ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 11, Issue, 08, pp.6102-6106, August, 2019

DOI: https://doi.org/10.24941/ijcr.35719.08.2019

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

HISTOPATHOLOGICAL SPECTRUM OF OVARIAN TUMORS - A TWO YEAR EXPERIENCE AT A TERTIARY CARE HOSPITAL

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ARTICLE INFO

Article History:
Received 12th May, 2019
Received in revised form
16th June, 2019
Accepted 20th July, 2019
Published online 31st August, 2019

Key Words:
Ovarian cancer,
Histopathology,
Serous cystadenoma,
Pain, CA125

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ABSTRACT

Background: Ovarian cancer encompasses a heterogenous group of malignancies that vary in etiology, molecular biology, and numerous other characteristics. Their complex nature, unpredictable behaviour, prognosis and varying therapeutic strategies, necessitates an accurate diagnosis. ***Aims and Objectives:*** The present study was undertaken to study the diverse histomorphological patterns of ovarian tumors over a period of 2 years(June-2010 to May-2012. ***Results:*** Out of 119 neoplastic ovarian lesions, 57.98% (69) were labeled as benign, 1.7% (2) as borderline and. 42.0% (48) as malignant. Age of the patients ranged from 1 to 70 years. with maximum cases (42.8 %) seen in the age group of 21-40 years. The commonest category of the ovarian tumors encountered in our series was epithelial tumors (73.94%) followed by germ cell tumors (16.8%). Abdominal pain was the most common presenting symptom. ***Conclusion:*** Benign ovarian tumours were more common than malignant ones across all age groups. Surface epithelial tumours were the most common histopathological type of ovarian tumour. Due to vague symptoms, patients present late. Development of methods for early diagnosis of ovarian neoplasia is therefore, a pressing need today. The relative frequency of incidence of different ovarian tumours shows regional variations, highlighting the need to identify region-specific risk factors.

Citation: Humira Bashir, Zubair Qureshi, M., Nazia Bhat and Saleem Hussain, **2019.** "Histopathological spectrum of ovarian tumors - A two year experience at a tertiary care hospital", *International Journal of Current Research*, 11, (08), 6102-6106.

INTRODUCTION

Ovarian cancer accounts for 2.5% of all malignancies among females but 5% of female cancer deaths because of low survival rates, largely driven by late stage diagnoses (Howlader *et al.,* 2017). According to hospital based cancer registry data ovarian tumors are third commonest tumor in Kashmir valley trailing behind carcinoma breast and esophagus. Ovarian tumors show histological heterogeneity. The classification of ovarian tumors by World Health Organization is based on the histogenesis of ovary Primary tumors are classified into surface epithelial tumors, germ cell tumors, sex cord stromal tumors, germ cell sex cord stromal tumors, tumors of rete ovarii and miscellaneous tumors of which surface epithelial tumors are most common (Scully *et al.,* 1999). Determination of various histopathologic patterns of ovarian tumors is important in the management as well as prognosis (Swamy and Satyanarayana, 2010). It has been seen that women diagnosed with localized-stage disease have more than a 90% five-year survival rate. The aim of this study was to see the morphological pattern of benign and malignant ovarian neoplasm in various age presenting at our center over a period of 2 years.

MATERIALS AND METHODS

This was a prospective observational study conducted over a period of 2 years (June-2010 to May-2012).All admitted cases diagnosed as ovarian neoplasms (Benign and malignant) were included in the study. Patients with functional ovarian cysts were excluded from the study. A detailed history, clinical examination, relevant laboratory investigation were obtained from the patients, histopathology requisition forms and wherever required from the medical record section.. Pre operative CA125 levels of the patients where ever available was also recorded. Wherever appropriate, special stains and immunohistochemical stains were used. The tumours were studied and classified as per the WHO classification of ovarian tumours

RESULTS

Out of the 119 ovarian tumours received, 57.98% (69) cases were benign where as 40.33% (48) cases were malignant (Scully *et al.,* 1999). Cases of borderline tumours were also reported.

Distribution of tumours in the different age groups: The ages of patients ranged from 1 month to 70 years. Maximum cases, 31 (26.1%) were reported in the age group of 41-50 years. Out of 67 benign cases, maximum 17 (25.4%) were in the age group of 31-40 years. Two (100%) tumours falling in the borderline category were found in the age group of 21-30 years. In the malignant category, 15 cases (30%) were in the age group of 41-50 years. Malignant tumours presented in higher age group than benign tumours. 58.2% of benign ovarian neoplasms were seen in patients less than 40 years of age where as 58% of malignant neoplasms were seen in patients more than 40 years of age (Table1).

Table 1. Showing Age-wise distribution of Benign, Borderline and Malignant Ovarian Neoplasms (n=119)

Age group (years)	Tumour type			Total
	Benign	Borderline	Malignant	
<10	1 (1.5%)	0	0	1 (0.8%)
11-20	6 (9.0%)	0	4 (8%)	10 (8.4%)
21-30	15 (22.4%)	2 (100%)	8 (16%)	25 (21%)
31-40	17 (25.4%)	0	9 (18%)	26 (21.8%)
41-50	16 (23.9%)	0	15 (30%)	31 (26.1%)
51-60	6 (9%)	0	11 (22%)	17 (14.3%)
61-70	6 (9%)	0	3 (6%)	9 (7.6%)
Total	67 (100%)	2 (100%)	50 (100%)	119 (100%)

Clinical presentation of the patients with ovarian tumor: The commonest symptom with which the patients presented was abdominal pain/discomfort, 77 cases (64.7%). Abdominal swelling/distention was present in 64 patients (53.8%). Ascitis was seen in 26 patients (21.8%). All the cases with ascitis were associated with malignancy except for one benign mucinous cystadenoma which had ruptured.

CA 125 level: CA 125 level was available in only 77 cases. Taking cut off values of >35U/ml as positive for malignancy, sensitivity of CA 125 was 90.9% and specificity was 83.7%. Our study was in accordance with the study done by Mani R (2007). Other studies (Torres *et al.,* 2002), Eagle (1997) showed lesser sensitivity and specificity. 16.3% of benign cases showed CA125 levels of greater than 35u/ml whereas in the study done by Eagle (1997) 22% cases had CA 125 levels greater than 35U/ml.

Laterality of ovarian tumours: Out of 119 cases 101 cases (84.9%) had unilateral involvement. Of these, right sided tumours, 71 cases (59.7%) were more common than left sided tumours, 30 cases (35.7%). There were 18 cases (15.1%) which were having bilateral ovarian involvement. Among the benign tumours 63 cases (94.0%) were unilateral and 4 cases (6%) were bilateral. Thirty six (72%) malignant tumours had unilateral involvement with 25 cases (50%) showing right sided involvement. Bilateral involvement was seen in 14 cases (28%)

Size ranges of ovarian neoplasms: Tumours ranged in size from 1 to 30 cm with majority, 76 (63.8%) falling in the range of 1-10 cm. The smallest tumour measured 1x1x1cm in size and was diagnosed as benign serous cystadenoma. The largest tumour measured 30x25x22 cm and was reported as benign mucinous cystadenoma.

Cut Section of ovarian tumors: Out of 119 neoplastic lesions 49.6% were cystic neoplasms, 16.8% were solid and 33.6% showed mixed consistency.

Table 2. Showing detailed analysis of Ovarian Neoplasms as per WHO classification (2003)

Histological type	No.	%age	Age (range) in years	Size (cms)	Consistency			Laterality	
					Cystic	Solid	Mixed	U/L	B/L
1. Surface epithelial tumour	89	74.8%	11 – 70	1 – 30	46	10	33	76	13
A. Serous tumours	71	59.7%	11 -70	1 – 28	39	9	23	62	9
a) Benign	42	35.3%	11 – 70	1 – 26	39	0	3	40	2
Cystadenoma	39	32.8%	11 – 70	1 – 23	39	0	0	37	2
Cystadenofibroma	3	2.5%	18 – 55	7 – 26	0	0	3	3	0
b) Borderline	2	1.7%	23 – 29	9 – 15	0	0	2	2	0
c) Malignant	27	22.7%	17 – 65	4 – 28	0	9	18	20	7
B. Mucinous tumours	15	12.6%	25 – 65	6 – 30	7	0	8	12	3
a) Benign	7	5.9%	35 – 65	6 – 30	7	0	0	7	0
b) Borderline	0	0%	0	0	0	0	0	0	0
c) Malignant	8	6.7%	25 – 60	7 – 21	0	0	8	5	3
C. Endometrioid carcinoma	1	0.84%	48	10	0	1	0	1	0
D. Clear cell carcinoma	1	0.84%	60	4 & 3	0	0	1	0	1
E. Mixed epithelial carcinoma	1	0.84%	45	6	0	0	1	1	0
2. Lipiod cell tumour	0	0%	0	0	0	0	0	0	0
3. Sex sord stromal tumour	2	1.7%	28 – 55	8 – 12	0	2	0	2	0
A. Granulosa cell tumour	0	0%	0	0	0	0	0	0	0
B. Thecoma	1	0.84%	55	14	0	1	0	1	0
C. Fibroma	1	0.84%	28	8	0	1	0	1	0
D. Sertoli ledig cell tumour	0	0%		0	0	0	0	0	0
4. Germ cell tumour	19	16.0%	0.8 – 45	3 – 26	12	3	4	18	1
A.Dysgerminoma	2	1.7%	15 – 18	11 –26	0	2	0	2	0
B. Yolk sac tumour	1	0.84%	12	9	0	1	0	1	0
C.Teratoma	16	13.4%	0.08 – 45	3 – 19	12	0	4	15	1
a) Mature	14	11.8%	0.08 – 42	3 – 19	12	0	2	13	1
b) Immature	0	0%	0	0	0	0	0	0	0
c) Monodermal(struma ovarii)	1	0.84%	45	9.5	0	0	1	1	0
d) Teratoma with squamous cellcarcinoma	1	0.84%	45	12	0	0	1	1	0
5. Gonadoblastoma	0	0%	00	0	0	0	0	0	0
6.Miscellaneous(Soft tissue tumour not specific to ovary)	1	0.84%	55	22 & 5	1	0	0	0	1
Lymphangioma	1	0.84%	55	22 & 5	1	0	0	0	1
7. Metastatic tumours	7	5.9%	25 – 57	2 – 12	0	5	2	4	3
8. Mixed epithelial and sex cord stromal tumour	1	0.84%	21	22	0	0	1	1	0

Table 3.

TYPE OF TUMOR	Ashraf et al. n=212	Swamy and Satyanarayana n=120	Raka Hota et al n=230	Agarwal et al	Mondal *et al* (2011) n=957	Present study (2019) n=119
Surface epithelial tumor	52.76%	61.6%	64.5%	73.68%	67.9%%	89 (74.8%)
Germ cell tumor	43.41%	21.7%	27%	23.69%	23.1%	19 (16%)
Sex cord stromal tumor	3.15%	11.7	5.2%	3.28%	5.6%	2 (1.7%)
Metastasis	0.78%	5%	2.6%	1.31%	2.61%	7 (5.9%)

Histological types of ovarian neoplasms: Tumours arising from the surface epithelium formed the largest group, 89 cases comprising 74.8% of total ovarian neoplasms. These were followed by 19 cases of Germ cell tumours (16.0%). 2 cases (1.7%) were reported as sex cord stromal tumour. 7 cases (5.9%) of metastatic ovarian tumour were also reported. Benign surface epithelial tumours constituted 73.1% of all benign neoplasms and its malignant counterpart constituted 76.0% of all malignant neoplasms. Among the individual neoplasms, serous tumours were the commonest (59.7%), followed by teratomas (13.4%), mucinous tumours (12.6%), metastatic tumours (5.9%) and dysgerminomas (1.7%). One case each of endometriod carcinoma, clear cell carcinoma, mixed epithelial carcinoma, thecoma, fibroma, yolk cas tumour, struma ovarii and lymphangioma was also reported in the present study (Table 2).

DISCUSSION

Ovary is a frequent site of primary and metastatic tumours. Due to its complex structure, primary ovarian neoplasms are of diverse histological types. The diversity of neoplasms makes it important to classify the tumours accurately by histopathological features by following universally accepted classification.

Frequency of benign and malignant tumors of ovary: Out of 119 neoplastic ovarian lesions, 57.98% (69) were labeled as benign, 1.7% (2) as borderline and. 42.0% (48) as malignant. Compared to studies in western countries, where 75-80%of tumours were benign, this study shows a relative decrease in the percentage of benign tumours and a consequent increase in the percentage of malignant tumours, which agreed with the findings of Mankar and Jain who reported incidence of benign, borderline and malignant of 162 (63.04%),15 (5.84%) and 80 (31.12%) respectively.

Clinical Presentations: The presenting complaint in most of our cases was abdominal discomfort /pain. 64.7% followed by abdominal distension/lump (52.0%). The results comply well with a study carried out by Pilli *et al.* (2002) and Goff (2014)**.**

Distribution of ovarian tumors in different age groups: In the present study patients ranged in age from 1 to 70 years, with maximum cases (42.8 %) seen in the age group of 21-40 years. In our study, the majority of benign tumours occurred in the age group of 21-40 years and malignant tumours occurred in patients more than 40 years of age. This was comparable to the studies done by Mankar and Jain (2015), Goyal *et al.* (2019), Vaidya (2014) and Ashraf *et al.* (2012).

Laterality of benign ovarian tumors: Out of 119 cases 101 cases (84.9%) had unilateral involvement. Of these, right sided tumours, 71 cases (59.7%) were more common than left sided tumours, 30 cases (35.7%).Study by Shadab8, Garg9 and Kuldeepa10 also showed similar results.

Comparison of size ranges: Tumours ranged in size from 1 to 30 cm with majority, 76 (63.8%) falling in the range of 1-10 cm. The smallest tumour measured 1x1x1cm in size and was diagnosed as benign serous cystadenoma. The largest tumour measured 30x25x22 cm and was reported as benign mucinous cystadenoma Our study was similar to the study conducted by Vaidya which had the mean size of 4-9 cm.

Consistency of ovarian neoplasms: Out of 119 neoplastic lesions 49.6% were cystic neoplasms, 16.8% were solid and 33.6% showed mixed consistency. Our study was similar to the study of Raka Hota *et al.* (2018). In their study majority of ovarian neoplasms (172 cases; 74.8%) showed cystic areas on cut section, with 50 cases (21.7%) showing mixed solid and cystic areas. Frequency of Histological Types of Ovarian Neoplasms

Surface epithelial tumour

Tumours arising from the surface epithelium formed the largest group, with 89 cases (74.8% of total ovarian neoplasms) in the present study. Serous tumours being the largest subgroup 71 cases (59.7%) Benign serous tumours included 42 cases comprising 35.3% of all ovarian tumours. Of these, 39 cases were benign serous cystadenomas and 3 cases were cystodenofibromas. Serous tumour of borderline malignancy was observed in 2 cases. Malignant serous tumours (serous cyst adenocarcinoma and papillary serous cystadenocarcinomas) constituted 22.7% (27 cases) of all the ovarian tumours, accounting for the commonest malignant tumours of the present series. This agrees with the findings of Mondal (2011) and Ashraf *et al.* (2012) (Table3)

Germ cell tumors

Germ cell tumor was the second major group of tumors in the present study with Teratoma, 16(13.4%) cases, was the largest subgroup. Of these, 14 (11.8%) were mature teratomas, 1 was monodermal teratoma and another 1 was teratoma with squamous cell carcinoma. 2cases of Dysgerminoma and 1 case of yolk sac tumor was also reported.Germ cell tumor was also the second major group in studies of swami3 and Agarwal (Deepti Agarwal *et al.,* 2018).

Metastatic tumour

Seven cases of metastatic ovarian tumours were reported comprising 5.9% of all ovarian tumours and was the third largest category.3 out of 7 cases were bilateral. All the metastatic tumours had primary in the Gastro-intestinal tract. Gupta SC,14and Swami et al et al (1986)[(67)] reported comparable incidence of 6.18% of metastatic tumors in their study. However study of Nayak et al showed only 0.4% of metastatic tumors.

CA 125 level: CA 125 level was available in only 77 cases. Taking cut off values of >35U/ml as positive for malignancy,

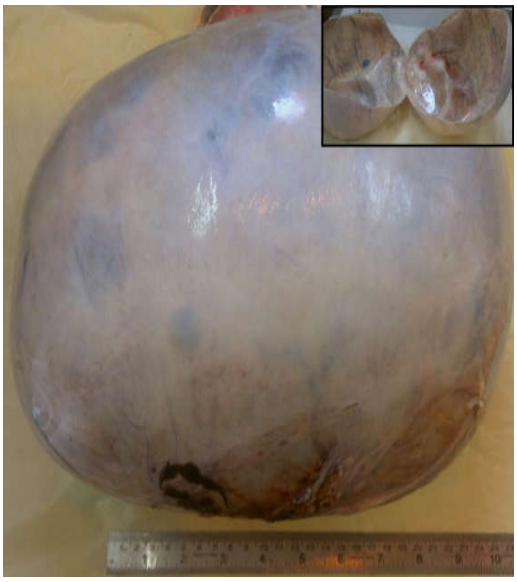

Figure 1.Serous cyst adenoma. large cyst with filled with serous fluid. Inset;showing inner smooth surface of the cyst wall Serous cystadenoma. Photomicrograph showing cystwall with lining epithelium composed of cuboidal to low columnar cells. (H&E-400X)

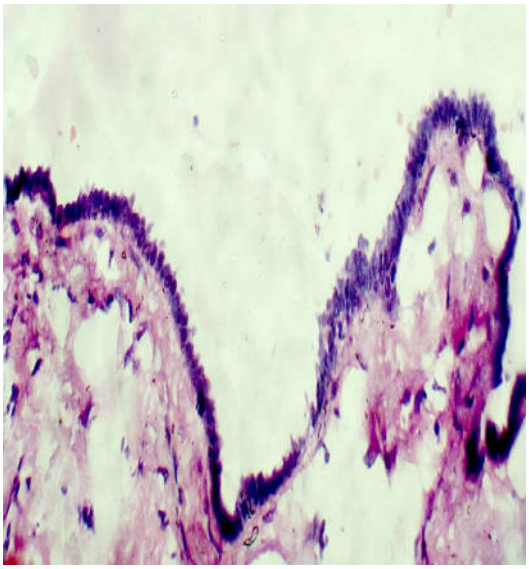

Figure 2. Serous cystadenoma. Photomicrograph showing cystwall with lining epithelium composed of cuboidal to low columnar cells. (H&E-400X)

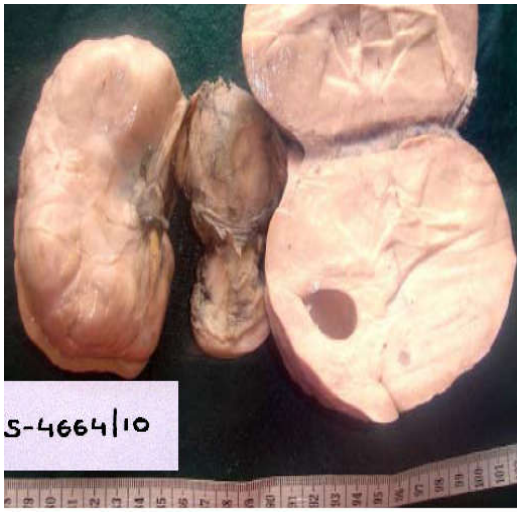

Figure 3. Krukenbergs tumour. Gross photograph showing bilaterally enlarged ovaries with smooth outer surface and predominantly waxy cut section.

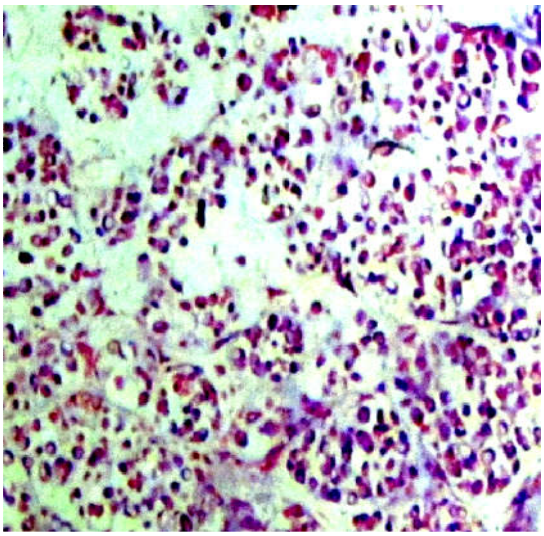

Figure 4. High power view showing tumor composed of signet cells

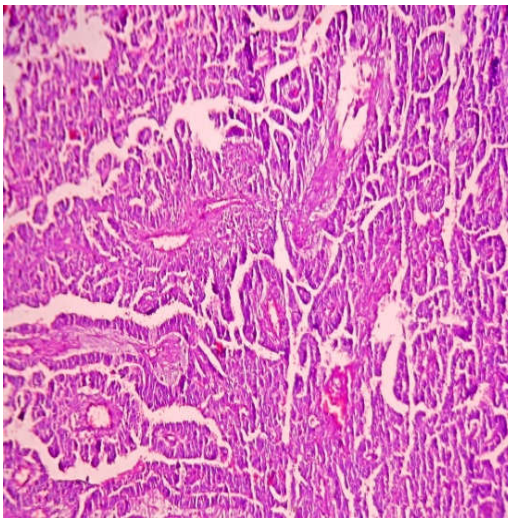

Figure 5. Yolk sac tumour. Photomicrograph showing characteristic Schiller Duval body characterized by the presence of a central vessel, surrounded by fibrous tissue and epithelial tumor cells, in a space lined by tumor cells

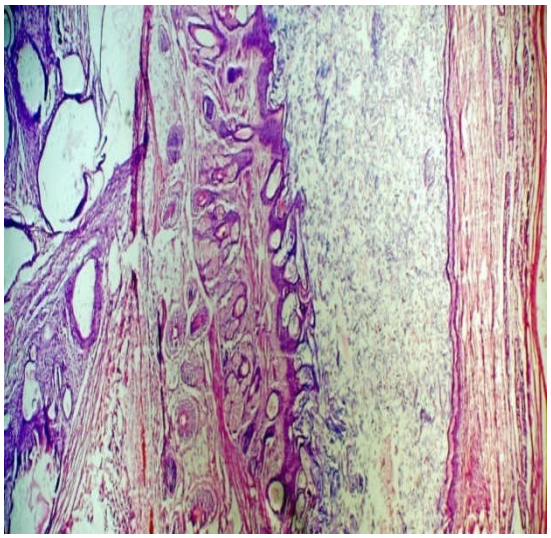

Figure 6.Mature cystic teratoma. Photomicrograph showing various mature elements comprising of squamous epithelium. Keratin, adnexal structures and glandular epithelium.(H&E-100X)

sensitivity of CA 125 was 90.9% and specificity was 83.7%. Our study was in accordance with the study done by Mani (2007). Other studies [Torres *et al.* (2002), Eagle (1997)] showed lesser sensitivity and specificity. 16.3% of benign cases showed CA125 levels of greater than 35u/ml whereas in the study done by Eagle (1997) 22% cases had CA 125 levels greater than 35U/ml.

Conclusion

To conclude, number of various clinical parameters such as age of the patient, location, dimensions and histological type of ovarian neoplasm affect the prognosis. In our study benign ovarian tumors were more common than malignant ones across all age groups. On morphological grounds, tumors originating from surface epithelium were the most common variant

Acknowledgement (optional)
Conflict of Interest; None
Funding statement

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