

Study of Ovarian Neoplastic Lesions

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Abstract: Ovaries are paired structures with an embryological, anatomic and functional complexity. Changes in their volume can be observed at ovulation, pregnancy and after menopause. Ovaries are normally resistant to diseases, but still ovary can be seat of more number of neoplastic lesions of benign and malignant. They may be primary or secondary, large or small, solid or cystic and also of mixed patterns and histological types of a broad spectrum. Ovaries are hormone influenced organs and so make a base for hormone related diseases. At the same time many other hormonally unrelated lesions are also seen in ovaries. They are asymptomatic and physical examination is difficult in early stages and hence ovarian neoplastic lesions are difficult to be diagnosed early. The present study is focused on parameters like incidence, bilaterality, age distribution, and spectrum of ovarian neoplasms. The risk of development of neoplasm in hormone influenced organs like breast and uterus is increased with hormone influenced ovarian neoplasms. The wide spectrum of ovarian neoplasms includes harmless simple cystic lesions to the fatal aggressive malignant lesions. The present study is focused on the incident rates of age, site and distribution of the various ovarian neoplastic lesions.

Keywords: Neoplastic Lesions, Granulosa cell tumor, Mature cystic teratoma, Yolk sac tumor, Krukenberg Tumor, surgical excision, chemotherapy, radiotherapy.

I. Introduction

Ovarian neoplasms pose a big challenge to the gynaecologist in finding out the causation of Cancer deaths. Available knowledge of the etiological factors is less and the oncologist may not achieve any considerable reduction in the mortality rate. The pathologist is often frustrated by the numerous neoplastic entities hosted by ovary and by so many histogenetic theories and to explain the occurrences. Ovarian neoplasms represent around 30% of all malignancies of the female genital system[1]. In the economically advanced countries, age adjusted incidence rates are high. Surface epithelial-stromal carcinomas contribute for 90% of all ovarian cancers in North America and Western Europe. In Japan like Asian countries, Germ cell tumours account for a considerable proportion (20%) of ovarian cancers. High parity and the usage of oral contraceptives are associated with a reduced risk of developing surface epithelial-stromal tumours, whereas prolonged estrogen replacement therapy increases the risk in postmenopausal women[1].

Ovarian cancer is the third most frequent malignancy with a higher mortality. By the time of diagnosis itself majority of the patients have tumour spread in the pelvis or abdomen. Regular ultrasound monitoring & bimanual examination of all women and also regular follow up in peri/postmenopausal women is helpful to detect early and to reduce the mortality of ovarian tumours. In the ovarian neoplasms with endocrine activity, which cause various clinical symptoms and signs, and in some feminizing ovarian tumours associated with endometrial carcinoma the problem is much more complicated. As the ovary is targeted to various hormones from menarche to menopause and repeated involutions there by prone to tumour formation. According to Silverberg grading is more helpful in predicting tumour response to chemotherapy and acts as a guide for therapeutic protocols. Histological typing is more useful than grading in predicting survival[2].

The present study comprised of 880 ovarian lesions, received during the study period of three years in the Pathology department, Siddhartha Medical College, Vijayawada. Out of 880 ovarian lesions 92 lesions were observed as neoplastic lesions (10.45%) which were included as study material. Bilateral incidence was 30.43% (28 of 92) and unilateral incidence was 69.57% (64 of 92) in neoplastic lesions. Age incidence varied from 21yrs to 65yrs with a peak between 31yrs to 50yrs age group (71%). Most of the lesions (more than 80%) were in the group of 21yrs to 50yrs. Benign lesions were observed in earlier (21yrs to 50yrs) when compared to the malignant lesions (31yrs to 60yrs). Surface epithelial tumours contributed major share of the neoplastic lesions, in both benign and malignant classifications. Serous cystadenomas are the commonest benign lesions reported (47.7%), whereas surface epithelial malignant lesions contributed 66.67% of that group. Serous cystadeno carcinomas were the commonly reported malignant tumors. Still a considerable number (646) of ovaries had normal histological picture and often no specific pathological changes noted.

II. Materials and Methods

Study period: three years

Study design: Prospective, Cross sectional and observational

Study material: all ovarian neoplastic specimens received during the study period in department of Pathology, Siddhartha Medical College, Vijayawada.

Inclusion: all the ovarian specimens which are diagnosed as neoplastic lesions received during study period in department of Pathology, SMC, Vijayawada.

Exclusion: specimens other than ovaries, ovarian non neoplastic lesions and also ovarian neoplastic specimens received before and after study period.

6.Methodology: As the department received good number of ovarian lesions regularly, the material was sufficient for this prospective study of the ovarian neoplastic lesions. With the help of case sheets and requisition forms particulars like age, clinical features, indication & operative findings, clinical diagnosis were recorded. After receiving the specimen its weight, colour, shape, measurements and consistency like features were recorded. Then the lesion was cut opened and the cut surface was described. Adequate number of bits were taken from representative sites for processing and then paraffin embedding. Routine Haematoxylin and Eosin staining was done. Special stains like PAS and Reticulin etc., were used wherever needed[3,13]. A descriptive study of ovarian neoplastic lesions was done over a period of 3 years considering details of general incidence of ovarian lesions and general incidence of ovarian neoplastic lesions in particular, Age incidence of ovarian neoplastic lesions, unilaterality (right or left) or bilaterality were also made out. Macroscopic appearances and histopathological features and also common and rare lesions were described.

III. Results

During the study period of three years, total number of 7384 specimens were received for histopathological examination out of which 880 were ovarian lesions, constituting 11.92% of total received specimens in the department of Pathology, Siddhartha Medical College, Vijayawada.

In the present prospective study, out of 880 ovarian lesions, 92 were diagnosed as neoplastic lesions (10.45%), which were included in the study. Out of 92, benign lesions were 66 and malignant lesions were 26 (7.50% and 2.95% of all ovarian lesions respectively) as shown in Table I. No neoplasm was reported as borderline tumor. Benign lesions contribute a major part of neoplastic lesions with 66 of 92 (71.74%) and remaining 26 of 92 (28.26) were malignant lesions. Various parameters like general and age incidences, uni or bilaterality, macro and microscopic features were discussed regarding overall neoplastic lesions and for benign and malignant lesions separately. Simple statistical tools were used in data analysis and presentation of results. Common features and histological types were discussed later.

IV. Discussion

Present prospective study of ovarian neoplastic lesions with three years study period, 880 ovarian specimens were received (11.92% of total received 7384 specimens) in Department of Pathology, Siddhartha Medical College, Vijayawada, Andhra Pradesh. In this part, important features of the present study are compared with the other similar studies[4,5].

4.1. Age incidence

In the present study, ovarian neoplastic lesions were observed in the range of 21 to 65 years age group with peak incidence between 31 to 50 yrs age group, covering 71% of the lesions. Ganga S. Pilli et al (2002) found the peak incidence of ovarian tumours in the 3rd and 4th decades accounting 55.7%[5]. Bhattacharya MM et al (1980) reported that the 2/3rd of the benign lesions were observed between 20 to 40 yrs and 2/3rd of the malignant tumours were seen after 40 yrs age. Present study also showed the similar observations and correlates with the above studies. Ovarian malignancy accounted for 12.0 new female cases per 100,000 population in Australia 2000 (AIHW and AACR, AIHW National Mortality Database, Australia's Health 2004, AIHW) [6].

4.2. Site incidence and Bilaterality

In neoplastic lesions of ovary, out of total 92 lesions 64 lesions were unilateral and remaining 28 were bilateral lesions. Benign tumours were more unilateral than the malignant lesions. Out of 66 benign lesions, 48 lesions were unilateral (72.73%) and remaining 18 lesions were bilateral (27.27%). Malignant tumours were 26 out of which unilateral were 16 lesions (61.54%) and bilateral were 10 lesions (38.46%). Ganga S. Pilli et al

reported 92.2% of the benign and 74.2% of the malignant tumours were unilateral[5]. Bhattacharya MM et al reported 85% of the neoplasms were unilateral and remaining 15% of the lesions were bilateral[4].

4.3. Benign lesions

Almost more than half of the benign lesions were covered under the group of surface epithelial tumors including surface epithelial serous, mucinous and also seromucinous tumors, shown in Table II. Out of 66 benign tumors, 48 were found as unilateral and the remaining 18 were bilateral tumors. Minimum age recorded was 21yrs and the maximum was 58yrs.

4.3.1. Surface epithelial serous tumors: In the present study, out of 66 benign lesions 26 were reported as surface epithelial serous tumors (39.39% of the benign lesions) and it was the major part of overall neoplasms (28.26%). Age of the patients varied from 21yrs to 60yrs, with a peak in 3rd and 4th decades. Few cases were partially solid with fibrous component or seromucinous type. Unilateralism is seen in 17 cases (65.38%) and in 9 cases(34.62%) bilaterality was seen. Majority of the tumors were more than 10cms in diameter in size, largest was of 32cms diameter found in a 60yrs old postmenopausal woman. It was smooth and with prominent vascular markings. On cut section the multiloculated cyst was filled with serous fluid and focal solid gray white areas were also observed. Microscopy gave the picture of serous cystadenofibroma.

4.3.2. Surface epithelial mucinous tumors: These have lower incidence rate than serous type. In this study, only 6 lesions were reported as mucinous type (9.09%) of 66 benign lesions. Out of 6 lesions, 5 were unilateral and one was bilateral. These were observed in the age of 22 to 50 yrs. Already cut opened ovarian specimens received from a patients of 22 yrs and 36yrs of age and other specimen was from 35 yrs aged woman. Grossly all were multilocular and filled with mucoid material on their cut surfaces and no solid areas were found[7]. Microscopically the mucinous columnar epithelium confirmed them as mucinous tumors[8,14]. Few of the sections studied also showed the focal calcifications.

4.3.3. Benign Brenner tumors : The present study had 4 lesions (6.06% of the benign lesions) reported as Benign Brenner tumors. Age of the patients was between 41 and 56yrs. All 4 lesions were unilateral with normal other ovary. One of these was 14cmx11cmx7cm sized firm and nodular tumour. Cut section showed well circumscribed lobulated gray white area with focal yellow areas and small cystic areas. Microscopic picture of epithelial cell nests and surrounded fibrous ovarian stroma with focal glandular patterns suggestive of benign Brenner tumor[9].

4.3.4. Mature cystic teratoma: Out of 66 benign lesions, 14 were diagnosed as mature cystic teratomas (21.21% of the benign and 15% of all neoplasms). Of 14 lesions, 8 were unilateral and the remaining 6 were bilateral. Age distribution was from 24yrs to 50yrs with a peak in 3rd decade. These tumors were observed generally as globular masses, varying from 5cms in diameter to 9x8x6cms sized. Cut section, almost of all the tumors showed the pultacious material and also tufts of hair. Yellow greasy material, myxoid areas and dark brown areas were also found in some of the lesions in addition. Histology showed mainly the ectodermal elements like squamous epithelial lining and subepithelial adnexae like hair follicles. Myxoid areas in the gross were corresponded with cartilage microscopically and yellow areas were adipose tissue, both were components of mesoderm. Incidence of the present study is 15% and comparable with the above studies of Ganga S. Pilli et al and Bhattacharya MM et al [4,5].

4.3.5. Struma ovarii: Present study included 2 lesions reported as struma ovarii (3.03% of the benign lesions). Both lesions were unilateral. Both lesions were observed as globular, firm and nodular gray white masses of 3cms and 4 cms in diameter. Cut section showed solid gray white with focal brown areas and partial cystic changes. Microscopically thyroid acinar cells were demonstrated as follicles along with normal ovarian histology[9]. Thyroid follicles were filled with colloid and separated by thin fibrous septae.

4.3.6. Fibrothecoma: These are common in postmenopausal women. Only 5% are bilateral. In the present study, 8 lesions were observed as fibrothecomas (12.12% of benign). All were unilateral and the age ranged from 48yrs to 61yrs. One lesion in 61yrs old patient was smaller (3x2x1cms sized) and the other lesion in 48yrs aged patient was larger (32x22x15cms). Small lesions were solid gray white with small yellow areas. The larger lesions showed cystic areas with focal solid areas which were gray white and yellow. Consistency varied from soft to firm. Microscopy showed thecoma cells show pale vacuolated lipid rich cytoplasm and bland oval nuclei. Spindle cells are also seen representing fibrous component. In Leutinized thecoma, leutein cells were seen discrete and in nests.

4.3.7. Fibroma: As per WHO classification, fibromas comprise 4% all ovarian neoplasms with a mean age incidence of 48yrs and mostly bilateral[11,12]. In this study, 4 fibromas were reported (9.09% of benign and 6.45% of overall neoplasms). Age incidence was from 48yrs to 53yrs. One was bilateral (25% of the fibromas). Size of the lesions varied from 1cm diameter to 5x3x2cms. Cut section showed solid and gray white picture in all lesions. Microscopy showed the fascicles of spindle cells with bland central oval nuclei.

4.3.8. Surface fibroma: Only one lesion in present study was observed as surface fibroma in a patient of 26 yrs age and it was unilateral (2.27% of benign and 1.67% of overall neoplasms). Macroscopically it was a normal sized ovary with a cauliflower like firm growth on one end of the ovary externally. On cut section it was gray white, solid and firm nodule. Microscopically it was observed as fibroma as it contained fibroblasts arranged in fascicles.

4.4 Malignant lesions

Present study consists of 26 malignant lesions (28% of neoplastic and 3.2% of overall ovarian lesions). Unilateralism is observed in 10 lesions and remaining 6 lesions were bilateral. Age group ranging from 36yrs to 65yrs, denotes later age group than the benign lesions. Epithelial ovarian cancer was the fourth most frequent cause of death in women. Surface epithelial tumors are the most common of the ovarian tumors, accounting for 90% of all ovarian malignancies. In the present study, all 26 were the primary malignancies and the epithelial malignancies were 19 in number comprising 73.08% of the primary malignancies. The epithelial malignancies in the present study included 10 serous malignancies, 3 mucinous, 1 is seromucinous, 2 endometrioid type, 1 clear cell carcinoma and 2 transitional cell carcinomas as shown in table III.

4.4.1. Serous cystadenocarcinoma: In present study 10 were reported as serous cystadenocarcinomas (38.46% of malignant and 10.87% of neoplasms). These were observed in the age group of 41yrs to 60yrs. Six lesions were unilateral and 4 were bilateral. All the lesions were grossly large masses. The size varied from 4x3x3cms to 16x16x12cms. All the lesions were uniloculated on cut section and three lesions showed papillary excrescences on inner surface. All the lesions were partly cystic and partly solid and had brown areas. Ragged inner surface was observed in one lesion. Histology showed the fallopian tube epithelium resemblance with stromal invasion and individual cell atypia[10]. Papillary tufting on cut section was seen in two cases. Extensive necrosis and congested blood vessels were present in almost all the lesions.

4.4.2. Mucinous cystadenocarcinoma: Three lesions in present study were reported as mucinous cystadenocarcinoma (11.5% of malignant lesions). Two were unilateral and one was bilaterally present in a patient of 40yrs old. One side lesion was of 12cms diameter sized and the other side lesion was smaller with 5cms in diameter. Both were multilocular with cystic areas filled with mucinous material and the inner surfaces showed the papillary excrescences. Microscopically epithelium was endocervical type with malignant features. Omental secondary deposits of the tumor were observed in this case.

4.4.3. Seromucinous cystadenocarcinoma: In this present study, one lesion was reported as seromucinous cystadenocarcinoma, observed in 59yrs old patient (3.85% of malignant lesions). The friable unilateral tumor of 6x4x3cms size was soft to cystic in consistency. Externally gray brown in color and the cut section showed myxoid material inside with focal solid gray white area. Histological combination of malignant serous and mucinous epithelium with papillary patterns was seen without vascular cores[11]. The other ovary was normal.

4.4.4. Endometrioid carcinoma: Two lesions (7.7% of malignant lesions) were reported as endometrioid carcinoma in the present study. One was bilateral lesion with omental secondary deposits and the other lesion was unilateral. Grossly the tumors were cystic and solid masses of 7x6x4cms and 5x5x4cms sized lesions respectively. Cut sections showed cysts with thickened cyst wall, filled with dark brown fluid. Solid areas were firm, gray white and nodular. Microscopy showed the tumor resembling the proliferative endometrial cells with malignant features[15]. There were areas of hemorrhages and necrosis. Some areas showed sarcomatoid changes.

4.4.5. Clear cell carcinoma: Only one unilateral case of clear cell carcinoma was observed in 44yrs old patient (3.85% of malignant lesions). It was solid, gray white tumor of 8cms diameter. Cut section showed cystic spaces with multiple yellow fleshy nodules. Histology comprised of polyhedral cells as sheets and papillary patterns. The individual cells showed abundant clear cytoplasm and malignant changes in the nuclei[16]. The epithelium was mimicking the gestational endometrium.

4.4.6. Transitional cell carcinoma: Present study had 2 reports of transitional cell carcinomas (7.7% of malignant lesions). Both were unilateral lesions and grossly solid, yellow to tan colored masses of 10 and 12cms diameter. Microscopy showed the nested patterns of transitional epithelium in multilayered and papillary patterns[17]. Primary Transitional cell carcinoma of urinary bladder was excluded to rule out the possibility of secondaries in these cases.

4.4.7. Gynandroblastoma: It was as an unilateral lesion (3.85% of malignant lesions) seen in 54yrs old woman. It was of 31x 28x 26cms sized multiloculated cyst with a solid area of 6x4x4cms. Solid area was firm and gray white and dark brown in color. Cyst was filled with brown coloured fluid. Microscopy showed oval to spindle and polygonal cells arranged in hyper and hypocellular patterns. In the cellular areas, the spindle cells were arranged in sheets with intervening areas of polygonal cells with scanty cytoplasm and vesicular nuclei arranged in trabecular form, linear rows and well defined tubular forms, lined with tall columnar cells. Nuclear grooving was seen in some of the cells. Hypocellular areas showed spindle and polygonal cells with vacuolated

clear cytoplasm. Mitotic activity was in a range of 4 to 6/10HPF. The histological picture was of mixed sex-cord stromal malignant tumor showing all the four components and reported as Gynandroblastoma[18].

4.4.8. Granulosa cell tumor: Two out of 26 (7.7%) malignant lesions were reported as Granulosa cell tumors, seen in 48yrs and 54yrs aged patients as unilateral lesions with other apparently normal ovary. Lesions were of 3x3x2cms and 4x3x3cms size respectively and grossly both were solid gray white with cystic areas[19]. Microscopically in both the lesions the tumor cells were arranged in sheets and trabecular patterns with characteristic focal Call-Exner bodies and nuclei showing longitudinal grooves (“coffee bean”).

4.4.9. Yolk sac tumor: Second most common germ cell tumor type next to mature cystic teratoma occurs in childhood, adolescence and early adult life (mostly <30yrs). Also called as endodermal sinus tumor[20,21]. Present study included 2 unilateral lesions (7.7% of malignant lesions) of yolk sac tumors reported in 19yrs and 24yrs aged patients. Grossly they were of 9 to 11cms diameter sized masses. Cut sections were solid and cystic with hemorrhagic and necrotic areas. Microscopy gave the picture of cystic areas with flattened epithelial lining showing various degrees of atypia and also classical pattern of perivascular formations (Schiller-Duval bodies). Hence the lesions were reported as yolk sac tumors.

4.4.10. Poorly differentiated carcinoma: Two unilateral lesions (7.7% of malignant lesions) were reported in 45yrs and 53 years old patients. Grossly gray-brown and solid. Microscopic picture of both showed pleomorphic epithelial cells with hyperchromatic nuclei infiltrating diffusely into adjacent adipose tissue and fibrous tissue alongwith areas of necrosis and hemorrhage. Tumor infiltration into ovarian stroma was also seen some areas. Thus picture is suggestive of poorly differentiated carcinoma infiltrating into ovarian stroma and fibrofatty tissue.

A recent study (W G McCluggage J.Clin. Pathol 2008) from Washington of consecutive cases of ovarian carcinoma operated in a large hospital (included ovarian carcinosarcomas and primary peritoneal carcinomas, particularly all with an epithelial component of serous type) showed a different frequency of the various types of ovarian carcinoma. In that study, 68% were ovarian carcinomas of serous in type. The next common was clear cell (13%), followed by endometrioid and mucinous (9% and 3% respectively). Six per cent of tumours were of mixed type and only 1% were transitional carcinomas.

In a study conducted by MM Bhattacharya et. Al[4], there were 17 sex cord stromal tumours forming about 6.80% of all ovarian neoplasms. Granulosa cell tumours numbered 8 out of which 2 were benign and 6 were malignant. Thecomas constituted 2; fibromas, 4; fibrothecomas were two and androblastoma was only one.

In a study (by Kataoka et al , Nippon Sanka Fujinka Gakkai Zashi.1989)[20] of malignant germ cell tumors at Kurume University Hospital, for 18 years, the total number of patients was 112, including 25 yolk sac tumors (YST), 10 mixed form germ cell tumors (MF), 36 dysgerminomas (DYS), 26 immature teratomas (IT), 2 choriocarcinomas (CHO) and 13 dermoid cysts with malignant transformation (DCMT). When DCMT cases were excluded, ages was closely related to the age of menarche in each patient.

The incidence, clinical appearance and the behavior of the different types of ovarian tumours is extremely variable. It is generally difficult to diagnose the nature of the ovarian tumour preoperatively just by clinical examination and even on exploration, though certain investigations like peritoneal fluid cytology, estimation of serum lactic dehydrogenase, fibrin degradation products and immunological tests have been reported to be of some help in predicting the nature of the pathology. Hence one has to depend on the microscopic appearance of the tumor for management of the ovarian neoplasms[4].

4.5 Radiotherapy(RT)

Radiotherapy was used as main line of management in certain type of ovarian cancers like Dysgerminomas which showed tremendous response[22]. But because of infertility caused by radiotherapy gradually being replaced by chemotherapy, except in such cases still radiotherapy is the line of management[23]. There was no improvement in survival in people with well differentiated ovarian cancers[23].

Radiotherapy was also used as part of palliative care of patients with cancers of advanced stage as helped in reducing the size of tumor which caused symptoms due to its larger size. This palliative RT was of shorter course when compared to non palliative RT course[24]. This was also used in chemotherapy resistant germ cell tumors[25].

V. Figures and Tables

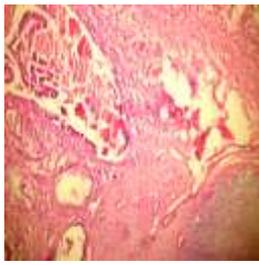


Fig.1

Mature cystic teratoma

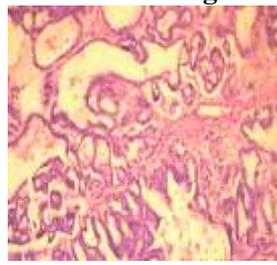


Fig.2

Papillary serous cystadenocarcinoma

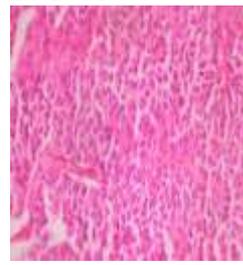


Fig.3

Granulosa Cell Tumor

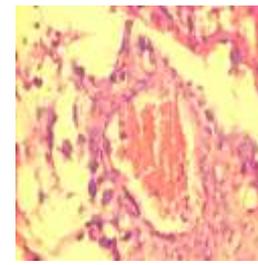


Fig.4

Yolk sac tumor

Table I: Distribution of Ovarian lesions

Non Neoplastic, 788
Neoplastic- Benign, 66
Neoplastic- malignant, 26

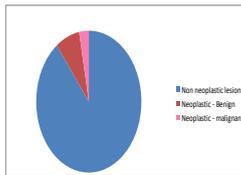


Table II: Distribution of benign ovarian lesions

- Surface epithelial tumour Serous - 26
- Surface epithelial tumour Mucinous -06
- Mature cystic Teratomas - 14
- Fibrothecoma - 08
- Fibroma - 05
- Surface Fibroma - 01
- Brenner Tumour - 04
- Struma Ovarii - 02

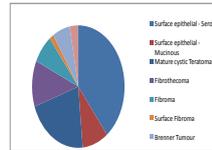
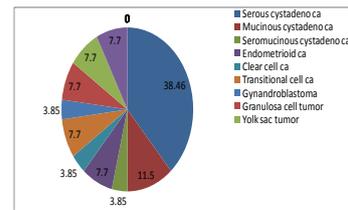


Table III Distribution of malignant ovarian lesions



VI. Conclusions

Ovarian neoplasms are one of the common types found in the women of reproductive age group. Accurate diagnosis and also typing & grading according to recent and standard classifications like WHO Classification is useful in the line of management as specific therapies, like chemo/ surgical/ radiotherapies including targeted therapies or combination of the various therapies depending on the type, stage and grade of ovarian cancer. An attempt was made to study the age incidence, prevalence, morphological types and histological variants among various ovarian neoplastic lesions. The results of the study are comparable with other similar studies and standard books substantiating the findings of the study. About 646 ovaries showed normal histology and no specific pathological changes noted. This may be due to the precautionary removal of ovaries at the time of hysterectomy to avoid further risk or similar surgery. There is a possibility of hidden minute pathology in these which had not appeared in the sections studied as the total ovary was not being processed and studied. Role of radiotherapy in ovarian neoplasms is also discussed.

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