Original Research Article

Histopathological classification of ovarian neoplasm: a retrospective study of 612 cases from a regional cancer centre, Odisha, India

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ABSTRACT

Background: Ovarian cancer is the leading cause of cancer related death amongst women in India. Identification of histological types helps to predict tumor behaviour and further appropriate management. Aims and objectives is to study the histopathological parameters of ovarian tumor.
Methods: This retrospective study was done on patients who presented ovarian mass and subsequently underwent surgery in a Regional Cancer Centre, Odisha, over a period of three years from January 2016 to December 2018. All datas such as age, site, gross findings and histological tumor types were retrieved from pathology and analyzed using MS Excel worksheet.
Results: A total 612 cases of ovarian tumor were included for study. Non-neoplastic to neoplastic tumor ratio was 1:7.74. Surface epithelial tumors comprised the majority of tumors, accounting for 452 cases (83.39%). Malignant lesions were predominant in this series 416 cases (76%). Majority of borderline tumors were of mucinous subtype 20 (76.92%). The Mean±SD ages of all benign comprising, borderline and malignant tumors were 47.4±11.9, 44.9±14.3 and 46.9±13, respectively. On the basis of two tired grading system, high grade malignant serous tumors were maximum, 226 (74.34%). Ovarian surface involvement, omental invasion, uterine invasion, LVSI, capsular invasion and pelvic lymph node involvement was observed in 146 (35.26%), 106 (25.6%), 12 (2.89%), 70 (16.9%), 6 (1.44%) and 12 (2.89%) respectively. According to the FIGO staging system, among primary malignant tumor, 58% patients were presented in late stage (III and IV).
Conclusions: The high incidence of malignant ovarian tumor with late presentation was observed in our study. So, further study is warranted to elucidate the major factors in our population.

Keywords: Histopathology, Ovarian neoplasm, Surface epithelial tumor

INTRODUCTION

Ovary is an important organ as it is concerned with the production of progeny. Typically, the mass lesion of this vital organ exists inherent heterogeneity with biological behaviour ranging from functional cysts to highly aggressive malignant tumors.[1]

Among ovarian neoplastic tumor, ovarian malignancy was found to be the 3rd most frequent gynaecological cancer with high mortality rate.[2] In India, it is the 4th most common cancer in women. The incidence is gradually escalating.[3]

Despite the improvement of treatment protocol, the prognosis of the ovarian cancer rate has not significantly changed. It is most probably due to its anatomical location, complex histology, nonspecific sign and symptoms and late presentation. Moreover, the etiology of this tumor is not fully understood.[4] It has been observed that the identification of various histological types according to the WHO classification helps to

predict tumor behaviour and to decide the further appropriate management.[5]

Distribution of the different ovarian neoplasm has been widely studied in western countries. However, paucity of such type of studies are available in eastern part of this country especially from Odisha.

Authors, aimed to study the histopathological parameters of various histological types and subtypes of ovarian neoplasm in a Regional Cancer Centre, Odisha.

METHODS

This hospital based retrospective study was conducted on patients who were clinically presented ovarian mass lesion and subsequently underwent surgery over a period of three years from January 2016 to December 2018.

Inclusion criteria

- Only histopathologically confirmed cases were included.

Exclusion criteria

- Cases having incomplete data.

The histopathology diagnosis was done on the basis of histo-morphologic features. The classification was done according to WHO guidelines. The histological data such as age, site, gross findings and histological parameters were retrieved from histopathology record. All the data were analyzed using MS Excel worksheet.

RESULTS

A total 612 cases of ovarian tumor were included in this study. Out of these, non-neoplastic to neoplastic tumor ratio was 1:7.74.

Among neoplastic tumors, surface epithelial tumors comprised majority of tumors accounting for 452 (83.3%) followed by germ cell tumor 16 (5.9%). Age wise distribution of ovarian tumor is shown in Table 1. Malignant lesions were predominated in this series 416 (76.75%) out of which 388 (93.26%) were primary and 28 (6.73%) were secondary. Of the primary ovarian malignant tumor, serous type constituted the highest percentage. Clinicopathological parameters distribution of ovarian tumors according to latest World Health Organization classification shown in Table 2.

Borderline tumor constituted 26(4.79%) of all neoplastic tumor among which majority were mucinous subtype 20 (76%).

Table 1: Age wise distribution of ovarian tumor.

Types of Tumor	<20 yrs	21-40 yrs	41-60 yrs	>61 yrs	Total (%)
Surface Epithelial tumor	3(33.3%)	47(72.3%)	142(88.7%)	34(91.8%)	226(83.3%)
Benign	1	9	20	8	38
Borderline	1	4	5	3	13
Malignant	1	34	117	23	175
Germ cell tumor	4(44.4%)	7(10.7%)	5(3.12%)	-	16(5.9%)
Benign	-	3	3	-	6
Malignant	4	4	2	-	10
Sex cord stromal tumor	1(11.1%)	4(6.1%)	8(5%)	2(5.4%)	15(5.5%)
Benign	1	2	3	-	6
Malignant	-	2	5	2	9
Metastatic tumor	1(11.1%)	7(10.7%)	5(3.12%)	1(2.7%)	14(5.1%)
Total (%)	9(3.32)	65(23.9)	160(59)	37(13.6)	271(100)

In germ cell tumor, mature cystic teratoma was the commonest benign tumor and yolk sac tumor was the commonest malignant tumor. Similarly, in sex cord tumor, fibroma was more common benign lesion and adult granulose cell tumor was predominated malignant tumor 18(60%).

The mean±SD ages of all benign, borderline and malignant tumors were 47.4±11.9, 44.9±14.3 and 46.9±13 respectively (Table 2).

Malignant surface epithelial tumors were significantly seen to be more common in older age group except serous borderline type. There were 29.15% and 72.69% cases below 40 years and above 40 years age respectively (Table 1). In below 20 years age, malignant germ cell tumor constituted the maximum numbers 16(44.4%) followed by surface epithelial tumor. Most sex-cord stromal tumors 20(66.6%) occurred in women above 40 years of age. Age wise distributions of ovarian tumors are shown in Table 1.

Table 2: Clinicopathological parameters distribution of ovarian tumors according to latest World Health Organization classification.

Tumor types	No (%)	Mean age±SD (range)	Mean size±SD (range) cm	Consistency			Laterality	
				Cystic	Solid	Mix	Uni	B/L
Benign Tumor types	50(18)	47.4±11.6 (15-80)	6.8±4.84(1.5-20)	20	19	16	38	12
Serous cystadenoma	28(56)	47.2±12.8 (15-72)	7.5±5.31 (1.5-18)	12	9	7	19	9
Mucinous cystadenoma	9(18)	49.5±15.3 (21-65)	10±7.1 (3.5-15.1)	5	4	4	8	1
Benign Brenner tumor	1(2)	45	8	-	1	1	1	-
Fibromas	5(10)	39.8±14.3 (18-550	14.9±6.4 (2.8-20)	2	2	1	4	1
Mature cystic teratoma	6(12)	42.2±9.21 (31-53)	8±3.46 (3-12)	1	3	2	5	1
Sertoli leyding cell tumor	1	22	5	-	-	1	1	-
Border line tumor types	13(4.7)	44.9±14.3 (20-72)	14.6±5.25 (6-20)	10	1	2	7	6
Serous borderline	3	28±6.92 (20-32)	9±2 (7-9)	1	1	1	2	1
Mucinous borderline	10	49.5±12.7 (30-72)	17.9±1.9 (2.1-20)	9	-	1	5	5
Malignant tumor types	208(76)	46.9±13 (14-80)	9.4±5.97 (0.4-27)	37	42	107	77	131
Serous cystadenocarcinoma	152	49.5±10.4 (23-80)	7.5±5.3 (1.5-18)	27	27	84	48	104
Mucinous cystadenocarcinoma	14	44.5±15.1 (26-72)	5.3±3.91 (1-9.7)	4	-	2	8	6
Endometroid adenocarcinoma	4	48.2±6.2 (40-55)	8±1.3 (2.1-8)	1	2	1	2	2
Clear cell adenocarcinoma	1	15	7	-	1	-	1	-
Malignant Brenner tumor	2	50±9.6 (40-62)	14	-	2	-	1	1
Transitional cell carcinoma	1	53	6	-	-	1	-	1
Adenosarcoma	1	80	3	-	1	-	-	1
Immature Teratoma	2	33.5±13.9 (20-47)	18.5±4.9 (15-22)	1	-	1	1	1
Embryonal cell carcinoma	1	14	6	-	1	-	1	-
Dysgerminoma	2	29±12.7 (20-38)	11.5±4.9 (8-15)	-	1	1	2	-
Yolk sac tumor	4	24.5±5.68 (16-28)	22.8±5.57 (16-27)	-	2	2	2	2
Mixed germ cell tumor	1	45	13	-	-	1		1
Adult granulose tumor	9	53.1±13.9 (31-70)	14.6±4.38 (9-19)	2	4	3	6	3
Metastatic	14(5.1)	45.8±14.3 (20-72)	8.2±4.5 (4-17)	2	1	11	5	9

Table 3: Histopathological parameters of borderline and malignant ovarian tumors.

Tumor types	Ovarian surface Involvemet	Omental invasion	Uterine invasion	Cervical invasion	LVSI	Capsular invasion	Pelvic LN +ve
Border line tumor types	6	2	2		2	-	-
Serous borderline	2	2	1		2	-	-
Mucinous borderline	4		1		-	-	-
Malignant tumor types	67	51	4		33	3	6
Serous cystadenocarcinoma	65	41	4	-	30	2	3
Mucinous cystadenocarcinoma	-	2	-	-	-	-	-
Endometroid adenocarcinoma	-						
Clear cell adenocarcinoma	-	1	-		1		1
Malignant Brenner tumor	1		-	1	-		
Transitional cell carcinoma	-	1	-		1	1	
Adenosarcoma	-	-	-	-	-	-	1
Immature Teratoma	1	1	-		-	-	1
Embryonal cell carcinoma	-	-	-		-	-	-
Dysgerminoma	-	-	-		-	-	-
Yolk sac tumor	-	3					
Mixed germ cell tumor	-	-	-		-	-	-
Adult granulose tumor	-	1	-		1	-	-
Sertoli leyding cell tumor	-	-	-		-	-	-

TAH with BSO was done in 57.6% cases where as unilateral salpengiooophrectomy, oophrectomy and cystectomies were done in 13.8%, 9% and 8.48% cases respectively.

Mean±SD size of tumor in epithelial tumor, germ cell tumor and sex cord stromal tumor was 8.93±5.8cm, 8.31±5.61cm and14.62±4.38cm with the size range of 0.4-25 cm, 8-27 cm and 2.8-20 cm respectively. The largest tumor was yolk sac tumor (27 cm) and smallest tumor was malignant serous tumor (0.4cm) (Table 2).

On gross examination, tumors were cystic in 134(24.72%) cases, solid in 124(22.87%) and mix (solid cystic) in 430(79.33%). In benign and borderline tumors, cystic lesions were common 58% and 76% whereas in malignant tumor mix consistency (solid and cystic) was observed in highest numbers 59%

The unilateral involvement was observed in 244(45%) and bilateral involvement was observed in 298(54%) cases. In surface epithelial tumor and metastatic tumors bilateral involvement was most common, while in germ cell tumor and sex-cord stromal tumor, unilateral involvement was most common (Table 2).

According to the nuclear grading system, poorly differentiated ovarian carcinoma cases predominated with 62%. On the basis of two tired grading system, high grade malignant serous tumors were maximum of 226 (74.34%), followed by low grade serous tumor of 78 (25.65%).

Ovarian surface involvement, omental invasion, uterine invasion, LVSI, capsular invasion and pelvic lymph node involvement was observed in 146 (35.26%), 106 (25.6%), 12 (2.89%), 70 (16.9%), 6 (1.44%) and 12 (2.89%) cases, respectively. Distribution of histopathological parameters of borderline and malignant ovarian tumors shown in Table 3.

According to the FIGO staging system, among primary malignant tumor, 58% patients were presented in stage III and IV.

DISCUSSION

Ovaries presents heterogeneous group of diseases with similar clinical and radiologic manifestation. So, diagnosis of ovarian lesion creates a big challenge. In this regard histomorphological classification of ovarian tumor was found to be an integral part of the evaluation as diagnosis and further management are based upon histo types. Moreover, knowledge of age, clinical presentation and histopathological parameters of tumor may also help to refine the diagnosis and further management.[6]

Ovarian tumor may be neoplastic or non-neoplastic. Incidence reported in this study regarding neoplastic lesions was higher which was concurred with other studies.[4,7]

According to morphological features, incidence of ovarian tumors varies globally. It has been observed that surface epithelial tumors forms the most common type followed by germ cell tumor.[6,8,9] The same result was found in this study, but in other study, conducted by Lancaster et al, GCT found to be the commonest of all ovarian neoplasm.[10]

In this study, malignant morphology comprised of highest percentage among all neoplastic tumor but in other study report from this country as well as western part of the globe, benign tumor found to be the highest numbers.[4,6,11,12] The high incidence of malignant tumor in this study could have been due to referral bias since this study was conducted in a regional cancer centre. In other hand, further complete research is needed to elucidate region specific factors behind the high incidence of ovarian malignancy in this area.

In this study serous cystadenoma formed the commonest benign tumor among all benign tumor followed by mucinous cystadenoma which was similar with the recent study findings.[11] But in another study from Bhutan, mature cystic teratoma was found to be the most common type (61.6%) followed by serous cystadenoma.[13]

Among malignant tumor, serous cystadenocarcinoma consisted of maximum. This was in agreement with the study done by Sharadha et al, Gupta et al, Kar et al, and Mondal et al.[4,6,11,12] But in other studies granulosa cell tumors were recorded as most predominant malignant type by Swamy et al, and endometroid carcinomas was found to be the most common ovarian malignancies by Yasmin et al.[14,15]

In a previous study the incidence of borderline tumors were 5.18% among all neoplastic tumors.[11] This was similar with this result but Mondal et al, found the higher incidence of borderline tumor in their study (7.31%).[6]

Borderline tumor can be classified histologically according to their epithelial characteristics as serous, mucinous, endometrioid, clear cell or Brenner tumors. The geographic variation is noted of these tumors in different part of the globe. It has been observed that, serous borderline types are most predominantly identified histologic type in North America, the Middle East, and most of Europe. In contrast, mucinous-type BOTs predominated in East Asia and parts of Europe.[16] Paucity of data are available from India.

In this study two types of borderline tumors, such as, serous and mucinous were observed among which, mucinous formed the highest number in this study. This finding was consistent with the previous report of this country.[11] But in other studies, serous borderline tumor was found to be maximum.[6,17]

In this present study, maximum number of mucinous tumors were malignant which was inconsistent with the

previous reports where majority of mucinous tumors were found to be benign.[6,11,18,19]

In molecular based study, it was suggested that invasive mucinous epithelial ovarian cancers develop via a sequence from benign through borderline tumor and this sequence can be prevented by surgical excision of identifiable precursor lesion. So, the accurate histology classification is crucial.[4]

In this study high grade serous ovarian cancer cases were most common that low grade which was in accordance with the study done by Allison et al, who found 95.7% high grade and only 4.3% low grade.[20] They also found that high-grade serous ovarian cancer patients were older at diagnosis compared to women with low-grade serous ovarian cancer (62.3 years versus 53.6 years; p<0.001). They were concluded that low grade tumor is associated with improved survival.

In this study the mean age of low grade and high grade serous tumor was 45±12.97 and 50±11.26 years age respectively.

According to the recent subdivision of epithelial ovarian cancers, type I epithelial tumors such as low-grade serous, endometrioid, clear cell, mucinous and transitional cell (Brenner) carcinomas comprised less common than type II, such as high-grade serous carcinoma, undifferentiated carcinomas and malignant mixed mesodermal tumors comprised. This was similar with the literature.[21] It has been found that type I epithelial ovarian cancer often present at an early stage, may arise from borderline ovarian tumors or endometriosis and typically have a good prognosis while Type II tumors typically present at an advanced stage and have a poor prognosis. Serous tumors, which are classified as type II epithelial, are the most common histological subtype among women with BRCA1 and BRCA2 mutations.[21]

According to the literature review, germ cell tumors accounts for 30.0% of primary ovarian tumors and malignant germ cell tumors account for 3.0% of all ovarian cancers. Teratomas to be the predominant GCT among which 95.0% were mature cystic teratomas and only 3.0% were immature. Immature teratoma (IT) of the ovary represents 1% of all ovarian cancers and 20% of malignant ovarian germ cell tumors.[22] In another study, the most common type of MGCT was dysgerminoma (38.2%) followed by yolk sac tumor (30.4%), and immature teratoma comprised of (15.7%).[23] where as in this study yolk sac tumor was found to be the most common type of MGCT.

It has been observed that sex cord-stromal tumors are uncommon than germ cell tumors. The proportion also varied widely between countries in Asia, Central and South America and Europe. Literature reviewed showed that sex cord-stromal tumors of the ovary include many of the most morphologically intriguing ovarian neoplasms among which adult granulose tumor were most common.[24] This was in agreement with this result.

Ovarian tumor may occur at any age, including infancy and childhood. The maximum numbers of ovarian neoplasm were found in 4th to 6th decade of life whereas in other studies the majority of cases were found 21-40 years age.[4,6,9,11,25]

Literature also showed that increased incidence at specific age group for each category of benign, borderline and malignant tumors. Data across cities in India revealed that the incidence of ovarian cancer increase from 35 years of age reaching its peak between 55-64 yrs while in other study the highest numbers of malignant tumors were found in the 40-60 years age which was similar with this findings.[26] Wasim et al, found ovarian cancers unusual before age 40.[27]

Prat et al, found a significant proportion (35%) of ovarian malignancies in women younger than 40 years.[9] This agreed with the findings of Jha et al, who found 26.90% of malignant neoplasms in women up to 40 years of age.[6]

According to the study report, there were 22.6% malignant cases in first two decades of life among which malignant germ cell tumors comprised of 66% and 9 were serous carcinoma.[28]

According to literature review it has been observed that dysgerminomas and ovarian yolk sac tumors occur in reproductive age usually in women under 30 years. [29, 30]

In OCCA, young age (<60 years) was considered as poor prognostic factors.[31] But in ovarian yolk sac tumors age had no apparent impact on the probability of event or death.[32]

In sex cord tumor, AGCTs occur more often in middle-aged and postmenopausal women, with a peak incidence between 50 and 55 years of age.[33] while Sertoli-Leydig cell tumor (SLCT) are seen during the second and third decades of life.

Nevertheless, accurate diagnosis primarily depends on the wide range of microscopic features they exhibit. Sometimes gross features help in differential diagnosis. It has been observed that most benign tumors of epithelial category are cystic, on the other hand, the finding of solid element and papillary projections make malignancy more likely which was consistent with this findings.[19] In a study, epithelial tumors were mostly found to be cystic, however the consistence of germ cell tumors and sex cord stromal tumors were mostly solid-cystic and solid respectively.[11] But in this study the epithelial tumors were most commonly mix (both solid and cystic) consistency while germ cell tumors and sex cord stromal tumors were mostly solid.

It is known that laterality gives the clue about the nature of the ovarian tumor. Although some studies has reported

the maximum unilateral involvement with side predilection but in this study we found maximum bilateral involvement.[11,34] Authors did not find the side (right or left) preponderance. Bilateral involvement by primary ovarian tumors varies with histological subtypes. Unlike other study report, the most common ovarian tumor with bilateral involvement was malignant serous tumor.[6] Sigismondi et al, found that bilaterality is rarely observed in malignant ovarian germ cell tumors (MOGTs).[35] The bilateral involvement represents a critical issue when diagnosed in young women desiring to preserve fertility.[35]

Pilli et al, found, none of sex cord stromal tumor was bilateral but in this study 26.67% of sex cord stromal tumors were presented bilateral involvement.[34]

In this study maximum no of malignant cases were diagnosed in late stage which was concordance with the previous report.[4,13]

Limitation of the study as it's single-centre hospital based retrospective study.

CONCLUSION

The high incidence of malignant ovarian tumor with late presentation was observed in this study. So further study is warranted to elucidate the epidemiological and genetical determinants of ovarian malignancy lesions in this population.

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