

**PRIMARY OVARIAN NEOPLASMS: 5-YEAR INSTITUTIONAL STUDY**

Nalini Modepalli<sup>1</sup>, Suguna Belur Venugopal<sup>2</sup>, Tirthankar Mukherjee<sup>3</sup>

<sup>1</sup>Assistant Professor, Department of Pathology, Rajarajeswari Medical College and Hospital, Bangalore.

<sup>2</sup>Professor and HOD, Department of Pathology, Kempegowda Institute of Medical Sciences, Bangalore.

<sup>3</sup>Assistant Professor, Department of General Medicine, Kempegowda Institute of Medical Sciences, Bangalore.

**ABSTRACT****BACKGROUND AND OBJECTIVES**

The wide variety of ovarian neoplasms makes it an interesting topic for study. The objectives of the present study was to study clinical and histopathologic features of various ovarian tumours and classify them according to WHO classification.

**METHODS**

Five year study was conducted on ovarian specimens received in Central Laboratory, Department of Pathology, Kempegowda Institute of Medical Sciences, Bangalore, from June 2006 to May 2011. All ovarian specimens which on histopathological examination was diagnosed as primary ovarian neoplasm was included in the study.

**RESULTS**

We studied 210 primary ovarian tumours of ovary of which 83.97% were benign tumours, 3.77% were borderline epithelial and 12.26% were malignant tumours. Surface epithelial tumours were more common followed by Germ cell tumours. Mean age of diagnosis was 40.43 years. Abdominal mass was the most common presenting symptom. Right sided tumours were more common than the left.

**CONCLUSION**

Even though immunohistochemical and chromosomal studies have made diagnosis and differentiation of tumours easier, in developing countries like India, cost effective histomorphologic studies still form the backbone of diagnosis of these tumours.

**KEYWORDS**

Primary Ovarian Neoplasms, Surface Epithelial Tumours, Germ Cell Tumours, Sex Cord Stromal Tumours.

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**INTRODUCTION**

Ovary is a small organ, unique in terms of variety of lesions that arise from it.<sup>1,2</sup> Ovarian cancer is 6<sup>th</sup> most common cancer among women worldwide,<sup>3,4</sup> 3<sup>rd</sup> leading site in India.<sup>5</sup> Tumours of the ovary are amazingly diverse pathological entities, attributable to 3 cell types that make up normal ovary—multipotent surface (Coelomic) covering epithelium, sex cord stromal cells and totipotent germ cells. Ovarian cancer has the worst prognosis among gynaecological malignancies, 5-year survival rate being 45%.<sup>4,6</sup> It is generally impossible to diagnose nature of ovarian tumours preoperatively. Histopathologic examination is needed for a confirmatory diagnosis.<sup>7</sup> Knowing the type of tumour helps in judicious management of the patient.

**MATERIALS AND METHODS**

Five year study was conducted on all ovarian specimens received in the Central Laboratory, Department of Pathology, Kempegowda Institute of Medical Sciences (KIMS), Bangalore, which on histopathological examination were diagnosed as tumour listed under WHO classification of primary ovarian

tumours.<sup>3</sup> Non-neoplastic lesions, tumour-like conditions, paraovarian lesions and metastatic tumours were excluded from the study.

Specimens were sent in 10% formalin. Weight, measurement, external appearance, appearance of capsule, features on cut section and other relevant features recorded. Representative sampling was ensured for accurate examination.

Material was processed routinely. Multiple thin sections of 4-5 micron thickness were obtained from paraffin blocks, stained with H and E for microscopic examination.

Clinical history was noted. Special stains and immunohistochemistry was done when necessary. All tumours were classified as per WHO classification.

**RESULTS AND OBSERVATIONS**

Our study included 210 cases (212 specimens) of primary ovarian neoplasms; 66.2% - Surface Epithelial Stromal (SES) tumours, 58 (27.6%) - Germ Cell (GC) tumours and 13 (6.2%) - Sexcord Stromal (SS) tumours (Table 1).

Two cases of bilateral SES tumours had 2 different diagnoses on either side and hence we have 212 diagnoses from 210 cases (141 diagnoses from 139 cases of SES tumours); 83.97% were benign, 12.26% malignant and 3.77% were borderline epithelial tumours. Of benign tumours, 65.2% cases SES, 29.2% GC and 5.6% were SS tumours. Among malignant tumours, 65.14% SES, 23% GC and 11.6% SS tumours reported.

Mean age at presentation was 40.43 yrs. GC tumours were seen in younger age group while SS tumours were in the older. (Table 2).

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*Corresponding Author:*

*Dr. Nalini Modepalli,*

*Flat No. 104, 2<sup>nd</sup> Floor,*

*Shravanthi Orchids, 1st Main,*

*Revenue Layout, Padmanabhanagar,*

*Bangalore-560070.*

*E-mail: doctor.nalini@gmail.com*

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Mass abdomen was most common presenting symptom. Menstrual disturbances were more common in SS tumours. (Table 3).

197 (93.8%) of primary ovarian neoplasms were U/L and 13 (6.2%) B/L. All bilateral cases were SES tumours.

132 (59.2%) cases were right sided and 91 (40.8%) left sided.

Size of tumours ranged from 2x2x1 cm (Mature cystic teratoma) to 43x30x15 cm (Mucinous cystadenoma).

Benign tumours showed 51.8% unilocularity and 48.2% multilocularity. Malignant tumours were more commonly multilocular (64.7%).

154 (72.6%) cases were purely cystic, 16 (7.5%) solid and 42 (19.8%) partly cystic and partly solid areas; 84.8% of benign tumours were purely cystic, 5.6% solid and 9.6% partly cystic and partly solid. Among malignant tumours, 20 (76.9%) were of mixed consistency and 6 (23.1%) purely solid. None of the malignant tumours were purely cystic.

Tumour Type	Frequency	Percent
SES	139	66.2
GC	58	27.6
SS	13	6.2
<b>Total</b>	<b>210</b>	<b>100.0</b>

**Table 1: Frequency of Primary Ovarian Neoplasms**

	Age (yrs.)							Total
	<20	20-29	30-39	40-49	50-59	60-69	≥70	
SES	4	22	25	49	21	9	9	139
	2.9%	15.8%	18.0%	35.3%	15.1%	6.5%	6.5%	100.0%
GC	6	22	11	14	2	3	0	58
	10.3%	37.9%	19.0%	24.1%	3.4%	5.2%	.0%	100.0%
SS	0	0	4	2	1	6	0	13
	.0%	.0%	30.8%	15.4%	7.7%	46.2%	.0%	100.0%
Total	10	44	40	65	24	18	9	210
	4.8%	21.0%	19.0%	31.0%	11.4%	8.6%	4.3%	100.0%

**Table 2: Age Distribution**

	SES	GC	SS	Total
Mass Abdomen	58.9% (83)	39.7% (23)	38.5% (5)	52.4% (111)
Pain Abdomen	35.5% (50)	29.3% (17)	23.1% (3)	33% (70)
Menstrual Disturbances	13.5% (19)	13.8% (8)	53.8% (7)	16% (34)
Ascitis	14.9% (21)	6.9% (4)	7.7% (1)	12.3% (26)
Urinary Symptoms	1.4% (2)	0%	0%	0.9% (2)
Infertility	1.4% (2)	3.4% (2)	0%	1.9% (4)
GIT Symptoms	2.8% (4)	0%	0%	1.9% (4)
Asymptomatic	11.3% (16)	19% (11)	0%	12.7% (27)

**Table 3: Clinical Presentation**

Sl. No.	Tumour	Number	Percentage
<b>Surface Epithelial Stromal Tumours</b>			
<b>Serous Tumours</b>			
1	Serous Cystadenoma	53	25%
2	Papillary Serous Cystadenoma	8	3.8%
3	Serous Cystadenofibroma	6	2.8%
4	Adenofibroma	2	0.9%
5	Papillary Serous Cystadenofibroma	2	0.9%
6	Borderline Serous Tumour	1	0.5%
7	Borderline Serous Cystadenofibroma	1	0.5%
8	Borderline Papillary Serous Tumour	1	0.5%
9	Serous Cystadenocarcinoma	5	2.4%
10	Serous Cystadenocarcinoma-Solid Type	1	0.5%
11	Papillary Serous Cystadenocarcinoma	7	3.3%
<b>Mucinous Tumours</b>			
12	Mucinous Cystadenoma	39	18.4%
13	Mucinous Cystadenofibroma	1	0.5%
14	Borderline Mucinous Tumour	2	0.9%
15	Borderline Mucinous Tumour with Intraepithelial Carcinoma	1	0.5%
16	Borderline Mucinous Tumour with Microinvasion	1	0.5%
17	Mucinous Cystadenocarcinoma	2	0.9%
18	Seromucinous Cystadenoma	2	0.9%
19	Borderline Seromucinous Tumour	1	0.5%
<b>Clear Cell Tumours</b>			
20	Clear cell carcinoma	1	0.5%
<b>Endometrioid Tumours</b>			
21	Endometrioid Adenocarcinoma	1	0.5%
<b>Brenner Tumours</b>			
22	Benign Brenner Tumour	3	1.4%
<b>Sex Cord Stromal Tumours</b>			
23	Granulosa Cell Tumour	7	3.3%
24	Granulosa-Theca Cell Tumour	1	0.5%
25	Luteinised Thecoma	1	0.5%
26	Fibroma	2	0.9%
27	Fibroma with Minor Sexcord Elements	1	0.5%
28	Stromal Luteoma	1	0.5%
<b>Germ Cell Tumours</b>			
29	Immature Teratoma	1	0.5%
30	Mature Teratoma	52	24.5%
31	Dysgerminoma	4	1.9%
32	Malignant Mixed Germ Cell Tumour	1	0.5%
<b>Total</b>		<b>212</b>	<b>100%</b>

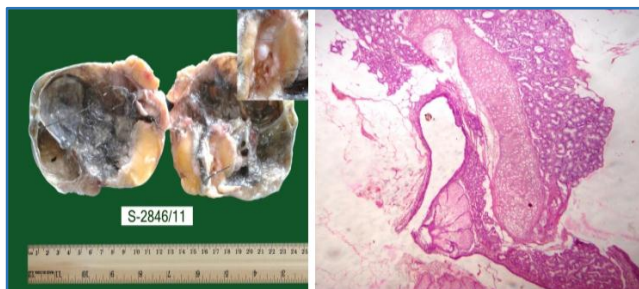
**Table 4: Distribution of Primary Ovarian Neoplasms**

	Benign	Malignant	Total
Seromucinous	2	1	3
Endometrioid		1	1
Clear cell		1 (PAS stain demonstrating hyaline globules)	1
Transitional	3		3
Mixed epithelial	Left ovary-serous cystadenofibroma with minor Brenner component (20%)		1

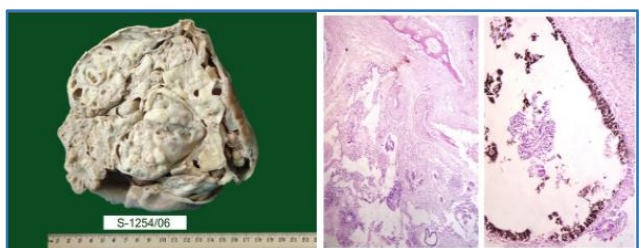
**Table 5: Other SES Tumours**



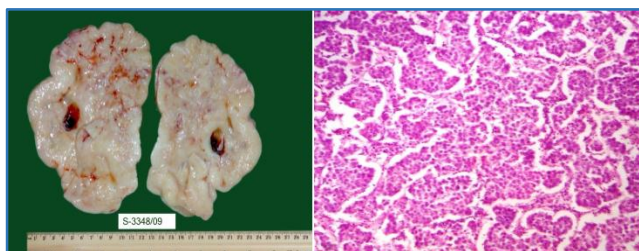
**Fig. 1: Serous Cystadenoma with Torsion**



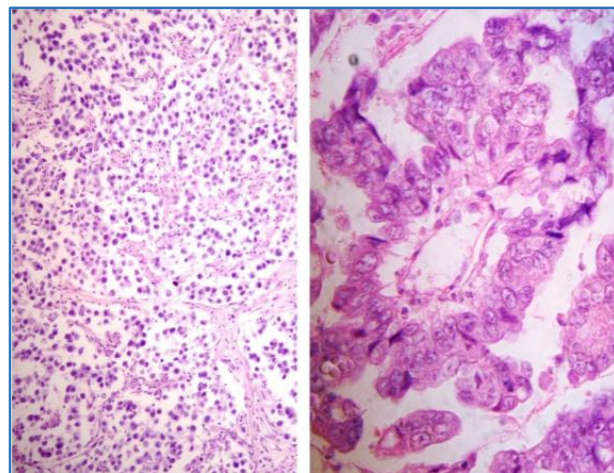
**Fig. 2: Mature Cystic Teratoma**



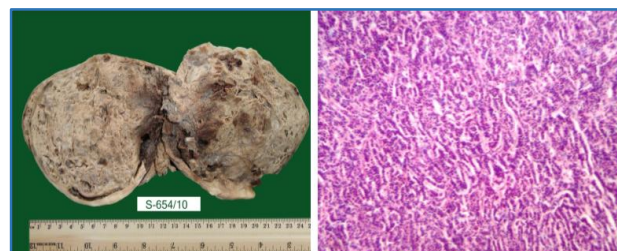
**Fig. 3: Immature Teratoma-Grade II**



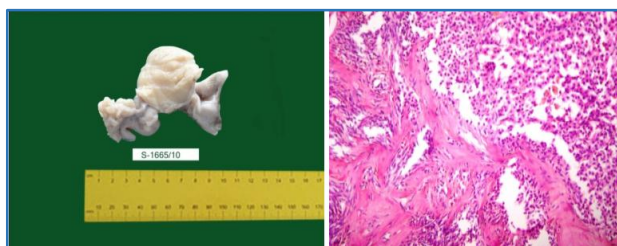
**Fig. 4: Dysgerminoma**



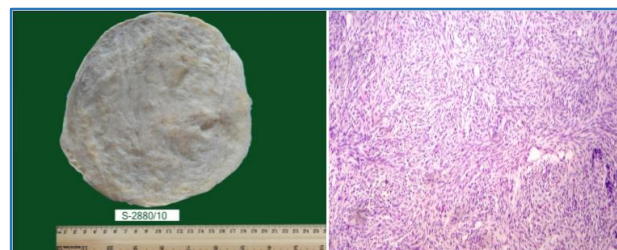
**Fig. 5A & B: Malignant Mixed Germ Cell Tumour (Dysgerminoma and Yolk Sac Components)**



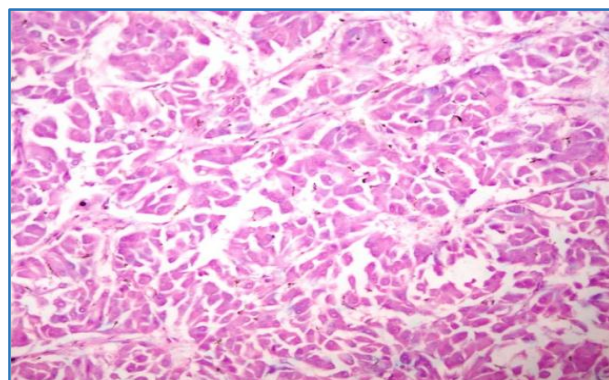
**Fig. 6: Granulosa Cell Tumour**



**Fig. 7: Luteinised Thecoma**



**Fig. 8: Fibroma**



**Fig. 9: Stromal Luteoma**

## DISCUSSION

### Primary Ovarian Neoplasms Are Broadly classified into

1. Surface Epithelial-Stromal Tumours (SES).
2. Germ Cell Tumours (GC).
3. Sex Cord Stromal Tumours (SS).

In our study, 66.2% of cases were SES, 27.6% GC and 6.2% SS tumours (Table 4), distribution comparable with studies done by Swamy et al<sup>8</sup>, Gupta et al<sup>2</sup> and Pilli et al.<sup>9</sup>

Incidence of malignant tumours was less compared to other studies, probably because study was undertaken in a general hospital and malignant tumours diagnosed before surgery get referred to speciality oncology centres.

Ovarian tumours can occur at any age. In our study, youngest patient was 14 year old, oldest 76 years old, comparable with studies of Swamy et al<sup>8</sup>, Kayasta S<sup>10</sup> and Kar T et al.<sup>11</sup>

Mass abdomen was most common presenting symptom followed by pain abdomen, comparable with findings of Gupta SC et al<sup>12</sup>, Bhuvanesh and Logambal<sup>13</sup> and Jagadeeswari et al<sup>14</sup>, Pilli GS et al<sup>9</sup>, Couto F et al<sup>15</sup> and Randhawa I et al<sup>16</sup> Menstrual symptoms noted in 16% of the cases, >50% of the patients had SS tumours (Functional tumours).

93.8% were unilateral, 6.2% were bilateral consistent with findings of Couto F et al<sup>15</sup>, Misra RK et al<sup>17</sup> and Prabakar BR et al.<sup>18</sup>

Right-sided tumours were more common than left, comparable with Ramachandran et al<sup>19</sup>, Pilli GS et al<sup>9</sup> and Saxena HMK et al.<sup>20</sup>

## SURFACE EPITHELIAL TUMOURS

### Serous Tumours

Benign serous tumours - 50.8%, borderline - 2.25% and malignant - 8% of all the SES tumours consistent with findings of Madan et al<sup>1</sup> and Maheshwari et al.<sup>21</sup>

### Mucinous Tumours

Benign mucinous tumours - 29.5%, borderline - 3% and malignant - 1.5%, of all SES tumours comparable to the findings of Couto F et al<sup>15</sup> and Madan A et al.<sup>1</sup> IHC was done for both cases of Mucinous cystadenocarcinoma, showed CK 7 positivity and CK 20 Negative, confirming that they were primary ovarian neoplasms.

Other SES tumours—described in Table 5.

One case of Synchronous Tumour of Ovary, Fallopian Tube and Cervix, comprising primary papillary cystadenocarcinoma of ovary and fallopian tube and adenosquamous carcinoma of the cervix. Synchronous multiple tumours of female genital tract are relatively rare comprising only 1-6% of genital neoplasms.<sup>22</sup> Cases of triple synchronous primaries are extremely rare and all cases reported till date involving cervix, endometrium and ovary.<sup>23</sup> To the best of our knowledge, this is the first case of synchronous cervical, fallopian tube and ovarian carcinomas.

2 B/L SES tumours with different diagnosis were reported. One had serous cystadenofibroma on the right side and serous cystadenoma on the left. Another had papillary serous cystadenoma on the right and borderline serous tumour on left side.

### Morphology of SES Tumours

- Mucinous tumours were comparatively larger than serous.

- 90.6% were U/L and 9.4% B/L.
- 75.9%-cystic, 2.8%-solid and 21.3%-partly cystic and partly solid.
- 57.9% had smooth external surface, 35.7% nodular/boselated; 4.2% showed surface papillary projections.
- All benign tumours had intact capsule; 4.3% showed breached capsule (All were malignant); 2.1% malignant tumours showed adhesions.
- 50.4% showed multilocularity, 46.8% were unilocular.
- Serous tumours were more commonly unilocular (66.7%)
- 84.8% of mucinous tumours-multilocular, 15.2%-unilocular.
- 25.5% showed papillary excrescences on cut section.
- Secondary changes in the form of haemorrhage, calcification, necrosis were more common in malignant tumours (84.6%).

### Germ Cell Tumours

Of the 210 cases 27.6% were germ cell tumours, comprising of 24.76% mature cystic teratomas (2 cases of struma ovarii, 1 strumal carcinoid and 1 squamous cell carcinoma arising in mature cystic teratoma reported), one case of immature teratoma with gliomatosis peritonei, 4 cases of malignant dysgerminoma and one malignant mixed germ cell tumour (dysgerminoma+yolk sac component). Findings were comparable to finding of Chhanda et al<sup>24</sup> and Sahu et al.<sup>25</sup> There are a very few cases reported in English literature on squamous cell carcinomas arising in dermoid cyst.<sup>26</sup>

Age range of mature cystic teratoma was 16-65 years, comparable to findings of Couto F et al<sup>15</sup> and Pilli GS et al.<sup>9</sup> Dysgerminomas was noted between 17-23 years comparable to findings of Gault EW et al.<sup>27</sup>

### Morphology of GC Tumours

- All GC tumours were U/L.
- External surface - smooth in 62.11%, nodular in others.
- Capsule was intact in 91.4%, breached in rest of the cases. Breached capsule was seen in malignant tumours.
- 55.6% of tumours—unilocular, 44.4%- multilocular.
- Smallest was mature cystic teratoma and largest GC tumour was immature teratoma (35 cm diameter).

### Sex Cord Stromal Tumours

13 sex cord stromal tumours were diagnosed. Meigs' syndrome was seen in 2 patients with ovarian fibroma. The age range was 30-65 years; 50% of patients presented with menstrual irregularities.

### Morphology of SS Tumours

- All the SS tumours were U/L.
- 66.7% had a smooth external surface, 33.3% were nodular.
- Capsule was intact in all except 2 malignant tumours.
- All tumours were solid, 50% soft and 50% firm in consistency.
- Silver impregnation for reticulin fibres was done for Granulosa and theca cell tumours. Granulosa cell tumours showed reticulin fibres surrounding aggregates of granulosa cells, whereas reticulin fibres typically surrounded individual tumour cells in theca cell tumours.

- Van Gieson stain was done for fibromas to highlight abundant dense collagen secreted by tumour cells.

### Complications

Torsion noted in 6.1% cases. Nonspecific inflammatory changes in 5.6% cases, comparable with findings of Bhuvanesh & Logambal.<sup>13</sup> Two cases of SES tumours were associated with endometriosis.

### Associated Findings in Cervix

Of the 55 hysterectomy specimens available, one case was of synchronous adenosquamous carcinoma of the cervix with primary papillary cystadenocarcinoma of ovary and fallopian tube. Another case was large non-keratinizing squamous cell carcinoma of cervix associated with serous cystadenoma of ovary; 91%- chronic cervicitis, 5.4% proclinal changes and 3.6% malignancy noted.

### Associated Findings in Fallopian Tube

33 fallopian tubes were unremarkable. One case was part of synchronous primary malignancies (Described above); 45.5% hematosalpinx, 9% hydrosalpinx and 13.6% non-specific salpingitis reported. One case had endometriosis and one case of ovarian adenofibroma showed tubercular salpingitis.

### Associated Findings in Uterus

29.09% proliferative, 9% secretory, 21.8% atrophic and 18.8% non-secretory endometrium noted; 11% endometrial hyperplasia and 3.6% cases with endometrial polyp seen. 23.63% cases had leiomyoma and 36.3% adenomyosis.

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