Section: Pathology

Research

CLINICOPATHOLOGICAL ANALYSIS OF OVARIAN TUMORS IN A TERTIARY CARE HOSPITAL

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Abstract

Background: Ovarian tumors accounts for 6% of all cancer in women 49. Ovarian tumors are the 5th leading cause of cancer death in women in India. Annual incidence rate in India is 9.0 per 100,000 population. Ovarian tumors accounts for 30% among all tumors of female genital tract. The aim and objective are to study and compare the incidence of ovarian tumors in our institution along with clinical correlation. **Materials and Methods:** A total of 157 cases of ovarian neoplasms referred from SKMCH, Muzzaffarpur, Bihar during 2018 to 2019 were included in this study. We received unilateral, bilateral salphingo-oophorectomy along with total abdominal hysterectomy and ovariotomy specimens. Specimens were fixed in to in 10% neutral buffered formalin and processed routinely. **Result:** In our study a total of 157 cases were evaluated with clinical, histopathological & immunohistochemistry and the following Result were made and presented. The incidence of ovarian neoplasms among all female neoplasms is 8.8%. The incidence of ovarian malignancies among all female malignancies is 3.6%. Ovarian malignancy ranks 2nd (5.7%) among the female genital tract Malignancies. The ratio of benign and malignant ovarian neoplasm is 3:1. **Conclusion:** The age specific incidence of ovarian cancer and its subtypes presented in this study will serve as a useful point of reference for future studies and would help to specify their trend in future and encompass the community health programs to solve health problems.

INTRODUCTION

Ovarian tumors accounts for 6% of all cancer in women. Ovarian tumors are the 5th leading cause of cancer death in women in India.[1] Annual incidence rate in India is 9.0 per 100,000 population. Ovarian tumors accounts for 30% among all tumors of female genital tract. Tumors of ovary generally are more prevalent in the upper socioeconomic groups due to their low fertility rate and there is aracial predisposition of ovarian cancers with increased risk of Caucasians and lower risk for black women.[2] About two-thirds of ovarian tumors occur in reproductiveage group. Many risk factors are associated with increased prevalence of ovarian tumors most importantly, age, positive family history, genetic factors, hormonal and reproductive factors.[3] Most cases are sporadic, only around 5-10% of ovarian cancers are Hereditary. Women having inherited mutations in BRCA-1 & BRCA2 tumor suppressor gene are at increased risk for developing the tumor.[4] Abdominal USG & Serum CA-125 measurement was used as screening methods for diagnosis of early ovarian carcinoma. Fine needle aspiration cytology is used for primary diagnosis in a patient with advanced disease and also to monitor recurrences after treatment with an overall accuracy of

Differentiating benign from malignant ovarian tumor ranging from 90-95%.[5] Preventive measures that could be recommended on population wide basis are diet modifications, cessation of smoking and prophylactic oophorectomy is usually done in patients having higher risk.[4] Despite the development of new diagnostic and therapeutic strategies to improve the 5- yr survival rate, ovarian cancer still remains the deadliest due to the fact that most of them are diagnosed only in advanced stages of disease where 5-yr survival rate falls less than 20% and partly it is due to paucity of knowledge about exact etiological factors.[6,7,8] Any persistent ovarian enlargement is an immediate indication for surgical assessment and actual diagnosis rests with the histopathological examination of specimen. WHO Histological Classification is used for the diagnosis of ovarian tumors. They are categorised into 3 major categories 1. Surface epithelial - stromal. 2. Sex cord –stromal 3. Germ cell tumors.[4,9] Histological subtyping of surface epithelial stromal tumorsinto Benign, Borderline &

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Malignant has therapeutic and prognostic significance. Histological grade is an important independent prognostic factor in patients with surface epithelial stromal tumor.[9] Ovarian serous carcinoma is classified according to 2-tier grading system into low and high grade and it is based on the biological evidence that these tumors develop from different pathways of gene alterations 3. P53 immunohistochemical staining is done to provide an update on pathogenesis of low- & high-grade serous carcinoma and also helps in understanding the pathogenesis of Type I & Type II ovarian carcinomas3. Ki-67 is a cell proliferation marker. MIB1 is a murine monoclonal antibody against ki-67 antigen8. Ki-67 labelling index helps in the differential diagnosis of surface epithelial stromal tumors of ovary.[3,4,5] This study is undertaken in order to evaluate theincidence of ovarian neoplasms in our institution with refrerrence to age, clinicopathological features, histopathological and immunohistochemical features along with immense review of journals and research publications.

Aims and Objectives

To study and compare the incidence of ovarian tumors in our institution along with clinical correlation.

MATERIALS AND METHODS

A total of 157 cases of ovarian neoplasms referred from SKMCH, Muzzaffarpur, during 2018 to 2019 were included in this study. We received unilateral, bilateral salphingo-oophorectomy along with total abdominal hysterectomy and ovariotomy specimens. Specimens were fixed in toto in 10% neutral buffered formalin and processed routinely. In cystic ovarian neoplasms, 4-5 bits were taken from the wall along with papillary excrescencess if present. In solid tumors, 3-4 bits were taken if the tumors were less than 5 cm. If more than 5 cm, one block per 1 cm of the tumor were taken across its greatest dimension, particularly if the appearance is variegated. 3-4 micrometre sections were cut and stained with haematoxylin and eosin. H&E-stained sections were reviewed in all cases. The following clinicaland histological parametres were evaluated in particular patients age, tumorsize stage of disease (FIGO staging), Histological Type & Subtypes were done according to WHO Classification criteria. For serous carcinomas, histological grade was done according to recent two-tier grading system. The immunohistochemical detection of biomarkers in suface epithelial stromal tumors was conducted using monoclonal primary antibody (anti-ki67 and anti-P53) against Ki-67 nuclear antigen and P53 gene respectively.

RESULTS

In our study a total of 157 cases were evaluated with clinical, histopathological & immunohistochemistry and the following Result were made and presented. The incidence of ovarian neoplasms among all female neoplasms is 8.8%. The incidence of ovarian malignancies among all female malignancies is 3.6%. Ovarian malignancy ranks 2nd (5.7%) among the female genital tract Malignancies. The ratio of benign and malignant ovarian neoplasm is 3:1. The incidence of ovarian neoplasm is highest during the 2nd decade followed by 4th decade. 90% of ovarian neoplasms are unilateral and 10% are bilateral at the time of presentation. Benign neoplasms are predominantly cystic, whereas malignant neoplasms are predominantly solid and cystic or purely solid. Surface epithelial tumors are the most common neoplasm of which Serous cysadenoma is the commonest.

Table 1: Clinical Features of Various Ovarian Tumors

SL.NO	CLINICAL FEATURES	NO.OF CASES	%
1.	Mass abdomen	119	79.3 %
2.	Pain abdomen	11	7.3 %
3.	Pregnancy associated	4	2.6 %
4.	Ascites	7	4.6 %
5.	Asymptomatic	9	6 %

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Table 2: Frequency Distribution of Individual Benign Tumors in Different Age Groups.

Diagnosis	Age 10-19 yrs	Age 20-29 yrs	Age 30-39 yrs	Age 40-49 yrs	Age 50-59 yrs	>60 Yrs	Total(%)
Serous cystadenoma	-	11	5	8	2	2	28 (25.6%)
Serous cystadenofibroma	-	4	5	7	2	2	20 (18.3%)
Mucinous cystadenoma	1	9	10	10	1	1	32 (29.3%)
Benign Brenner	-	-	-	1	2	-	3 (2.75%)
Fibroma	-	1	-	1	-	1	3 (2.75%)
Mature cystic teratoma	-	10	4	5	3	-	22 (20.1%)
Fibrothecoma	-	-	-	1	-	-	1 (0.9%)
Total	1	35	24	33	10	6	109 (100%)

Table 3: Frequency Distribution of Individual Malignant Tumors in Different Age Groups

Diagnosis	Age 10-19 yrs	Age 20-29 yrs	Age 30-39 yrs	Age 40-49 yrs	Age 50-59 yrs	Age >60 yrs.	Total%
Papillary Serous cystadenocarcinoma	-	-	1	2	5	2	10(34.4%)
Mucinous cystadenocarcinoma	-	1	2	-	1	-	4(13.6%)
Granulosa cell tumor	-	1	2	3	3	-	9(31.2%)
Dysgerminoma	-	1	-	-	-	-	1(3.4%)
Mixed germ cell tumor	1	-	-	-	-	-	1(3.4%)
Metastatic adeno/krukenberg	-	-	1	1	2	-	4(13.6%)
Total	1	3	6	6	11	2	29(100%)

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DISCUSSION

Ovaries are common sites of non-neoplastic and neoplastic lesions. The anatomy of ovary is complex and its physiology peculiarly shows constant cyclical changes from puberty to menopause giving rise to different cell types, each of which is capable of giving rise to complex varieties of tumors.[2,3] Two thirds of ovarian tumors occur in women of reproductive age group92. According to Glen mc clugge et al ovarian cancer is considered to be a silent Killer, as most of these tumors are identified at advanced stage of the disease(FIGO III or IV)and hence overall prognosis is poor.[2,3] Although ovarian tumors are considered as one disease clinically; it is being increasingly realised that the different morphological subtypes has different pathogenesis and are associated with distinct molecular alterationsand have different prognosis.[2,4] In this study, about 11,726 surgical pathology specimens werereceived and analysed over a period of 2 1/2 years. Of these 626 weregynaecological tumors, among which ovarian neoplasms constitutes 150cases, accounting for about 23.9% of all gynaecological tumors. In our study we observed that the ovarian malignancy accounted for 2.6%of all female malignancies .it is evident that, of the total 29 malignant ovarian tumors, most common was papillary serous cystadenocarcinoma accounting for about 35.5% (10/29), followed by granulosa cell tumor accounting for 312% (9/29) and mucinous adenocarcinoma & metastatic tumorsaccounting for 15% (4/29) each. The least common type in this study was dysgerminoma (1/29 cases). Incidence rate of 8.8% and the least is Dindigul ambilikai cancer registry with the incidence rate of 4.3%. This study conducted in a semi urban area; showed an incidence rate of ovarian malignancy (3.6%) is in midway between rural and urban area. it was observed that ovarian malignancies are the second common (5.7%) malignancy among all female genital tract malignancies. It was also observed that uterine cervix (92%) was found to be the first most common site to be involved, and the least common site is vulva. The age specific incidence of ovarian neoplasms ranges from 20-70 years. According to Min jae kim et al the incidence of benign neoplasms peaks in 2nd -3rd decade of life.[4,9] In this study, benign neoplasms were commonly observed in 20-29 yrs of age which is well correlated with our study. According to Debra et al, the incidence of borderline ovarian tumors peaks in 4th decadeIn our study borderline ovarian tumors are common in 40-50yrs age group. This finding is well correlated with previous studies and literature. In this study malignant ovarian tumors are common in 5th-6th decade. This in accordance with study conducted byshruti shah et al88, who showed that 44.5% patients with malignant tumors were in the age group of 51-60yrs. Similar findings were noted in other studies. Ovarian cancers are considered as a silent killer, as they present at an advanced stage of the disease due to the nonspecific symptoms. Most common presenting symptom in our study was abdominal mass (81%), followed by pain abdomen (7%). This is similar to a study conducted by Hiermath et al in Pondicherry which showed that abdominal mass is presenting symptom accounting for 85% cases followed by abdominal pain (13%). In this study; 14 cases, constituting for about 10% of all ovarian tumors showed bilateral involvement at the time of presentation. Of which 5 cases (65%) were benign, 1 case (8%) were borderline, 9 cases (58%) were malignant. Among malignant tumors, bilaterality is commonly observed in malignant serous group (4/8, 51%), followed by metastatic tumor (3/8,38%). This is inaccordance with study conducted by R Jha et al. In this study, 72.6% ovarian tumors were benign and 19.3% were malignant. This is similar to the data from a study by Pilli et al in India which showed that 75.2% were benign, and a similar study conducted by samina et alin Pakistan which showed similar results with 78% benign tumors and 21 % were malignant. Comparison of incidence of benign and malignant ovarian tumors in our study in relation to various other studies. Among all ovarian tumors, surface epithelial tumors was the most common, accounting for about 72.6% followed by germ cell tumors(16%) and sex cord stromal tumors (8.6%).The data obtained in this study well correlates with the study conducted by sumaira et al in Pakistan which showed that surface epithelial tumors predominates with 76.5% ,followed by germ cell tumors(18%). In this study among the surface epithelial tumors, most common wereserous tumors accounting for 56%, followed by mucinous tumors (41%). Among serous tumors, 78.6% were benign, 4.9% were borderline, and 16.3% were malignant. This is in accordance with study conducted by R Jha et al in Nepal which showed that benign serous tumors were the commonest (78.9%) followed by malignant serous tumors (22%). Compares the incidence of histological subtypes of surface epithelial tumors in relation to other studies. According to the Jefferey et al and Geza et al, Serous borderline ovarian tumors are the most common histological subtype of borderline tumors accounting for 65% of all borderline ovarian tumors. In contrast, mucinous borderline tumors were common in our study accounting for about 75% cases and serous borderline for 25%. There are about 3 benign Brenner tumors in this study accounting for 3% of all benign surface epithelial tumors. This is in accordance with the journals andliterature16 Brenner tumors are often associated with other tumors such as ucinous cystadenoma and mature cystic teratoma.[10] Inthis study one suchassociation of Brenner tumor with mucinous cystadenoma was found. According to Tsunehisa kaku et al presence of endometriosis is associated with high incidence of ovarian carcinomas, particularly endometrioid

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carcinoma, clear cell carcinoma, mucinous and serous carcinomas. In contrast none of the ovarian tumors in this study was found to be associated with endometriosis. In this study there are about 24 cases of germ cell tumors, accounting for 16% of all ovarian tumors. Among germ cell tumor group, mature cysticteratoma was the commonest accounting for 91.6%, followed by dysgerminoma,4.1% and mixed germ cell tumor, 4.1%. This is in accordancewith the study conducted by Fred ureland et al,[1,5] and Kwok et al.[4,6] According to P.Singh et al,[9] age at presentation for malignant transformation in dermoid cyst is older than those with benign disease and is more common in postmenopausal age group. In contrast there were three cases in postmenopausal age group in our study but none of them showed malignant transformation. According to P. Singh et al and Gary et al, Dermoid cysts were the commonest ovarian tumor associated with pregnancy.[9,10] Similarly in our study, common tumor associated with pregnancy was dermoid cyst, followed by benign mucinous cystadenoma. One case of dysgerminoma and 1 case of mixed germ cell tumor with combination of dysgerminoma and yolk sac tumor component was observed in ourstudy. In this study, a total of 13 cases, of sex cord stromal tumor accountingfor 8.6% of all ovarian tumors was observed. Of which granulosa cell tumor was the most common type with 9 cases (69%), followed by fibroma with 3 cases (23%), followed by fibrothecoma 1 case, (8%). This finding in our study well correlates with thestudy conducted by R Jha et al,[7,8] According to Lawrence et al,[4,9,10] more than 95% of adult granulosa cell tumors are unilateral. Similarly in this study 9/9 cases were unilateral at the time of presentation. According to Fattaneh et al,[1,6] granulosa cell tumors can be associated with endometrial neoplasia. However in this study, none of the 9 cases had any association with endometrial neoplasia. According to Sung-Jong et al,[8,9] metastatic tumors to the ovaryaccounts for about 5-10% of all ovarian neoplasms. General features of ovarian metastases include bilaterality, surface involvement, extensive extraovarian spread, vascular invasion, desmoplastic reaction & unusual clinical history. According to masaki mandai et al, Krukenberg tumor is the most common form of ovarian metastatic carcinoma, often found in the 4th decade. It is applied to a clinicopathological entity characterised by presence of mucin – filled, signet ring tumor cells within cellular stroma.[5,9] In this study, 3 cases of krukenberg tumor and one case of metastatic adenocarcinomatous deposits in one ovary of intestinal origin was observed.

CONCLUSION

This study is an institution based one and has small sample size of 157 cases. So the results obtained may or may not reflect the actual histological pattern and age distribution of ovarian cancer in Indian women. Them epidemiological pattern of cancers in developing countries differs in many aspects from developed nations. The age specific incidence of ovarian cancer

And its subtypes presented in this study will serve as a useful point of reference for future studies and would help to specify their trend in future and encompass the community health programs to solve health problems.

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