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Original Research Article

A Clinico-Pathological Correlation and an Analysis of Ovarian Tumours in Tertiary Care Hospital

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ABSTRACT

Background: Tumours of the ovary are common forms of neoplasms in women. The pathology of ovarian neoplasms is one of the most complex areas of gynaecology, because the ovary gives rise to the greater and larger variety of tumours than any other organ.
Aim: This study was done to analyse the frequency of ovarian tumours and their clinical and histopathological features in rural set up.
Materials and Methods: This is a retrospective study of 132 ovarian tumours in tertiary care hospital over a period of two years. All the relevant clinical data of the patients were searched from the ward records.
Results: The total number of ovarian tumours studied during the three year period was 132 cases, among that 76(57.5%) cases were benign, 17 (13%) cases were borderline and 39 (29.5) cases were malignant. In benign ovarian tumours, the most common neoplasm was serous cystadenoma, followed by benign germ-cell tumours (cystic teratoma). In malignant tumours, serous cystadenocarcinoma was the most common, followed by mucinous cystadenocarcinoma and metastatic tumours.
Conclusion: Ovarian tumours are composed of wide range of histology. Correlation of age, clinical features, gross, various histopathological pattern and categorizing according to WHO classification helps in arriving at the correct diagnosis as well as helps to assess the prognosis of ovarian tumours.

Key words: Benign, Malignant, Histopathology, Periodic Acid Stain (PAS), Reticulin.

INRODUCTION

Ovarian neoplasms have become increasingly important not only because of the large variety of neoplastic entities, but more because they have gradually increased the mortality rate in female genital malignancies.

Worldwide, ovarian tumor is the sixth most common tumor in women. In the western countries, ovarian carcinoma is the fifth most common malignancy and ranks fourth in cancer mortality. In U.S women, ovarian cancer accounts for 5% of cancer deaths. In India, breast is the leading site of cancer, followed by the cervix and ovary. In Chennai, ovarian cancer stands in the fourth position. [(1)] About two thirds of ovarian tumours occur in women in their reproductive age group. Several risk factors have been identified, such as age at the birth of first child, breast feeding, weight, diet, talc, smoking, certain types of viral infections in childhood and ionizing radiation. [(2)] Genetic factors are an important ovarian cancer risk. Hereditary predisposition conferred by the BRCA 1 and BRCA 2 tumour suppressor genes is responsible for approximately 10% cases due to the markedly increased risk associated with it.

Regarding prevention of ovarian cancer, preventive measures could be

recommended on a population wide basis, such as diet modifications, cessation of smoking and prophylactic oophorectomy in those with BRCA mutations. [2]

This study is undertaken in view of evaluating the actual incidence of ovarian neoplasms in a semi urban area in relation to the age, clinical features and histopathological features. In addition, the recent literatures, journals and research publications regarding ovarian tumors are also immensely reviewed.

MATERIALS AND METHODS

This is a retrospective study of 132 ovarian tumours in a tertiary care hospital over a period of two years. All the relevant clinical data of the patients were searched from the ward records. We had received ovariotomy specimens along with hysterectomy specimens. A detailed history with particular attention to clinical symptoms and signs were recorded and thorough gross examination of the specimens was also done. The specimens were fixed in toto in buffered 10% neutral formalin and processed routinely. In cystic ovarian neoplasms, four to five bits were taken from the wall along with papillary excrescences if present. In solid tumours, three to four bits were taken if the tumors were less than five centimeters. If more than five centimeters, one block per centimeter of the tumour were taken across its greatest dimension, particularly if the appearance is variegated. Three to five micrometer sections were cut and stained with haematoxylin and eosin. Reticulin or PAS were applied in doubtful cases.

OBSERVATION AND RESULTS

This retrospective study covered a total number of 132 ovarian neoplasms during the period of two years.

I. Incidence

We had diagnosed 1616 cases in female neoplasms; among them 132 cases were ovarian neoplasms. The average incidence of ovarian neoplasms (including benign and malignant) among females was 8.17 %.

II. Age

The distribution of cases according to their age is given in the following table. The neoplasms were also divided into benign, borderline and malignant categories as given in the following table1.

Sl. no	Age in yrs	Benign	Borderline	Malignant
1	10 – 19	10	-	3
2	20 – 29	22	4	5
3	30 - 39	14	6	4
4	40 – 49	20	5	14
5	50 – 59	07		11
6	60 – 69	03	-	1
7	70 – 79	-	-	1
	Total	76(57.5%)	17(13%)	39(29.5%)

In our study, the incidence of benign neoplasm was highest in the age group 20 – 29 yrs (22 out of 76 cases, 29%), borderline neoplasm was seen in the age group 30 – 39 yrs (6 out of 17 cases, 35.2%) and malignant neoplasm was seen in the age group 40 – 49 yrs (14 out of 39 cases, 36%). We noted that most of the ovarian masses were malignant after 50 years of age and in those below 20 years of age [bimodal peak] (3 cases, 7.7%).

III. Clinical Evaluation

All the cases were evaluated clinically at the time of admission along with basic investigations as in the following table.

Table 2: Clinical presentation

Sl. no	Clinical features	No. of cases	%
1	Mass abdomen	86	65.15
2	Pain abdomen	20	15.15
3	Acute abdomen	2	1.52
4	Ascites	8	7.58
5	Bleeding Per vaginum	5	3.79
6	Associated with pregnancy	6	4.55
7	Asymptomatic	5	3.79

Abdominal mass was the most common clinical presentation (86 cases, 65.15%) followed by pain (20 cases, 15.15 %). Few cases presented as acute abdomen necessitating emergency laparotomy. Abnormal vaginal bleeding in the post menopausal period was the presenting symptom in five cases. Six cases were found to be associated with pregnancy, which was removed during LSCS. Five cases were asymptomatic and detected during routine

abdominal ultrasonography done for other causes.

IV. Laterality

Likewise tumours were also categorised as unilateral / bilateral ovarian involvement as in the given table.

Table 3:

Sl. no	Tumours	Unilateral	%	Bilateral	%
1	**Serous**				
	Benign	32		1	
	Borderline	8		2	
	Malignant	9		6	
	Total	**49**	**37.1**	**9**	**6.8**
2	**Mucinous**				
	Benign	26		1	
	Borderline	6		1	
	Malignant	4		2	
	Total	**36**	**27.3**	**4**	**3.0**
3	Endometrioid carcinoma	1	0.8	1	0.8
4	Transitional	1	0.8	0	
5	Sexcord- stromal tumor	6	4.5	0	
6	Germ cell tumor	18	13.6	1	0.8
7	Metastatic	-		5	3.8
8	Gonadoblastoma	1	0.8	0	
	Grand Total	**112**		**20**	

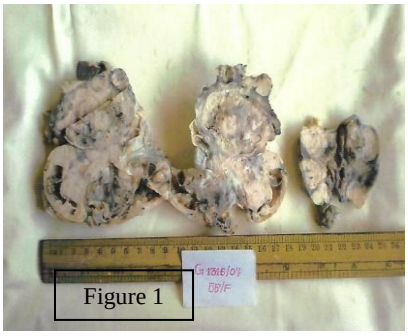


Figure 1

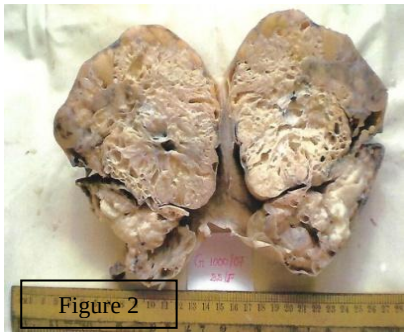


Figure 2

Fig.1: Bilateral serous cystadenocarcinoma. Predominantly solid, with areas of necrosis and haemorrhage.
Fig.2: Mucinous cystadenicarcinoma. Cut surface shows predominantly solid areas with mucin containing cystic spaces.

Forty nine cases(37.1%) with Serous tumours (Fig 1), 36 cases(27.3 %) with mucinous tumours (Fig 2) and 18 cases with germ cell tumors (13.6%) had unilateral ovarian involvement at the time of presentation. Bilateral ovarian involvement in serous and mucinous tumours taken as a whole was less than 9.8%. (13cases). All cases of metastatic ovarian tumours were bilateral at the time of presentation (5 cases, 3.8 %).

V. Gross/ Histomorphology of Ovarian Neoplasms

Table 4:

Sl. no	Gross morphology	Number of cases
1	Pure Solid	10
2	Pure Cystic	83
3	Mixed Solid & Cystic	9
4	Cystic with Papillary excrescences	21
5	Solid with variegated appearance	05
6	Solid & Cystic with areas of calcification	04
	Total	**132**

The ovarian neoplasms were divided into following types as in table 4 according to Histomorphology.

Vi. Distribution of Ovarian Neoplasms According to Histological Classification

Table 5:

Sl.no	Classification	No. Of cases	Total cases	%
1	**Surface epithelial Tumour**			
	Benign	59		
	Borderline	17	101	76.5
	Malignant	25		
2	**Germ-cell Tumour**			
	Benign	14		
	Malignant	4	18	13.6
3	**Sexcord-stromal**			
	Benign	1		
	Malignant	6	7	5.3
4	Metastatic	5	5	3.7
5	Gonadoblastoma	1	1	0.76
	Total	**132**	**132**	

Out of 132 neoplasms, surface epithelial tumours predominate with 101 cases (76.5 %), followed by germ cell tumours 18 cases (13.6 %) and sexcord-

stromal tumours 7 cases (5.3 %).Rare case such as gonadoblastoma was also observed in this study.

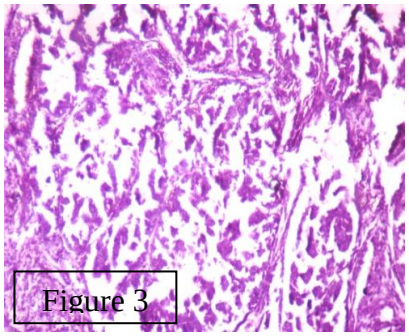
VII. Sub Classification of Surface Epithelial Tumours

Surface epithelial tumours were also classified according to WHO classification as in the following table 6.

Serous tumours (Fig 3) predominate in our study (53 cases, 52.4%) followed by mucinous tumours (Fig 4) (43 cases, 42.5%). Two cases of endometrioid tumour and one case of transitional cell tumour were also observed.

Table 6: Sub-classification of surface epithelial tumours

Sl.no	Classification	No. of cases	%	Average %
1	**Serous**			
	Benign	29	54	
	Borderline	7	13	
	Malignant	17	22	
	Total	**53**		**52.0**
2	**Mucinous**			
	Benign	27	63	
	Boderline	10	23	
	Malignant	6	14	
	Total	43		43.0
3	**Endometrioid**			
	Malignant	2	50	
	Total	**2**		**4.0**
4	Clear cell tumour	-	-	-
5	**Transitional**			
	Benign Brenner	1		1.0
	Grand Total	**101**		



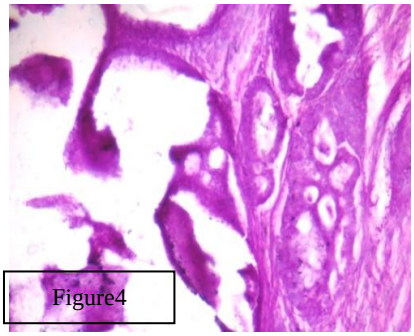


Fig.3: Serous cystadenocarcinoma .The tumor cells are arranged in paillary pattern with hyperchromatic pleomorphic nuclear features. H & E, X 100.

Fig. 4: Mucinous cystadenocarcinoma showing glands lined by stratified layers of malignant cells. H & E, X 100.

VIII. Sex cord-stromal Tumours

Table 7-A : Sexcord-stromal Tumours

Sl.no	Classification	No of cases	%
1	Granulosa cell tumour		
	Adult	4	71.4
	Juvenile	1	
2	Fibrothecoma	1	14.3
3	Fibroma with sarcomatous change	1	14.3
4	Others	-	
	Total	7	

Table-7-B: Germ Cell Tumours

Sl.no	Classification	No. Of cases.	%
1	Teratoma		
	Benign	14	77.7
	Malignant	-	
2	Dysgerminoma (Fig 8)	1	5.5
3	Mixed Germ cell tumour	3	16.6
4	Others	-	
	Total	18	

Likewise Sex cord-stromal tumours and germ cell tumours were also classified according to the following table 7 - A & B.

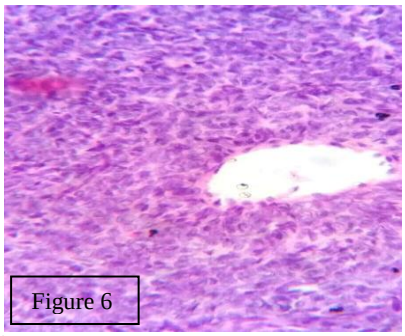


Fig.5: Granulosa cell tumor, adult type, Cut surface shows homogenous tan yellow solid areas.

Fig.6: Granulosa cell Tumor-Adult type, Diffuse pattern with Call-Exner body, H&E, X 100.

In our study, seven cases of sex cord - stromal tumours were observed. Of which, five cases of granulosa cell tumours (Fig 5&6) (71.4 %), one case of fibrothecoma and one case of fibroma with sarcomatous changes that typically had mitosis of more than 4/10 HPF, nuclear atypia and necrosis was also been observed.

In Germ cell tumours, most of the tumours were benign mature cystic teratomas (14 cases, 77.7 %) followed by mixed germ cell tumours (Fig 7) (3 cases, 16.6%).

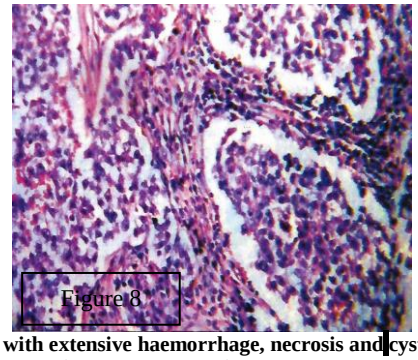


Fig7: Mixed germ cell tumor. The cut surface is heterogenous with extensive haemorrhage, necrosis and cystic degeneration
Fig8: Dysgerminoma, Well–defined nests of tumor cells separated by fibrous strands infiltrated by lymphocytes, H & E X 100.

DISCUSSION

Ovarian cancer has emerged as one of the most common malignancy affecting women. The absolute number of new cancer patients in India is increasing rapidly due to increase in the size of the population as well as due to increase in the proportion of elderly persons due to improved life expectancy. [(3)]

Most ovarian cancers are environmental in origin. Hence an increase in exposure to risk factors also plays a pivotal role in the incidence of ovarian cancer. Nandagudi Srinivasa Moorthy et al has observed that some of the very widespread changes in the incidence of ovarian cancer may be accounted for by the trends, in aspects of reproductive behavior such as progressively smaller family size, nulliparous women and proportion of unmarried women. Parity and combined oral contraceptive use have been consistently documented as the protective factors. [(4)]

Women with a family history of ovarian and breast cancer in first degree relatives have also been reported to be at increased risk. [(4)] No such association has been found in our study. Nandakumar et al has observed that tubectomy as a method of family planning appeared to reduce the risk of development of ovarian cancer, but the follow up data is unavailable. [(5)]

A COMPARATIVE ANALYSIS

In our study we observed that the total number of malignancies in female were 1152 cases .Out of these 39 cases were ovarian malignant neoplasms. It was accounted for about 3.39% of total malignancies in a period of two years.

The incidence of ovarian carcinoma by various studies as per the literature and journals is given below [(6)]

Place Of Study	Incidence
1. Indian Cancer Society Mumbai.	7.27%
2. Dr. B.R. Ambedkar Institute Rotary Cancer Hospital All India Institute of Medical Sciences, New Delhi.	7.19%
3. Gandhi Medical College, Bhopal.	6.53%
4. The Gujarat Cancer and Research Institute, Ahamadabad.	6.06%
5. Kidwai Memorial Institute of Oncology, Bangalore	5.19%
6. Cancer Institute, WIA, Adyar Chennai.	5.11%
7. Nargis Dutt Memorial Cancer Hospital, Barshi.	3.37%.
8. PRESENT STUDY	3.39%

Of all these studies, Mumbai holds the top ranking with the incidence rate of 7.27%, and the least was Barshi with the incidence rate of 3.37%. These observations suggest that the possible environmental and lifestyle changes have an influence on the incidence rate. India is rapidly stepping towards industrialization. Hence, in urban areas like Mumbai changes in lifestyle and factors such as increase in

age of marriage, delay in age at first birth, reduction in parity and improved socio-economic conditions might have contributed to the increase in incidence in contrast to the rural area like Barshi with the lowest incidence. [6] In our study conducted in a semi urban area, the incidence of ovarian malignancy was at the midway between rural area like Barsi and urban area like Chennai.

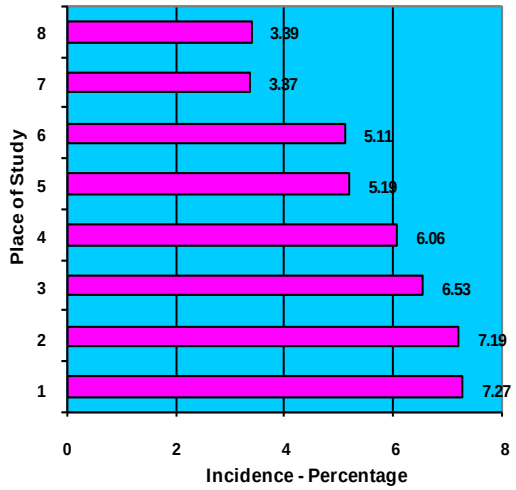


Diagram 2: Bar chart depicting comparative analysis of the incidence of ovarian cancer in our study with various other studies

1. Indian Cancer Society, Mumbai. 2. Dr. B.R. Ambedkar Institute Rotary Cancer Hospital, All India Institute of Medical Sciences, New Delhi. 3. Gandhi Medical College, Bhopal 4. The Gujarat Cancer and Research Institute, Ahamadabad. 5. Kidwai Memorial Institute of Oncology, Bangalore. 6. Cancer Institute, WIA, Adyar Chennai. 7. Nargis Dutt Memorial Cancer Hospital, Barshi. 8. Present Study.

The incidence of benign neoplasms peaks at 2nd to 4th decade in accordance with the literatures. As per the literature and studies conducted by various authors, borderline forms were detected after 40 years and 30-40% of them occur after the age of 65 years. [7] In contrast, in our study borderline tumours peak at the 3rddecade. In contrast, in our study 7.6% of cases were noted in first two decades. According to the studies of BD Rufford et al 87% had abdominal symptoms, 41% had gastrointestinal, 29% had constitutional symptoms and only 2% presented with mass abdomen. [8] Bilaterality is a common feature of tumour that has metastasized to the ovary and is an important diagnostic clue. [9] In our studyabdominal mass was the most common clinical presentation (86 cases, 65.15%) followed by pain (20 cases, 15.15 %) which is in contrat to their study.

In our study, surface epithelial tumour were observed in 101 cases (76.5%) and it was the most common ovarian neoplasms diagnosed, followed by germ cell tumour with 18 cases (13.6%).Of the surface epithelial tumours serous tumours contribute to 52.4% of which 54% were benign serous cystadenoma, 13% were border line and 17% were carcinomas in accordance with the literature. [10,11]

The diagnostic challenge associated with Low malignant potential (LMP) or borderline ovarian neoplasms begins at the time of exploratory laparotomy. At this time the gynaecologic surgeon must assess several issues, including (1) Ovarian or Para ovarian location and extent of problems. (2) Presence of adhesions between ovary and surrounding structures. (3) Indication for staging omentectomy, sub diaphragmatic smears and peritoneal washings.(4) Involvement of contralateral ovary and (5) Preservation of fertility. For accurate sampling the surgeon should indicate to the pathologist the presence and location of any adhesions. [12] According to Russel et al allow malignant potential ovarian neoplasms represented 15% of all ovarian surface epithelial tumours. [13] This correlates well with the observation of 16% of borderline cases in our study.

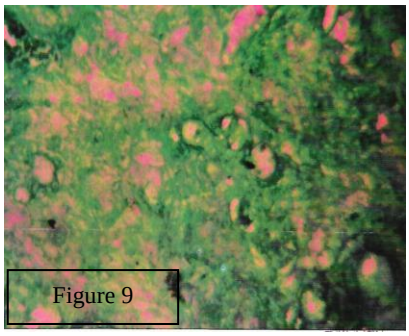
In most series of studies by Katsube et al, Koonings et al and Petterson et al mucinous borderline tumours were less common than serous borderline tumours. [10,11-14] But in our study, mucinous borderline tumours outnumber the serous borderline tumours in accordance with the studies by Isarangkul in Thailand. [15] In the studies conducted in Japan and Norway, both types of tumours were equally prevalent.

Brenner tumours are often associated with other tumours such as mucinous cystadenoma, mature teratomas and transitional cell carcinoma of bladder. [16] In our study one such association with mature cystic teratoma was observed.

Germ cell tumours constitute a heterogeneous group of tumours reflecting the capacity for multiple lines of differentiation of the main stem cell system. 14 cases of benign teratomas were observed in our study. According to Hurwitz et al, malignant transformation in a dermoid cyst was more common in post menopausal women. [17] In contrast, in our study two cases of mature teratoma in post menopausal age group without any evidence of malignant transformation were observed.

Metastatic ovarian tumors account for about 6 % of adnexal masses that prove to be malignant ovarian tumors on pathological examination. Recent emphasis on the pathology of metastatic ovarian tumors has centered mainly on the problems caused by metastatic colorectal carcinomas, metastasis from the appendix, and pancreas which can resemble closely primary mucinous borderline tumors and carcinomas. [18] Four cases of Krukenberg tumour and one case small cell-neuroendocrine tumour of intestinal origin have been observed in our study

The PAS (Periodic Acid Stain) technique is without question the most versatile and widely used technique for the demonstration of carbohydrates or glycoconjugates. The first histochemical use of this technique was by McManus (1946) for the demonstration of mucin. As typically employed in the histology laboratory, the PAS technique is based upon the reactivity of free aldehyde groups within carbohydrates with the Schiff reagent to form a bright red/magenta end product. In Krukenberg tumors, intracellular material is PAS - positive, and diastase resistant. Mucin pools are positive in mucinous carcinoma of ovary. [19] In our study, mucinous carcinoma of ovary and Krukenberg tumour was stained positive with PAS (Fig 9)



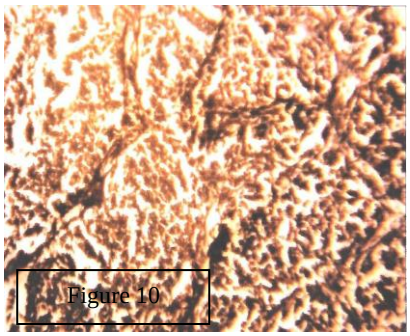


Fig .9: Krukenberg tumor.Intracytoplasmic mucin exhibiting PAS positivity, x 100.
Fig .10: Granulosa cell tumor, Exhibiting reticulin wrapping around nests. RETICULIN STAIN, X 100.

Reticulin stain is helpful, since granulosa cells typically grow in sheets or aggregates bound by reticulin fibrils, whereas thecomas contain an abundance of intercellular fibrils surrounding individual cells. The distinction is important since granulosa cell tumors have an aggressive potential, whereas thecomas are benign with rare exceptions. [20] In this study, we applied reticulin stain for granulosa cell tumours and fibrothecoma. The reticulin stain showed fibrils surrounding nests and larger aggregates of granulosa cells (Fig 10). In thecoma, reticulin stain highlighted the individual cells.

CONCLUSION

The incidence of ovarian neoplasms among the female neoplasms in our study was 8.17%. Ovarian malignancy ranked second among the female genital tract malignancies. The ratio of benign and malignant ovarian neoplasm was 2.3:1.The incidence of ovarian neoplasm was highest

during the fifth decade followed by the third decade. Eighty five percentages of ovarian tumours were unilateral in presentation. Benign neoplasms were predominantly cystic, whereas malignancies were predominantly solid and cystic or purely solid. Surface epithelial tumours were the most common neoplasm, of which serous cystadenoma is the commonest. Reticulin and PAS stain still have their value in the initial evaluation to distinguish Thecoma and Granulosa cell tumour and to demonstrate mucin filled signet ring cells in Krukenberg tumour and mucinous nature of high grade mucinous cystadenocarcinoma respectively.

Advanced diagnostic tools and awareness of screening periodically for malignancies in those who have risk factors helps in the early detection of ovarian neoplasms and thereby reduces the morbidity and mortality.

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