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Histopathological Study of Ovarian Lesions

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Abstract: ***Introduction: Ovarian lesions manifest with a wide spectrum of clinical, morphological and histological features. The complex nature, unpredictable behavior, prognosis and controversial management make ovarian lesions a difficult problem for gynecologist hence this study was undertaken with following aims & objectives. Objectives: This study is undertaken to characterize the ovarian lesions based on histopathological features and to find out the frequency of benign and malignant neoplasms with their clinicopathological correlation. Results: Of the 485 cases of ovarian lesions studied, 109 cases were benign, 17 cases were malignant & 3 were borderline lesions. The tumors can occur at any age. The most common symptom was abdominal pain. Commonest benign epithelial tumors were Serous cystadenoma (55.4%). Among primary malignant tumors clear cell carcinoma(2-3%) was most common. Conclusion: The ovary is a frequent site for primary and metastatic tumors. Due to its complex structure, primary ovarian neoplasms are of diverse histological types. Certain neoplastic lesions of the ovary frequently form a pelvic mass and potentially mimic on ovarian neoplasm. Their proper recognition is therefore important to allow appropriate therapy.***

Keywords: Ovary, neoplastic, histomorphological patterns.

1. Introduction

The ovaries are paired intra-pelvic organ of the female reproductive system. Ovary being complex and unique organ has been described to be involved by wide varieties of neoplasms.

Tumours of the ovary are common forms of neoplasia in women[1]. In general benign ovarian tumours are more common and account for 80% of all ovarian neoplasms. Ovary being a common site of primary malignancy[2], metastasis may occur. Among cancers of the female genital tract ovary is the third most common site of primary malignancy in Indian females. About 80% are benign and occur in women of 20-45 years and malignant tumours are more common in 40-65years.

Risk factors for ovarian cancer are much less clear than for other genital tumours, but nulliparity, family history, and heritable mutation play a role in tumour development[3,4]. Serum HCG, serum CA125, serum alpha – fetoprotein, placental alkaline phosphatase and lactate dehydrogenase are useful tumour markers.

Screening for ovarian epithelial cancer may be improved by genetic study and by Doppler colour flow ultrasonography and transvaginal ultrasonography.

2. Methods/Approach

The present study is based on histomorphological evaluation of ovarian specimen received at the department of Pathology, Government Medical College, Bhavnagar from July 2012 to June 2015. The gross specimens received were fixed in 10% formalin for 12-24 hours and specimen multiple sections were taken. The sections were prepared using paraffin technique and were stained with H & E stain. Special stains like Periodic Acid Schiff (PAS), reticulin stains were done whenever necessary.

3. Literature Survey

Several epidemiologic studies suggest that disordered endocrine function may contribute to the development of ovarian cancer. A higher incidence of epithelial ovarian cancer is seen in women with lower number of pregnancies, nulliparous women and women with history of infertility. Familial and genetic association has been reported but is uncommon. Several unusual genetic disorders seem to predispose to ovarian neoplasms, although tumour that develop are benign and stromal in origin. The neoplasm arising from ovaries inherit a spectrum of histogenetic background, much more varied than any other organ. This pathological complexity had led to a number of classifications among which WHO classification is most important which provide a communication between different workers in the field of oncology be they surgeons, pathologists, radiotherapists or epidemiologists.

4. Results

The specimen & biopsies of ovaries were studied under the present study for the period from July 2012 to June 2015. Total contained 485 cases were studied. The clinical presentation, symptoms and ovarian parameters were recorded. The specimens were studied in detail as per method described in materials and methods. Out of 129 cases of ovarian lesions, 109 cases (84.5%) were benign, 3 cases (2.3%) were borderline and 17 cases (13.2%) were malignant tumors in the present study.

Table 1: Age distribution among ovarian lesions

Sr. No	Age range (years)	Benign lesions		Borderline lesions		Malignant lesions		Total	
		Cases No	%	Cases No	%	Cases No	%	Cases No	%
1	<19	6	4.7	0	0	3	2.3	9	7
2	20-39	31	24.1	0	0	2	1.5	33	25.6
3	40-59	57	44.2	3	2.3	9	7	69	53.5
4	>60	15	11.6	0	0	3	2.3	18	13.9
5	Total	109	84.6	3	2.3	17	12.6	129	100

Age distribution among ovarian lesion according their morphological patter is shown in Table 1. Among all the lesions, majority of the cases of malignant, benign & borderline lesions were seen in age group of 40-59 years i.e., 53.5% .The youngest patient was 14 years old and the oldest patient was 100 years old.

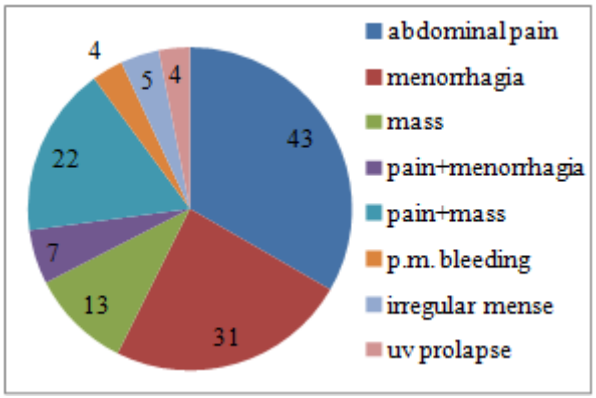

Figure 1: Mode of presentation of neoplastic lesions of ovary

Abdominal pain was the single most common presenting symptom followed by menorrhagia. In non-neoplastic lesions menorrhagia was the commonest symptom.

Table 2: Consistency of ovarian lesions

Lesion	Solid	Cystic	solid+cystic
Benign	11	73	25
Borderline	0	2	1
Malignant	6	0	11
total	17	75	37

Majority of the benign lesions were cystic in consistency (73 cases; 56.6% of total lesions) while few cases had both solid and cystic consistency. While majority of borderline & malignant lesions were solid & both solid & cystic in consistency.

Table 3: Frequency according to WHO classification

Histological subtype according to WHO classification			*No of cases*	*%*
SES tumors	Serous	Benign	70	55.4%
		Borderline	2	1.5%
		Malignant	2	1.5%
	Mucinous	Benign	9	7%
		Borderline	2	1.5%
		Malignant	0	0%
	Endometrioid	Benign	1	0.8%
		Borderline	0	0%
		Malignant	2	1.5%
	Clear cell	Benign	0	0%
		Borderline	0	0%
		Malignant	3	2.3%
	Transitional cell(Brenner tumor)	Benign	2	1.5%
		Borderline	0	0%
		Malignant	0	0%
	Epithelial-stromal	Adenosarcoma	0	0%
		Malignant mixed mullerian tumor	1	0.8%
SCS tumors	Granulosa cell tumor		2	1.5%
	Fibromas		4	3.1%
	Fibrothecomas		0	0%
	Thecomas		0	0%
	Sertoli-leydig cell tumor		2	1.5%
	Steroid lipid cell tumor		0	0%
Germ cell tumor	Teratoma	Immature	1	0.8%
		mature	Solid 7	5.4%
			Cystic 9	7%
		Monodermal	4	3.1%
	Dysgerminoma		2	1.5%
	Yolk sac tumor		0	0%
	Mixed germ cell tumors		0	0%
Metastasis from non ovarian primary			3	2.3%

Amongst all types, the serous tumors formed the largest group (65.4 %) followed by germ cell tumors (17.8 %) which was followed by mucinous tumors which accounted to 8.5 % of the total found in the study. Sex cord stromal tumor constituted for 6.1 %.

5. Discussion

Of the 485 cases of ovarian lesions studied in the present study, 109 cases were benign, 17 cases were malignant & 3 were borderline lesions.

Table 4: Comparison of percentage incidence of benign, borderline and malignant tumors in different studies and present study

Sr No	*Authors (year)*	*Benign*	*Malignant*	*Borderline*
1	Couto et al[5] (1993)	80.76%	16.91 %	2.33%
2	Maheshwari V et al[6] (1994)	71.7%	23.7%	4.4%
3	Pilli et al[7] (2001)	76 %	21.2%	2.8%
4	Gupta N et al[8](2005)	72.9%	4.2%	22.9%
5	Present study(2015)	84.5%	13.2%	2.3%

The result was similar to the findings by other workers where benign tumors were more common, than malignant tumors.

Table 5: Percentage distribution of cases in various age groups in comparison with present study

Sr No	*Authors (year)*	*Age groups in years*			
		0-19	*20 - 39*	*40- 59*	*> 60*
1	Ramachandran et al[9] (1972).	7.9%	53.00%	30%	9.10%
2	Pilli et al[7] (2001)	7%	58%	30%	5%
3	Kar et al[10] (2005)	7.4%	41.79%	46.28%	4.47%
4	Present study(2015)	**7%**	**25.6%**	**53.5%**	**13.9%**

In the present study maximum numbers of cases were in 5th to 6th decade of life. Present study is in concordance with Pilli et al[7] and Ramachandran et al[9] where incidence of ovarian neoplastic lesions was more common in 20- 39 years of age group. Kar et al[10] reported high incidence of ovarian tumors in 40-59 years age group.

Table 6: Mode of presentation of cases in various studies in comparison with present study

SrNo	Authors (year)	Mode of presentation		
		Abdominal Pain	Mass per abdomen	Menstrual Irregularities
1	Couto et al[5](1993)	40%	90%	39%
2	Maheshwari V et al[6](1994)	39%	71%	3%
3	Pilli et al[7](2001)	70%	63%	10%
4	Present study(2015)	**33.3%**	**10%**	**24%**

In present study almost half of the patients presented with combination of abdominal pain, mass per abdomen and menstrual irregularities. Present study concorded well with studies by Pilli et al[7] where pain in abdomen was the commonest symptom. Study by Couto et al[5] and Maheshwari V et a[6] showed more cases with mass per abdomen.

Table 7: Relative percentage of different histological types of ovarian tumors in different studies and present study

Sr No	Authors (year)	Tumor type			
		Epithelial	Sex cord	Germ cell tumor	Metastatic
1	Gupta SC et al[11](1986)	54.70%	7.06%	31%	6.18%
2	Pilli et al[7](2001)	71%	7%	21%	0.70%
3	Kar et al[10] (2005)	79%	1.50%	16%	1.20%
4	Present study(2015)	**73.8%**	**6.1%**	**17.8%**	**2.3%**

Histologically, 129 ovarian lesions were classified according to WHO classification. Present study results correlated with studies by Kar et al[10] and Pilli et al[7] but not with Gupta SC et al[11] which showed relatively more number of germ cell tumors. Among the individual tumors, the commonest benign epithelial tumors were serous cystadenoma (55.4%), followed by mucinous cystadenoma (7%) & mature cystic teratoma (7%). Among primary malignant tumors clear cell carcinoma (2.3%) was most common, followed by serous cystadenocarcinoma (1.5%) & endometriod carcinoma(1.5%). Similar findings were seen in studies by Maheshwari V et al[6] and Gupta et al[11] However, the incidence of mucinous cystadenocarcinoma was more when compared to our study.

Germ cell tumor was second most common group of ovarian tumor. Among 23 cases of germ cell tumor, most common one was mature cystic teratoma accounting for 7% of total neoplastic lesions. Among malignant lesions dysgerminoma was commonest accounting 1.5% of total tumors. This result correlated with studies by Misra RK et al[13], Prabakar BR et al[12], Gupta SC et al[11]. In present study, one case of immature teratoma with is noted with accounting for 0.8% of total lesions.

Incidence of sex cord stromal tumor in the present study was composed of two case of granulosa cell tumor accounting for 1.5 % of total tumors, four cases of fibroma accounting for 3.1 % of total tumors & 2 cases of sertoli-leydig cell tumor accounting for 1.5 % of total tumors, which was comparable to studies by Gupta N et al[8], Misra RK[13] & Prabhakar BR[12].

Table 8: Laterality of ovarian neoplastic lesions in different study and present study

Sr No	*Authors (year)*	*Laterality*	
		Unilateral	*Bilateral*
1	Prabhakar et al[12](1989)	90.90%	9.10%
2	Misra RK et al[13](1990)	95.50%	4.50%
3	Couto F et al[5](1993)	91.25%	8.75%
4	Kar et al[10](2005)	73.13%	26.87%
5	Present study(2015)	**88.4%**	**11.6%**

In present study, out of total 129 ovarian lesions, 114 cases were unilateral and 15 cases were bilateral. The present study is concordant with studies by Misra RK[13], Prabhakar et al[12] and Cousto F et al[5]. Kar et al[10] reported more number of bilateral tumors compared to present study. Most of the benign tumors (75.5%) were unilateral and most of malignant tumors (10.9%) were also unilateral tumors which was concordant with studies by Misra RK et al[13] & Prabhakar et al[12].

In present study the tumors ranged in size from 2 to 35cms in diameter. The smallest tumor had a size of 2x2×1cm that was diagnosed as simple serous cyst of ovary. The largest tumor measured 35x26x14cm in a 56-year-old woman, who presented with mass in abdomen and was diagnosed as mucinous cystadenoma.

Table 9: Percentage incidence of consistency of ovarian lesions in different study and present study

Sr No	*Authors (Year)*	*Consistency*		
		Cystic	*Solid*	*Solid & Cystic*
1	Gupta SC et al[11](1986)	76.20%	2.40%	21.50%
2	Misra RK et al[13] (1990)	78%	4.09%	18%
3	CoutoF et al[5] (1993)	61.23%	10.20%	28.57%
4	Present study(2015)	**58.1%**	**13.2%**	**28.7%**

Present study is concordant with studies by Gupta SC et al[11] and Misra RK et al[13] and with Cousto F et al[5] which showed high incidence of malignant tumor having more number of tumors with solid and mixed consistency. Majority of the benign lesions (56.6%) in the present study were cystic in consistency. And majority of malignant lesions (8.5%) were having mixed consistency. This result is concordant with studies by Gupta N et al[8] and Misra RK et al[13].

Serous cystadenoma: Accounted for 70 cases (55.4 %) and the findings are in accordance with Misra RK et al[13] and Maheshwari V et. al[6] reported an incidence of 49% and 46.01% of serous cystadenoma. In our study most of the tumors were unilateral and cystic in consistency.

Borderline serous cystadenoma: 2 (1.5 %) case of benign borderline serous cystadenomas were found in present study. Both tumors were unilateral. One case was cystic and other one was having mixed consistency.

Malignant serous cystadenocarcinoma: 2 cases of serous cystadenocarcinoma have been observed in present study. Randhawa et al[14] reported 12% incidence and Pilli et al[7]

reported 10.3% of malignant serous tumors in their series. Peak age of occurrence of serous cystadenocarcinoma were seen in 5th to 6th decade of life in present study, a finding similar to that of Pilli et al[7].

Mucinous cystadenoma: Mucinous cystadenoma accounted for 9 cases (7%) out of 129 cases of ovarian neoplastic lesions. Similar findings have been reported by Prabhakar et al[12] (18%), Maheshwari et al[6] (13 %). Age incidence was more common in 30-59 years. Most of them were cystic in consistency in this study.

Borderline mucinous cystadenocarcinoma: Two cases of borderline mucinous cystdenocarcinoma was reported in present study accounting for 1.5% of all neoplastic lesions. The other authors like Maheshwari et al[6], Pilli et al[7] , Prabhakar et al[13] showed similar incidence.

Endometrioid carcinoma ovary: There were 2 cases of endometrioid carcinoma (1.5%) , similar incidence was seen in studies by Prabhakar BR et al[13] (1.1%) . Studies by Maheshwari et al[6] and Dawar R et al[15] showed higher incidence (3.65% and 5.7% respectively). Their study was confined only to surface epithelial tumors of the ovary. Both of the cases were in 40 to 60 years of age group.

Epidermoid cysts of ovary: There was one rare tumor of epidermoid cysts accounting 0.8% of total neoplastic lesions. Patient was of 65 years of age. It was unilateral swelling measuring 13x9×7.6 cms. Young RH et al[16] reported 3 cases and Nogales and Silverberg reported 5 cases of epidermoid cysts. All cases were unilateral and size was varying from 2- 46 mm, age of patients was ranging from 21 to 64 years.

Granulosa cell tumor: There were two cases of granulosa cell tumor accounting 1.5% of total neoplastic lesions. Incidence was slightly less compared to the study done by Ramachandra et al[9] with granulosa cell tumour accounting for 2.7%.

Germ cell tumours: These accounted for 23 cases (17.8%) of the total ovarian tumors. Out Of these cases 16 were mature teratoma, 2 were cases of struma oavrii, 1 was immature teratoma and 2 cases were dysgerminoma.

Mature cystic teratoma: Mature cystic teratoma most common germ cell tumor, accounted 7% of total neoplastic lesions 39.1% among germ cell tumors. Studies by Tyagi et al[17], Gupta SC et al[11] and Couto F et al[5] which showed an incidence of 18 .46 %, 23.13 %, 15.45 % respectively. In the present study 8 out of 9 cases of mature cystic teratoma were unilateral and one case was bilateral. Studies by Tyagi SP et al[17] showed 8.33% of bilateral tumors. Majority of the cases in the present study were ranging from 2nd decade to 7th decade of life. Studies by Couto F et al[5] showed a wide variation of age range (13-54 years) among cases of mature cystic teratoma.

Dysgerminoma: There were 2 cases (2.4%) of total ovarian neoplastic lesions. Both patients were in 2nd & 3rd decade of life. Studies by Couto F et al[5], Tyagi SP et al[17] and Gupta GC et al[11] showed an incidence of 2.90%, 3.08% and 3.53% respectively.

6. Conclusion

Our study of 485 ovarian lesions in Government Medical College, Bhavnagar aimed to classify the ovarian tumours according to WHO classification (2005). The results of present study are comparable to other series of studies regarding occurrence with respect to age, laterality, gross features and microscopy.

Surface epithelial tumours are the commonest ovarian tumours followed by germ cell tumours as observed in other studies. Majority of the cases occurred in 40 -59 years of age. Certain non - neoplastic lesions of the ovary frequently form a pelvic mass and potentially mimic an ovarian neoplasm. There proper recognition is therefore important to allow appropriate therapy.

Effective therapeutic management of ovarian malignant tumours continues to be a challenge to the oncologist. An accurate histopathological diagnosis combine with clinical staging will help in rendering prompt and appropriate treatment to the patient.

7. Future Scope

Although accurate diagnosis of ovarian tumours can be rendered in all most all of most cases by ancillary methods such as correlating the clinical presentation, radiographic appearance, gross morphology and light microscopic features of H & E stained sections of the tumours, there is a vast scope for reaching most specific & reliable diagnosis of ovarian lesion such as special stains e.g. PAS, Reticulin., immunohistochemical markers e.g. Vimentin, Carcino Embryonic Antigen (CEA), Keratin, Epithelial Membrane Antigend (EMA), Human Chorionic Gonadotropin (HCG), Estridiol., ultrastructural studies, cytogenetics(chromosomal aberration, Kras expression, BRCA1, & BRCA2 expression).

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