HISTOPATHOLOGICAL ANALYSIS OF NEOPLASTIC AND NON-NEOPLASTIC LESIONS OF OVARY : A 4 YEAR STUDY IN EASTERN NEPAL

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ABSTRACT

Introduction

Ovarian neoplastic and non–neoplastic lesions form a pelvic mass and cause gynaecological problems. Therefore, proper recognization and classification is important for appropriate therapy.

Objective

To study the morphological pattern and classify the neoplastic and non–neoplastic ovarian lesions in terms of age and size.

Methodology

A retrospective study conducted at Sriram Diagnostic Clinic, Biratnagar, Nepal and Birat Medical College, Tankisinwari, Morang, Nepal during a period of March 2012 to February 2016. All abdominal hysterectomy specimens with bilateral or unilateral salpingo-oophorectomy and all ovarian surgeries presenting with either solid or cystic ovarian lesions were included in the study for histopathological analysis. Normal appearing ovaries on gross and microscopic examination were excluded from the study.

Results

A total of 522 cases were studied. Out of which 329 (63%) were non-neoplastic and 193 (37%) were neoplastic. Follicular cysts comprised of 112 (34%) cases, and it was the most common non neoplastic lesion. The age of patients with non-neoplastic lesions and neoplastic lesions varied from 16-54 years and 13-72 years respectively. Size of non-neoplastic and neoplastic lesions varied from 2-12 cm and 2-19 cm respectively. Among the 193 neoplastic ovarian lesions, 181 (94 %) were benign, as well as 4 (2%) were borderline and 8 (4 %) were malignant. Mature cystic teratoma was the commonest benign tumor followed by Serous cystadenoma. Serous cystadenocarcinoma was the commonest occurring malignant tumor followed by Mucinouscystadenocarcinoma.

Conclusion

Varying types of both non neoplastic and neoplastic ovarian lesion were seen. Among the non-neoplastic and neoplastic lesion, the most commonly encountered lesion was follicular cyst and mature cystic teratoma respectively.

KEY WORDS

INTRODUCTION

The ovary consists of both germ and mesenchymal cells, resulting in varied types of neoplastic and non-neoplastic lesions. Most of the ovarian lesions are benign which can be seen from neonatal to post menopausal period. Pelvic ultrasonography, CT imaging and MRI can detect ovarian cystic and solid lesions. However, it is difficult for imaging modalities to categorize the non neoplastic lesions and to differentiate benign ovarian tumors from malignant ovarian tumors.[1] That is why many women even with non-neoplastic lesions of ovary have to undergo surgery. On the other hand the neoplastic ovarian cyst/mass can remain asymptomatic in the early stage, so early diagnosis becomes difficult. Therefore study on ovarian lesion offers a broad field for analysis.[2]

The present study is to ascertain the relative frequency, histologic types, age distribution of both neoplastic and non–neoplastic ovarian lesions in the hospitals of Eastern Nepal and compare the results with similar studies in other regions of this country and abroad.

METHODOLGY

This is a retrospective study based on surgical biopsies from histopathologically diagnosed cases of ovarian neoplastic and non-neoplastic lesions at Birat Medical College, Tankisinuwari, Morang and Sriram Diagnostic Clinic, Biratnagar over the period of four years from March 2012 to February 2016. The cases for study were identified and the original requisition forms were retrieved for relevant clinical information and bio-data. Oopherectomy specimens showing no pathological changes were excluded from the study. The gross study of ovarian lesions like size and external surface were noted. On cut sections in the cystic lesions the wall of the cysts (whether thick and thin wall), loculations (whether uniloculated or multiloculated) and the content of the cysts (whether clear, mucinous, hemorrhage, blood fluid, hairs etc) were noted. In solid ovarian tumors, the consistency as well as areas of hemorrhage and necrosis were also observed. The tissues were processed by routine paraffin techniques and sections were stained with Haematoxylin and Eosin. All histopathology slides were reviewed individually by four different pathologists. The ovarian tumors were classified according to World Health Organization (WHO) classification. The results obtained were analyzed using descriptive statistical methods.

RESULTS

A total number of 522 biopsies were reviewed. Among these 329 (63 %) cases were non-neoplastic and 193 (37%) cases were neoplastic (Figure 1). Among the neoplastic lesions 181 were benign, 4 were borderline and 8 were malignant.

The age range of patients of non-neoplastic lesion was 16 to

Figure 1: Frequency of Ovarian Lesions (n = 522)
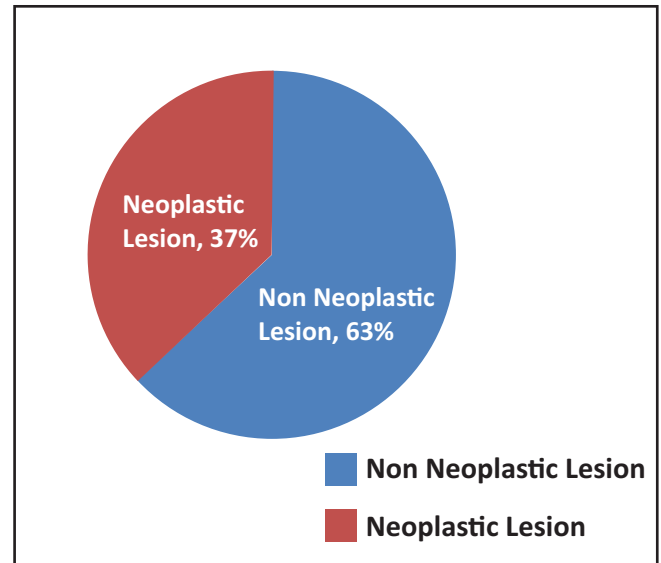
54 years. Similarly the age range of patient of neoplastic lesion was 13 to 72 years.

Out of the 329 non-neoplastic lesion, majority were follicular cyst (34%), followed by Corpus Luteum Cyst (31.3%), Simple serous cyst (18.2 %) hemorrhagic cyst (16.2 %) and endometriosis (0.3%) respectively (Table 1). Follicular cysts were predominantly thin walled and were filled with clear fluid. Grey brown areas of hemorrhage were appreciated in Corpus luteal as well as Endometriotic cysts. Among the non neoplastic lesions 53 (16.2%) cases reveal massive areas of hemorrhage as well as infarction. So specific pathological diagnosis was not possible in these cases.

Out of 193 neoplastic lesions, Mature cystic teratoma was the most commonly encountered lesion comprising of 122 (63.4%) cases, followed by Serous cystadenoma comprising of 40 (20.8%) cases (Table 2). Sizes of non-neoplastic and neoplastic ovarian lesions varied from 2 cm to 12 cm and 2 cm to 19 cm respectively. Non-neoplastic ovarian lesions were all cystic in nature, where as the neoplastic ovarian lesions were predominantly cystic, partially cystic and solid or predominantly solid in nature.

Table 1: Types of Non-Neoplastic Lesions (n = 329)

Types	Number of cases	Percent
Follicular cyst	112	34 %
Corpus luteum cyst	103	31.3 %
Simple serous cyst	60	18.2 %
Hemorrhagic cyst	53	16.2 %
Endometriosis	01	0.3 %

Table 2: Types of Neoplastic Lesions (N = 193)

Types	Number of Cases	Percent
Surface Epithelial tumor (63)		
Serous Cyst Adenoma	40	20.8 %
Mucinous Cystadenoma	15	7.8 %
Serous Papillary Cystadenoma	1	0.5 %
Borderline Serous Tumor	1	0.5 %
Borderline Mucinous tumor	3	1.5 %
Serous Cystadeno Carcinoma	2	1 %
Mucinous Cystadeno Carcinoma	1	0.5 %
Germ Cell Tumor (125)		
Mature Cystic Teratoma	122	63.4 %
Immature Teratoma	1	0.5 %
Strumma Ovarii	1	0.5 %
Squamous Cell Carcinoma Arising in Teratoma	1	0.5 %
Sex- Cord Stromal Tumor (4)		
Sertoli - Leydig Cell Tumor	1	0.5 %
Granulosa Cell Tumor	1	0.5 %
Fibroma	1	0.5 %
Thecoma	1	0.5 %
Matastatic–Krukenberg Tumor (1)	1	0.5 %

Figure 2: Gross picture of multiloculated mucinous cystadenoma, ovary. The loculi contains gelatinous material.

Figure 3: Gross picture of mature cystic teratoma. Cut surface show a unilocular cyst containing greasy material and grey white hard tissue resembling tooth.

Figure 4: Gross picture of ovarian fibroma . A solid ovarian tumor with grey white firm area.

Figure 5: Histopathological findings in Borderline papillary serous neoplasm. (Hematoxylin and eosin stain)X10x. Microscopy picture showing pronounced papillary pattern lined by cuboidal to columnar nuclei revealing mild atypia.
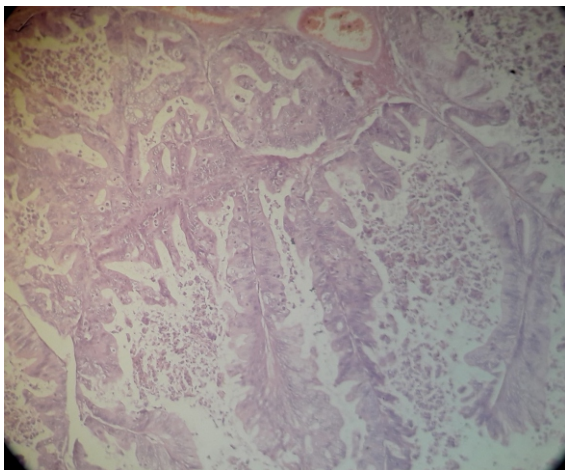

Figure 6: Histopathology findings in immature teratoma (Hematoxylin and eosin stain) X10x Microscopy showing immature neural tissue.
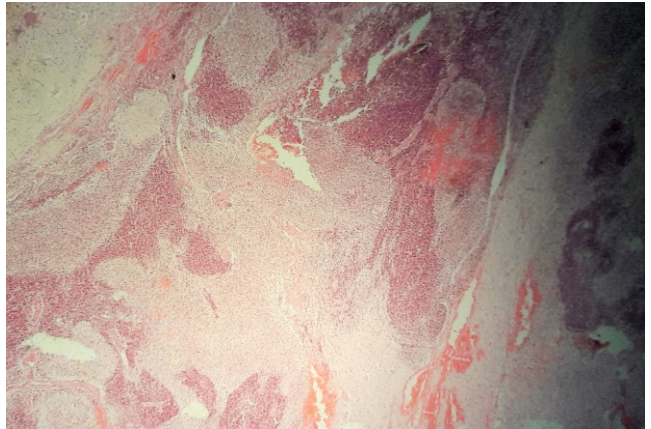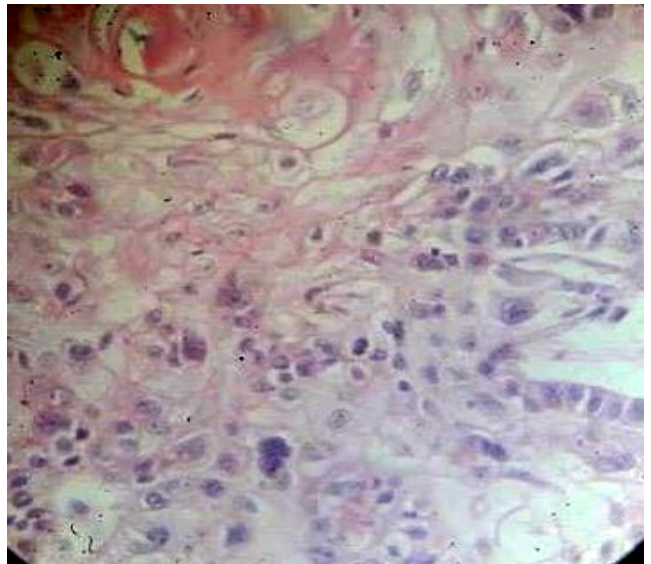

Figure 7: Histopathology findings in a case of ovarian teratoma (Hematoxylin and eosin stain) × 40 x Microscopy is showing squamous cells revealing nuclear atypia.

DISCUSSION

Diagnosis of cystic or solid lesions of ovaries is important whether it is benign or malignant. Benign lesions can relieve the anxiety of a patient whereas a malignant lesion is necessary to be diagnosed on time for further appropriate therapy. Ovarian cancer is the one of the most deadly malignant tumor which comprises of 25% of all gynecologic malignancy.[3,4]

The exact nature of ovarian tumor cannot be confirmed preoperatively either by clinical evaluation or by ultrasono- graphic examinations. Hence it is removed prophylactically in routine oopherectomy and hysterectomy operating procedure. That is why the microscopic diagnosis of the ovarian lesions are necessary to find out the histopathological patterns upon which further management is based on. In our study 522 both non-neoplastic and neoplastic ovarian lesions were studied to find out the incidence and morphological patterns in various age groups.

Out of the 132 ovarian lesions during Martisnez -Onsurbe et al study, they found 55 (41.67%) non-neoplastic lesions.[5] In a study of 203 ovarian lesions by Kruezer GF et al, 82 (40.39%) non-neoplastic lesions were found.[6] Eriksson et al found that two third of cystic ovaries undergoing surgery comprised of functional cyst, which was quoted by De Kroon et al.[7] In this study we found that non-neoplastic lesions constituted 63% of cases. In our study follicular cysts (34%) were the commonest non neoplastic ovarian lesion followed by corpus luteal cysts (31.3%). This is also similar to the study done by Choi et al, and Tayyiaba et al.[8,9]

Follicular cysts are the common non neoplastic cysts which are painless and harmless to the patients. It can be developed in both the ovaries. In our study, we found most of these cysts in the reproductive age group. Corpus luteal cysts were less prevalent than follicular cysts, resulting from intra-cystic hemorrhage. These cysts are also harmless and can resolve without leaving any complication. However it can sometimes rupture or cause ovarian torsion.

This study also showed that about 53 (16.10%) of ovarian cysts were hemorrhagic and many showed areas of infraction as well. Thus hemorrhagic cysts also constitute a high proportion of non neoplastic cysts. Frequency of hemorrhagic infracted cysts was found to be 14.75% in a study by Sumaira Jasmin.[10] Endometriosis is also known as chocolate cyst of ovary. When the endometrial tissue is found outside the endometrium and myometrium, it is called as endometriosis, which can lead to infertility. Endometriosis in our study was seen in only one of the cystic ovary. The prevalence of endometriosis is difficult to identify. We reported a confirmatory diagnosis of endometriosis only after seeing the presence of endometrial glands and stroma in the ovary under microscopic examination. Cysts only showing hemorrhage and hemosiderin laden macrophages under microscopic examinations were diagnosed under the category of hemorrhagic cysts and were advised to correlate with surgical and clinical findings. That may be the reason for less cases of endometriosis and a high percentage of hemorrhagic cysts in this study. Other non neoplastic cysts in the present study were simple/serous cysts. Many other studies have also commonly reported simple serous cyst.[11,12,13] Other functional ovarian cysts like bilateral theca lutein cysts encountered in the present study were relatively rare. This is also in accordance with report of other researchers.[12,13]

The World Health Organization (WHO) has classified ovarian tumors on the basis of histogenesis of the normal ovary.[14] Using the WHO criteria to classify ovarian tumors, it is conventionally known that the surface epithelial tumors of ovary are the most common lesions seen globally. However, the commonest category of ovarian tumors encountered in our study were germ cell tumors followed by surface epithelial tumors. Studies done in Asian and African countries have shown that germ cell tumors of ovaries are more common than surface epithelial tumors.[15]

The result of our study is also in accordance with reports from Lagos by Onyiaorah et al., where germ cell tumor was the most common ovarian lesion followed by surface epithelial tumors.[16]

Among the neoplastic lesions, most common was benign tumor comprising of 93.78% cases, whereas malignant tumor comprised of 4.14% cases and 2.07% of tumors were in borderline category. Gupta et al found 22.9% malignant, 4.1% borderline and 72.9% benign ovarian tumors respectively.[17] However study done by Mondal et al showed 29.6% malignant ,7.3% borderline and 63.1% benign ovarian tumors respectively.[18] In this study, we found a less percentage of malignant tumor and a high percentage of benign tumors. One of the reasons for this could be that the surgeons might have referred the clinically and radiologically suspected malignant ovarian tumors for surgery and further management to higher centers. Other reason could be that we do not have the ancillary techniques like immunohistochemical markers for confirmation and categorization of tumors, so the surgeons might have sent biopsy of suspected malignant tumors to higher centers. Most common benign tumor in this study was mature cystic teratoma (Figure 3) followed by serous cyst adenoma. A study done by Thanikasalam K et al among Malaysian women also reveals mature cystic teratoma as commonest benign tumor.[19] We also found a case of struma ovarii in a mature cystic teratoma. Most cases of struma ovarii are benign and usually unilateral, same was seen in our patients as well. Struma ovarii can be hormonally active with ascites and hydrothorax.[20-22] We could not access the hormone status as the patient did not come for follow up.

This study also showed a case of squamous cell carcinoma arising in a mature teratoma. (Figure 7). We know that the squamous cell carcinoma of the ovary is quite rare and usually arises in mature cystic teratoma of the ovary up to 2%, which has a poor prognosis.[23] In this study, we found that atypical squamous cells were seen arising from the squamous lining of teratoma. A case of immature teratoma of ovary was also seen in our study (Figure 6). Our patient was a 16 year old female, presented with solid cystic ovarian mass. Immature ovarian teratomas are uncommon malignant germ cell tumors of ovary. Along with the mature components they predominantly contain immature neural tissue. In this study, majority of non-neoplastic lesions and benign tumors were cystic except for ovarian fibroma and thecoma, which presented as solid ovarian tumor (Figure 4). Majority of malignant tumors were both solid and cystic. This is almost similar to the studies of Fusey et al who found that solid or solid-cystic tumors were predominantly malignant and cystic swellings were either non-neoplastic or benign in nature.[24]

Next to mature cystic teratoma, the second common benign tumor in this study was serous cystadenoma. Grossly, the tumor showed cystic area filled with serous fluid. Microscopy

showed cysts lined by tall columnar ciliated epithelial cells revealing no nuclear atypia and architectural complexity. Microscopic examination of mucinous cystadenoma revealed tall columnar lining epithelial cells of the cysts with presence of apical mucin. Grossly, mucinous neoplasms showed multiloculated cysts filled with gelatinous material (Figure 2). We know that the borderline tumors have a favourable outcome as compared to malignant ovarian tumor. Stromal invasion is not appreciated in borderline tumors. The two commonest histologic subtypes of borderline ovarian tumors found in our study were serous and mucinous. There is an important role of pathologist in the diagnosis of these tumors and to categorize them in various histologic subtypes. Present study also showed 3 cases of borderline mucinous ovarian tumor and one patient with borderline serous tumor (Figure 5). All these tumors were predominantly cystic in nature.

Present study showed serous cystadenocarcinoma (1%), as the commonest malignant epithelial tumor. These tumors showed numerous branching papillary fronds, nuclear stratification with atypia, nests and clusters of tumor cells infiltrating the ovarian stroma. In mucinous cystaden-ocarcinoma (0.5%), the atypical cells were also seen invading the ovarian stroma. Ovarian sex cord-stromal tumors are uncommon neoplasms that represent approximately 7% of all ovarian tumors.[25] Only single case of fibroma as well as a single case of fibroma-thecoma was found in our study. Both the tumors were solid in nature and did not reveal any microscopic features suggestive of malignancy. In our study we also found only one patient presenting with Sertoli -Leydig cell tumor (SLCTs). SLCTs are also called as Androblastoma. They are the subset of ovarian tumors that constitute less than 0.5% of all ovarian tumors.[26] On microscopic examination, we saw many areas with undifferentiated histology with focal areas revealing variable proportion of sertoli and leydig cells. After giving a provisional diagnosis of SLCTs, patient was advised for immunohistochemical examinations for further diagnostic confirmation.

One case of granulosa cell tumor was seen in 60 years old female. We know that the adult granulosa cell tumor is a rare ovarian malignancy. On histopathological examination, the tumor cells were present in cords and sheets revealing nuclear grooving with atypical mitosis. A provisional diagnosis of adult granulosa cell tumor was given and patient was asked for immunohistochemical examinations for further diagnostic confirmation.

Metastatic tumor in the ovary seen in this study was Krukenberg tumor. Patient was a 21 year old female, already diagnosed with a primary malignant tumor of stomach on endoscopic biopsy.

Majority of the non-neoplastic cysts and the benign ovarian tumor in our study occurred in reproductive age groups. This is similar to other reports where most of the benign ovarian lesions occur in women of reproductive age groups. [27]

In this study, ovarian malignancies were seen in all age groups including reproductive, perimenopausal, and postmenopausal women. However, majority of cases in the western world were seen in elderly postmenopausal women.[28] The data available from this study can help in recognizing the pattern of ovarian tumors prevalent in this part of the world.

CONCLUSION

The functional ovarian cysts were the most commonly encountered ovarian lesions occurring in reproductive age group comprising of follicular cysts followed by the corpus luteal cysts. Among the ovarian neoplastic lesions, germ cell tumors showing mature cystic teratoma were the most common tumor followed by serous cystadenoma.

RECOMMANDATIONS

The best method of correctly categorizing ovarian lesions is histopathological examination of routinely stained hematoxylin and eosin (H&E) slides. However in complicated cases, immunohistochemistry (IHC) and special stains are required. Clinical features, radiological and operative findings as well as gross findings of the lesions also play an important role in diagnosis.

LIMITATIONS OF STUDY

In our study, immunohistochemical markers were not available. Some of the poorly differentiated ovarian tumors for correct categorization need further immunohisto-chemical analysis. Such cases in our study were referred to higher centers along with relevant slides and blocks for diagnostic confirmation after immunohistochemistry analysis. We also found a less percentage of malignant ovarian tumors. A further study of frequency and prevalence of malignant ovarian tumors in other parts of Nepal is needed.

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CONFLICT OF INTEREST

There is no conflict of interest

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