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Study Of Neoplastic Lesions Of The Ovary

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Abstract:
Ovary is a structure with an embryological, anatomic and functional complexicity. It changes its volume at ovulation, pregnancy and after menopause. Though ovaries are resistant to diseases, still ovary can be seat of large number of neoplastic lesions of benign and malignant, primary and secondary, large and small, solid and cystic and mixed patterns with wide spectrum of histological types.

Ovaries are common hormone influence organs and make a base for related diseases. Many other lesions unrelated to hormonal influence are also seen in ovaries. Ovarian neoplasms are difficult to be diagnosed early as they are asymptomatic and physical examination is difficult. This study is focused on features like incidence, spectrum, bilaterality and age distribution of ovarian neoplasms. In many cases of hormone influenced ovarian neoplasms, the risk of development of neoplasms is increased in other hormone influenced organs like uterus and breast. The spectrum of ovarian neoplasms is wide with harmless simple cystic lesions at one end and the fatal aggressive malignant lesions at the other end. The present study is aimed to observe the incident rates and distribution of the various neoplastic lesions of the ovary.

Keywords: Neoplastic Lesions, Benign Brenner, Struma Ovarii, Endometrioid Carcinoma, Krukenberg Tumor

I. INTRODUCTION

Neoplasms of the ovary pose a widespread challenge to the gynaecologist in causation of death from Cancers. There is paucity of full knowledge of the etiological factors and the oncologist is frustrated by the failure to achieve any notable reduction in the mortality rate. The pathologist is often challenged by the profusion of neoplastic entities to which the ovary becomes host and by the wide variety of histogenetic theories that are proffered to explain the occurrences.

Tumours of the ovary represent about 30% of all cancers of the female genital system[1]. Age-adjusted incidence rates are highest in the economically advanced countries. Carcinomas of surface epithelial-stromal origin account for 90% of these cancers in North America and Western Europe. In some Asian countries, including Japan Germ cell tumours account for a significant proportion (20%) of ovarian malignancies. High parity and the use of oral contraceptives are consistently associated with a reduced risk of developing surface epithelial-stromal tumours while long-term estrogen replacement therapy appears to increase the risk in postmenopausal women[1].

Cancer of ovary is the third most frequent malignancy It carries a higher mortality. Most of the patients already have tumour spread in the pelvis or abdomen by the time of diagnosis. Periodic bimanual examination & ultrasound monitoring of all women and regular follow up in peri/postmenopausal women will be helpful in

early detection and helps in reducing the mortality of ovarian tumours.

In the ovary the problem is further complicated by the endocrine activities of tumour causing a variety of clinical symptoms and signs, and some feminizing ovarian tumours are associated with endometrial carcinoma. Further ovary is a target organ for a variety of hormones from menarche to menopause and repeatedly undergoes involutions there by giving rise to tumour formation.

Silverberg opines that histological typing is more valuable than grading in predicting survival. Grading is better for predicting tumour responsiveness to chemotherapy and helps as a guide to proceed with therapeutic protocols.[2]

The present study comprised of 600 ovarian lesions, received in the department of Pathology, Siddhartha Medical College, Vijayawada during the study period of 2 yrs. Out of 600 ovarian lesions studied 62 lesions are observed as neoplastic lesions (10.33%). Incidence of bilateral lesions was 57.5% and unilateral incidence was 42.5%.

Age of the patients varied from 22yrs to 64yrs with a peak incidence between 31yrs to 50yrs age group (72%). More than 80% of the lesions were in 22yrs to 50yrs age group. Age incidence of the benign lesions is earlier (22yrs to 50yrs) when compared to the incidence of the malignant lesions (30yrs to 60yrs).

In the neoplastic lesions, surface epithelial tumors have the major percentage in both benign and malignant classifications. Serous cystadenomas are the commonly reported benign lesions (47.7%). All types of surface epithelial malignant lesions consist 66.67% of that group. Commonly reported malignant lesions are serous cystadeno carcinomas. About 414 ovaries showed normal histology and often no conspicuous pathological changes noted.

The current study revealed the age incidence, distribution of various types of neoplastic ovarian lesions and the incidence of the common and rare types of the lesions of the ovary, reported in the department of Pathology, Siddhartha Medical College, Vijayawada during the study period.

II. BODY TEXT

The present study comprises 600 ovarian specimens received in the department of Pathology, Siddhartha Medical College, Vijayawada. During the study period of two years, 5281 specimens were received for histopathological examination, out of which 600 were ovarian lesions – constituting of 8.8% of the total.

The clinical data was collected from the case sheets and requisitions and recorded as per the proforma. The details of the specimens and macroscopic findings were noted at the time of grossing and relevant tissue samples were subjected for processing. The microscopic findings were documented.

A. Materials And Methods

1.Study design: Prospective, Cross sectional and observational

2. *Study period:* two years

3. Study material: Ovarian specimens received in Pathology department, Siddhartha Medical College, Vijayawada during the study period.

4. Inclusion: all the ovarian specimens received in Pathology department, SMC, Vijayawada during study period.

5. Exclusion: specimens other than ovaries and ovarian specimens received before and after study period.

6.Methodology: As a quite good number of ovarian lesions were reported regularly, the volume of material has prompted this prospective study of the ovarian lesions.

In the study, following particulars like age of patient, clinical features, indication & operative findings, diagnosis, gross characteristics and histopathological features were recorded. Each lesion was described in detail as regards to weight, colour and shape, consistency (when fixed), size, appearance of the cut surface. Several bits were taken from appropriate sites for processing and paraffin embedding. Special stains like reticulin, PAS etc., were used wherever necessary[3,13].

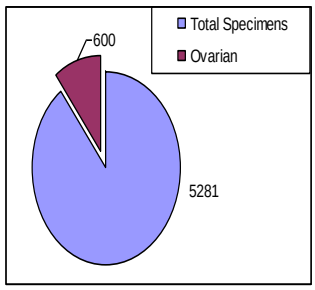
Finally a detailed study of ovarian lesions was done over a period of 2 years taking into account the following details of General incidence of ovarian lesions, Age incidence, Unilaterality (right or left) or bilaterality, Gross appearances and histopathological features and also about Common and rare lesions.

III. Results & Discussion

During the study period of two years, 5281 specimens were received in the department of Pathology, Siddhartha Medical College, Vijayawada for histo pathological examination, out of which 600 were ovarian lesions as shown in table I (8.8% of the total specimens).

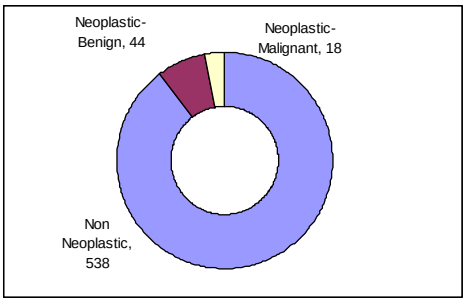
Table I: Incidence of Ovarian lesions

Total number of specimens received during the study period	5281
Number of ovarian specimens received during the study period	600
Incidence of ovarian lesions in total specimens	7%



In the present study of 600 lesions, 62 were neoplastic lesions (10.33%). Out of 62, benign lesions were 44 and malignant lesions were 18 (7.33% and 3% of all ovarian lesions respectively) as shown in table II. None of the neoplastic lesions were reported as borderline tumors.

Table II: Distribution of Ovarian lesions



In this part, salient features of the present study are discussed and compared with the other similar studies[4,5]. In the present study, neoplastic lesions are recorded in the range of 22 to 64 years age group. Peak incidence is between 31 to 50 yrs age group, covering 68% of the lesions.

Ganga S. Pilli et al (2002)[5] reported the peak incidence of ovarian tumours in the 3rd and 4th decades accounting 55.7%. Bhattacharya MM et al (1980) reported that the 2/3rd of the benign tumours were seen between 20 to 40 yrs and 2/3rd of the malignant tumours were seen after the age of 40 yrs. Present study correlates with the above studies Incidence (annual) of Ovarian Cancer in USA is 23,300 (SEER 2002 estimate). Ovarian cancer 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].

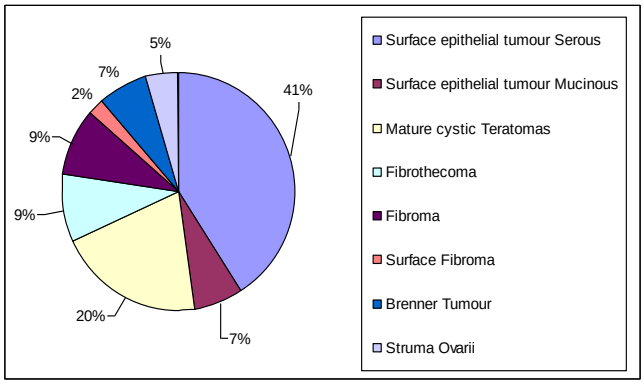
In neoplastic lesions, benign lesions are more unilateral when compared to malignant lesions. Out of 44 benign lesions, 33 lesions are unilateral (66.67%) and remaining 11 lesions are bilateral (33.33%). Malignant lesions are 18 and of which unilateral are 11 lesions (61.12%) and bilateral are 7 lesions (38.88%).

Ganga S. Pilli et al reported 92.2% of the benign lesions are unilateral and 74.2% of the malignant lesions are unilateral[5]. Bhattacharya MM et al reported 85% of the neoplasms as unilateral and 15% of the lesions as bilateral[4]

A.Benign lesions

Nearly half of the benign tumors are come under the group of surface epithelial tumors which include surface epithelial serous, mucinous and rarely seromucinous tumors.

Table III: Distribution of benign lesions



1.Surface epithelial serous tumors: In the present study, out of 44 benign lesions 18 are reported as surface epithelial serous tumors (40.91% of the benign lesions) and it is also a major part of overall neoplasms (29.36%). Age of the patients varied from 22yrs to 60yrs, with a peak incidence in 3rd and 4th decades. Few cases have solid fibrous component or of seromucinous type. Unilateralism is observed in 12 cases (66.67%) and in 6 cases(33.33%) bilaterality was observed. Most of the tumors were of more than 10cms in diameter. In a 60yrs old postmenopausal woman, a lesion of 28cms diameter was noted. Its surface was smooth and prominent vascular markings were noted. Grossly it was multiloculated and filled with serous fluid. Focal solid gray white areas were observed. Microscopy gave the picture suggestive of serous cystadenofibroma.

*2.Surface epithelial mucinous tumors:*These have lower incidence rate when compared to serous type of surface epithelial tumors. In our study, only 3 lesions were reported as mucinous type (6.82%) of 44 benign lesions. All 3 lesions are unilateral and observed in the age of 20 to 50 yrs.

Already cut opened ovarian specimen received from a patient of 20 yrs age and other specimen is from 35 yrs aged woman. Grossly both were multilocular with mucoid material on their inner surfaces and no solid areas were found[7]. Microscopy showed the mucinous columnar epithelium confirming it as mucinous tumor[8,14]. The sections studied also showed the focal areas of calcification. Microscopically they were reported as surface epithelial mucinous tumors.

3.Benign Brenner tumors : The present study has 3 lesions (6.82% of the benign lesions) reported as Benign Brenner tumors (2 are benign and 1 is borderline). Age of the patients is between 40 and 56yrs.

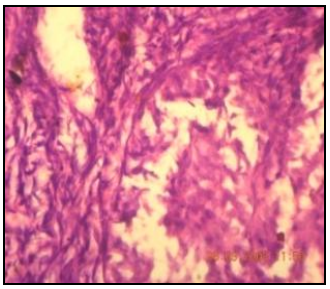


Fig.1 Benign Brenner

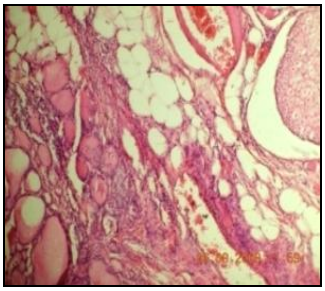


Fig.2 Struma Ovarii

All 3 lesions are unilateral with normal other ovary. One of three was from 56yrs aged patient, 15cmx10cmx7cm sized firm ovarian tumor with nodular external surface. Cut section showed a well circumscribed lobulated gray white mass with focal yellow areas and small cystic areas. The remaining two lesions are also showed the similar gross findings but smaller in size. Histology gave a picture of epithelial cells arranged in the patterns of nests and surrounded by ovarian fibrous stroma with focal glandular patterns. The picture was suggestive of benign Brenner tumor[9].

*4.Mature cystic teratoma:*Out of 44 benign lesions of the present study, 9 lesions were reported as mature cystic teratomas (20.45% of the benign lesions) and this is 14% of overall neoplasms. Of 9 lesions, 5 were unilateral and the remaining 4 were bilateral. Age distribution is from 22yrs to 48yrs and had a peak in 3rd decade.

In general these tumors were observed as globular masses, varying in sizes from 5cms in diameter to 9x8x6cms sized. On cut section, almost all the tumors showed the pultacious material and tufts of hair. One lesion showed yellow greesy material in addition and the other lesion showed the myxoid areas. Dark brown areas were also found in two lesions. Histology predominantly showed the ectodermal elements like squamous epithelial lining, hair follicles and other subepithelial adnexae. Myxoid areas in the gross were seen as cartilage microscopically and yellow areas were observed as adipose tissue, both were components of mesoderm. Incidence of the present study is 14% and comparable with the

above studies of Ganga S. Pilli et al and Bhattacharya MM et al[4,5].

5.Struma ovarii: Present study included 2 lesions reported as struma ovarii (4.55% of the benign lesions). Both lesions were unilateral and observed in 4th decade.

Both lesions of struma ovarii were observed as globular, firm and nodular masses of 2cms and 4 cms in diameter. Cut section showed solid gray white appearance with focal brown areas with partial cystic changes. Microscopically thyroid tissue was demonstrated as follicles along with normal ovarian structures[9]. Thyroid follicles filled with colloid and separated by thin fibrous septae were observed.

6.Fibrothecoma: These are common in postmenopausal women. Only 5% are bilateral. In our study, 4 lesions are observed as fibrothecomas (9% of benign). All are unilateral and the age ranging from 43yrs to 60yrs. One lesion in 60yrs old patient was found as small as 4x2x1cms sized and the other lesion in 48yrs aged patient was as large as 30x20x15cms. Small lesions on cut section were solid gray white with focal yellow areas. The larger lesions predominantly showed cystic areas with focal solid areas which are gray white. Consistency is variable – soft to firm. Microscopy showed thecoma cells with pale vacuolated lipid rich cytoplasm and bland oval nuclei. Spindle cells are also seen. Leutinized thecoma showed leutein cells individually and in nests.

7.Fibroma: According to WHO classification, fibromas comprise 4% of overall neoplasms with a mean age incidence of 48yrs and 5 to 10% are bilateral[1,12]. In the present study, 4 lesions are reported as fibromas (9.09% of benign and 6.45% of overall neoplasms). Age group is from 47yrs to 53yrs. One lesion is bilateral (25% of the fibromas). Size of the lesions varied from 1x1x1cm to 6x3x2cms. On cut section all were solid and gray white. Microscopy showed the spindle shaped cells with bland central oval nuclei arranged in fascicles.

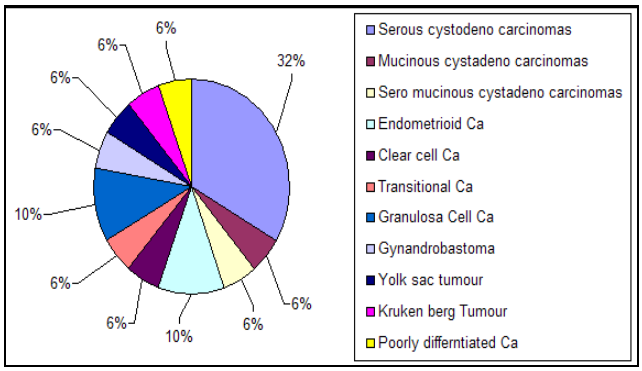
*8. Surface fibroma:*Only one lesion in present study is observed as surface fibroma in a patient of 26 yrs age and it is unilateral (2.27% of benign and 1.67% of overall neoplasms). Macroscopically it was a normal sized ovary with a cauliflower like firm growth on one end of the ovary externally. On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

B.Malignant lesions

Present study consists of 18 malignant lesions (29% of neoplastic and 3% of overall ovarian lesions). Unilateralism is observed in 11 lesions and remaining 7 lesions are bilateral. Age group ranged from 35yrs to 64yrs, seen in later age group than the benign lesions.

Epithelial ovarian cancer is the fourth most frequent cause of death in women. Epithelial tumors are the most prevalent of the ovarian tumors, accounting for 90% of all ovarian malignancies. In the present study, all 18 are the primary malignancies and the epithelial malignancies are 13 in number comprising 76.5% of the primary malignancies. The epithelial malignancies in the present study include 6 are serous malignancies, 1 is mucinous, 1 is seromucinous, 2 are endometrioid type, 1 is clear cell carcinoma and 2 are transitional cell carcinomas (as shown in table IV).

Table IV: Distribution of malignant lesions



1.Serous cystadenocarcinoma: Six lesions in present study are reported as serous cystadenocarcinomas (33.3% of malignant and 9.67% of neoplasms). These are observed in 40yrs to 60yrs age group. Four lesions are unilateral and two are bilateral.

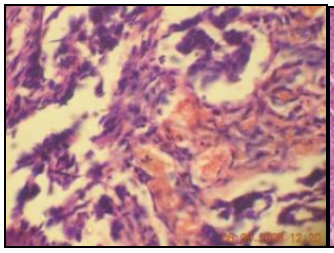
All the lesions are large masses. The size of the lesions varied from 5x3x3cms to 16x12x8cms. All the lesions are multi loculated on cut section and two lesions showed papillary excrescences on inner surface. All the lesions are partly cystic and partly solid. The solid areas in three lesions showed gray brown areas. Inner surface of one lesion is observed as ragged. Histology showed the epithelium resembling the fallopian tube epithelium with stromal invasion and cytological atypia[10]. Papillary tufting was seen in two cases. Extensive areas of necrosis and congested blood vessels were observed in almost all the lesions.

2.Mucinous cystadenocarcinoma: One lesion in present study was reported as mucinous cystadenocarcinoma (5.56% of malignant lesions). This was bilaterally present in a patient of 39yrs old. One side lesion was of 15cms diameter sized and the other side lesion measured 5cms in diameter. The larger mass cut section showed multilocular with cystic areas. Mass was filled with mucinous material and the inner surface showed the papillary excrescences. The other lesion also a multiloculated cystic lesion, filled with mucus and with papillary excrescences are observed. Microscopically endocervical type of epithelium was found with malignant features. Omentum showed secondary deposits of the tumor. Fallopian tube showed the hydrosalphingitic changes.

3.Seromucinous cystadenocarcinoma: In the present study, one unilateral lesion is included as seromucinous cystadenocarcinoma, observed in 60yrs old patient (5.56% of malignant lesions). The lesion was received along with the uterus and the other ovary. The friable tumor measured 6x4x3cms and it was soft to cystic in consistency. Gray brown in color and the cut section showed abundant myxoid material inside the lesion along with solid gray whte focal area. Histologically the combination of serous and mucinous type of epithelium with malignant changes & papillary patterns were seen without vascular cores[11]. The opposite ovary was normal.

4.Endometrioid carcinoma: Two lesions were reported as endometrioid carcinoma in our study (11.12% of malignant lesions). One was bilateral lesion found in 35yrs aged woman with omental secondary deposits and the other was unilateral in 47yrs old patient. Grossly the tumors were cystic and solid masses of 8x6x3cms and 5x5x3cms sized lesions respectively with variable consistency. Cut section of the both lesions showed thickened cyst wall, cysts filled with dark brown fluid. Solid areas are firm, gray white and nodular. Microscopically the tumor resembled the proliferative type of endometrial cells with malignant changes[15]. There are foci of hemorrhages and necrosis. Occasional areas showed sarcomatoid changes. Sections from the omentum and the mesentery showed the secondary deposits.

5.Clear cell carcinoma: Only one case of clear cell carcinoma was observed unilateral lesion in 44yrs old patient (5.56% of malignant lesions). Grossly it was solid, gray white mass of 8cms diameter. Cut section showed multiple yellow fleshy nodules placed in cystic spaces. Histology comprised of polyhedral cells arranged in sheets and papillary patterns. The tumor cells had abundant clear cytoplasm with malignant changes in the nuclei[16]. The epithelium resembled the gestational endometrium.



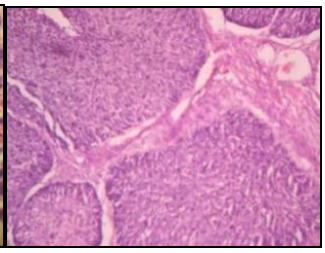


Fig.3 Endometrioid Ca. Fig.4Transitional Cell Ca.

6.Transitional cell carcinoma: Present study consists of 2 reports of transitional cell carcinomas (11.12% of malignant lesions). Both are unilateral lesions and the age of the patients is 48yrs and 53yrs. Gross appearance was solid, yellow to tan colored masses of 10 and 12cms diameter respectively. Microscopy showed the nested patterns of the tumor cells. The transitional epithelium was also seen in multilayered and papillary patterns[17]. Transitional cell carcinoma of urinary bladder was excluded in these cases (as it resembles).

7.Gynandroblastoma: It was observed in a 55yrs aged patient as an unilateral lesion (5.56% of malignant lesions). It was of 30x 28x 28cms sized multiloculated cystic mass with a solid area of 5x4x2cms. Solid area was gray white and dark brown in color. Cystic area was filled with hemorrhagic fluid.

Microscopically the tumor composed of oval to spindle and polygonal cells in hyper and hypocellular patterns. In the cellular areas, the 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. Some of the cells showed nuclear grooving. Hypocellular areas showed spindle to polygonal cells with vacuolated clear cytoplasm. Mitotic activity was about 4 to 6/10HPF. The histological picture was suggestive of mixed sex- cord stromal malignant tumor with all the four components and reported as Gynandroblastoma[18].

8.Granulosa cell tumor: Two out of 18 malignant lesions were reported as Granulosa cell tumors (11.12% of malignant lesions), seen in 50yrs and 56yrs aged patientas as unilateral lesions with size of 3x2x2cms and 4x3x3cms respectively. Grossly they were solid gray white with cystic areas[19]. The opposite ovary was apparently normal in both the cases. Microscopically both the lesions showed the tumor cells arranged in sheets and trabecular forms with characteristic focal Call-Exner bodies (small cavities filled with eosinophilic material) and nuclei showing longitudinal grooves (“coffee bean”).

9.Yolk sac tumor: This is the second most common type of germ cell tumor next to mature cystic teratoma. Occurs in childhood, adolescence and adult life (mostly <30yrs). Also known as endodermal sinus tumor[20,21]. In the present study included a single unilateral lesion of yolk sac tumor reported in a patient of19yrs age (5.56% of malignant lesions). Grossly it was of 9x9x 7cms sized mass. Cut section was solid and cystic with areas of hemorrhage and necrosis.

Microscopically cystic areas were lined by flattened epithelial cells with various degrees of atypia. Histologic picture was suggestive of classical pattern of perivascular formations (Schiller-Duval bodies) and the lesion was reported as yolk sac tumor.

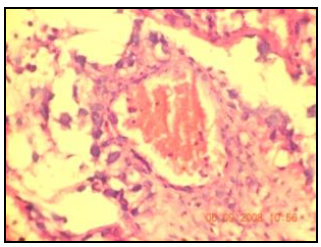


Fig.5 Yolk sac tumor

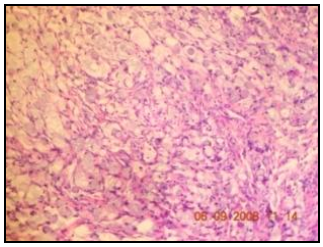


Fig.6 Krukenberg Tumor

10.Krukenberg tumor: The term Krukenberg tumor refers to a metastatic mucionous/signet-ring cell adenocarcinoma of the ovaries which typically originates from primary tumors of the G.I.tract, most often colon and stomach. Single case of Krukenberg tumor was reported in the present study as a bilateral lesion in 46yrs aged patient (5.56% of malignant lesions). Grossly the lesions are firm and yellow-white masses of 3x3x2cms each. Microscopic picture was resembling the primary tumor of the stomach. The signet-ring cells are observed. Focal segmental necrosis of the glands, oocasional presence of goblet cells were seen.

11.Poorly differentiated carcinoma: This is identified in a 45yrs old patient as an unilateral lesion (5.56% of malignant lesions). Gray-brown and solid macroscopically. Microscopic picture showed pleomorphic epithelial cells with bare hyperchromatic nuclei infiltrating diffusely into adipose tissue and fibrous tissue. there are areas of necrosis and hemorrhage. Some areas showed the tumor infiltration into ovarian stroma. The picture is suggestive of poorly differentiated carcinoma infiltration into ovarian stroma and into fibrofatty tissue.

A recent study (W G McCluggage J.Clin. Pathol 2008) from the Washington area of consecutive cases of ovarian carcinoma operated in a single large hospital (excluded consultation cases and included ovarian carcinosarcomas and primary peritoneal carcinomas, essentially all of which have an epithelial component of serous type) showed a different frequency of the various types of ovarian carcinoma. In that study, 68% of

ovarian carcinomas were 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 Bhatacharya 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 , Nipppon 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 impossible 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].

IV. CONCLUSIONS

Ovarian lesions are one of the common types of lesions found in the women of reproductive age group. Accurate diagnosis and typing according to recent and standard classifications like WHO Classification is helpful in the development of specific therapies, possibly including targeted therapies, for management of the various types of ovarian cancer. An attempt was made to study the age incidence, prevalence, morphological patterns and histological variants among various neoplastic lesions that occur in ovary. The results of the study are comparable with other similar studies and standard books substantiating the findings of the study.

About 414 ovaries showed normal histology and no specific pathological changes noted. This is may be due to the precautionary removal of ovaries at the time of hysterectomy or similar surgery. Some of these may contain hidden minute pathology which possible had not appeared in the sections studied as the total ovary was not being processed and studied.

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