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STUDY OF HISTOPATHOLOGICAL SPECTRUM OF OVARIAN LESION AT A TERTIARY CARE HOSPITAL

Pathology

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ABSTRACT

Introduction: Ovary is complex in its embryology, histology and steroid genesis with potential to develop non-neoplastic and neoplastic lesions. No definite screening program and the difficulty in early detection are main reasons for poor prognosis of ovarian cancer. **Aim:** To study frequency, clinical findings and histopathological spectrum of non- neoplastic and neoplastic lesions of ovary. **Methods:** The Study was descriptive observational cross sectional and conducted in the Pathology department from January 2019 to June 2022 at a tertiary care Hospital. **Results:** The commonest age presentation was 21-50 years of age group (67%). The symptoms of ovarian lesions were not very specific and pain in abdomen and menstrual disturbance were common symptoms. Most of the ovarian tumors were unilateral (86.92%) and of cystic in consistency (48.46%). Out of 214 lesions, 64 (30%) were non- neoplastic and 150 (70%) were neoplastic. Simple cyst was most common (29.9%) non-neoplastic lesion. Out of total 150 neoplastic lesions 89 (59.4%) were benign, 6 (04%) were borderline and 55 (36.6%) were malignant lesions. Among the neoplastic lesions, epithelial tumor (80%) was the most common. Out of them serous epithelial tumors (53.33%) were the common. The commonest germ cell tumor was mature teratoma and commonest sex cord stromal tumors was adult granulosa cell tumors. **Conclusion:** Non-neoplastic and neoplastic ovarian lesions include various morphological features with particular age wise distribution and majority lesions were neoplastic.

KEYWORDS

Neoplastic, Non-neoplastic, ovarian tumors

INTRODUCTION:

Ovaries are concerned with progeny production which are consist of totipotent sex cells and multipotent mesenchymal cell (Sawant & Mahajan, 2017). Ovarian cancer is one of the most lethal gynecologic malignancy. In 2018, it is the eighth most common cancer diagnosis and cause of cancer deaths in female, with estimated 2,95,000 cases and 1,84,000 deaths worldwide (Höhn et al., 2021). In most of the population-based cancer registries in India, the age-adjusted incidence rates of ovarian cancers vary between 5.4 to 8.0 per 100,000 population in different parts of the country (Indian Council of Medical Research, 2008; Parkin et al., n.d.).

Ovarian lesions have silent nature progression and vague nonspecific symptoms for which no satisfactory method of detection has been detected as yet. Ovarian neoplasms remain asymptomatic until massive ovarian enlargement causes compression of pelvic structures, ascites, abdominal distention or distant metastasis (Whittemore, 2010). By the time the tumor is discovered, in many cases the tumor has already spread beyond the ovary and is not amenable to cure.

Ovarian diseases of surgical importance can be broadly divided into Nonneoplastic lesions and Neoplasms (Ahmad et al., 2019). The WHO histological classification, which separates ovarian neoplasms according to the most probable tissue origin, from any of the three cell types in the normal ovary: The multipotent surface (coelomic) epithelium, the totipotent germ cells, and the sex cord-stromal cells. Surface epithelial tumors constitute the large majority of ovarian neoplasms and, their malignant forms, account for almost 90% of ovarian cancers. Germ cell and sex cord-stromal cell tumors are comparatively less common; although they account for 20–30% of ovarian tumors, they are collectively responsible for 10% of ovarian malignancies (Kumar, 2017). Histological subtyping of ovarian epithelial cancers is important as they differ in their mean age of presentation, 5-year survival, molecular abnormalities, association with familial syndromes, and sensitivity to chemotherapy and other treatment modalities. The findings of recent molecular studies, for the most part, support morphology-based classification system and also demonstrate that it accurately reflects both histogenesis and the underlying molecular abnormalities of the different ovarian tumor subtypes (John R. Goldblum, 2018). Some non-neoplastic lesions of ovary present with pelvic mass and associated with abnormal hormonal manifestations often mimicking ovarian neoplasm causing diagnostic confusion. Therefore, distinguishing non-neoplastic lesion from a neoplastic lesion is important for appropriate therapy and prognosis thereby avoiding unnecessary oophorectomy (M Maru & B. Menapara, 2019).

Histopathological examination is the most accurate way to differentiate between benign and malignant lesions and help in making the correct diagnosis and further management (Ahmad et al., 2019). No definite screening program and the difficulty in early detection are main reasons for poor prognosis of ovarian cancer. However, in the present time due to availability of sensitive imagine techniques & advancement of cytodiagnosis, early detection and prognostic predilection is possible (M Maru & B. Menapara, 2019).

The purpose of this institutional study was to determine the histopathological spectrum and frequency of ovarian lesions in relation to age, laterality and clinical findings & compare their trends reports from other studies.

MATERIAL AND METHODS:

The present study was conducted in the Department of Pathology at tertiary care hospital affiliated to Medical College. The cases included were those specimens and biopsies received from Department of Obstetrics and Gynecology and further processed at the Department of Pathology from January 2019 to June 2022. It was a Descriptive Observational cross-sectional retrospective study. Total 191 cases with 214 histopathologically diagnosed ovarian lesions were included.

Inclusion Criteria: All biopsies and specimens of ovary, which were adequate and histopathologically proven non-neoplastic and neoplastic lesion received as either as a solitary specimen or part of total abdominal hysterectomies or cystectomies.

Exclusion Criteria: The following criteria were excluded from the study:

- Normal ovaries
- Inadequately preserved specimens with handling artefacts
- Specimens with Improper clinical record (History and

examination)
- Specimen of post-chemotherapy ovaries

Data And Sample Collection:
The records of specimens received in histopathology section, department of pathology. The biopsies and specimens were received in glass or plastic vials containing 10% formalin solution. Gross examination of specimens was done under heads of laterality, size, external surface, consistency and cut-section appearance like solid, cystic or both. Biopsies/specimens were fixed as early as possible by 10% neutral buffered formalin & processed preferably within 24 hours. Following fixation, the tissues were processed, embedded in paraffin and 5 µ thick sections were cut, which was stained with Hematoxylin and Eosin for morphological assessment. Hematoxylin & Eosin Staining (H & E) were done by manual method. Tissue sections were examined under light microscopy for histomorphological features. Special stains such as reticulin and Periodic Acid Schiff (PAS) were performed whenever required. The neoplastic lesions were classified according to WHO International Classification of Ovarian Tumours 2020.

Statistical analysis: Patient details, clinical presentation, along with gross examination and histomorphological findings, were entered into an Excel sheet. Descriptive statistical analysis was performed, appropriate charts and graphs were created, and the results were expressed as a percentage.

OBSERVATION AND RESULTS:
The present study was conducted in department of pathology, tertiary care hospital affiliated to medical college during period from January 2019 to June 2022. The specimens of 191 patients with 214 ovarian lesions on either and/or both sides were examined in the present study. Out of 214 ovarian lesions, 64 (30%) were non- neoplastic and 150 (70%) were neoplastic.

Age Wise Distribution: In present study, the ovarian lesions had wide range of distribution and found to occurs in age group of patients ranging from 1st to 8th decade of life. As seen from the above table no 1, the youngest age of presentation was 5 years while the oldest was 80 years. The most common age of presentation i.e. 67% cases were in 21-50 years age group. Among non-neoplastic lesions, maximum 38.1% cases were in 31-40 years age group, while among benign neoplastic lesions, highest number of cases i.e. 25.9 % cases were in 31-40 years age group. However, among malignant lesions, highest number of cases i.e. 32.65 % were in 51-60 years of age group.

Table 1: Age group wise case distribution of ovarian lesions according to nature of lesions (n=191)

Age group	Non-neoplastic	Neoplastic			Total
		Benign	Borderline	Malignant	
0-10	-	1	0	0	1
11-20	05	4	0	1	10
21-30	18	18	1	7	44
31-40	21	21	2	4	48
41-50	07	15	1	13	36
51-60	02	10	1	16	29
61-70	02	7	1	7	17
71-80	-	5	0	1	6
Total	55	81	6	49	191

Clinical Features: Patients presented with variety of symptoms and clinical complaints. Commonest complaint was pain in abdomen for 136(70.1%) cases followed by menstrual disturbances for 65(33.5%) cases. Other presenting features included abdominal distension for 37 (10.1%) cases, ascites for 14(7.2%) cases and discharge per vagina 4(2.06%) cases.

Laterality Of Lesions: Out of total 191 cases of ovarian lesions 25(13.08%) cases were bilateral and rest 166 (86.92%) cases involved either right or left ovary.

Consistency Of Lesions: In present study, out of 214 lesions, 194 were received as specimen and rest 20 cases were biopsy for which gross details were not possible. According to gross findings and consistency of 194 lesions, majority of the lesions were of cystic in consistency i.e. 94 (48.45%). Amongst the rest cases, 77 (39.7%) were mixed in consistency showing both solid and cystic areas. 23 (11.85%) were solid in consistency.

Non-neoplastic Lesions: out of total 64 non-neoplastic lesions, the most common lesion reported was simple cyst in 20 (29.9%) cases followed by corpus luteal cyst in 15 (22.5%) cases. Other non-neoplastic lesions include follicular Cyst 07 (10.8%) cases, chocolate Cyst 07 (10.8%) cases, hemorrhagic Cyst 07 (10.8%) cases, ovarian Torsion 4 (6.1%) cases, ectopic Pregnancy 03(4.6%) and hydatid Cyst01(1.5%) cases.

Neoplastic Lesions: Among 150 ovarian neoplastic lesions, most common was benign tumors with 89(59.4%) lesions followed by malignant tumors in 55(36.6%) lesions and borderline tumors in 6(4%) lesion.

Histopathologic Types: The tumors are classified according to WHO classification of ovarian tumor, 2020 and frequency of different types of tumors noted as per table 2. Histopathologically, surface epithelial tumors (120 cases; 80%) were the most common subtype followed by germ cell tumors (17 cases; 11.33%) and then sex cord tumors (9 cases; 06%). The most common neoplastic lesion as well most common benign tumor was serous cystadenoma (39 cases: 26%). Serous carcinoma (35 cases; 23.4%) was the most common malignant tumor. The most common germ cell tumor was mature cystic teratoma (14 cases; 9.33%). The most common sex cord-stromal tumor was adult granulosa cell tumor (4 cases; 2.67%.). Other neoplastic lesions include lymphoid tumor-Non-Hodgkin Lymphoma (01 case; 0.67%) and secondary tumors (3 cases; 2%) of the total neoplastic ovarian lesions.

Table 2: Distribution Of Histopathological Spectrum Of Various Neoplastic Ovarian Lesions (n=150)

	Types of Tumors		No. of cases	Percentage (%)
I	**Epithelial tumors**		**120**	**80**
A.	Serous tumors		80	53.33
	Benign	Cystadenoma	39	26
		Cystadenofibroma	04	2.6
	Borderline		02	1.30
	Malignant		35	23.40
B.	Mucinous tumors		35	23.40
	Benign	Cystadenoma	27	18
	Borderline		04	2.67
	Malignant		04	2.67
C.	Endometrioid Carcinoma		02	1.30
D.	Benign Brenner tumors		01	0.67
E.	Clear cell Carcinoma		01	0.67
F.	Carcinosarcoma		01	0.67
II	**Sex-cord stromal tumors**		**09**	**06**
	Fibroma		03	02
	Fibro-thecoma		01	0.67
	Adult Granulosa cell tumor		04	2.67
	Sex-cord stromal tumors with Annular Tubules		01	0.67
III	**Germ Cell tumors**		**17**	**11.33**
	Mature cystic Teratoma		14	9.33
	Dysgerminoma		03	02
IV	**Others**		**04**	**2.67**
	Lymphoid Tumor	Non-Hodgkin Lymphoma	01	0.67
V	**Secondary tumors**		**03**	**02**
	Metastatic carcinoma		02	1.33
	Krukenberg tumor		01	0.67

Distribution Of Surface Epithelial Tumor
Out of 120 surface epithelial tumor, serous epithelial tumors were most common i.e. 80 (66.7%) followed by mucinous tumor i.e. 35(29.3%). Among 80 serous tumors, 39 (32.5%) lesions were of serous cystadenoma which was most common. Most commonly encountered malignant surface epithelial tumor was serous carcinoma was accounting for 25 (29.3%) lesions.

Among 35 lesions of serous carcinoma 22 lesions were diagnosed as a high- grade serous carcinoma, 01 lesion was low grade serous carcinoma and remaining 12 lesions were biopsies which were not sufficient to be classified as high grade or low-grade serous carcinoma. Rest of the epithelial tumors are subdivided as per chart no. 1

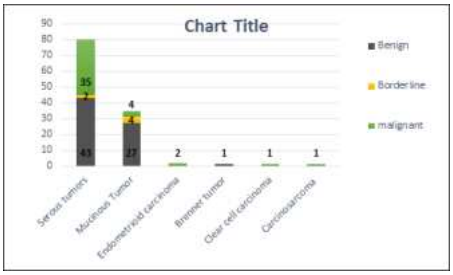

Chart no. 1: Subtypes distribution of Surface Epithelial Tumor (n=120)

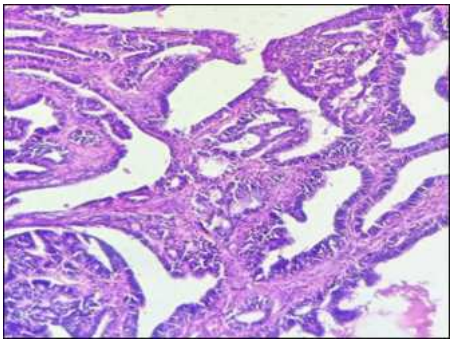

Figure 1: Endometrioid Carcinoma (H&E;10x)

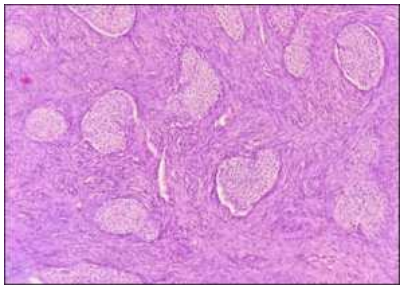

Figure 2: Benign Brenner Tumor (H&E;10x)Distribution of germ cell tumors

Out of 17 Germ cell tumors, benign mature cystic teratoma was the commonest germ cell tumor i.e. 14(82.4%) followed by 3 (17.6%) lesion of malignant germ cell tumor was reported as a dysgerminoma (Figure 3).

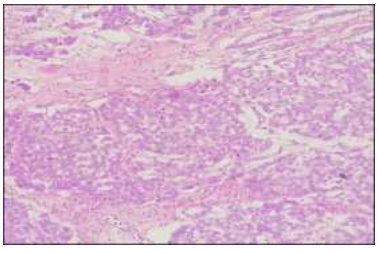

Figure 3: Dysgerminoma (H&E; 40x)

Distribution Of Sex Cord Stromal Tumor

Out of 9 sex cord stromal tumor, most common was adult granulosa cell tumor for 4 (44.44%) lesions (Figure 4) followed by fibroma accounting 3 (33.34%) lesions. There were 1 (11.11%) lesion of fibro-thecoma (Figure 5) and 1 (11.11%) lesion of sex-cord stromal tumor with annular tubules reported in this study.

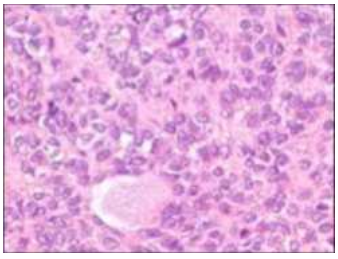

Figure 4: Adult granulosa cell Tumor (H&E; 40x)

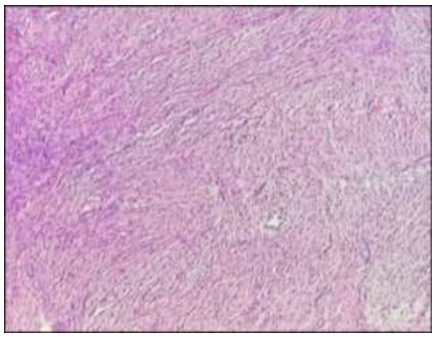

Figure 5: Fibroma of ovary (H&E; 10x)

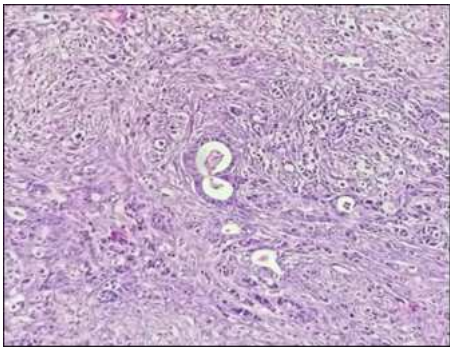

Figure 6: Krukenberg Tumor (H&E; 10x)

DISCUSSION:

In this present study histopathologically diagnosed 217 ovarian lesions from 194 patients were evaluated at Department of Pathology, tertiary care hospital affiliated to medical college during the period from January 2019 to June 2022.

In present study, no age group was exempted from occurrence of ovarian lesions and the majority of the cases reported were in the age group of 31-40 years, which is in concordance with Garg N et al (Neha Garg, 2017) and M Uma et al (M et al., 2015) studies as mentioned above except in Ahmad N et al (Ahmad et al., 2019) study in which majority of the lesions occurred in 21-30 years. This difference may be due to varying local demographic profile of the patients attending the institute. The age distribution also varied according to the nature of the ovarian lesions. The most common age group for incidence of non-neoplastic lesions was 31-40 years in present study which is similar to study by Modi et al (Modi et al., 2018) while is it 21- 30 years in the study by Ahmad N et al (Ahmad et al., 2019).

The majority of benign tumors were occurred between 31-40 years of age group followed by 21-30 years of age group, which is in concordance with other similar studies (Jha R, 2008; Modi et al., 2018; M et al., 2015; S. A. Badge, 2013).In present study, the majority of malignant tumors were occurred between 51-60 years of age group which is similar with Sampurna K et al (Sampurna & Jyothi, 2022) while in contrast with R. Jha & S Karki et al (Jha R, 2008) in which 41-50 years of age group is more common.

Most common clinical presentation was pain in abdomen in 70.1% of case. This is in concordance with Mankar D et al (Mankar & Jain, 2015) who reported 33.48% of cases while in contrast with Gupta SC et al (SC Gupta, 1986) in which abdominal distension is most common clinical findings (60.5%). The ovarian cancer remains usually asymptomatic until the size of the tumor becomes large enough to interfere with other pelvic or abdominal organs or until it entraps nerve tissue and causes pain as observed by Blansterin (Blaustein A., 1981) . All the percentage of clinical complains been calculated in present study are not by considering one main clinical complaint for each patient. It was based on the fact that one patient might present with pain in abdomen as chief complaint but might be suffering from abdominal fullness and menstrual disturbance simultaneously. That is why in present study percentage value for each clinical complaint may be different than other comparative studies.

In present study, 25 cases (12.89%) of bilateral ovarian lesions were

reported. Similar findings have been reported by Gupta N et al (N. Gupta et al., 2019) and Verma et al (Verma K, 1981) who reported bilateral ovarian specimen with 12.3% and 11.91% respectively. This is higher than 9.1% reported by Tyagi et al (Tyagi SP, 1993).

On gross examination, cystic consistency of ovarian tumor was most commonly observed. Similar findings have been reported by Gupta N et al (N. Gupta et al., 2019), Kanthikar S. N. et al (Nagnath, 2014) and Kanpurwala et al (Kanpurwala, 2016) who reported cystic as a most common consistency with 56%, 44.78% and 63.69% respectively. However, the second common consistency was solid in Kanpurwala et al (Kanpurwala, 2016)with 18.47%. Possibly because of inclusion of a greater number of malignant tumors (35.66%) which are commonly solid in consistency.

Out of total 214 specimens of ovary studied, 64 (30.8%) accounted for non-neoplastic lesions. Amongst those, the highest number of cases reported were of simple cysts (29.9%) followed by corpus luteal cysts (22.5%) of the total non-neoplastic lesions. This finding in present study was in concordance with studies conducted by Modi et al (Modi et al., 2018) and Parvataka A et al (Annapurna Parvatala, 2015) who also reported similar results .However, these similar studies are in contrast with study done by Ahmad N et al (Ahmad et al., 2019) and Choi and Kim et al (Choi et al., 2003) where corpus luteum cyst was the commonest while studies done by Thakkar N. et al (Nirali N. Thakkar, 2015) from India and Maliheh et al (Maliheh Arab, 2010) from Iran in their studies reported follicular cysts as the most common non-neoplastic lesion. The reason for this variation cannot be fully ascertain, but may be attributable to environmental, hormonal, and genetic influences.

In present study, out of 150 neoplastic lesions most common neoplastic lesion was benign tumors 89(59.4%) lesions followed by malignant tumors in 55(36.6%) lesions and borderline tumors in 6(4%) lesion. Our findings are in concordance with other studies as per table no 3.

Table 3: Comparative Analysis Of Benign, Borderline And Malignant Tumors Of Ovary

Study	Benign (%)	Borderline (%)	Malignant (%)
Tyagi et al (Tyagi SP, 1993)	71.7	4.4	23.7
Mankar DV and Jain et al (Mankar & Jain, 2015)	63.04	5.8	31.2
Gupta N et al (N. Gupta et al., 2019a)	63.7	5.2	31.1
Present study	59.4	04	36.6

Based on histomorphological features, frequency of surface epithelial tumors was the commonest (80%) followed germ cell tumors (11.33%), sex-cord stromal tumors (6%) and other tumors include lymphoid tumor- Non-Hodgkin Lymphoma (0.67%) and secondary tumors (2%). Ovary is a common site for metastasis. The most common sources are stomach, large bowel, appendix, breast, uterus, lung and skin. Adenocarcinoma of Large bowel are important because of their relatively high frequency and their ability to stimulate primary ovarian carcinoma, mainly the mucinous and endometrioid type and sometimes clear cell type al (Rosai and Ackermann's Surgical Pathology: First South Asian Edition., n.d.) so. Similar observations seen in others study as per table 4.

Table 4: Comparative Analysis Of Histopathogical Spectrum Of Neoplastic Ovarian Lesions

Histological Types	H. Makwana et al (Makwana et al., 2014)	R Jha & S Karki et al (Jha R, 2008)	Gupta N et al (N. Gupta et al., 2019)	Vaishali B. et al (Vaishali Bhankhodia, 2018)	Present Study
Surface Epithelial Tumor	65.7	52.1	59.3	53.04	80
Sex cord stromal tumors	9.29	3.1	3.8	9.56	06
Germ Cell Tumors	22.86	42.2		36.5	11.33
Others- Lymphoid tumor-NHL	-	-	0.5	-	0.67
Metastasis	2.1	2.4	1.9	0.9	02
Metastatic carcinoma	-	1.2	1.9	-	1.30
Krukenberg tumor	2.1	2.4	-	0.9	0.67

In present study, Out of 120 epithelial tumor, most common was serous tumor for 80 cases (66.7%) followed by mucinous tumor for 35 cases (29.3%). This is similarly seen in S. A. Badge et al (S. A. Badge, 2013) , H makawana et al (Makwana et al., 2014), Gupta N et al (N. Gupta et al., 2019) and Vaishali B. et al (Vaishali Bhankhodia, 2018) and Chhanda SC et al (Chhanda M. Dasgupta A, 1991). Benign brenner tumor, endometrioid carcinoma, clear cell carcinoma and carcinosarcoma (malignant mixed muellerium tumor) are rarely found in present study and other studies also as per table no. 5

Table 5: Comparative Analysis Of Surface Epithelial Tumors

Histological Types	S. A. Badge et al(S. A. Badge, 2013)	H. Makwana et al (Makwana et al., 2014)	Chhanda SC et al(Chhanda M. Dasgupta A, 1991)	Gupta N et al(N. Gupta, 2019)	Vaishali B. et al(Vaishali Bhankhodia, 2018)	Present Study
Serous Tumors	52.7	65.3	59.5	41.4	62.1	66.7
Mucinous tumor	32.2	15.6	38.7	34.8	32.7	29.3
Benign Brenner tumor	1.2	3.2	1.6	-	1.6	0.8
Endometrioid Carcinoma	1	4.3	-	2.6	-	1.6
Clear Cell Carcinoma	3	2.1	-	1.6	1.6	0.8
Carcinosarcoma (malignant mixed muellerium tumor)	-	-	-	-	1.6	0.8

In present study, out of 17 germ cell tumors, mature cystic teratoma (14 cases; 82.3%) was the most common germ cell tumor followed by dysgerminoma. This was similarly observed in S. A. Badge et al (S. A. Badge, 2013) , H. Makwana et al (Makwana et al., 2014), Vaishali B. et al (Vaishali Bhankhodia, 2018)and Gupta N et al (N. Gupta et al., 2019a).

In present study, out of 9 sex cord stromal tumor, most common was adult granulosa cell tumor for 4 (44.44%) lesions followed by fibroma accounting 3 (33.34%) lesions. There were 1 (11.11%) lesion of fibro-thecoma and 1 (11.11%) lesion of sex-cord stromal tumor with annular tubules reported in this study which is similarly found in study done by chhanda SC et al (Chhanda M. Dasgupta A, 1991) with 75% lesions. while fibro-thecoma was most common sex-cord stromal tumor in studies done by S. A. Badge et al (S. A. Badge, 2013) with 66.66% and R Jha & S Karki et al (Jha R, 2008) with 80%.

CONCLUSION:

Ovarian lesion is a silent menace that reveled as a tremendous clinical challenge to gynecologist, oncologist and radiotherapist. So, correct histopathological diagnosis of ovarian lesions is of prime importance in view of their behavior prediction and also for proper management of patient. The present study reveals that ovarian tumors are common neoplasm of female genital tract having broad group of lesions from non-neoplastic to neoplastic benign, borderline and malignant lesions. We have compared these lesions with various parameters like age, clinical presentation, location and different histological subtypes which guide the overall management and prognosis of various ovarian lesions. The ovarian neoplasms in our institute represented a wide histomorphological spectrum. The frequency of the distribution of neoplasms was similar to the reports in the literature. However, the incidence of malignant tumors was higher in our setup, as our institute is a tertiary care center. The observations of our study and their assessment will provide valuable insight of distribution pattern of ovarian neoplasms.

Limitation Of Study: This present study had some limitation like long term follow up of patients was not possible and thus the prognosis of most patients was not known. Other limitation is that this is single center study. Multicentric studies with large number are needed to validate our results.

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