Original Article

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Pathology Section

Histopathological Study of Non-neoplastic and Neoplastic Lesions of Ovary at a Tertiary Health Care Centre in Mangalore, Karnataka, India

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ABSTRACT

Introduction: Ovarian tumours are one of the leading causes of gynaecologic malignancy and death in women. Carcinoma of ovary represents 30% of all cancers of the female genital tract. Morphologic diversities and non-specific symptoms of these tumours often pose a diagnostic challenge.

Aim: To observe the histopathological spectrum of ovarian lesions in a tertiary care hospital and to find the distribution of benign and malignant neoplasms.

Materials and Methods: This was a prospective study done at a tertiary care hospital in Mangalore, Karnataka, India on 100 ovarian lesions over the period of three years from September 2013 to September 2016. The specimens of ovaries, both neoplastic and non-neoplastic, were processed by routine histopathological techniques and stained by Haematoxylin and Eosin (H&E) stains. Chi-square test was used to find association between spectrum of lesions.

Results: Of the 100 cases of ovarian lesions studied, majority were neoplastic lesions which constituted 51 cases (51%) and the remaining 49 (49%) were non-neoplastic. Among the non-neoplastic lesions, majority were corpus luteal cysts 25 (51%) followed by follicular cyst 17 (34.7 %). Out of the 51 neoplastic ovarian lesions, 32 (52.4%) were benign, 2 (3.2%) were borderline and 17 (27.8%) were malignant. Among the benign ovarian neoplasms, most commonly seen was serous cystadenoma followed by mucinous cystadenoma. In malignant cases, maximum were of serous cystadenocarcinoma (6 cases, 35.3%), followed by two cases each of mucinous cystadenocarcinoma and mixed germ cell tumour. There was one case of metastatic tumour to the ovary.

Conclusion: Histopathological observations in this study provide valuable baseline information regarding the frequency and distribution of ovarian tumours. Histopathology remains the gold standard in the diagnosis of ovarian lesions and their proper recognition is important for appropriate therapy.

Keywords: Cancer, Distribution, Microscopy, Morphology

INTRODUCTION

A variety of non-neoplastic and neoplastic lesions are seen within the ovaries. They show a wide range of age distribution [1,2]. Majority of ovarian lesions are functional, either follicular cysts/cystic corpus luteum, which usually resolve with minimal treatment. Ovarian tumours can be benign, malignant or borderline. Ovarian neoplasms are common tumours in females comprising of 23% of all gynaecologic tumours and are the most common gynaecologic malignancy [3,4]. Ovarian carcinoma is the leading cause of death from gynaecologic malignancy. Incidence of malignancy in ovaries is 20- 30% [1,2]. Ovarian malignancy is a silent killer and most patients present with vague or non-specific symptoms. Most ovarian cancers are inoperable at the time of diagnosis and the five year survival rate varies from only 30-40% [1]. Determination of the histological patterns of ovarian tumours helps in diagnosis and prognosis. The exact aetiology of ovarian cancer remains unclear. Variety of factors have been implicated which includes, hormonal and reproductive factors (nulliparity, late age at menopause, and family history of ovarian/breast cancer). Breast Cancer Gene (BRCA) mutations have been found to be associated with hereditary ovarian cancer. Two-thirds of these cases are found to be in association with BRCA1 gene mutations and one-third with BRCA2 [5,6].

Studies have shown that, age at first birth was associated with serous borderline and endometrioid/clear cell tumours and age at last birth with endometrioid/clear cell tumours [7,8]. Association of ovarian cancer and Hormonal Replacement Therapy (HRT) still remains unclear. Recent case-control studies showed an increased risk of epithelial ovarian cancer in patients with history of usage of HRT. There is also epidemiologic evidence suggesting the role of elevated androgen and oestrogen levels and decreased progesterone levels in the pathogenesis of ovarian cancer [9-11].

Different pathways have been described for the development of the major histologic types of ovarian carcinoma [12]:

1. Low grade serous carcinoma originates along an adenoma–(borderline tumour)- carcinoma sequence and is associated with mutations in Kristen Rat Sarcoma (KRAS) and v-raf murine sarcoma viral oncogene homolog B1 (BRAF). High grade serous carcinomas originate due to alterations in surface epithelial inclusion glands and are associated with mutations involving Tumor protein 53 (Tp53) and dysfunction of BRCA1 and/or BRCA2.
2. Mucinous carcinomas progress along an adenoma-(borderline tumour)-carcinoma sequence and are associated with mutations of KRAS.
3. Catenin beta-1 (CTNNB1)-the gene encoding b-catenin and Phosphatase and Tensin Homologue (PTEN) mutations are seen in endometrioid carcinomas. These tumours arise from endometriosis.
4. The origin of clear cell carcinoma has not been studied much, but an origin from endometriosis has been suggested.

Objective of this study was to observe the histopathological spectrum of ovarian lesions in a tertiary care hospital and to find the distribution of benign and malignant neoplasms to provide valuable baseline information regarding the frequency and distribution of ovarian tumours.

MATERIALS AND METHODS

A prospective study of all the ovarian cystectomy specimens, total hysterectomy, oopherectomy specimens presenting to the Department of Pathology of KS Hegde Medical Academy, Mangalore, Karnataka, India, was studied. The study was done

from September 2013 to September 2016 for a period of three years. Institutional Ethical Committee (IEC) approval was obtained (No.- INST.EC/EC/37/2013-14). A total of 100 cases were studied. All the specimens of ovaries, both neoplastic and non-neoplastic, of all age groups received in the department during the three years were included and ovarian biopsies after chemotherapy and cytoreduction were excluded.

The specimens were processed by routine histopathological techniques; microsections of 5 microns thickness were taken on the glass slides and stained by standard H&E stains. Sections were dewaxed and hydrated through graded alcohol to water and was stained in alum haematoxylin for 5 minutes. Then they were washed in running tap water until sections were blue for 5 minutes or less. Differentiation was done in 1% acid alcohol for 5-10 seconds and then the sections were washed well in tap water until sections were again blue. Sections were blued by dipping in an alkaline solution (ammonia water) followed by a 5 minutes tap water wash and counter stained in 1% eosin Y for 30 seconds to 1 minute. Then the sections were dehydrated, cleared and mount in DPX.

STATISTICAL ANALYSIS

Statistical Package for the Social Sciences (SPSS) SPSS version 16.0 was used for statistical analysis. The study variables were represented using frequency and percentage. Fisher's-exact test was performed to find the association between spectrum of lesions and risk factors. A p-value <0.05 was taken as statistically significant.

RESULTS

The present study included histopathological evaluation of 100 ovarian lesions of which 32 (32%) were benign tumours, 2 cases (2%) borderline tumours, 17 (17%) malignant tumours and 49 (49%) non-neoplastic lesions. The cases had a wide range of age distribution ranging from 1st to 8th decade. Majority of the patients were in the age group of 41 to 50 years. Age wise distribution of benign, borderline, malignant and non-neoplastic lesions is shown in [Table/Fig-1].

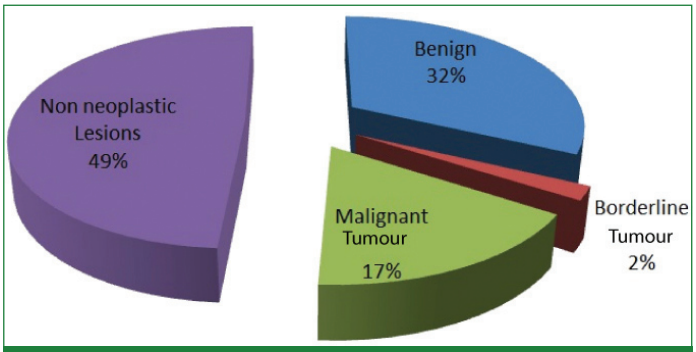
Age (Years)	Benign N (%)	Borderline N (%)	Malignant N (%)	Non-neoplastic N (%)	Total N (%)
1-10	2 (6.3)	0	0	0	2
11-20	3 (9.4)	0	0	1 (2)	4
21-30	4 (12.5)	0	3 (17.6)	6 (12.2)	13
31-40	10 (31.3)	0	0	9 (18.3)	19
41-50	7 (21.9)	0	6 (35.3)	27 (5 5.1)	40
51-60	1 (3.1)	2 (11.7)	2 (11.7)	5 (10.2)	10
61-70	4 (12.5)	0	5 (29.4)	1 (2)	10
71-80	1 (3.1)	0	1 (5.8)	0	2
Total	32	2	17	49	100

[Table/Fig-1]: Age group distribution of benign, borderline, malignant and non-neoplastic lesions.
Fishers-exact test p=0.001, highly significant

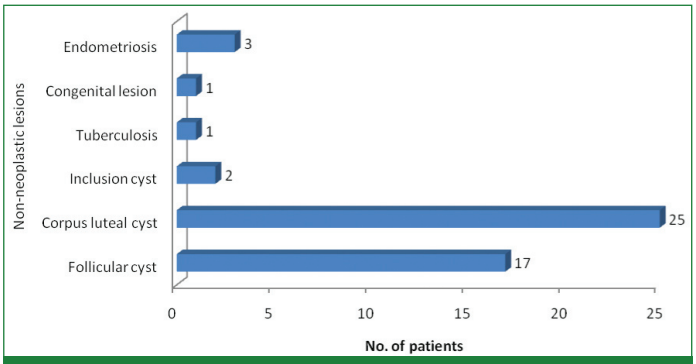
Among the 51 patients of ovarian tumours, majority presented with abdominal pain 36 cases (70.6%) followed by mass per abdomen 17 cases (33.3%) and menstrual disturbances 14 cases (27.5%). Majority of the ovarian lesions were cystic 51 cases (51%) and 12 cases (12%) showed both cystic and solid features, 37 cases (37%) were purely solid. In present study, 40 patients with ovarian tumours were married out of which 38 patients were parous with one or more pregnancies. Two married women were nulliparous and 11 patients were unmarried. Incidence of malignancy was found to be inversely proportional to parity. 2 (6.25%) out of total 32 benign tumors and 12 (70.5%) out of total 17 malignant tumors were bilateral in involvement. The largest lesion was 30 cm in maximum diameter and the smallest lesion was 1 cm in maximum diameter.

The ovarian lesions were broadly categorised as benign, borderline, malignant and non-neoplastic. The distribution of cases among these categories is shown in [Table/Fig-2]. Non-neoplastic lesion was the commonest ovarian lesion in this study accounting for 49 cases (49%). The distribution of non-neoplastic lesions is given in [Table/Fig-3]. Histopathologically, no ovarian tissue was identified.

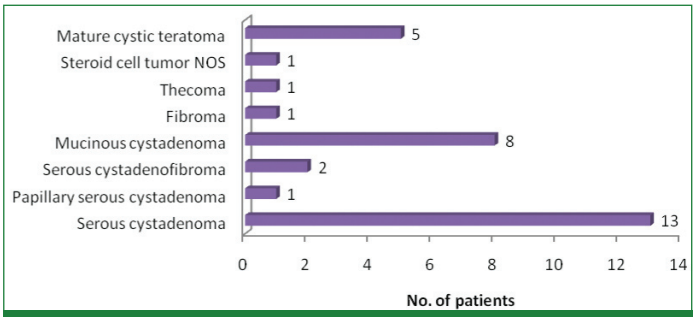
The distribution of lesions diagnosed as benign neoplastic is given in [Table/Fig-4].



[Table/Fig-2]: Distribution of ovarian lesions.

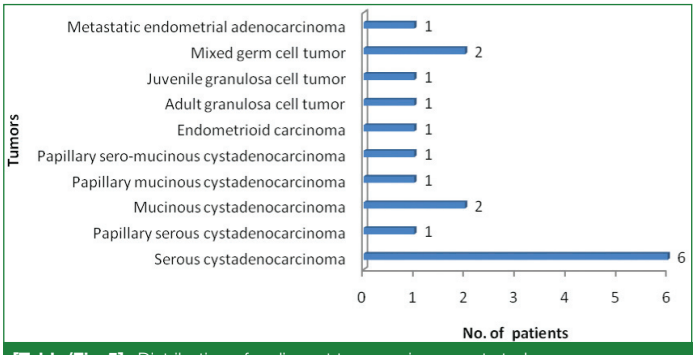


[Table/Fig-3]: Distribution of non-neoplastic lesions in the present study.



[Table/Fig-4]: Distribution of benign tumours in present study.

There were two borderline tumours in this study, one case each of serous borderline and mucinous borderline tumour. Seventeen malignant tumours were diagnosed the distribution of which is given in [Table/Fig-5]. The distribution of histological types of ovarian lesions is given in [Table/Fig-6].



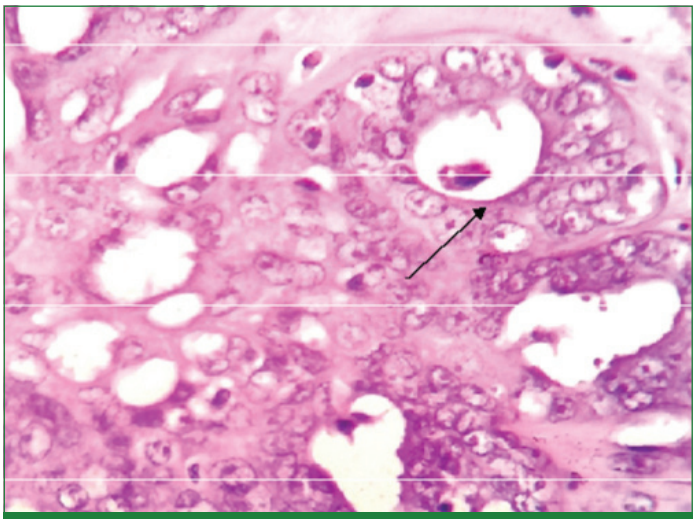
[Table/Fig-5]: Distribution of malignant tumours in present study.

Out of the 38 cases of surface epithelial stromal tumours, the commonest was serous tumour which constituted 24 cases (63%),

Types of ovarian lesions	No. of cases (%)
Surface epithelial- stromal tumours	38 (38)
Sex cord-stromal tumours	5 (5)
Germ cell tumours	7 (7)
Metastatic tumours	1 (1)
Non-neoplastic lesions	49 (49)
Total	100

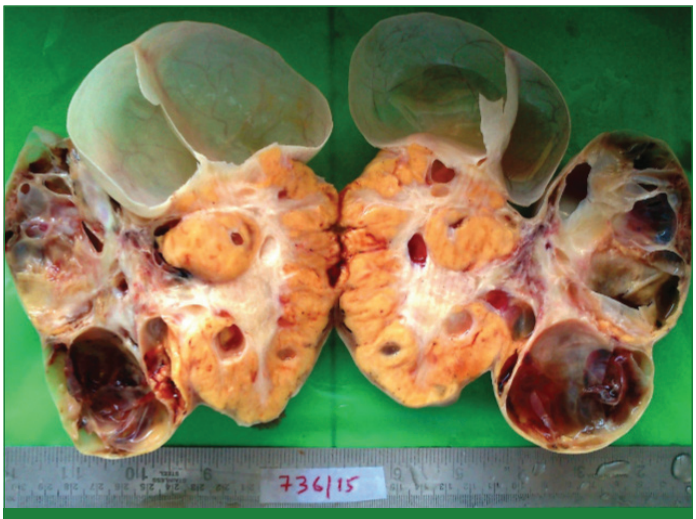
[Table/Fig-6]: Distribution of histological types of ovarian lesions.

followed by mucinous tumour which constituted 12 cases (32%). One case of malignant endometrioid tumour was encountered in a 43-year-old female who presented with pain abdomen and bilateral adnexal mass on ultrasonography. Histopathology confirmed the diagnosis of endometroid carcinoma [Table/Fig-7]. One case of papillary seromucinous cystadenocarcinoma in a 64-year-old female who presented with abdominal pain and bilateral adnexal mass on ultrasonography.

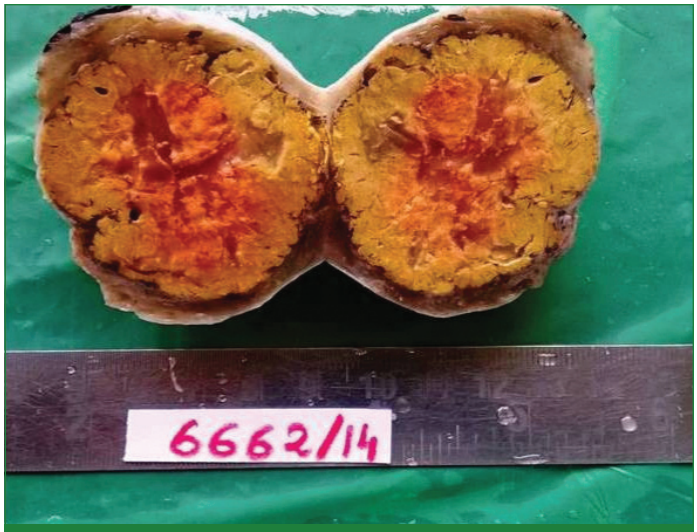


[Table/Fig-7]: Neoplastic glands (black arrow) lined by stratified columnar epithelium of endometroid carcinoma of ovary (H&E 40X).

There were two cases of granulosa cell tumour, one case each of adult and juvenile granulosa cell tumour and one case each of fibroma, thecoma and steroid cell tumour [Table/Fig-8,9]. There were five cases of mature cystic teratoma. The youngest patient was seven years and the oldest patient was 40 years of age. All cases were unilateral. One case of mixed germ cell tumour showing both yolk sac and embryonal component was seen in a 26-year-old female involving the right ovary and one case of metastatic endometrial adenocarcinoma was encountered in a 68-year-old unmarried female who presented with post-menopausal bleeding. The endometrium of the patient showed well differentiated endometrial adenocarcinoma.



[Table/Fig-8]: Gross specimen of adult granulosa cell tumour of ovary showing both solid and cystic areas. Solid areas are yellow.



[Table/Fig-9]: Gross specimen of steroid cell tumour of ovary showing well circumscribed solid, lobulated mass with yellowish cut surface.

DISCUSSION

Ovarian lesions are diverse in morphology and their precise diagnosis is required for optimal management [1,3]. Majority of benign, borderline and malignant tumours in present study were unilateral which was in correlation with the studies of Kuladeepa AVK et al., and Janaki M et al., [8,13]. In contrast to the studies of Kuladeepa AVK et al., (31.58%), and Janaki M et al., (33.33%), bilaterality was seen in 70.5% of malignant tumors in present study [8,13]. Ovarian lesions showed wide range of age distribution. Majority of ovarian lesions in present study were found in the age group of 31-50 years, which was comparable to the studies by Ashraf A et al., Makwana H et al., and Prathima G and Shastry S [14-16].

In this study, the most common symptom with which the patients presented was abdominal pain. The next most common clinical symptom was abdominal mass. In contrast, majority of the patients in the studies of Bodal VK et al., presented with abdominal mass followed by abdominal pain [17]. Majority of benign, borderline and malignant tumours in present study were unilateral which was in correlation with the studies of Kuladeepa AVK et al., and Janaki M et al., [8,13]. Benign tumours were predominantly cystic which correlated with the study Janaki M et al., [13]. Malignant tumours in present study were mostly mixed in consistency. In contrast in the study by Janaki M et al., malignant tumours were predominantly solid [13]. Borderline tumours in present study showed both cystic and mixed consistency. The borderline tumours were predominantly cystic in the study by Janaki M et al., [13].

In the current study, non-neoplastic lesions like follicular and corpus luteal cysts were the commonly encountered lesions which were in accordance with the findings of Zaman S et al., Makhwana HH et al., Kanthikar SN et al., and Iqbal J et al., [1,15,18,19]. Ovary is a common location of endometriosis [18]. There were 6.1% of ovarian endometriosis cases in present study which was coincided with the study of Makhwana H et al., and Kanthikar SN et al., [15,18]. But in contrast, studies by Zaman S et al., and Iqbal J et al., showed a higher incidence of ovarian endometriosis [1,19]. In present study, 4.1% of inclusion cyst were found which was comparable with the findings of Kanthikar SN et al., and Iqbal J et al., [18,19] and 2% of oopheritis which was similar to the study of Makhwana H et al., [15]. There was one case of swyers syndrome (congenital) in present study which was not reported in any of these studies.

In present study, 32% of ovarian tumours were benign, 2% were borderline and 17% were malignant. The distribution of benign, borderline and malignant tumours in present study was in

concordance to the studies conducted by Bodal VK et al., Gupa N et al., Nabi U et al., and Hasan Y et al., [17,20-22].

Among the histologic types, the most prevalent category encountered in present study was surface epithelial stromal tumours followed by germ cell tumours and sex-cord stromal tumours. Similar observations were made by Ashraf A et al., Makwana H et al., Gupta N et al., Bodal VK et al., and Hasan Y et al., [14,15,17,20,22]. One case of metastatic ovarian tumour was observed in present study. Two percent of metatstatic ovarian tumours were reported by Gupta N et al., and Bodal VK et al., [17,20], whereas no metastatic tumours were reported by Hasan Y et al., [22].

The commonest benign tumour in present study was benign serous tumour which was similar to the study by Makwana H et al., and Bodal VK et al., [15,17]. But Hasan Y et al., has reported mature cystic teratoma as the most common benign tumour [22]. Most common malignant tumour in present study was malignant serous tumour which was similar to the study by Makwana H et al., and Bodal VK et al., [15,17]. But present study findings were in contrast to the study by Hasan Y et al., where malignant mucinous tumours were found to be the most common [22]. Serous tumours were more common than mucinous tumours in present study. Similar observations were made by Janaki M et al., Bodal VK et al., and Gupta N et al., [13,17,20].

HRT has been shown to be associated with an increased risk for ovarian carcinoma whereas oral contraceptive pills have consistently shown to reduce the risk of ovarian cancer [11]. Surprisingly, in present study no patient gave history of usage of such drugs which can be due to the fact that majority of them came from a rural background and the prevailing social pressures might have contributed to the non-acceptance. There was no significant family history in any of the cases.

Limitation(s)

Limitation of this study was that it did not reveal the status of tumour markers and gene at the time of presentation in the ovarian cancer patient.

CONCLUSION(S)

Since non-neoplastic lesions of ovary can present as a pelvic mass and potentially mimic an ovarian neoplasm, their proper recognition is important to provide appropriate therapy. Histopathological study is still a gold standard method and the clinical and histomorphological observations in this study provide valuable baseline information regarding the frequency and distribution of ovarian tumours.

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