Histomorphological study of ovarian tumors – A study from tertiary care centerin north Karnataka.

Dr. Anuradha Patil[1] , Dr. Ranjana Ranade[2], Dr. N.S. Kamkeri[3]

[1](Assistant professor,Department of pathology,MGM medical college and Hospital,Aurangabad,Maharashtra)
[2](Associate professor, Department of pathology, JGMMC, Hubli,Karnataka)
[3](Professor,Department of Pathology, KIMS, Hubli, Karnataka)
Corresponding author - Dr. Anuradha Patil

Abstract
Background :Ovary is an important site for both benign and malignant tumors in the female genital tract. Due to the deep seated nature of ovarian cancers, lack of screening tests and non specific clinical features these patients often present at an advanced stage of disease. Accurate histopathological typing and grading of ovarian tumors is needed for early diagnosis and appropriate treatment of the patient.
Materials and methods:This was a descriptive cross sectional study conducted over a period of three and a half years from 1stDecember 2008 to 31stMay 2012 in a medical college in north karnataka. Sample consisted of all the neoplastic specimens of ovary received in this time frame. Clinical, gross and histomorphologic features of all benign and malignant ovarian tumors were evaluated. Percentage , frequency and chi square test was used for quantitative data as required, a p value of <0.05 was considered significant.
Results:amongst a total of 218 cases of ovarian tumors studied, surface epithelial tumors were the most common category accounting for 72% followed by germ cell tumors(16%) , sex cord stromal tumors(10%) and metastatic tumors and other tumors(2%). Serous cystadenoma was the most commonon benign tumor followed by mucinous cystadenmoma. Serous cystadenocarcinoma (37% of malignant tumors) was the most common malignant tumor with two thirds cases presenting with bilateral ovarian involvement. One rare case of cavernous hemangioma was also seen.
Conclusion :surface epithelial tumors account for vast majority of both benign and malignant ovarian tumors . Bilateral involvement of ovaries is more common in malignant ovarian tumors.Accurate histomorphological diagnosis and grading of ovarian tumors is important for proper management of the patient.
Key words:Ovarian tumors, serous cystadenoma, histomorphology.

I. INTRODUCTION

The ovary is made up of germ cells,follicular cells and mesenchymal tissues each with its own potential to form tumor. Therefore, ovarian neoplasms exhibit a complex wide spectrum involving a variety of histological tissues ranging from epithelial tissue, connective tissue,specialized hormone secreting cells and germinal and embryonal cells.[1] Indian cancer registry data project ovary as an important site of cancer in women comprising up to 8.7% of cancers in different parts of country.[2].Lack of cancer awareness, unavailability of proper screening tests and variable pathology are responsible for the patients presenting in advanced stage of disease.[3] In todays era of molecular pathology, histological typing and grading of ovarian tumors is still important for further molecular and immunohistochemical tests and appropriate treatment of the patient.

Considering wide variation in histopathological presentations of different neoplasms of ovary systematic evaluation on large samples is much felt need. This study is undertaken to analyze histopathological spectrum of ovarian tumors in different age groups over a good time frame.

II. MATERIALS AND METHODS

This study was conducted over a period of three and a half years from 1stDecember 2008 to 31stMay 2012 in the Pathology department of a tertiary care hospital in north Karnataka. Sample consisted of all the neoplastic specimens of ovary received in this time frame. With this purposive sampling method, we could assess 218 samples of ovarian neoplasms.
Study design: Observational cross sectional retrospective study.

Study location: this study was done in a tertiary care center of north Karnataka in the department of Pathology, Karnataka institute of medical sciences, Hubli, Karnataka.

Study duration : 1[st]December 2008 to 31[st]May 2012

Sample size :218 samples of ovarian tumors.

Inclusion criteria:All neoplastic lesions of ovary received in the department of pathology were included in the study.

Exclusion criteria:Non neoplastic lesions of the ovary were excluded from the study.

Procedure: Demographic and clinical data was recorded in a predesigned proforma. Gross examination of specimen was done carefullywith special attention to solid areas, areas adjacent to ovarian surface and papillary projections and these details were recorded in the proforma. After overnight fixation in 10% formalin sections of specimen were given.Sections of 3-5 microns thickness were cut and stained with hematoxylin and eosin in all cases. Special stains were done wherever needed. A minimum of 4 to 5 sections from representative area of tumor were selected for histological assessment. The tumors were classified and studied as per WHO classification[4]. All these details were recorded in proforma.

Statistical analysis: Quantitative data was analyzed by using descriptive statistics. Frequency, percentage and Chi-squire test was used as applicable. Significance of p value was set as <0.05. Qualitative data was grouped together as per WHO Classification of ovarian tumors.

III. RESULTS

The total of 14628 histopathology specimens were received in the department during study period, of which the ovarian neoplasms constituted only 218 (1.49%). Out of 218 tumors, 175(80.28%) were benign, 3(1.38%) were borderline and 40(18.35%) were malignant. Majority (49.10%) of cases were seen in the reproductive age group that is 21 -40 years of age. Majority (92, 52.57%) of benign neoplasm were seen between 20-40 years age. Most of the malignant tumors (11, 27.5%) were seen in age group 41- 50 years (Table 1)). When laterality of tumor was assessed, 199 (91.28%) cases were unilateral and nineteen (8.71%)cases were bilateral (table 2). Majority (170,97.15%) of benign ovarian tumors were unilateral, and significant number (14, 35%) of malignant ovarian tumors had bilateral presentation.This difference in laterality was highly significant (χ^2=33.16, P < 0.0001

Gross features of ovarian tumors -Mean size of ovarian neoplasms was 14.52 (SD=5.2) centimeters. In the present study, majority, 146 (66.97%) of ovarian neoplasm were cystic in consistency, of which most of them were benign tumors 145 (99.31%). Forty seven (21.56%) had mixed consistency i.e. solid and cystic areas, among them 29 (61.70%) were malignant tumors. Twenty five (11.47%) had solid consistency, of which 11(44%) were malignant and 14(56%) were benign (Table 3) The association between gross findings and nature of neoplasm were found to be statistically highly significant.

Table 1: shows age distribution of different categories of ovarian tumors

Age	Benign	Borderline	Malignant	Total	Percentage
1-10	0	0	0	0	0
11-20	10	0	5	15	6.88
21-30	46	0	7	53	24.31
31-40	46	1	7	54	24.77
41-50	35	1	11	47	21.56
51-60	19	0	6	25	11.47
>61	19	1	4	24	11.01
Total	175	3	40	218	100

Table 2:Showing laterality of ovarian tumors. $\chi^2$33.16, P < 0.0001

Laterality	Benign	Borderline	Malignant	Total	Percentage
Unilateral	170	3	26	**199**	**91.28**
Bilateral	5	0	14	**19**	**8.71**

Table 3: Showing gross consistency of ovarian tumors .

Gross consistency	Benign	Borderline	Malignant	Total	Percentage
Cystic	145	1	0	146	66.97
Solid	14	0	11	25	11.47
Mixed	16	2	29	47	21.56

Histopathological Classification:

Based on microscopic appearance, these tumors were classified as per then prevalent WHOclassification system of ovarian neoplasms.(Table 4)Surface epithelial tumors were most common(72%) followed by germ cell tumors(16%), sex cord stromal tumor(10%), metastatic tumors(1.3%). Serous cystadenoma was the most common benign tumor seen in this sudy followed by mucinous cystadenoma. Serous cystadenocarcinoma was the most common malignant tumor encountered in this study. Amongst the germ sell tumors benign cystic teratoma was the most common tumor while in the sex cord stromal tumor category granulosa cell tumor was the most common tumor encountered in this study. There were three metastatic tumors to ovary in this study, in one case the primary as carcinoma colon while in other two cases the primary was not known. One rare case of cavernous hemangioma was also seen.

Table 4: Shows classification of ovarian tumors according to WHO classification.

		Histopathological type	No. of cases	%
		Surface epithelial Stromal tumors	**157**	**72.02**
I	1	Serous Cystadenoma	73	28.44
	2	Serous cystadenocarcinoma	15	6.8
	3	Mucinous cystadenoma	52	23.8
	4	Mucinous borderline tumor	3	1.38
	5	Mucinous cystadnenocarcinoma	7	3.2
	6	Benign Brenner tumor	2	0.92
	7	Benign mixed epithelial tumor	2	0.92
	8	Endometroid cystadenofibroma	3	1.38
		Sex-cord stromal tumors	**22**	**10.09**
II	9	Adult Granulosa cell tumor	10	4.59
	10	Fibroma	5	2.29
	11	Fibrothecoma	7	3.21
		Germ cell tumor	**35**	**16.06**
III	12	Benign cystic teratoma	27	12.39
	13	Immature teratoma	2	0.92
	14	Malignant mixed germ cell tumor	2	0.92
	15	Dysgerminoma	3	1.38
	16	Struma ovarii	1	0.46

IV	Metastases to ovary	3	1.38
V	Mesenchymal tumors	1	0.46

Fig 1: Gross photograph of endometroid cystadenofibroma showing cystic and solid areas.

Fig.2 Microphotograph of endometriod cystadenofibroma showing benign endometrial type glands in a fibrous stroma.(H&E,100X)
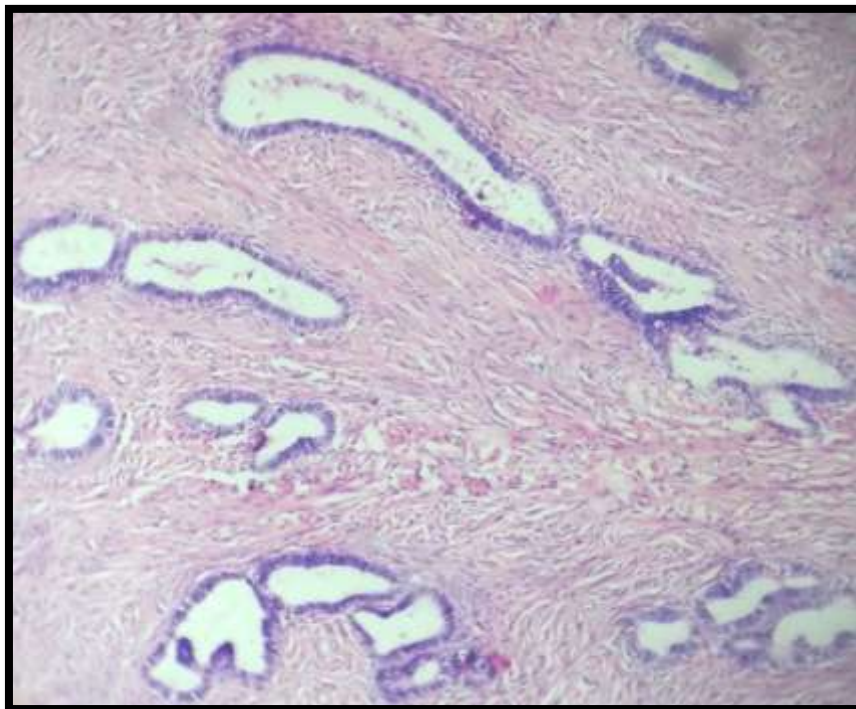
Fig. 3: Gross picture of benign Brenner tumor with nodular external surface and stretched fallopian tube

Fig. 4: Microphotograph of benign Brenner tumor showing nests of transitional cells in a fibrous stroma.(H&E,100)
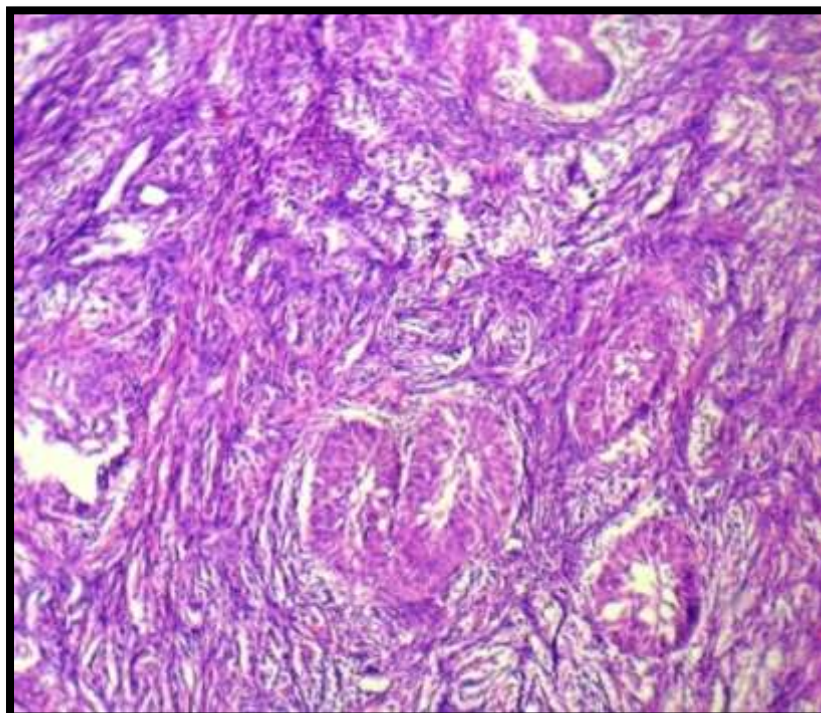
Fig. 5:Microphotograph of adult granulose cell tumor showing groups of cells surrounded by reticulin. (Reticulin stain, 100X)
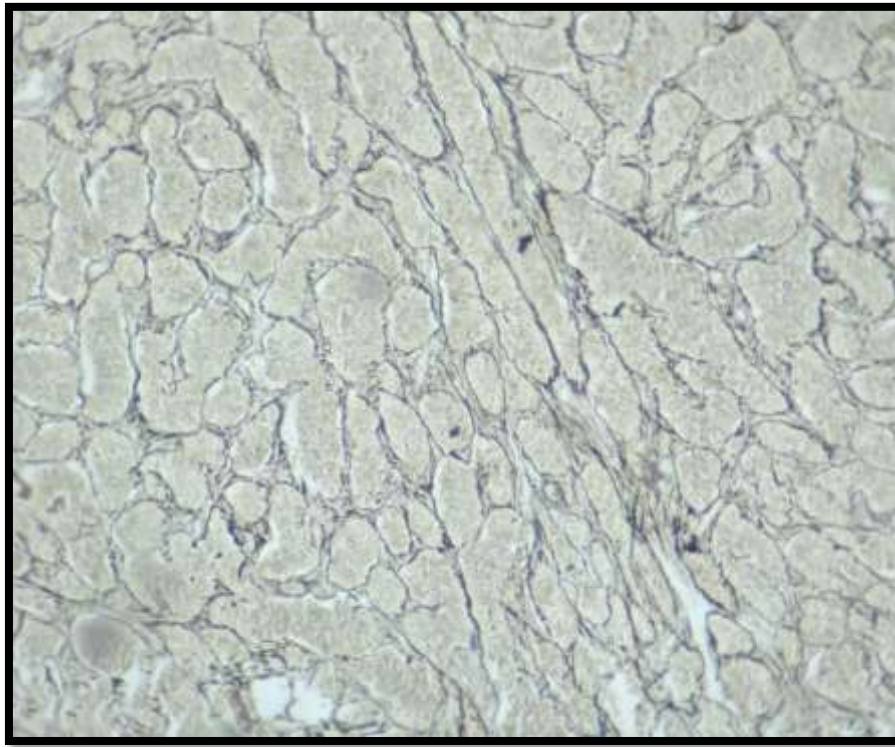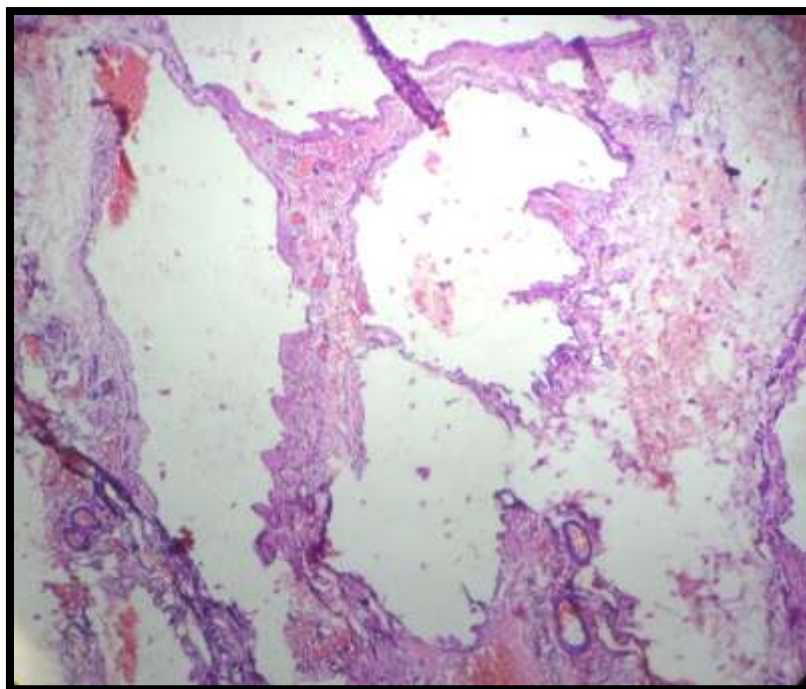

Fig. 6: Microphotograph of cavernous haemangioma showing dilated vascular channels.(H&E, 100X)

IV. DISCUSSION

Diagnosis of ovarian tumors can be difficult due a variety of conditions that can affect the ovaries and present with similar clinical and radiological manifestations. Knowledge of morphology and age specific characteristics can help refine the diagnosis.[5]A wide range of age distribution of ovarian tumors was seen in our study, youngest being 14 years old and eldest was 84 years old lady. Majority of ovarian tumors were seen in reproductive age group of 3rd to 5th decade similar to the studies by Mondal et al.; andSheikh et al.[6,7]Majority of benign ovarian tumors were seen in 3rd and 4th decade, similar results were reported in two other studies.[6,8] The incidence of ovarian carcinoma increases with age and peaks between the ages of 55-64 years.[2]In our study most of the malignant tumors were seen in 5th and 6th decade ,similar observations were made in a study by R Sindhuja et al. [9]

Majority of ovarian tumors in our study were of cystic consistency (67%) followed by tumors with mixed consistency(21.5%) and tumors of solid consistency(11.5%) . Similar results were reported by Gupta N et al and Garg et al.[10,11] Majority of benign tumors were cystic in consistency while most of the malignant tumors were solid or of mixed consistency, this is in agreement with studies by Kanthikar et al., and Geeta et al.[12,13] Out of 218 cases 175(80.3%) were benign, 3(1.4%) were borderline and 40(18.3%) were malignant, similar findings were observed in in other studies.[6,10]

Histomorphological distribution of ovarian tumors was similar to that seen in studies by Mankar et al et al. and Patil RK et al.[14,15]withsurface epithelial tumors being most common (72%) followed by germ cell tumors (16%), sex cord stromal tumors (10%) and metastatic tumors(1.5%).When laterality of the tumors was assessed it was noted that bilaterality was common in malignant tumors (74% of bilateral tumors). Most common malignant tumor that had a bilateral presentation was serous cystadenocarcinoma accounting for 10(52%) out of a total of 19 bilateral cases , similar observation was made in studies by Mondal et al.[6]ovarian serous carcinomas usually present as large mass with bilateral presentation in two thirds of cases. [16]

Serous cystadenoma (41.4%) was the commonest benign tumor in this study followed by mucinous cystadenoma (33.12%) and mature cystic teratoma. Similar observations were made in a study by Gupta N et al and Kalyani et al.[10,17]However, sheikh et al. reported mature cystic teratoma(30.6%) as the most common benign tumor in their study[.7]Serous cystadenocarcinoma(25% of all malignant tumors) was the most common malignant tumor which was comparable to two other studies.[7,17]

Other interesting epithelial tumors were three cases of benign endometroid cystadenofibroma (figures 1 and 2), two cases of benign brenner tumor (figures 3 and 4) and two cases of benign mixed tumors were seen. Mixed tumors showed benign Brenner and mucinous cystadenoma components. Brenner tumors are associated with another tumor type, usually mucinous cystadenoma in 20% of cases.[18]

Amongst germ cell tumors mature cystic teratoma was most common. Other tumors in this category were dysgerminoma, immature teratoma, mixed germ cell tumors and one case of strumaovariiwas seen. Both the cases of immature teratoma showed primitive neuroepithelial tissue based on which they were graded.In the sex cord stromal tumor category adult granulosa cell tumor(figure 3) was most common. Similar observations were made in other two studies.[6,10] The tumor cells in a case of adult granulosa cell can sometimes be spindled mimicking cellular fibroma or sometimes the cells can be luteinized mimicking a thecoma, we encountered one such case in our study, so we performed a reticulin stain(figure 5) . Reticulin stain is of great aid in his differential as it outlines aggregates of neoplastic cells in zones of granulosa cell neoplasia whereas in thecomas and fibromas there is individual cell investment.[19]

One rare case of cavernous hemangioma was seen in our study. It was seen in 18-year-old girl and measured 7x7 cms. Microscopy showed thin-walled cavernous spaces lined by endothelial cells (Figure 6). These are rare tumors with only 60 cases reported so far.[20] Most of these tumors are small and detected incidentally while larger tumors may present with abdominal pain and ascitis. It has been postulated that hyperestrogenism caused by pre existing stromal leuteinization of ovaries may stimulate the development of ovarian hemangioma due to the growth stimulatory effects of estrogn and expression of estrogen receptors by hemangioma. [21]

V. CONCLUSION

Surface epithelial tumors are most common category of ovarian tumors followed by germ cell tumors and sex cord stromal tumors in this study. Serous cystadenoma was the most common benign tumor and serous cystadenocarcinoma was the most common malignant tumor in our study. Two thirds of serous cystadenocarcinomaspresented with bilateral ovarian involvement.

Mature cystic teratoma was the most common germ cell tumor while granulosa cell tumor was the most common sex cord stromal tumor. One rare case of ovarian cavernous hemangioma and benign mixed epithelial

tumor consisting of mucinous cystadenoma and benign Brenner component were encountered in our study. With proper histological diagnosis and categorization of ovarian neoplasms in conjunction with recent diagnostic modalities a more accurate diagnosis can be made which helps in the proper management of the case.

REFERENCES

[1]. Padubidri VG, Shirish N Daftary. Disorders Of Ovary. In: Howkins And Bourne., Editors. Shaws Textbook Of Gynecology. 13th Ed. Churchill Livingston: London; 2004. P352-485.
[2]. Murthy NS, Shalini S, Suman G, Pruthvish S, Mathew A. Changing Trends In Incidence Of Ovarian- The Indian Scenario. Asian Pac J Cancer Prev 2009;10:1025-30.
[3]. Maheshwari A, Kumar N, Mahantshetty U. Gynecological Cancers:A Summary Of Published Indian Data. South Asian J Cancer 2016;5:112-20
[4]. Tavassoli FA, Devilee P. World Health Organization Classification Of Tumors Of Female Reproductive Organs. IARC Press: Lyon 2014.
[5]. Sutton C I, Mckinney CD, Jones JE, Gray SB. Ovarian Masses Revisited- Radiologic And Pathologic Correlation. Radiographics1992;12:953-77.
[6]. Mondal SK, Banyopadhyay R, Nag DR, Roychowdhury S, Mondal PK, Sinha SK. Histologic Pattern, Bilaterality And Clinical Evaluation Of 957 Ovarian Neoplasms. A 10 Year Study In A Tertiary Hospital Of Eastern India. J Can Res Ther 2011; 7:433-7.
[7]. Sheikh S, Bashir H, Farooq S, Beigh A, Manzoor F, Reshi R. Histopathological Spectrum Of Ovarian Tumours From A Referral Hospital In Kashmir Valley, Jammu And Kashmir, India. Int J Res Med Sci [Internet]. 2017 Apr. 26 [Cited 2023 Nov. 9];5(5):2110-4. Available From: Https://Www.Msjonline.Org/Index.Php/Ijrms/Article/View/2863.
[8]. Jha R, Karki S. Histological Pattern Of Ovarian Tumors And Their Age Distribution. Nepal Med Coll J 2008;10:81-5.
[9]. R Sindhuja, V. Bhagyalakshmi, K Shantaraman. Histological Profile Of Ovarian Tumors In Rural South Tamil Nadu – A 3 Year Retrospective Analysis. IP Journal Of Diagnostic Pathology And Oncology , 2017; 2 (3): 49-52.
[10]. Quaranta M, Nath R, Mehra G, Diab Y, Sayasneh A. Surgery Of Benign Ovarian Masses By A Gynecological Cancer Surgeon: A Cohort Study In A Tertiary Cancer Centre. Cureus. 2020 Jul 15;12(7):E9201. Doi: 10.7759/Cureus.9201. PMID: 32821556; PMCID: PMC7429623.
[11]. Gupta N, Yadav M, Gupta V, Chaudhary D, U.Patne SC. Distribution Of Various Histopathological Types Of Ovarian Tumors : A Study Of 212 Cases From A Tertiary Care Center Of Eastern Uttar Pradesh. J Lab Physicians 2019;11:75-81.
[12]. Garg N, Anand AS, Annigeri C. Study Of Histomorphological Spectrum Of Ovarian Tumors . Int J Med Healthres 2017:3;12-20.
[13]. Kanthikar SN, Dravid NV, Deore PN, Nikumbh DB, Suryavanshi KH. Clinico – Histological Analysis Of Neoplastic And Non-Neoplasticlesions Of Ovary: A 3-Year Prospective Study In Dhule, North Maharashtra, India. J Clin Diagn Res 2014;8(8):FC04- 7
[14]. Pachori G, Meena U, Sunaria R, Pachori P, Jethani N, Bayla T. Histopathological Study Of Ovarian Tumors In Ajmer Region. Int J Med Sci Public Health 2016;5(7):1400-1403.
[15]. Mankar DV, Jain GK. Histopathological Profile Of Ovarian Tumors : A Twelve Year Institutional Experience . Muller J Med Sci Res2015;6107-11.
[16]. Daniel GR,Zhihong Zhang, Weiwei Shan And Jinsong Liu. Morphological And Molecular Basis Of Ovarian Serous Carcinoma. J Biomed Res 2010:7;24(4): 257-63.
[17]. Kalyani S,Muraliprasath SR. A Two Year Retrospective Study Of Ovarian Tumors In A Rural Tertiary Care Hospital. Indian J Pathol Oncol 2018;5(4):563-570.
[18]. Sridevi S, Rao V Manmadha, Kumar S Satish, Baghyalakshmi A. Mucinous Cystadenoma With Brenner Tumor : A Case Report. J Evid – Based Med Healthcare. 2015:2(4):455-458.
[19]. Robert H Young. Ovarian Sex Cord Stomal Tumors And Their Mimics. The Journal Of The Royal College Of Pathologists Of Australasia 2017;50(1):5-18.
[20]. Uppal S, Heller DS, Majumdar B. Ovarian Hemangioma – Report Of Three Cases And Review Of Literature. Arch Gyneol Obstect 2004; 270(1):1-5.
[21]. D Miliaras, S Papaemmanouil, G. Blatzas. Ovarian capillary hemangioma and stromal leutenization: A case study with hormonal receptor evaluation. Eur J Gynaecol Oncol 2001;22: 369-371.