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**5 YEAR RETROSPECTIVE STUDY OF HISTOPATHOLOGICAL SPECTRUM OF
OVARIAN TUMOURS AND TUMOUR-LIKE LESIONS IN A TERTIARY
REFERRAL CENTRE, PIPARIA**

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ABSTRACT

Introduction:

Ovary and its neoplasms show a wide histological spectrum and clinical behavior. They present from neonatal period to post menopause. About 30% of all cancers of the female genital system are represented by ovarian tumors. Ovarian tumor is the seventh leading cause of cancer death. As symptoms are vague and insidious, ovarian tumors are often difficult to detect until they are advanced in stage or size. An accurate and early diagnosis of malignant lesions will essentially help in the optimal management of these cases.

Method:

A retrospective study of all cases of ovarian lesions received during November 2016 – November 2021 at SBKS MI & RC was done. Routine H and E staining was performed. Immunohistochemistry (IHC) was done in difficult cases.

Result:

Among the samples received, 59.2% of them belonged to the age group of 20-39 years of age. A total of 92% of lesions were unilateral. 29.6% of the ovarian lesions were non-neoplastic amongst which follicular cyst constituted 33.3% of these lesions. 16.9% of all the pathologies of ovary were constituted by malignant lesions. Amongst the neoplastic lesions,

serous cystadenoma was predominant lesion diagnosed that is 14.6% of all the neoplastic lesions.

Conclusion:

The morphologic diversity of ovarian masses poses many challenges. A specific diagnosis can usually be made by evaluating routinely stained slides but sometimes immunohistochemistry is required in difficult cases.

Keywords: Brenner tumor, Krukenberg's tumor, Serous cystadenoma

INTRODUCTION

Ovaries show various lesions, which can be non-neoplastic or neoplastic.

Ovarian lesions show diverse morphology and are associated with relatively mild symptoms and are therefore unusual [1]. These lesions can be observed from the neonatal period to the post-menopausal period. Many of these ovarian lesions are functional ovarian cysts which can be treated with minimal intervention [2, 3]. Among gynaecological admissions, the prevalence of ovarian cysts and tumour-like lesions is between 2 to 4% [4]. Clinically, intraoperatively as well as on histopathological examination few of the benign lesions may be confused with neoplasm [5]. Various cystic ovarian abnormalities need to be differentiated from non-malignant features as histological presentation decides proper treatment.

Ovarian tumours are 6th most common female cancer and the 4th leading cause of death due to cancers in women [6]. Pathology of ovarian tumours and Tumour-like conditions is one of the most complex areas in gynaecology, because the ovary

gives rise to a great range and variety of tumours than any other organ in the body. The tissue from which the ovarian tumour arises as well as the mode of development of the presumptive tissue is often uncertain and disputed [7].

Neoplastic disorders can arise from either, mullerian epithelium, germ cells or sex cord stromal cells [1]. As ovarian neoplasms present with mild symptoms, they are usually detected at a late stage and are large in size [8]. However, an accurate and early diagnosis of malignant lesions will be beneficial in optimal management of these cases [8].

The aetiology of ovarian cancers is poorly understood. Previous epidemiological studies have classified aetiological factors of epithelial tumours which include family history of ovarian cancer, advanced age, and nulliparity associated with increased risk for ovarian cancers. Other factors that are responsible for decreased risk for ovarian cancers are history of tubal ligation or hysterectomy, number of pregnancies & oral contraceptive (OC) use. There are

certain factors that have inconclusive relation with the occurrence of ovarian cancers like smoking, consumption of alcohol or coffee, use of fertility and infertility drugs, Hormone Replacement Therapy (HRT), talc use, diet, obesity, age at first childbirth, age at menarche/menopause and breastfeeding. Whereas some studies that focused on aetiology of non-epithelial ovarian tumours have found that there is an increased risk of germ cell ovarian cancer among the mothers of females who were under 20 years of age at time of pregnancy, girls and young women who had a high pre-pregnancy body mass or had used exogenous hormones during the pregnancy, whereas factors like history of oestrogen replacement therapy or oral contraceptives use was found to be associated with a decreased risk of developing sex cord-stromal ovarian tumours [9, 10, 11].

Maximum cases of ovarian tumours are seen in women of reproductive age group of 20 and 45 years whereas most cases of neoplastic ovarian tumours are seen in elder women between the ages of 45 and 65 years [12, 13]. Primary tumours are classified into surface epithelial tumours, germ cell tumours (both primitive germ cell and mature teratomas) and also monodermal like struma ovarii, sex cord stromal tumours like granulosa stromal cell and thecomas out of which Surface

epithelial tumours are most common. The laterality and stage of the tumour also indicates their nature for example, the sex cord stromal tumours are almost always confined to a single ovary. On the other hand, approximately 65% of the metastatic tumours are bilateral (Krukenberg) [12, 13].

METHODS

This is a retrospective study. Data regarding age, size and tumour histology were collected from medical records. Different non neoplastic and neoplastic cases of ovaries were counted from the histopathological records of pathology department. Details of the histopathological diagnoses of the ovarian masses evaluated, as well as the age distribution of the patients, were analyzed. Routine H and E staining was performed. The study was approved by Institute of Ethical Clearance and informed consent was obtained. Age of the patient, histopathological type of ovarian lesion has been noted and accordingly, percentage is been calculated. Immunohistochemistry (IHC) was done in difficult cases that included cytokeratin, Epithelial Membrane Antigen (EMA), Inhibin and Leukocyte Common Antigen (LCA). All patient data were kept confidential.

Materials

Study design: A retrospective analytical study.

Study Setting: Department of Pathology, SBKS MI & RC.

Study Period: November 2016 - November 2021

Sample Size: All cases of functional ovarian cysts, benign ovarian neoplasms and ovarian cancer, received during 5-year period at pathology department of SBKS MI & RC, Pipheria, who attained the inclusion criteria during the study period were taken into study.

Inclusion criteria: All cases of ovarian lesions both neoplastic as well as non – neoplastic that were received, in the Department of Pathology, SBKS MI & RC, Pipheria, during above mention period were included in the study.

Exclusion criteria: Autolysed specimen and normal ovaries and ectopic pregnancy etc. were excluded from the study.

This study was carried out to analyse the gross morphological features and various histopathological changes of ovarian lesions with respect to various parameters like age, laterality, clinical symptoms and associated conditions as well as to evaluate the association between these parameters with risk of malignancy.

RESULT

A total of 455 cases were included in this study with the age range from 21-80 years [Table – 1 & 2]. Minimum age of the patients presenting with the ovarian lesion in our study was 22 years while maximum age was 79 years. Ovarian lesions were most common in the age group of 31-40 years, comprising of 147(32.3%) cases [Table 1& 2]. Overall a total of 271 cases were seen in the reproductive age group range of 21-40 years [Table 1 & 2].

Maximum number of non-neoplastic lesions were seen between the age of 21-30 years (62 cases) followed by 31-40 years (56 cases) [Table 1].

Maximum number of neoplastic benign lesion were seen between the age of 31-40 years (91 cases) followed by 21-30years (62 cases) [Table 2].

Based on the microscopic features, the tumour were broadly classified into various groups as per WHO classification and surface epithelial tumors was the most common (219 cases) followed by Germ cell tumors (70 cases) and sexcord stromal tumors (6 cases) [Table 2].

Table 1: Distribution of tumor like lesions of ovary in different age groups

Age in years	Corpus luteal Cyst	Follicular Cyst	Twisted Ovarian Cyst	Chocolate Cyst	Polycystic Ovary	Inflammatory	Total
21-30	22	20	01	01	16	02	62
31-40	28	18	01	05	03	01	56
41-50	06	05	00	01	01	00	13
51-60	01	02	00	00	00	00	03
61-70	01	00	00	00	00	00	01
71-80	00	00	00	00	00	00	00
Total	58	45	02	07	20	03	135

Table 2: Frequency of different classes of tumors in different age groups

Age in years	Surface epithelial tumors	Germ cell tumor	Sex cord stromal tumors	Metastatic tumor	Undifferentiated tumor	Total
21-30	52	10	00	00	00	62
31-40	60	22	09	00	00	91
41-50	59	14	08	01	00	83
51-60	24	06	01	01	01	33
61-70	12	10	05	02	00	29
71-80	11	08	01	02	00	22
Total	219	70	24	06	01	320

Table 3: Clinical presentation of various ovarian tumors

Clinical presentation	Number of cases	Percentage of cases
Pain in abdomen	209	46%
Profuse menstruation	58	12.7%
Pain in abdomen with mass per abdomen	46	10.1%
Irregular menses with mass per abdomen	41	9%
Mass per abdomen	37	8.1%
Distension of abdomen, ascites	36	8%
Amenorrhoea	11	2.4%
Infertility	09	2%
Asymptomatic	08	1.7%

Most of the ovarian lesion presented with pain in abdomen (209) followed by profuse menstruation (58). Other presenting symptoms were infertility, amenorrhoea and mass per abdomen in occasional cases. 8 cases were asymptomatic [Table 3].

Majority ovarian tissues were received as total abdominal hysterectomy specimens. Other specimens were received in the form

of unilateral or bilateral salpingo-oophorectomy samples and as trucut incisional biopsies.

A total of 419(92%) cases were unilateral amongst which 218(47.9%) cases were seen on the right ovary and 201(44.1%) cases were seen on the left ovary while 36(8%) cases were bilateral.

Table 4: Non-neoplastic lesions of Ovary with laterality and number

Sl. NO.	HISTOPATHOLOGICAL TYPE	Right	Left	Bilateral	NUMBER (%)
1	Corpus luteal cyst	27	22	09	58
2	Follicular cyst	20	18	07	45
3	Polycystic ovary	06	08	06	20
4	Chocolate cyst	03	04	00	07
5	Twisted ovarian cyst	01	01	00	02
6	Inflammatory	00	01	02	03
	TOTAL	57	54	24	135

Based on the microscopic features corpus luteal cyst was the most common non-neoplastic lesion with 58 cases (42.9%) followed by 45 cases each of follicular cyst

(19.8%) and polycystic ovary (14.8%) [Table 4]. Other non-neoplastic lesions were chocolate cyst, twisted ovarian cyst and inflammatory lesions.

Ovarian lesions were diagnosed into non-neoplastic and neoplastic types in which benign, borderline and malignant category were differentiated on the basis of morphological features. Majority of the ovarian tumors belonged to benign category [Table 5 & 6].

Based on the microscopic features, among the benign lesions, serous cystadenoma was the most commonly encountered lesion with 32 cases, followed mucinous

cystadenoma with 29 cases. Cases of serous cystadenofibroma and Brenner's tumour [Fig-1] are also seen. Among Borderline lesions, 24 cases of Borderline Papillary cystadenomas were recorded. Among the malignancies, serous carcinoma was the most common comprising of 25 cases, [Fig-2] while six cases of Metastatic carcinoma from different sites to bilateral ovary are recorded. Few cases of Endometroid carcinoma were also seen [Table 6].

Table 5: Neoplastic lesions with laterality and number

Category	Type of neoplastic lesion	Right	Left	Bilateral	Total number
Benign	Serous cystadenoma	12	12	08	32
	Serous cyst	06	12	09	27
	Mucinous Cystadenoma	12	14	03	29
	Fibromas	10	09	00	19
	Brenner tumor	04	06	00	10
Borderline tumors	Borderline Papillary cystadenomas	11	07	06	24
Malignant	Serous carcinoma	11	10	04	25
	Endometroid carcinoma	08	07	07	22
	Mucinous adenocarcinoma	07	06	11	24
	Malignant Brenner	00	01	00	01
	Krukenberg tumor	00	00	03	03
	Metastatic tumor	00	00	03	03
	TOTAL	81	84	54	219

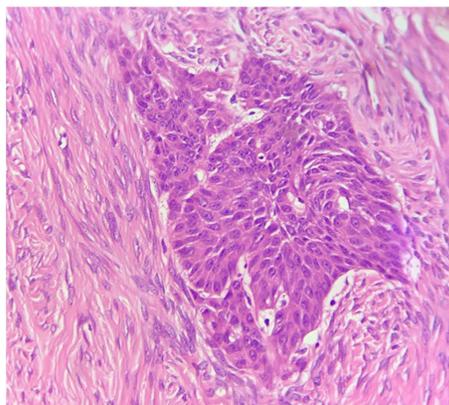


Figure 1: Brenner tumor
Epithelial nests composed of cells with oval nucleus many of which exhibit longitudinal grooves embedded into fibrous tissue.

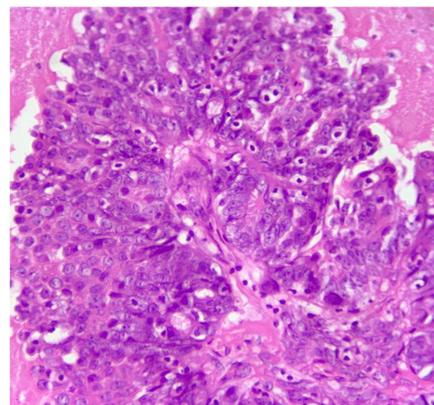


Figure 2: Serous cystadenocarcinoma
Complex papillary architecture and high nuclear grade

Table 6: Associated conditions with Ovarian Lesions

Associated conditions	No. of Cases
Adenomyosis	05
Leiomyoma	29
Adenomyosis & Leiomyoma	12
Chronic cervicitis	23
Prolapse	01
Hydrosalpinx	03
Carcinoma Endometrium	04
Hypothyroidism	04
Endometrial intraepithelial Neoplasia	01
Carcinoma Cervix	01
Diabetes Mellitus	02
Hypertension	02
Total	87

In specimens of Hysterectomy with salpingo-oophorectomy many associated findings were also found. Most common was leiomyoma either alone or in combination with adenomyosis. Other associated findings were chronic cervicitis, carcinoma endometrium, cervical carcinoma, hydrosalpinx, etc. [Table 6]. Systemic symptoms were found in some of the lesions which were ascites, hypothyroidism, diabetes mellitus, hypertension, etc.

DISCUSSION

Ovarian neoplasm is a very interesting tumour of women in terms of histogenesis, clinical behaviour and malignant potentiality. Ovarian masses consist of functional and pathological lesions [14]. Histomorphological classification of ovarian tumours forms an integral part of the evaluation of the neoplasms [17]. Given the location of these paired organs and the

mildness of symptoms associated with lesions arising in them, these lesions usually attain a fairly large size before they are detected and removed, accounting for a disproportionate number of fatal cancers, being responsible for almost half of deaths from cancer of female genital tract [8, 15, 16]. Ovarian Neoplastic disorders can arise from (1) mullerian epithelium, (2) germ cells or (3) sex cord stromal cells. Precise diagnosis of lesions of the ovary is essential for optimal management of these lesions [5].

The peak incidence of the ovarian tumours in the present study was in the age group of 31-40 years (32.3%) which was very much similar to the observations of Jha and Karki *et al* in 2008 and Kuldeepa *et al* in 2011 who reported maximum number of cases in third decade of life with 26.7% cases and 36.7% cases in third decade respectively [18, 19].

Authors	Age group in years		
	20-40	41-60	>60
Ramchandran <i>et al</i> [20]	53%	30%	9.1%
Pilli <i>et al</i> [21]	58%	30%	5%
Kar <i>et al</i> [22]	41.7%	46.2%	4.4%
Present study	59.4%	29%	1.8%

The most common presenting symptom in the present study was pain in abdomen (45.93%) followed by menstrual irregularities & mass per abdomen. It was similar to the studies done by Mankar *et al* in 2015 (33.48%) and Kanthikar *et al* (53.33%) where abdominal pain was the commonest symptom [22, 23]. In a study done by Bodal *et al*, the commonest presenting feature was mass per abdomen (in 69.33% cases) [24].

Grossly, it was found in our study that non-neoplastic and benign tumours were mostly cystic as compared to malignant, which were solid in consistency followed by partly cystic and partly solid which is in accordance with other studies [21].

The present study revealed that out of 455 ovarian specimens 419 were unilateral (92%) and only 36 (8%) were bilateral. The

findings of the present study are in concordance with other studies, out of 229 masses, 208 were unilateral (90.8%) and 21 were bilateral (9.2%) [25, 26]. Many cases were unilateral and while certain cases were bilateral [27]. It was observed that 90.8% of lesions were unilateral [28]. In another study conducted, the majority of the tumors were unilateral about 68% (34/50) with right side predominance, bilateral in 32% (16/50) [29]. Our findings are in concordance with other studies (Prabhakar and Kalyani-90.9% unilateral; Couto *et al*-91.25% unilateral [30]; Thakkar and Shah- 88.4% unilateral) [31, 32].

Laterality of ovarian neoplastic lesions in various studies in comparison with present study

Authors	Laterality	
	Unilateral	Bilateral
Prabhakar <i>et al</i> [30]	90.9%	9.1%
Misra <i>et al</i> [33]	95.5%	4.5%
Couto F <i>et al</i> [31]	91.2%	8.7%
Kar <i>et al</i> [16]	73.13%	26.8%
Present study	92%	8%

In present study, most of the cases were benign (70.3%) followed by malignant (24%) and borderline (8.75%). A similar pattern of benign, borderline and malignant tumours have been reported in most of the

studies performed in the past. In the study by Bodal *et al*, there were 75% benign, 1.66% borderline and 14% malignant tumors [24]. Similarly, in another study performed by Bhagyalaxmi *et al* in 2014,

there were 78.3% benign, 18% malignant and 3.7% borderline tumours [34]. In a study conducted by Dimpal Modi *et al*, Gunvanti B Rathod *et al*, K.N Delwadia *et al* and H.M. Goswami *et al* [1] out of 97 cases, 82 cases (84.5%) were benign, 2 cases (2.1%) were borderline and 13 cases (13.4%) were malignant tumors.

In present study, surface epithelial tumours were 68.4%, germ cell tumours were 21.8% cases and sex cord stromal tumours were 7.5% cases. The results of surface epithelial tumours were close and similar to Bodal *et al* 2014 (71.67%) and Willis *et al* 2016(71.6%) [24, 35].

The most common primary malignant tumor was serous cystadenocarcinoma (7.8%) followed by mucinous adenocarcinoma (7.5%) and endometrioid carcinoma (6.8%). Serous cystadenoma (52.7%) was the commonest benign tumor followed by Mucinous cystadenoma (28.4%). The results were similar to studies done by Ahmad *et al* (19.81%) [36].

In present study 2.1% of the lesions were metastatic ovarian tumor and all of them were bilateral [37], which were close to the observations of Jha *et al* 2004 (3.64). Bodal *et al* in 2014 reported 1.7% cases of metastatic ovarian tumours in their study [24, 38]. Metastases to the ovaries are relatively frequent with the most common being from the endometrium, breast, colon, stomach, and cervix. In the present study

three cases of Krukenberg tumour and one case of metastases from breast tumour and one from endometrial tumor were observed. Non-Hodgkins Lymphoma is very rare and can present as bilateral ovarian masses. We diagnosed a single case of NHL in young female of 41 years presenting with bilateral ovarian masses. Mucinous cystadenomas tend to be larger than serous cyst at presentation. Immunohistochemistry is an important diagnostic tool in evaluation of ovarian tumors [39]. It is especially useful in diagnosing tumours with follicles or other pattern which bring a sex-cord stromal tumour into differential. We performed different markers for proper diagnosis in difficult cases.

CONCLUSION

Ovary, despite being a small pair of organ in female genital system has complex architecture with different cell types. Hence it encompasses broad group of lesion from non-neoplastic to neoplastic - benign, borderline and malignant lesions. Symptoms of ovarian tumours are vague and insidious; therefore, they are often difficult to detect until they are advanced in stage or size. They usually present as pain in abdomen and menstrual abnormality in females of third to fifth decade of age group. In our study we have compared these lesions with multiple parameters like age, clinical presentation, and location of lump, associated lesions, and different

histological subtypes. All these clinical and histomorphological parameters and advanced newer diagnostic modalities can help to arrive at early definitive diagnosis and to plan the line of treatment and also have prognostic significance. Both non-neoplastic as well as neoplastic lesions of ovary often present with similar clinical, radiological and surgical features. So histopathological study is essential to diagnose ovarian tumours and predict their prognosis. A specific diagnosis can usually be made by evaluating routinely stained slides, but much less often, special stains and IHC staining is also required. In cases of benign functional cysts spontaneous resolution may take place, so symptomatic treatment and observation may help to minimize surgery in these patients. Since most of the malignant cases are detected at a later stage, their early diagnosis can help in patient's long survival and prognosis; but this requires surgery. Differentiation of a benign tumor from a malignant one is important for determining better management and prognosis; hence further similar studies are warranted.

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