Original Article

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Histomorphological Study of Ovarian Tumors at a Tertiary Care Centre

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ABSTRACT

Background: Ovarian tumors account for about 30% of female genital tract tumors and is fourth leading cause of cancer deaths in females. This study was conducted to evaluate the frequency and distribution of histological types of ovarian tumors.

Methods: This was a retrospective seven years observational study based on histomorphological evaluation of 151 ovarian tumours received in department of pathology. Statistical analysis was done and chi-square test was used to see the association.

Results: Out of 151 cases, 149 were primary ovarian tumors and two were metastatic tumors to ovary. There were 124 benign tumors, one was borderline and 26 were malignant.Most common age group affected was 31 to 45 years. Benign tumors were common in 16 to 30 years age group, whereas malignant tumors in 46-60 years. For all age group, benign tumors were more common than malignant tumors.

Surface epithelial tumors (72.2%) were the most common followed by germ cell tumors (19.9%) and then sex cord stromal tumors (6.6%). Serous cystadenoma (41.93%) was the most common benign tumor followed by mucinous cystadenoma (32.25%). Serous cystadenocarcinoma (38.46%) was the most common malignant tumor. Most common germ cell tumor was mature cystic teratoma (73.3%) and granulosa cell tumor (50%) was the most common sex cord stromal tumor.

Conclusion: Diagnosis of neoplastic ovarian lesions requires correlation between clinical, gross and microscopy features as the morphologic diversity of ovarian tumors poses many challenges. In difficult cases, immunohistochemistry and molecular diagnosis may be often required.

Keywords: *Ovarian tumors, Surface epithelial, Serouscystadenoma, Endometroid*

Introduction

Tumors of the ovary are amazingly diverse pathologic entities due to the three cell types that make up the normal ovary: the multipotential surface (coelomic) covering epithelium, the totipotential germ cells, and the multipotential sex cord/stromal cells. Each of these cell types gives rise to a variety of tumours.[1]

In most of the population based cancer registries in India, ovarian cancer is the third leading site of cancer among women trailing behind cervix and breast cancer.[2,3] Ovarian tumors account for about 30% of female genital tract tumours and is the fourth leading cause of death among cancer deaths in females.[4,5] The age adjusted incidence rates of ovarian cancer vary between 5.4 and 8 per 100,000 populations in different parts of the country.[3] It is estimated that about 1 in every 70 women have a life time risk of developing ovarian cancer.[6]

Ovarian tumorsare often difficult to detect until they are advanced in stage or size, as symptoms are vague and insidious and there is no definite screening programme for early detection. The incidence, clinical appearance and the behaviour of the different types of ovarian tumors is extremely variable.[3,4]Knowledge of various histomorphological patterns of ovarian tumors is important for diagnosis as well as prognosis. Hence this study was conducted with the aim to evaluate the frequency and distribution of histological types of ovarian tumors at department of pathology of our tertiary care centre.

Materials and Methods

This was a retrospective seven years observational study based on histomorphological evaluation of 151 ovarian tumors received in department of pathology from January 2009 to December 2015. Institutional ethical committee approval was taken for the study.All histopathologically proven cases of ovarian tumors irrespective of the type of surgery done, were included in the study. Functional cysts and tumor-like condition of ovary were excluded. The clinical data was achieved from hospital records. The paraffin blocks and respective haematoxylin & eosin stained slides were retreived and studied. The world health organization (WHO) classification of ovarian tumours was used for classifying the tumors.

Statistical analysis was done using statistical package for social sciences-22 (SPSS-22). Chi-square test was used to see the association. The p-value of less than 0.05 was considered statistically significant.

Results

Out of the total 151 cases studied, 149 were primary ovarian tumorsand two were metastatic tumors to the ovary. Among the 151 ovarian tumors, 124 were benign, one was borderline and 26 were malignant (Table 1).Age of the patient ranged from 12 years to 82 years. The most common age group affected was 31 to 45 years (Table 2). Benign tumors were most commonly seen in 16 to 30 years age group, whereas malignant tumors were more common in 46-60 years.

Out of the total 109 surface epithelial tumors, 84.4% were benign, 0.91% were borderline and 14.67% were malignant. Benign surface epithelial tumors comprised 74.2% (92/124) of all benign tumors while their malignant counterpart formed 61.5% (16/26) of all malignant ovarian tumors. Serous cystadenoma (41.93%) was the commonest benign tumor followed by mucinous cystadenoma (32.25%)(Table 3). Among the malignant tumours, serous cystadenocarcinomas (38.46%) was the most common tumor (Table 4).

Among the 30 germ cell neoplasms, 73.3%were benign and reported as mature cystic teratomas or dermoid cysts (Figure 1a, 1b). Most germ cell tumors, both benign and malignant, were seen in women younger than 30 years. Germ cell tumor was the most common malignant tumor upto 30 years of age. The youngest patient in the present study was a 12 year old girl with dysgerminoma (Figure 1c, 1d). There were ten cases of sex cord stromal tumors, all of which were benign. Most sex cord stromal tumors occurred in women above 30 years of age. Only two (1.3%) cases of metastasis to ovary was seen in the present study, both affecting patients above 30 years.

For all age group, benign tumors were more common than malignant tumors. Out of 52 patients below 30years, 46 (88.46%) had benign tumors and 6 (11.54%) had malignant tumors. Germ cell tumors was the most common malignant tumour below 30years, accounting for 83.33%. Out of 99 tumors affecting patients above 30years, 78 (78.78%) were benign, 1 (1.01%) was borderline and 20(20.20%) were malignant. Serous cystadenocarcinoma was the most common malignant tumor above 30 years accounting for 50%. The borderline surface epithelial tumour was of mucinous type. There were three cases of patient aged below 15 years. All three cases were of germ cell tumors.

Surface epithelial tumors were more common in 31-45 years (37.61%), Germ cell tumors were more common in 16-30years (53.33%) and sex cord stromal tumors were more in 46-60 years (50%).

Discussion

Ovarian neoplasm has become increasingly important not only because of its large variety of histomorphological patterns but more because they have gradually increased the mortality rate in female genital cancers. A female's risk at birth of having ovarian tumour sometime in her life is 6% to 7%, of having ovarian cancer is almost 1.5% and dying from ovarian cancer is 1%.[7] The poor survival is due to the fact that they do not clinically manifest early and approximately 60% to 70% of the neoplasm present as either stage III or stage IV.[8]Though certain investigations like peritoneal fluid cytology, estimation of serum lactate dehydrogenase, fibrin degradation products and immunological tests have been reported to be of some help in predicting the nature of the pathology, it is generally impossible to diagnose the nature of the ovarian tumor preoperatively just by clinical examination and exploration. Hence, one has to depend on the microscopic appearance of the tumor for further management of the ovarian tumors.[9]

Table 1: Frequency of different classes of benign and malignant ovarian tumors

Classes of tumor	Benign (%)	Borderline	Malignant (%)	Total
Surface Epithelial tumors	92 (74.2%)	1	16(61.5%)	109
Germ cell tumors	22 (17.7%)	-	8(30.8%)	30
Sex cord stromal tumors	10 (8.1%)	-	-	10
Metastatic tumors	-	-	2(7.7%)	2
Total	**124**	**1**	**26**	**151**

Table 2: Frequency of different classes of ovarian tumors in different age group

Age group in years	Surface epithelial tumor	Germ cell tumor	Sex cord stromal tumor	Metastatic tumor	Total
Upto 15	-	3	-	-	3
16-30	31	16	2	-	49
31-45	41	5	3	1	50
46-60	25	4	5	-	34
>60	12	2	-	1	15
Total	**109**	**30**	**10**	**2**	**151**

Table 3: Frequency of individual benign ovarian tumor in different age group

Diagnosis	Upto 15 years	16-30 years	31-45 years	46-60 years	>60 years	Total
Serous cystadenoma	-	17	24	7	4	52
Mucinous cystadenoma	-	13	13	12	2	40
Benign Teratoma	1	13	4	2	2	22
Granulosa cell tumor	-	1	2	2	-	5
Fibroma	-	-	-	2	-	2
Fibrothecoma	-	-	1	1		2
Sex cord tumor with annular tubules	-	1	-	-	-	1
Total	**1**	**45**	**44**	**26**	**08**	**124**

Table 4: Frequency of individual malignant ovarian tumor in different age group

Diagnosis	Upto 15years	16-30years	31-45years	46-60years	> 60years	Total
Serous cystadenocarcinoma	-	-	3	4	3	10
Mucinous cystadenocarcinoma	-	1	-	1	-	2
Endometroid tumor	-	-	-	1	-	1
Undifferentiated/poorly differentiated tumors	-	-	-	-	3	3
Immature teratoma	-	1	-	-	-	1
Teratoma with malignant transformation	-	-	1	2	-	3
Dysgerminoma	1	1	-	-	-	2
Yolk sac tumor	1	-	-	-	-	1
Mixed germ cell tumor	-	1	-	-	-	1
Metastatic tumors	-	-	1	-	1	2
Total	**2**	**4**	**6**	**8**	**7**	**26**

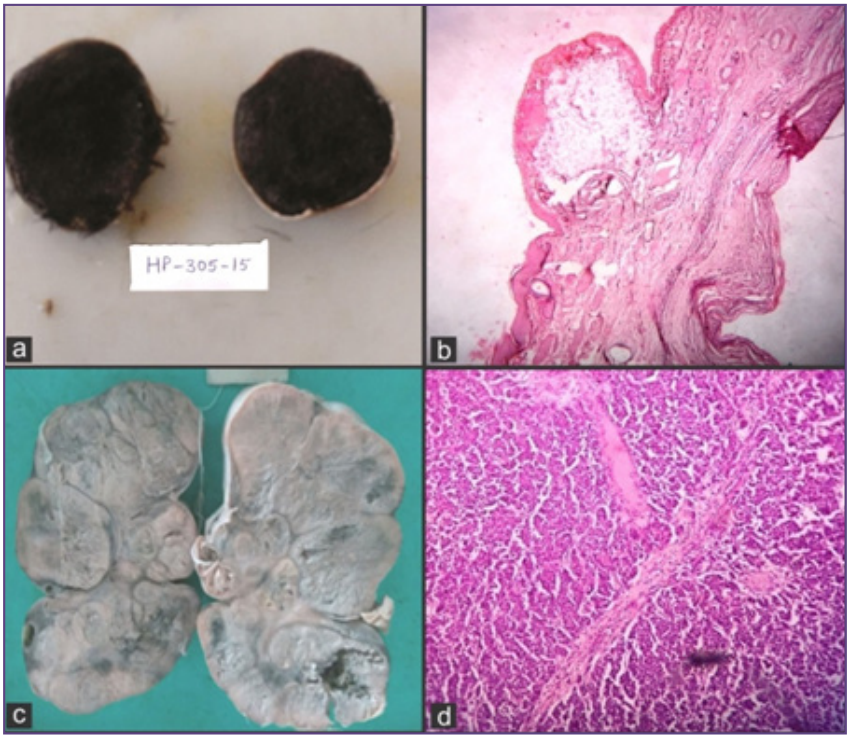

Fig. 1: a) Cut section of mature cystic teratoma showing tuft of hair, b) Microphotograph of mature cystic teratoma (H and E, x100), c) Cut section of dysgerminoma, d) Microphotograph of dysgerminoma (H and E, x100).

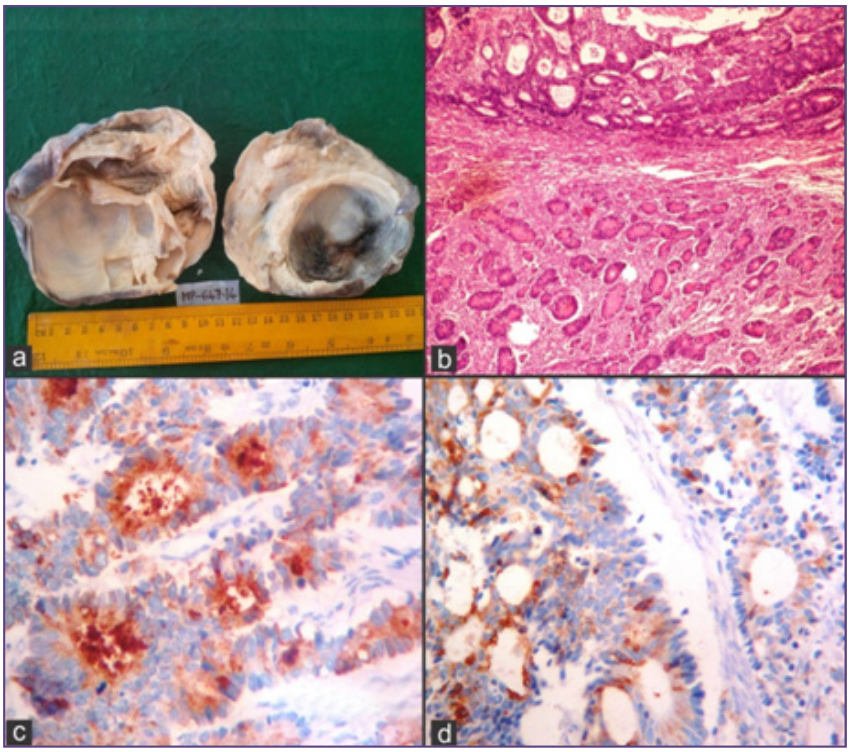

Fig. 2: a) Cut section of sertoliform endometrid tumor showing solid and cystic areas, Microphotograph showing b) conventional endometrid carcinoma with sertoliform pattern (H and E, x200) c) EMA positivity (IHC, x400) d) CK positivity (IHC, x400).

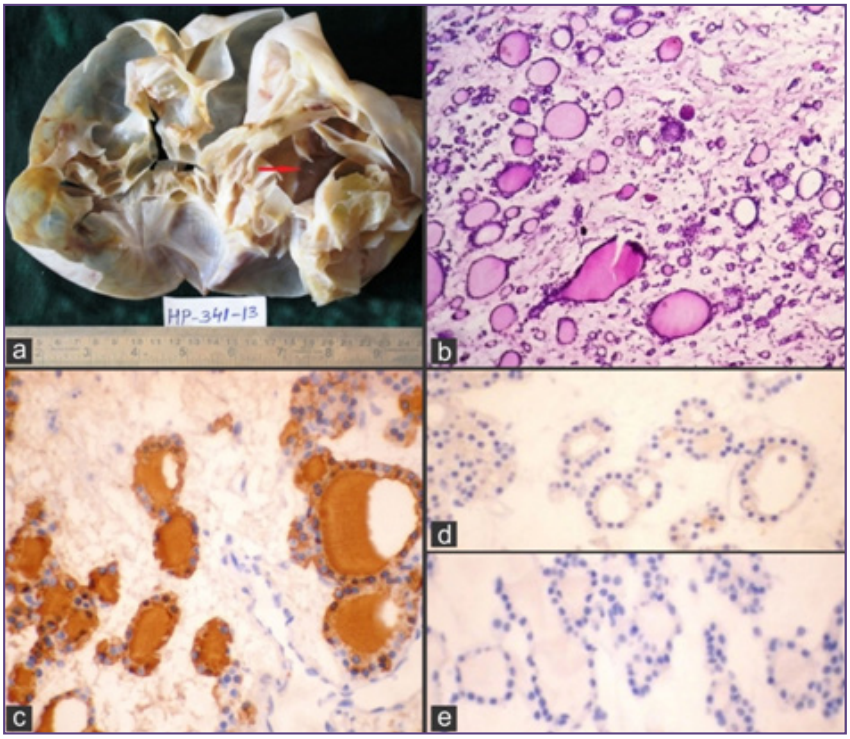

Fig. 3: a) Cut section showing cystic multiloculated (arrow) struma ovarii, b) Microphotograph showing struma ovarii (H and E, x100), Microphotograph showing thyroid follicular cells positive for thyroglobulin (c), negative for synaptophysin (d) and chromogranin (e) (IHC, x400).

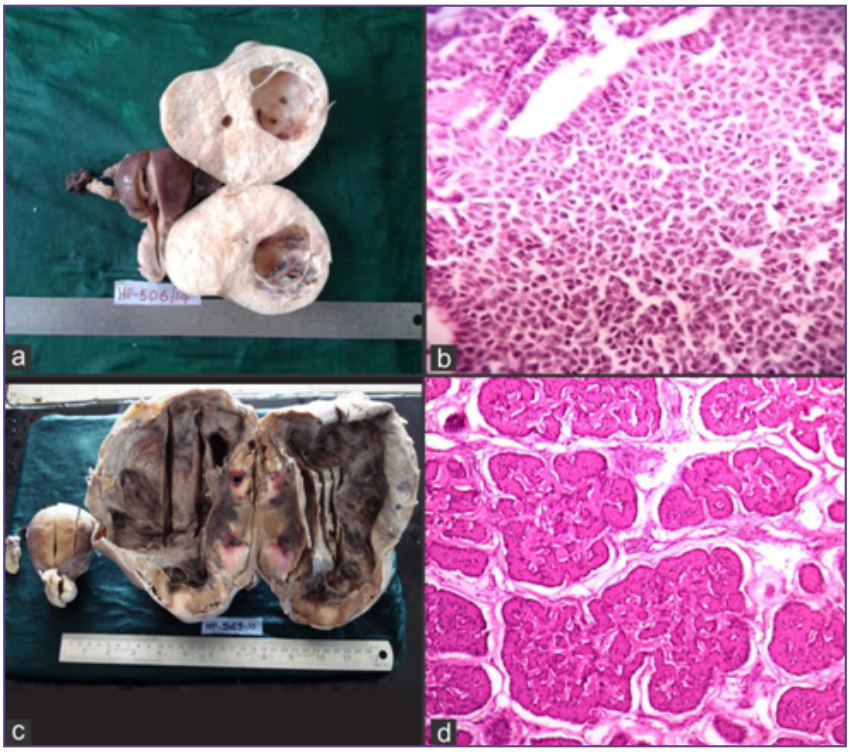

Fig. 4: a) Cut section of granulosa cell tumor, b) Microphotograph showing granulosa cell tumor (H and E, x200), c) Gross photograph of SCTAT, d) Microphotograph of SCTAT (H and E, x200).

In this study, 82.1% cases were benign, 0.7% were borderline and 17.2% were malignant. This was in concordance with study done by Modi et al, where 84.5% were benign, 2.1% were borderline and 13.4% were malignant.[9] In study done by Kuladeepa et al, 82.35% were benign , 3.68% were borderline and 13.97% were malignant.[4] However, in study done by Nishal et al (51%) and Ahmad et al (59.18%) , the incidence of benign tumours was less compared to the present study.[3,10]The incidence of borderline tumours was more in study done by Nishal et al (5%) and Mondal et al (7.3%) compared to our study. [3,11]Tejeswini et al andMalli et al didn't find any borderline tumour in their study.[8,12] Tumors in the borderline category are characterised by epithelial proliferation greater than that of the benign tumor but an absence of destructive invasive stroma.

In the present study, 98.68% tumors were primary and 1.32% tumors were metastatic to the ovary. Our findings corroborated well with study done by Tejeswini et al, wherein 98.92% were primary and 1.08% were secondary ovarian tumors.[8]

Among the major histological classes, commonest type of ovarian neoplasm seen in the present study was surface epithelial tumors accounting for 72.2%, followed by germ cell tumors (19.9%) and sex cord stromal tumors (6.6%). Studies done by Modi et al and Yogambal et al had similar findings.[9,13] However Guppy et al documented higher incidence of surface epithelial tumors (90%) than in the present study.[14] Gupta et al documented lower incidence of surface epithelial tumors (48.8%).[15]

In the present study, 84.4% of surface epithelial tumors were benign, 0.91% were borderline and 14.67% were malignant. This was similar to study done by Modi et al and Danish et al.[9,16] Serous cystadenoma was the most common surface epithelial tumour in our study as well as study done by Singh et al, Tejeswini et al and Modi et al.[6,8,9]Among the malignant surface epithelial tumors, endometroid tumor constituted 0.66% in the present study, similar to study done by Tejeswini et al and Pilli et al, constituting 0.72% and 0.7% respectively. [8,17] A case of sertoliform variant of endometroid tumor was diagnosed in a 55 year old lady who presented with torsion of ovary. On immunohistochemistry (IHC), the tumor cells showed positivity for epithelial membrane antigen(EMA) and cytokeratin(CK) and were negative for inhibin, thus confirming sertoliform endometroid tumor (Figure 2).

One case of struma ovarii was diagnosed in a 45 year female presenting with mass per abdomen and pain abdomen since 1 month. Due to suspected carcinoid foci along with struma ovarii, IHC was done. It was positive for thyroglobulin and negative for synaptophysin and chromogranin (Figure 3). In study done by Tejeswini et al, the incidence of strumaovarii was found to be 0.36%(1 case). In the present study, as well as study done by Tejeswini et al, one case of immature teratoma was reported.[8] We reported one case of mixed germ cell tumor having dysgerminoma and yolk sac component. Three cases were reported as teratoma with malignant transformation, two out of which was transformed into squamous cell carcinoma and one into adenosquamous carcinoma.

The frequency of sex cord stromal tumors in our study was 6.6%. This value is comparable with study done by Modi et al (6.1%).[9] All the sex-cord stromal tumors in the present study were benign, 50% of which were granulosa cell tumour (Figure 4a, 4b). One rare case of sex cord tumor with annular tubules (SCTAT) was reported in a 26years nulliparous female who presented with amenorrhea and mass per abdomen since 3 months (Figure 4c, 4d).

Undifferentiated/ poorly differentiated tumors were detected in 3 cases accounting for 11.53% of all malignant tumors. All three patients were aged more than 60 years. On conventional histomorphology, we could not further subtype these tumors. Due to financial constraints, IHC was not done, which was a limitation of our study. In study done by Danish et al, 19.2% of tumors were undifferentiated or poorly differentiated.[16]

In the present study, we reported 2 cases of metastasis to the ovary. One case was of a 70 year female with papillary adenocarcinoma of fallopian tube and other was of a 40 year female with mucinous carcinoma of colon. In study done by Singh et al , Tejeswini et al and Gupta et al the incidence of metastatic tumors were 0.83%, 1.08% and 2% respectively.[6,8,15]

Among the benign tumors, serous cystadenoma (41.93%) was the commonest followed by mucinous cystadenoma (32.25%) in the present study as well as study done by Modi et al.[9] Our study differs from Nishal et al and Mankar et al who documented mucinous cystadenoma as the most common benign tumor and from Jha et al and Ahmad et al who documented benign cystic teratoma as the most common benign tumor.[3,7,10,18]

Among the malignant tumors, serous cystadenocarcinoma (38.46%) outnumbered all others in our study. This observation is consistent with most other studies with few exceptions. In study done by Sharma et al, mucinous cystadenocarcinoma was the most common malignant tumour.[1] Swamy et al recorded granulosa cell tumours and Yasmin et al observed endometroid carcinoma as the most common ovarian malignancy.[19,20]

In the present study, right ovary was more commonly involved than left ovary. Two cases of bilateral serous cystadenoma and 1 case of bilateral mucinous cystadenoma were seen in the present study. This differed from other studies which had higher incidence of bilateral tumours. Nishal et al reported 13% bilateral tumors, 1 out of which was benign and 1 borderline and rest were malignant.[3]

The histopathological type of ovarian tumor correlates with the prognosis of the tumors. Role of histopathology is critical in recognizing the distinct patterns of ovarian tumors as they have different epidemiological and genetic risk factors, precursor lesion, patterns of spread, response to chemotherapy and prognosis.

Conclusion

It is concluded from this study that the benign ovarian tumors were more common for all age groups. Surface epithelial tumors were the most common class of tumors, similar to the western and local data from other medical institutions. Considering individual tumors, serous cystadenoma was the most common ovarian tumor overall as well as the most common benign tumor, whereas serous cystadenocarcinoma was the most common ovarian malignancy. Malignant ovarian tumors were more common above 40 years. Histopathological study is still the gold standard in diagnosing most of primary ovarian tumor. However, it may be supplemented by newer techniques like IHC, morphometric analysis, cytometric analysis of ploidy status to resolve the difficult, dilemmatic cases and to predict prognosis.

Abbreviations

WHO: World health organisation

IHC: Immunohistochemistry

EMA: Epithelial membrane antigen

CK: Cytokeratin

SCTAT: Sex cord tumor with annular tubules

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