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ORIGINAL RESEARCH

Histopathological Spectrum Of Ovarian Neoplasms: A 15 Months Prospective Study At A Tertiary Care Centre Of Rajasthan

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Abstract

Background: The ovaries are reproductive organ, the source of female fertility, and at the same time, the origin of many of the most complex as well as lethal neoplasms. Worldwide, ovarian cancer is the most frequent cause of death from gynecological cancers.

Aim & Objectives: To study the histopathological spectrum of ovarian tumors, their clinical presentation and age distribution.

Materials & Methods: A prospective study was conducted over a duration of 15 months (April 2021 to June 2022) in the Department of Pathology, SMS Medical College, Jaipur, Rajasthan. A total of 134 cases were studied and analyzed for age, histopathological findings and clinical presentations.

Results: Out of 134 cases of ovarian neoplasms, 84 cases (62.7%) were benign, 6 cases (4.4%) were borderline, 44 cases (32.8%) were malignant. Among the histologic subtypes, 77 cases (57.5%) were of surface epithelial histotype, 32 cases (23.9%) were of germ cell histotype, 23 cases (17.2%) were sex-cord stromal tumors and 1 case each of metastatic and miscellaneous tumors were observed. Tumors were seen over age range of 6-82 years with maximum number of cases in 3rd to 5th decade (68.7%). Most of the cases presented with chief complaint of abdominal pain and lump abdomen, seen in 77.6% and 66.4% cases respectively.

Conclusion: Surface epithelial tumors are the most common variant followed by germ cell tumors and sex-cord stromal tumors. Correlation among clinical details, radiology, serology and gross morphology gives important clue for proper histopathological diagnosis, thereby helping the gynecologists in initiating proper and timely management of the patient.

Keywords: Ovarian Tumors, Histopathology, Surface Epithelial Tumor.

INTRODUCTION

The ovaries are reproductive organ, the source of female fertility, and at the same time, the origin of many of the most complex as well as lethal neoplasms. Ovarian cancers are amongst one of the common malignancies affecting women. Ovarian cancers consists 4% of all female cancers[1] and accounts for 30% of all cancers of female genital system.[2] It is the fifth leading cause of cancer death in women.[2]

The prognosis of ovarian tumors is determined by its tumor stage, specific histological type and grading. Staging of ovarian tumors is done mainly by TNM system, established by American Joint Committee on Cancer, and also by the International Federation of Gynaecology and Obstetrics staging system. Histological typing and grading are done mainly by World Health Organization (WHO) classification of ovarian tumors.[1] Ovarian tumors are broadly classified as benign, borderline and malignant types. About 80% tumors of ovary are benign, mostly occur in 20-45 year age group. The malignant tumor are more common in age groups between 40-65 year.[3] The diversity of the pathologic entities of ovarian tumors is due to the three cell types that make up the normal ovary. These are the multipotent surface (coelomic) covering epithelium, the totipotent germ cells, and the multipotential sex cord/stromal cells and each of these cell types gives rise to a variety of tumors.[4] Primary lesions include epithelial ovarian carcinoma, germ-cell tumors, sex-cord stromal tumors, and other more rare types. Metastases to the ovaries are relatively frequent, the most common are from the breast, colorectal, endometrial, stomach, and appendix.[5]

A number of epidemiological studies have evaluated a variety of risk factors for ovarian neoplasms. These risk factors include : age, chronic inflammation, non-steroidal anti-inflammatory drug (NSAIDs) usage, diet, ethnicity, infertility, obesity, low parity, smoking, and talc use/asbestos exposure. Use of combined oral contraceptive pills is found to be a protective factor.[6] Early ovarian cancer causes minimal, nonspecific, or no symptoms, and so, most cases are diagnosed in an advanced stage, thus earning itself the term “silent killer”. [7]

Ovarian tumors are associated with high mortality due to lack of symptoms in the early stage of the disease in most of the patients. Ovarian cancers have worst prognosis amongst all gynecological malignancies. The overall survival is approximately 45%, primarily due to diagnosis at late stage of disease.[8] Diagnosis of various pattern of ovarian tumors is very important in the treatment and prognosis which is confirmed by histopathological examination of ovary. The purpose of this descriptive type of observational study is to evaluate the complete histopathological spectrum of various ovarian neoplasms and to correlate them with their clinical findings.

MATERIALS AND METHODS

A prospective observational study was conducted over a period of 15 months (April 2021 to June 2022) in the Department of Pathology, SMS Medical College, Jaipur, Rajasthan and a total of 134 cases of ovarian tumors were included in the study by applying inclusion and exclusion criteria.

Inclusion Criteria

(1) Formalin fixed biopsies or specimens of ovary received in the Department of Pathology S.M.S Medical College, Jaipur, Rajasthan.

(2) Patients with written informed consent.

Exclusion criteria

(1) Poorly fixed specimens.

(2) Inadequate biopsies.
(3) Patient not willing to be a part of the study.
A detailed clinical history, radiological and serological investigations were obtained from the patients and histopathology requisition forms. The formalin fixed specimen was then subjected to gross according to Grossing of Surgical Oncology Specimens by Tata Memorial Hospital.[9] The grossed specimens were then subjected to histopathological examination under microscope and reported according to CAP protocol and classified as per WHO Classification of Ovarian tumors 2021.[10]

RESULTS

A total of 134 cases of ovarian tumors were included in the present study, out of which 84 cases (62.7%) were benign, 6 cases (4.5%) were borderline and 44 cases (32.8%) were malignant.
Table 1 illustrates the incidences of ovarian neoplasms with respect to age. The age ranged from 6 – 82 years with a mean age of 40.71 years. The maximum number of ovarian neoplasms were noted in the 3rd and 5th decades with 33 (24.6%) and 32 cases (23.9%) respectively. Benign ovarian tumors were most commonly observed during 3rd to 5th decade while malignant ovarian tumors were more common during 4th to 7th decade of life.
In present study most patients presented with multiple complaints. The most common presenting complaints in patients with ovarian neoplasms was pain abdomen in 104 cases (77.6%) followed by lump abdomen in 89 cases (66.4%). Heavy menstrual flow and irregular cycles were seen in 24 (17.9%) and 17 cases (12.7%). 8 patients presented with complaints of post-menopausal bleeding while 4 patients presented with chief complaint of primary infertility. The occurence of ovarian tumors were mostly seen during parity 3 (42 cases, 31.3%) followed by parity 2 (39 cases, 29.2%). 16 cases (11.9%) of ovarian tumors were diagnosed in nulliparous females. Out of 134 total cases, 118 cases (88.1%) had unilateral involvement of ovaries, without any predominant side while bilaterality was noticed in 16 patients (11.9%).
Out of total 134 samples of ovarian tumors received in our department during the study period, 9 samples (6.7%) were of linear core biopsies. Out of the remaining 125 specimens, most of the ovaries had mixed consistency (65 cases, 48.5%). 45 specimens (33.6%) had cystic consistency while the remaining 15 specimens (11.2%) were solid.
The tumors were classified according to WHO histologic classification of ovarian tumors 2021 and the incidence of various histological types were noted (Table 2). In the present study, Surface Epithelial tumors were the most common of all (77 cases, 57.5%), followed by Germ Cell tumors (32 cases, 23.9%) and Sex-Cord Stromal tumors (23 cases, 17.2%). 1 case each of Miscellaneous tumor and Metastatic tumor was found. The most common benign tumors observed were benign serous tumor (28 cases, 20.9%) followed by mature cystic teratoma (26 cases, 19.5%) and most common malignant tumors observed were malignant serous tumor (20 cases, 14.9%) followed by granulosa cell tumor (8 cases, 6.5%). 6 cases of borderline ovarian tumors were found comprising of 3 cases (50%) each of borderline serous and borderline mucinous tumors.

Table 1: Distribution of tumor in different age groups

Age (in yrs)	Benign	%	Borderline	%	Malignant	%
<10					1	2.3
11-20	5	5.9			3	6.8
21-30	25	29.7	3	50	5	11.4
31-40	19	22.7			8	18.2
41-50	19	22.7	1	16.6	12	27.3
51-60	8	9.5	1	16.7	5	11.4
61-70	7	8.3	1	16.7	9	20.3
71-80	1	1.2				
>80					1	2.3
	84	100	6	100	44	100

Table 2: Histologic Types and Percentage distribution of various Ovarian Neoplasms

S.No	Histologic Type of Ovarian Neoplasm	Number of patients (n=134)	Percentage (%)
I	**EPITHELIAL TUMORS**	**77**	**57.5**
A	**Serous Tumors**	**51**	**38**
	Benign Serous Tumor	28	20.9
	Borderline Serous Tumor	3	2.2
	Malignant Serous Tumor	20	14.9
B	**Mucinous Tumors**	**24**	**17.9**
	Benign Mucinous Tumor	16	11.9
	Borderline Mucinous Tumor	3	2.2
	Malignant Mucinous Tumor	5	3.8
C	**Endometrioid Tumor**	1	0.8
D	**Brenner Tumor**	1	0.8
E	**Clear Cell Tumor**	0	0
II	**SEX-CORD STROMAL TUMORS**	**23**	**17.2**
A	**Granulosa Cell Tumor**	8	6.5
B	**Fibroma, Thecoma and Fibrothecoma**	8	6.5
C	**Sertoli-Leydig Cell Tumor**	1	0.7
D	**Myxoma**	1	0.7
E	**SCST With Annular Tubules**	1	0.7
F	**SCST, NOS**	4	3.1
III	**GERM CELL TUMORS**	**32**	**23.9**
A	**Dysgerminoma**	4	3
B	**Mature Teratoma**	26	19.5
C	**Immature Teratoma**	0	0
D	**Yolk Sac Tumor**	1	0.7
E	**Struma – Ovarii**	1	0.7
IV	**MISCELLANEOUS**	**1**	**0.7**
V	**METASTATIC**	**1**	**0.7**
	Total	**134**	**100.0**

DISCUSSION

Oophorectomy is a commonly performed major gynecological surgical procedure throughout world. It is a successful operation in terms of symptom relief and patient satisfaction. It also provides symptomatic relief to the patient from various diseases afflicting the ovary, often when medical treatment fails to alleviate disabling symptoms. The current study was conducted during the study period of approximately 15 months and 134 samples of ovarian neoplasms were analyzed for detailed histopathological diagnosis and their correlation with age and clinical features were noted.

The age of patients in our study ranged from 6-82 years. Majority of the cases (44.8%) were encountered in the age group of 20-40 years followed by 34.3% cases in 40-60 years. This corroborates with the findings of Mondal S. et al[11], Ranjana et al[12], Amita S. et al[13], Gupta N. et al[1] and Aishwarya et al[8] (Table 3).

Table 3: Comparison of distribution of ovarian neoplasms in different age groups

Age (years)	Mondal S. et al (2011)[11]	Ranjana et al (2017)[12]	Amita S. et al (2018)[13]	Gupta N. et al (2019)[1]	Aishwarya et al (2020)[8]	Present study
<20	6.8%	7.6%	6.7%	14.6%	6.65%	6.7%
20-40	58.0%	58.8%	57.5%	48.2%	49.2%	44.8%
40-60	32.7%	25.2%	32.7%	34.9%	37.5%	34.3%
>60	2.5%	8.4%	3.1%	2.3%	6.65%	14.2%

Most of the ovarian neoplasms in our study were benign in nature followed by malignant tumors. Benign ovarian neoplasms were reported in 84/134 cases (62.7%). These findings were corroborated with the findings of Mondal S. et al[11], Gupta N. et al[1] and Aishwarya et al[8] with benign tumors reported in 63.1%, 63.7% and 67.6% of the cases respectively. Benign tumors were reported in 56.3% cases of ovarian tumors in the study conducted by Sofi et al[6] and 78.36% benign cases in the study by Anitha PV et al[14]. In the studies conducted by Ranjana et al[12] and Amita S. et al[13], benign ovarian neoplasm was reported in 91.5% and 93.2% cases respectively.

The benign ovarian neoplasms were followed by malignant tumors, which were more common than borderline tumors. The present study observed malignant ovarian neoplasms in 32.8% cases (44/134 cases). Similar results were obtained in the studies conducted by Mondal S. et al[11] with 29.6% malignant cases, Gupta N. et al[1] with 31.1% malignant cases and Aishwarya et al[8] with 30.2% malignant cases. Sofi et al[6] in his study observed 42% of the malignant ovarian neoplasms while Ranjana et al[12], Amita S. et al[13] and Anitha PV et al[14] observed slightly lower percentage of malignant neoplasms, which were seen in 8.5% of the cases, 6.2% of the cases and 15.11% of the cases respectively.

In present study, a low percentage (4.5%) of ovarian neoplasms were reported as borderline in nature. These findings corroborated with the results obtained in the studies conducted by Mondal S. et al[11], Sofi et al[6], Gupta N. et al[1], Aishwarya et al[8] and Anitha PV et al[14]. In the study conducted by Amita S. et al[13], out of a total of 162 ovarian neoplasms, only 1 case (0.6%) was observed to be borderline in nature. No case of borderline ovarian neoplasm was reported in the study conducted by Ranjana et al[12].(Table 4)

Ovarian tumors are divided in epithelial, germ cell, and sex cord-stromal. In present study, surface epithelial tumors constitute the majority of ovarian neoplasms, seen in 77/134 ovarian tumors 57.5% similar to the studies conducted by Mondal S. et al[11], Nirali N. et al[15], Ranjana et al[12], Sofi et al[6], Amita S. et al[13], Gupta N. et al[1], Aishwarya et al[8] and Anitha PV et al[14]. In our study, germ cell tumors were observed in 32/134 cases 23.9%. Similar findings were observed in

the studies conducted by Mondal S. et al[11], Nirali N. et al[15], Ranjana et al[12], Sofi et al[6], Amita S. et al[13], Gupta N. et al[1] and Anitha PV et al[14]. 1 case each of metastatic and miscellaneous tumors was also reported in our study similar to the findings observed in studies conducted by Mondal S. et al[11], Nirali N. et al[15], Sofi et al[6], Gupta N. et al[1] and Anitha PV et al[14].

Table 4: Comparison of the Incidence of various Ovarian tumors

	Benign	Borderline	Malignant
Mondal S. et al (2011) [11]	63.1%	7.3%	29.6%
Ranjana et al (2017) [12]	91.5%	0%	8.5%
Sofi et al (2018) [6]	56.3%	1.7%	42.0%
Amita S. et al (2018) [13]	93.2%	0.6%	6.2%
Gupta N. et al (2019) [1]	63.7%	5.2%	31.1%
Aishwarya et al (2020) [8]	67.6%	2.2%	30.2%
Anitha PV et al (2021) [14]	78.36%	6.53%	15.11%
Present Study	62.7%	4.5%	32.8%

Benign serous epithelial tumors were the most common benign tumors observed in our study, reported in 20.9% of the total ovarian tumors, followed by mature teratoma, reported in 19.5% of the total cases. Similar results were also observed in the studies conducted by Mondal S. et al[11], Nirali N. et al[15], Sofi et al[6] and Anitha PV et al[14]. In the studies conducted by Gupta N. et al[1] and Aishwarya et al[8], most common benign tumors observed were benign serous epithelial tumors followed by benign mucinous tumors and mature teratomas.

In our study, 3/134 cases 2.2% each of borderline serous and mucinous tumors were observed. These results corroborated with those observed in the studies conducted by Mondal S. et al[11], Nirali N. et al[15], Sofi et al[6], Gupta N. et al[1], Aishwarya et al[8] and Anitha PV et al[14].

The most common malignant ovarian neoplasms observed in our study were serous adenocarcinomas, reported in 20/134 cases 14.9%, followed by granulosa cell tumors, which were reported in 8/134 cases 6.5%. Similar results were also observed in the studies conducted by Anitha PV et al[14]. In the studies conducted by Mondal S. et al[11], Nirali N. et al[15], Sofi et al[6], Gupta N. et al[1] and Aishwarya et al[8], malignant serous epithelial tumors were the most commonly reported malignant ovarian neoplasm, followed by malignant mucinous epithelial tumors [Table 5].

Abdominal pain and lump abdomen were the most common presenting complaint in the present study observed in 77.6% cases and 66.4% cases respectively. 29.9% cases also presented with accompanying complaint of weight loss. 20.9% cases had accompanying menstrual irregularities. Post menopausal bleeding and uterine prolapse were presenting complaints in 6% and 1.5% of the patients. These findings were similar to those observed in the studies conducted by Geeta et al[16], Sofi et al[6], Amita S. et al[13], and Aishwarya et al[8].

The parity in our study ranged from 0-5. Maximum cases had parity of 2 and 3 (60.5%). 22 cases (16.5%) had parity of 4 and 5. 15 cases (11.2%) had a parity of 1 while 16 cases (11.9%) were nulliparous. 3 cases (2.2%) were found to be pregnant at the time of surgery. These findings were similar to an Indian study performed by Aishwarya et al[8] in which, maximum cases had parity of 1 and 2 (59.5%). 8.8% cases had parity 3 and 7.3% cases had parity of 4 and above. 20.5% cases were nulliparous while 3.6% of the total cases were found to be pregnant at the time of surgery.

Table 5: Comparison of percentage distribution of various histologic types of Ovarian tumors

S.No	Type of Tumor	Mondal S. et al 2011[11]	Nirali N. et al 2015[15]	Sofi et al 2018[6]	Gupta N. et al 2019[1]	Aishwarya et al 2020[8]	Anitha PV et al 2021[14]	Present Study
I	**Surface Epithelial Tumor**							
A	Serous Tumors							
	Benign	29.98%	55.4%	35.3%	18.9%	39.7%	42.85%	20.9%
	Borderline	5.33%	1.5%	1.7%	0.9%	1.5%	2.04%	2.2%
	Malignant	11.38%	1.5%	22.7%	9.9%	13.3%	5.71%	14.9%
B	Mucinous Tumors							
	Benign	11.18%	7%	5.9%	14.6%	15.4%	14.69%	11.9%
	Borderline	1.98%	1.5%	0%	4.2%	0.7%	4.48%	2.2%
	Malignant	3.34%	0%	6.7%	6.1%	6.6%	2.04%	3.8%
C	Endometrioid Tumor	1.25%	2.3%	0.84%	12.7%	1.5%	2.04%	0.8%
D	Brenner Tumor	2.0%	2.3%	-	1.4%	0.7%	0.8%	0.8%
E	Clear Cell Tumor	1.5%	1.5%	0.84%	-	-	0.4%	0%
II	**Sex-Cord Stromal Tumor**							
A	Granulosa Cell Tumor	2.51%	1.5%	0%	1.4%	1.5%	2.04%	6.5%
B	Fibroma, Thecoma, Fibrothecoma	1.57%	3.1%	1.68%	1.9%	3%	2.87%	6.5%
C	Sertoli-Leydig Cell Tumor	1.15%	1.5%	0%	-	-	0.4%	0.7%
D	Myxoma	-	-	-	-	-	-	0.7%
E	SCST with annular tubules	-	-	-	-	-	-	0.7%
F	SCST, NOS	-	-	-	0.5%	-	-	3.1%
III	**Germ Cell Tumors**							
A	Dysgerminoma	2.61%	1.5%	1.7%	0.5%	-	0.81%	3%
B	Mature Teratoma	15.98%	12.4%	11.8%	13.2%	7.4%	16.32%	19.5%
C	Immature Teratoma	1.57%	0.8%	0%	2.4%	0.7%	0%	0%
D	Yolk Sac Tumor	1.25%	-	0.84%	0.5%	-	0.4%	0.7%
E	Struma-Ovarii	-	-	0.84%	1.4%	-	-	0.7%
IV	**Miscellaneous**	**0.62%**	**-**	**1.7%**	**0.5%**	**0.7%**	**0.8%**	**0.7%**
V	**Metastatic**	**2.61%**	**2.3%**	**5.9%**	**1.9%**	**0.7%**	**-**	**0.7%**

Table 6: Comparison of the mode of presentation of various Ovarian neoplasms

Chief Complaint	Geeta et al 2015[16]	Sofi et al 2018[6]	Amita S. et al 2018[13]	Aishwarya et al al 2020[8]	Present Study
Pain Abdomen	76.45%	64.7%	48.8%	83.1%	77.6%
Lump/Distended Abdomen	40.50%	53.8%	20.9%	27.2%	66.4%
Menstrual	25.62%	8.4%	19.7%	7.4%	20.9%

Irregularities					
Post-Menopausal Bleeding	-	-	1.9%	0.7%	6%
Weight Loss	-	-	-	6.6%	29.9%
Uterine Prolapse	-	-	0.6%	-	1.5%

In the present study, most of the ovarian neoplasms were found to involve unilateral ovary without any side predominance, which were reported in 118/134 cases (88.1%). Similar findings of unilateral ovary involvement were observed in the studies conducted by Nirali N. et al[15] with 88.4% cases, Amita S. et al[13] with 89.5% cases, Gupta N. et al[1] with 87.7% cases and Aishwarya et al[8] with 80.9% cases.

In the present study, on cutting the gross of oophorectomy specimen, most of the ovarian masses had cystic consistency along with some solid areas, giving it mixed solid-cystic consistency. This was observed in 65/134 cases (48.5%). Mixed solid-cystic consistency were observed in 28.7% of the cases in study conducted by Nirali N. et al[15], 25.3% cases in the study by Amita S. et al[13], and 32.1% cases in the study by Gupta N. et al[1]. In our study, cystic consistency was observed in 45 out of 134 ovarian neoplasm cases (33.6%). In the studies conducted by Nirali N. et al[15], Amita S. et al[13] and Gupta N. et al[1], cystic consistency was observed in 58.1% cases, 68.5% cases and 56% cases respectively. Solid consistency of ovarian neoplasms was observed in 15 out of 134 cases (11.2%) in our study. These findings were similar to the findings obtained in the studies conducted by Nirali N. et al[15], Amita S. et al[13] and Gupta N. et al[1].

CONCLUSION

Ovary is a common site of neoplasia in female genital tract and present with a variety of clinical and histological features. The present study provides a fair insight into histopathological patterns of ovarian neoplasms in the biopsy samples received in our institute. Our study concluded that benign tumors were far more common than malignant tumors. Based on histopathology, surface epithelial tumors were the most common variant followed by germ cell tumors and sex-cord stromal tumors. In our study, ovarian neoplasms were seen in all age groups, with predominance in 3rd to 5th decades of life. This study has shown primary ovarian neoplasms in younger as well as elder age groups, hence, possibility of malignancy should not be neglected in younger females. Abdominal pain and abdominal mass were the most common clinical presentations in our study. So, correlation of proper clinical details, radiological findings, serological findings and gross morphology can give important clues for the diagnosis. A proper and detailed histopathological diagnosis and categorization according to WHO classification of ovarian tumors helps the gynecologists in initiating proper and timely management to the patient. To conclude, histopathological profile of ovarian tumors remains the gold standard for treatment and determining the prognosis of the patient.

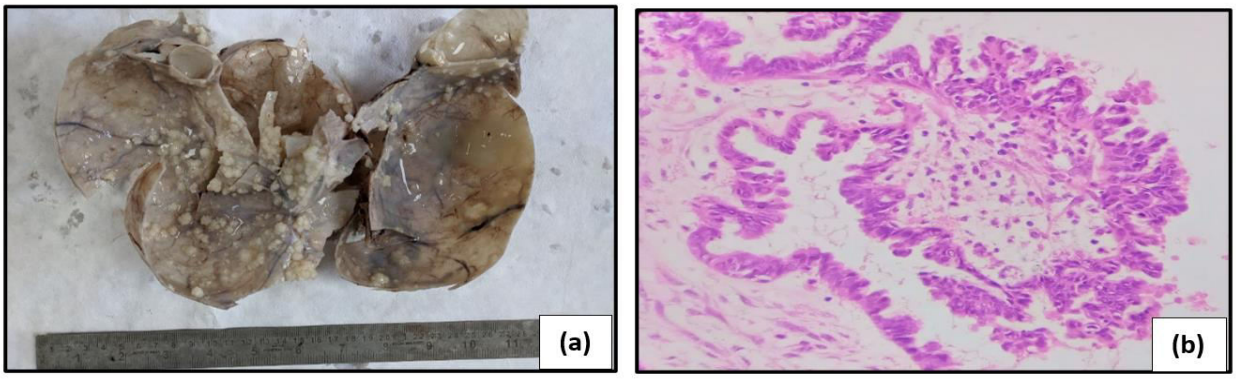

Figure 1: a) Gross image of cut open multiloculated ovarian cyst showing prominent vessels and numerous pearly white papillary excrescences. Wall thickness varies from papery thin to 0.3cm
b) H & E-Stained section (100x) of Serous Borderline Ovarian tumor showing numerous slender to broad irregular variably sized papillae with fibrous and hyaline cores. Hierarchical complex branching noted.

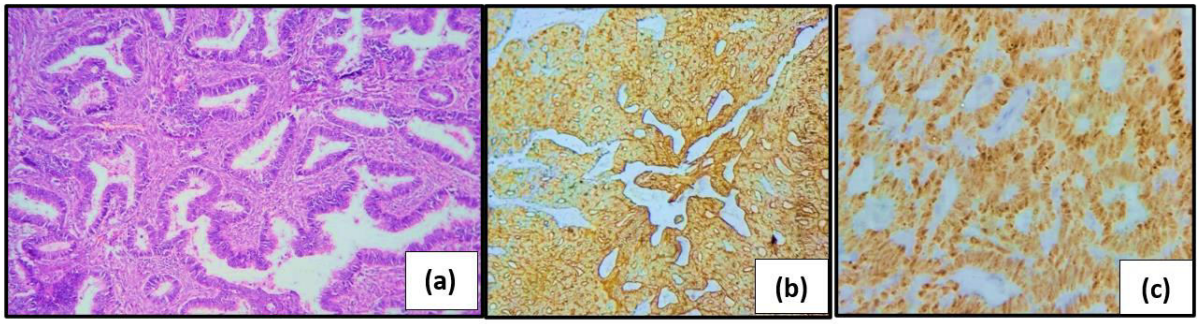

Figure 2: a) H & E-Stained section (100x) of High-Grade Serous Neoplasm showing papillary and micropapillary architecture with fibrovascular core. The neoplastic cells show high grade nuclear features.
b) IHC Stained section of High-Grade Serous Neoplasms showing strong membranous positivity for EMA (100x) and
c) nuclear positivity for WT-1 (400x)

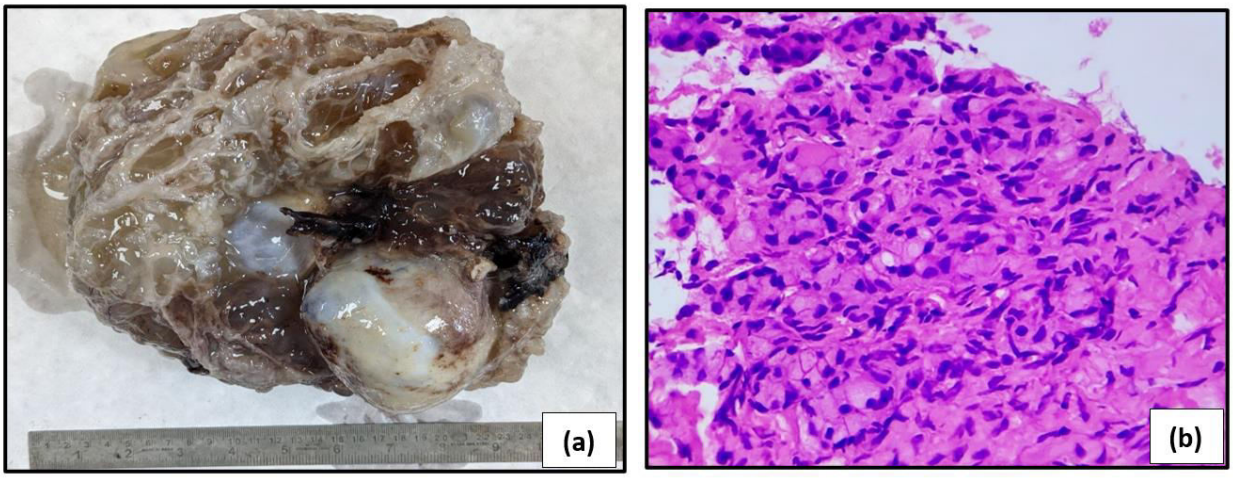

Figure 3: a) Gross image of Ovarian cyst filled with mucinous fluid.
b) H & E-Stained section (400x) of signet ring type of Mucinous Adenocarcinoma

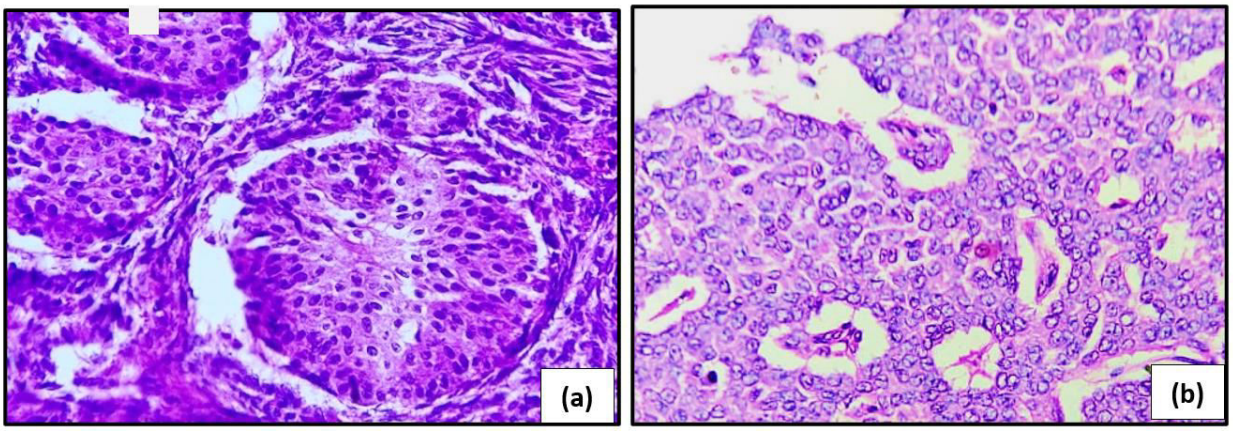

Figure 4: a) H & E-Stained section (400x) of Brenner tumor showing characteristic solid nests of epithelial cells resembling transitional epithelium surrounded by abundant stromal component
b) H & E-Stained section (100x) of Granulosa cell tumor showing characteristic Call-Exner bodies and coffee bean nuclei

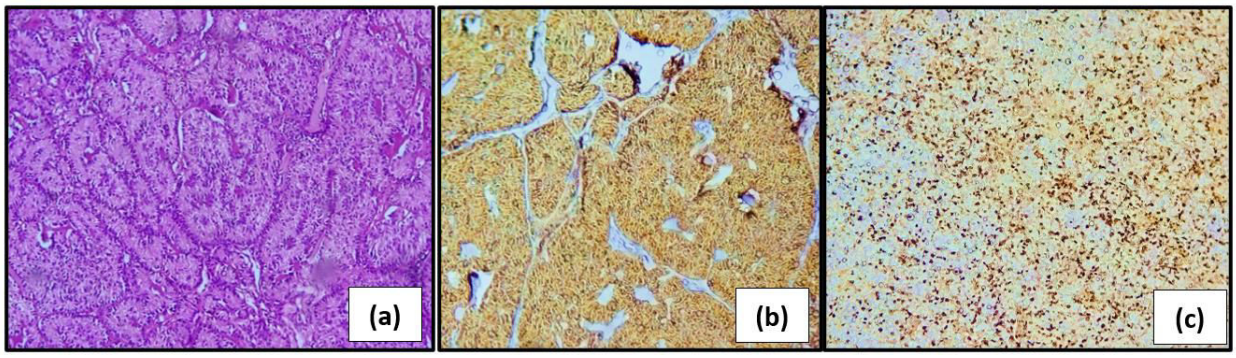

Figure 5: a) H & E-Stained section (100x) of SCST with annular tubules showing ring shaped simple and complex annular tubules with peripherally oriented nuclei around a central hyalinized body composed of basement membrane material.

b) IHC Stained section (100x) of SCST with annular tubules showing strong diffuse positivity for Inhibin and

c) nuclear positivity for Calretinin

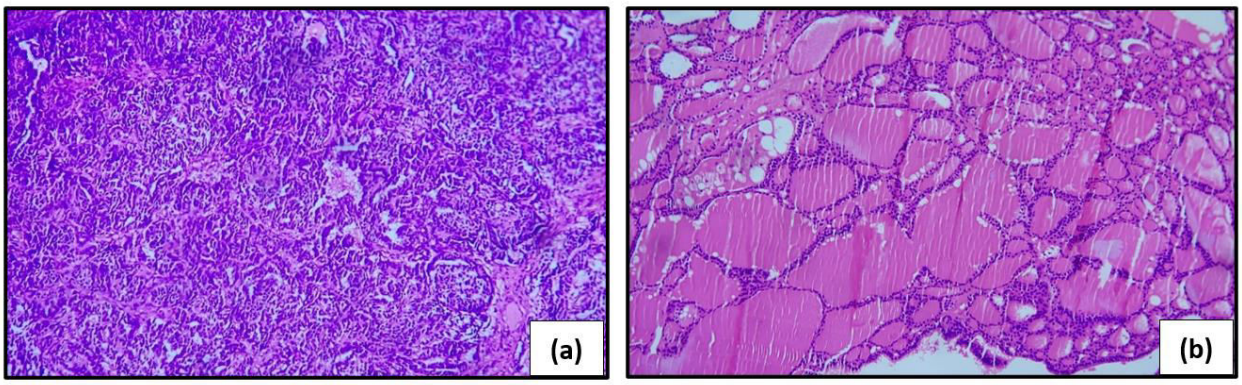

Figure 6: a) H & E-Stained section (100x) of Yolk Sac Tumor showing tumor cells arranged in endodermal sinus pattern and characteristic Schiller-Duval bodies.

b) H & E-Stained section (100x) of Struma ovarii showing colloid filled macro and microfollicles

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