specimens was followed. After conventional processing, paraffin sections of 5µm thickness were stained by haematoxylin and eosin for histopathological study.

The tumors were categorized according to the WHO 2020 classification. Histological types, appearance on gross were also determined. The data was collected, statistically evaluated and represented in terms of frequency distribution tables. The categorical and counting variables were presented by frequencies and percentages. The proportion of subjects according to the various subgroups such as age, histological type, subtype, benign vs malignant and was estimated.

RESULTS

A total sample of 120 cases were studied and evaluated. A standard protocal for grossing and histopathological techniques were followed.

Maximum patients were seen between 31 – 50 years of age Based on their morphological features, ovarian tumours were divided into three categories: benign, borderline, and malignant. In the present study, 102(85%) cases were benign, 11(9.1%) were malignant and 7(5.8%) were borderline tumors. Majority of benign tumors were seen between the age group of 31-50 years. Where as two-thirds of all malignant tumors were seen between 41-50 years of age.

Table 1 : Distribution of benign, borderline and malignant ovarian neoplasms in different age groups.

Age	Nature of neoplasms			Total
	Benign n (%)	Borderline n (%)	Malignant n (%)	
11-20	5(4.16)	0(0)	1(0.83)	6(4.99%)
21-30	20(16.66)	1(0.83)	1(0.83)	22(18.32%)
31-40	31(25.83)	4(3.33)	1(0.83)	36(30%)
41-50	24(20)	2(1.6)	7(5.83)	33(27.43%)
51-60	16(13.33)	0	0	16(13.33%)
>60	6(5)	0	1(0.83)	7(5.83%)
Total	**102(85)**	**7(5.8)**	**11(9.1)**	**120(100)**

Based on microscopic features, the tumors were broadly classified as per WHO 2020 Classification. Histologically, Surface epithelial tumors accounted for 80% of all ovarian tumors, followed by germ cell tumors(15%) and sex cord stromal tumors constituted only 5%.

Serous cystadenoma(52 cases, 43.3%) was the most common benign surface epithelial tumor and followed by mucinous cystadenoma (21 cases, 17.5%), seromucinous cystadenoma (11 cases, 9.3%). The most common malignant surface epithelial tumor was High grade serous carcinoma.

Among germ cell tumor, Mature cystic teratoma was the most common tumor (17 cases, 14.2%). Adult granulosa cell tumor was the most common sex cord stromal tumor in our study.

Figure 1: Photomicrograph of Adult granulosa cell tumor showing solid cystic mass

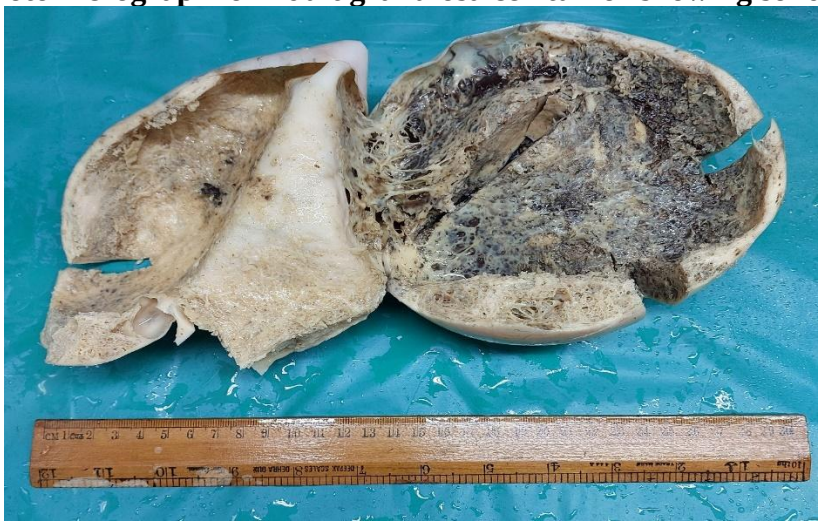


Table 2: Distribution of ovarian neoplasms based on histological subtype

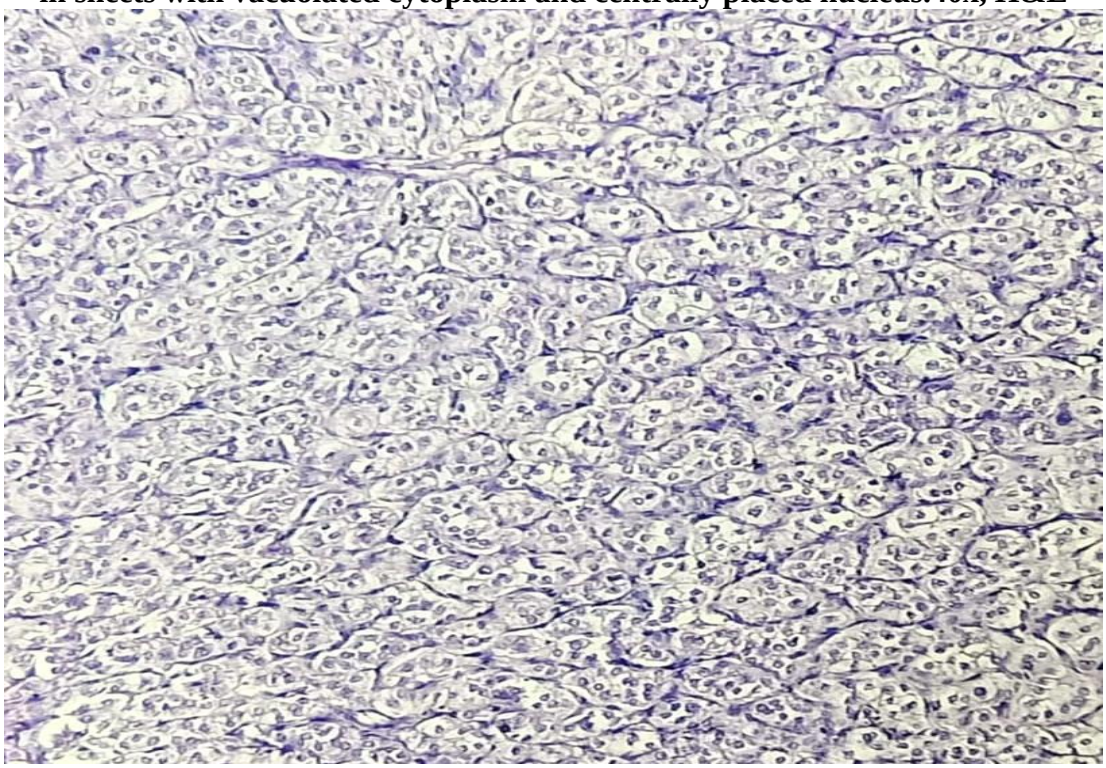
Histological type	Histological subtype	Frequency (n)	Percentage(%)
Surface Epithelial tumors	Benign Brenner tumor	1	0.8
	Borderline mucinous tumor	6	5
	Borderline serous tumor	1	0.8
	Mucinous cystadenoma	21	17.5
	Mucinous cystadenocarcinoma	1	0.8
	High grade serous carcinoma	3	2.5
	Seromucinous cystadenoma	11	9.3
	Serous cystadenoma	52	43.3
Germ cell tumors	Mature cystic teratoma	17	14.2
	Struma ovary with papillary carcinoma	1	0.8
Sex cord stromal cell tumors	Adult granulosa cell tumor	5	4.2
	Steroid cell tumor-NOS	1	0.8
Total		**120**	**100**

Table 3: Distribution of ovarian tumors according to consistency.

Consistency	Frequency (n)	Percentage (%)
Cystic	100	83.4
Solid Cystic	16	13.3
Solid	4	3.3
Total	**120**	**100**

Out of 120 cases studied, the majority of the tumors were unilateral, only 4 cases were Bilateral tumors. Majority of the tumors were cystic (100 cases, 83.4%), followed by solid and cystic (16 cases, 13.3%).

Figure 2: Photomicrograph of microscopy of steroid cell tumor -NOS showing cells arranged in sheets with vacuolated cytoplasm and centrally placed nucleus.40x, H&E



The most common presenting symptom was pain abdomen in more than half of the cases(62 cases, 51.7%), followed by abnormal uterine bleeding(31 cases, 25.8%) and mass per abdomen(24 cases, 20%).

Figure 3: Microscopy of Struma Ovarii with papillary carcinoma, showing Follicles with nuclear features of papillary carcinoma.10x, H&E

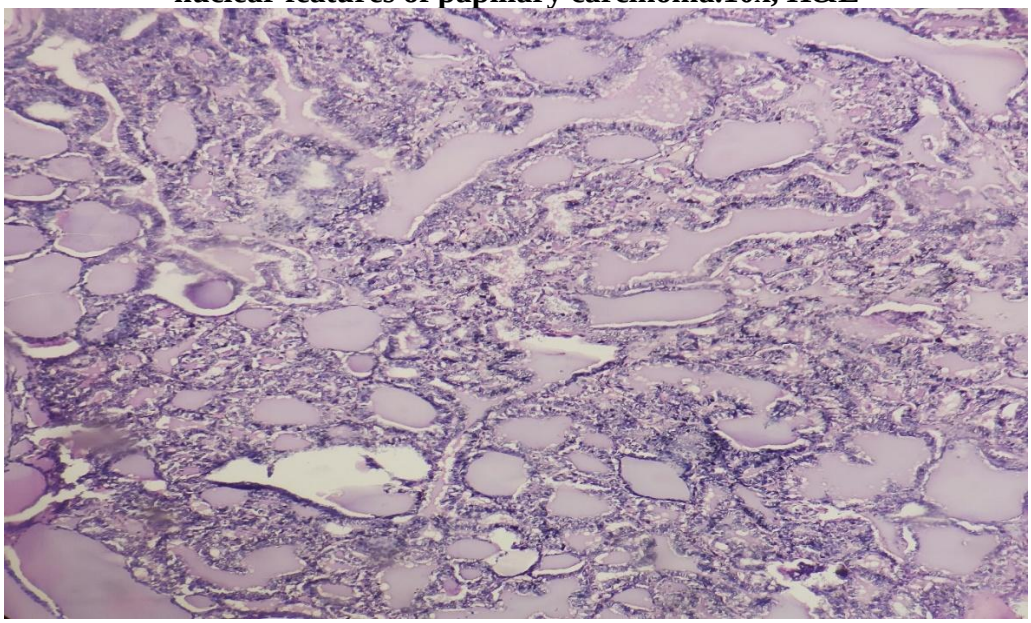
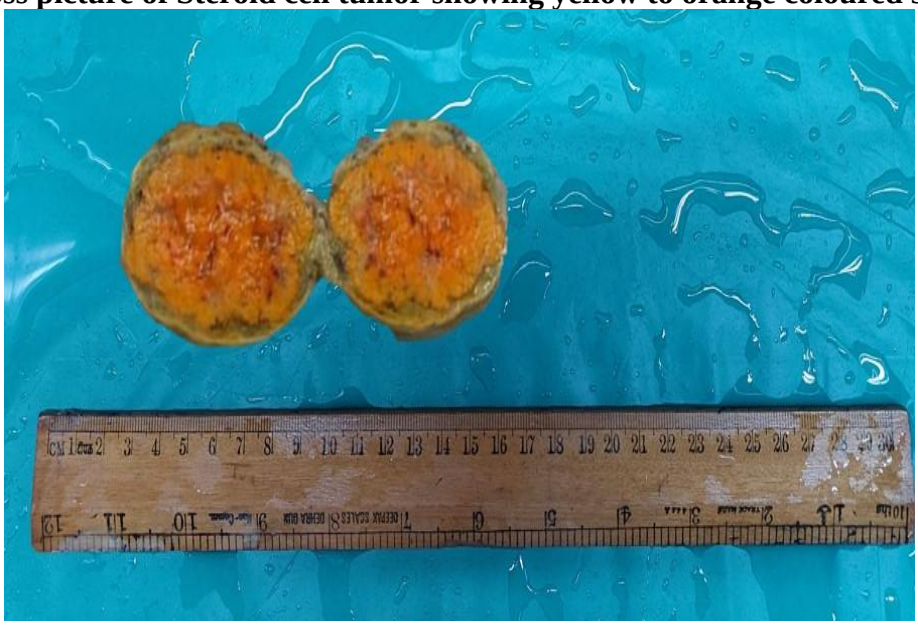


Table 4: Distribution of ovarian neoplasms according to symptoms

Symptoms	**Frequency (n)**	**Percentage (%)**
Pain abdomen	62	51.7
Abnormal uterine bleeding	31	25.8
Mass per abdomen	24	20
Amenorrhea	01	0.8
Infertility	01	0.8
Postmenopausal bleeding	01	0.8
Total	**120**	**100**

Figure 4: Gross picture of Steroid cell tumor showing yellow to orange coloured solid mass



DISCUSSION

Ovarian neoplasms have grown in significance due to their wide range of histomorphological patterns, but more significantly, since they have been linked to a progressive rise in the death rate from female genital cancers due to their ambiguous symptoms and advanced stage diagnosis. The many forms of ovarian tumours vary greatly in their occurrence, clinical presentation, and behaviour. Even though clinical or gross examination offers valuable diagnostic hints for developing a differential diagnosis, it is typically not sufficient to determine the type of ovarian tumour. Therefore, in order to accurately type ovarian tumours, one must rely on the tumor's microscopic morphology.[11]

The peak incidence of the ovarian neoplasms in the present study was in the fourth decade (30%) which was very similar to the observations done by Neetu GV et al.[12] in their study, who reported 31.1% cases in 4th decade. Where as, Sharma P et al.[13] reported that majority of the cases occured in the fifth decade of life which was slightly higher than our study.

In the present study, Most of the cases were benign tumors (85%) followed by malignant (9.1%) and borderline (7%). A similar pattern was seen in most of the studies done in the past. In the study by Sharma S et al[14], there were 52% benign, 06% borderline and 42% malignant tumors, which displayed relatively higher incidence of malignant tumors than ours.

Comparing the relative percentage of different histological types of ovarian neoplasm with different studies and the present study, it was found that epithelial tumors comprised 80% of all tumors, followed by germ cell tumors 15%. Sex cord/stromal tumors were found in only 5% cases. Hashmi AA et al [15] found epithelial, germ cell and sex cord stromal tumors in relative percentage of 67.2%, 27.2% & 4.9% respectively. Aparna et al [16] found it to be 53%, 40% and 7% respectively.

Surface epithelial tumors out numbered all the other neoplasms, a common finding in all other studies. However, Aparna et al [16] reported slightly higher incidence of germ cell tumors in contrary to the present study.

In the present study, Serous cystadenoma (54.16%) was found to be the most common neoplasm among the surface epithelial tumours. Studies on ovarian tumours carried out by Deepesh Kumari et al.[17] and Gaikwad et al.[18] have also reported similar results where the serous cystadenoma were the most common. High grade Serous carcinoma (3.12%) was the most common tumour diagnosed among the malignant surface epithelial tumours in the present study, which was consistent with Gaikwad SL et al .[18]and Wills V et al[19]. On the contrary, Deepesh Kumari et al. [17]reported mucinous cystadenocarcinoma as the most common malignant surface epithelial tumor.

Table 5: Comparison of Surface epithelial tumors with other studies

Histological Subtype of Surface epithelial tumors	Deepesh kumari et al n (%)[17]	Gaikwad SL et al n (%)[18]	Wills V et al n (%)[19]	Present Study n(%)
Benign Brenner tumor	-	02(3.17)	-	01(1.04)
Borderline mucinous tumor	01(1.69)	01(1.58)	01(2.5)	06(6.25)
Borderline serous tumor	-	01(1.58)		01(1.04)
Mucinous cystadenoma	05(8.47)	24(38.09)	10(25)	21(21.87)
Mucinous cystadenocarcinoma	04(6.77)	02(3.17)	02(5)	01(1.04)
High grade serous carcinoma	01(1.69)	02(3.17)	01(2.5)	03(3.12)
Sero mucinous cystadenoma	-	-	-	11(11.45)
Papillary Serous Cystadenoma	01(1.69)	-	-	-
Endometrioid carcinoma	01(1.69)	01(1.58)	01(2.5)	-
Serous cystadenoma	46(77.96)	30(47.61)	25(62.5)	52(54.16)

The incidence of germ cell tumours was 15% of all ovarian tumors. The most common subtype was mature cystic teratoma, which constituted 94.4% of all germ cell tumors. Studies by Wills V et al[19]., Deepesh Kumari et al.[17], and Gaikwad SL et al.[18] showed an incidence of mature cystic teratomas to be 92.30%, 77.77%, and 82.35% of all germ cell neoplasms, respectively, which were consistent with the present study. Only one case of struma ovary papillary carcinoma was noted in the present study, accounting for 5.55%.

The incidence of sex cord stromal tumor in the present study was 5% and predominately comprised adult granulosa cell tumor which accounted for 83.33% of sex cord stromal tumors and a single case of steroid cell tumor – NOS noted. However, Wills V et al.[19] and Gaikwad SL et al.[18] observed that the most common sex-cord stromal tumors were fibroma-thecoma group tumors.

In the present study, 96.7% of cases were unilateral and only 3.3% were bilateral. This is in agreement with the study conducted by Prakash A et al.[20] and Sharma S et al. [14],where as Swarnalatha P et al.[21] reported relatively higher incidence of bilateral neoplasms. In the present study, Bilateral lesions were seen in 4 (3.3%) cases out of which, two were serous cystadenomas and two were mature cystic teratoma. These observations indicated an association of bilaterality with benign tumors.

In the present study almost half of the patients presented with abdominal pain (51.7%), followed by abnormal uterine bleeding (25.8%). Other symptoms observed were mass per abdomen, postmenopausal bleeding and infertility. It was concorded well with study by Thakkar NN et al.[23] . In a study done by Chandanwale SS et al[24], the commonest symptom was mass per abdomen.

One of the study's limitations is that it was conducted on a small group at a single institute. Therefore, we advise multicentric research on a broader study population.

CONCLUSION

Ovarian neoplasms are the widest and most complex problems in gynecology, and has wide spectrum of clinical and histopathological features. Early diagnosis is very crucial to help in decreasing the morbidity and mortality among the patients.

As ovarian cancer is a leading cause of cancer related mortality worldwide, proper categorization into exact morphological types will help the gynecologists for better management. The observations and analysis of the present study will provide valuable baseline information regarding the pattern, distribution of ovarian tumors. Histopathological Examination remains the Gold standard in the diagnosis of the Ovarian neoplasms

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