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Post-Operative Clinico-Pathological Spectrum of Oophorectomy Specimens (A Rural Scenario).

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ABSTRACT

Ovaries are common site for non-neoplastic and neoplastic lesions,that vary in their incidence, clinical presentation and exhibit a wide range of histological features. These lesions sometimes behave adversely and generally escape detection, until they attain a large sized pelvic mass and sometime associated with abnormal hormonal manifestations. Ovarian lesions have adverse histopathologies reflecting different cells of their origin. To distinguish a non-neoplastic lesion from neoplastic clinically, is a great challenge. It is also important for guiding appropriate therapy and future outcome. To study and characterize various ovarian lesions and to provide a specific diagnosis based on Histomorphological features using special stains and serological markers. Fifty Oophorectomy specimens of all age groups were received in Pathology department, over a period of two yrs. All clinical, gross and histological findings were recorded, compiled and analyzed to achieve a final diagnosis. All Specimens were formalin fixed overnight, processed and stained with H& E stain. Special staining procedures like Reticulin, PAS, mucicarmine, Alcian blue and IHC markers were also used. Out of 50 cases, 62% were neoplastic and 38% non-neoplastic respectively. Majority of neoplastic lesions (62%) were found in women aged between 31-50 years. Commonest non neoplastic lesion was follicular cyst (36.84%) followed by endometriosis (31.57%). Among neoplastic tumors, largest proportion was benign (70.96%) and malignant (29.03%) respectively. Primary ovarian malignancies were more common than secondaries. Overall surface epithelial tumors constituted majority of primary neoplasms accounting for 51.61%, followed by germ cell tumors (32.25%) and sex cord stromal tumors (6.45%). Serous cyst was commonest benign tumor followed by mature cystic teratoma and mucinous cyst adenoma. Commonest malignant tumor was serous cystadenocarcinoma. Histological assessment of ovarian lesions remains mainstay of final diagnosis till date. With proper histological categorization in conjunction with other diagnostic modalities like Ultrasound examination, special staining & CA-125 biomarker study, a more accurate diagnosis can be made, that may be helpful for proper management and improving prognosis.

Keywords: Histological, Metastatic, Stromal, Cyst.

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INTRODUCTION

Ovaries are paired pelvic organs of about 4×2×1cm each and weighing 5-8 gms, which shrinks to its half size during menopause [1]. They carry potential for malignancy and are the commonest site to harbour malignant lesions, that may be missed till, they attain huge size and become symptomatic with abnormal hormonal manifestations [2]. To distinguish malignant from benign lesions clinically is a great challenge. About 15-25% of all primary malignancies of female genital tract arise in the ovaries [7]. Moreover, ovaries have a special predilection for metastatic deposits from breast, lung and abdominal cancers [3]. It is 5th common gynecological malignancy worldwide. Asian population have rates of 2-6.5 new cases /10,000 women /year, while in our country [4, 5], it stands second in the order of malignancy of female genital tract while, first being carcinoma cervix [6]. For a local disease, five year survival is 94% (FIGO STAGE 1). Surprisingly, only less than a third of cases, according to US statistics, are diagnosed at this stage. Despite advances in Radical surgery and other newer armontarian eg, neo Chemotherapy and Radiotherapy, the overall survival rate is very grim and had remained stationary for past 50 yrs. At present, WHO histological typing on the basis of tissue of origin, has been used. It has removed the dilemma of categorizing ovarian neoplasms. Of all primary ovarian tumors, approximately 70-80% is of epithelial origin (benign 80%, malignant 20%, stromal origin 10%, germ cell 5%) and remaining fall into other groups [8].

These tumors do not spare any age and are highly nebulous and indefinite. Symptoms may include abdominal swelling, pain/pressure, increased urinary urgency/frequency, backache and seldom unusual vaginal bleeding. Adding to misery, no definite screening test is available except ultrasound examination and CA-125 (non specific serological biomarker) for ovarian cancers, which is also raised in other conditions like diverticulitis, endometriosis, liver abscess, normal menses, pregnancy and uterine fibroids. Moreover, risk factors for ovarian cancers are not well understood however, there is an agreement on two parameters like nully parity and family history. Higher incidence of carcinoma ovary is seen in unmarried and women of low parity [11]. Life time risk of ovarian cancer in women without family history is 1.6% with one affected first degree relative [9, 10]. Though clinically, it is considered as one disease, but different ovarian cancers have different pathogenesis, natural behavior and prognosis. The determination of histological pattern is very important in proper diagnosis, management and prognosis.

Aim and Objective

To study and characterize various ovarian lesions and to provide a specific diagnosis based on Histomorphological features using special stains and serological markers.

MATERIAL AND METHODS

Fifty Ovarian specimens of all age groups were received in Pathology department, MMIMS&R Mullana, Ambala (HR), for histopathological diagnosis during the period from Oct 2012 - Sept 2014. All clinical information regarding patients was obtained, recorded and analyzed.

Oophorectomy specimens after fixing in 10% buffered formalin overnight, were dehydrated in ascending alcohol, cleared in xylene and finally embedded in paraffin. 3-5 µm thick paraffin sections was cut, dewaxed and finally stained with Hemotoxylin and Eosin stain. Special staining procedures like reticulin, Periodic acid schiff(PAS), mucicarmine, Alcian blue and Immunohistochemical markers used.

OBSERVATIONS

Fifty cases of ovarian lesions from all age group patients received in Pathology department. All specimens were processed and examined to make a proper diagnosis and later confirmed by special staining& serological markers. Out of total 50 cases studied, 19(38%) were non neoplastic and 31(62%) neoplastic respectively. Out of 31 neoplastic cases, 22(70.96%) were benign and 09(29.03%) malignant. (figure 1) No case of borderline malignancy seen. Study age ranged from 14-80 yrs. Most of ovarian lesions were found in women age group, between 31-40yrs (34%) followed by (28%) in 41-50 yrs and only (2%) were above 60 yrs of age. Non neoplastic lesions were usually seen between 31-50 yrs and uncommon below 21yrs & above 50yrs of age. Neoplastic tumors were seen more frequently between 31- 40 years. 3 cases of neoplastic tumors were seen below 21 years and 6 cases reported above 50 years of age.

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Table 1: Age wise distribution Of Histological types of Ovarian Lesions.

NON –NEOPLASTIC	<=20	21-30	31-40	41-50	51-60	>60
Follicular Cysts	0	0	03	04	0	0
Corpus Luteal Cysts	0	02	02	0	0	0
Inclusion Cysts	0	0	0	01	0	0
Inflammation	0	0	01	0	0	0
Endometriosis	0	03	01	02	0	0
NEOPLASTIC						
Surface Epithelial Tumors	02	03	03	04	05	0
Germ Cell Tumors	0	02	06	02	0	0
Sex-Cord Stromal Tumors	01	0	0	01	0	0
Metastatic	0	0	01	0	01	01

Out of 19 cases of non-neoplastic lesions, follicular cysts (4 cases) were seen between 41-50 yrs, followed by 3 cases in 31- 40 years of age group. Endometriosis usually peaked between 21-30 yrs (3 cases), whereas 1 case each of xanthogranulomatous oophoritis & multiple inclusion cyst were detected in age group of 31- 40 yrs & 41-50 years respectively. . All non-neoplastic lesions were unilateral and less than 10 cms in size Out of 31 neoplastic tumors, germ cell tumors (19.35%) were commonest tumors seen in 31-40 years of age followed by surface epithelial tumors (16.12%) in the age group of 51-60 years respectively. Clinically, 90% cases presented with pain followed by mass abdomen (42%). Sixteen (32%) cases complained of menstrual disturbances, (menorrhagia). Disturbances of gastrointestinal tract were seen in 5 cases (10%). Fever & burning micturition(08%) & (06%) cases respectively. Infertility reported in 2 cases (4%) only. Three cases (6%) in our study had past history of carcinoma at extra ovarian site.

Table 2: Carcinoma at extra ovarian sites.

Extraovarian carcinoma.	Number of cases (n=50) (%).
Myometrium	1 (02%)
Endometrium	1(02%)
Cervix	1 (02%)

Out of total 50 cases, 31 cases (62%) had preoperative CA-125 levels done. 12(37.5%) cases had raised CA125 levels (>35 IU/ml) ranging from 5.8 to 366 IU/ml.

Table 3: showing Consistency of Lesions.

NON – NEOPLASTIC	CYSTIC	SOLID	MIXED
Follicular Cysts	06	0	01
Corpus Luteal Cysts	03	0	01
Inclusion Cysts	0	0	01
Inflammation	0	01	0
Endometriosis	01	02	03
TOTAL(n=19)	10	03	06
PERCENTAGE	52.63%	15.78%	31.57%

Microscopic findings; Out of 19 non- neoplastic lesions, commonest diagnosis was follicular cysts (36.84%) followed by endometriosis (31.57%) & corpus luteal cysts (21.05%) and 1 case each of xanthogranulomatous oophoritis & multiple inclusion cyst, respectively.

Table 4: Histological Subtypes (Non-Neoplastic Lesions).

TYPES	TOTAL (n=19)	% age
Follicular Cysts	07	36.84%
Corpus Luteal Cysts	04	21.05%
Inclusion Cysts	01	05.26%
Inflammation	01	05.26%
Endometriosis	06	31.57%

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Histological Findings (Neoplastic): All neoplastic lesions were unilateral and were of size ranged from 4-22 cms in greatest dimension. These lesions had irregular surface as nodular and papillary projections. Capsule was intact in 24 neoplastic cases (77.41%) and breached in7cases (22.58%). On cut section, majority of tumors showed cystic appearance (48.38%) mainly surface epithelial tumors, both Unilocular (11cases) & multilocular (4 cases). Solid appearance was observed in 6 cases (19.35%). Germ cell tumors were common to show both cystic and solid areas (70%). Papillary projections were seen in 3 cases (09.67%). 9 cases (29.03%) showed pultaceous material with hair in it.

Table 5: Gross & Microscopic Patterns (Neoplastic Lesions).

NEOPLASTIC	CYSTIC	SOLID	MIXED
Surface Epithelial tumors	12	01	03
Germ Cell Tumors	03	0	07
Sex Cord Stromal Tumors	0	02	0
Metastatic	0	03	0
TOTAL (n=31)	15	06	10
PERCENTAGE	48.38%	19.35%	32.25%

Microscopic findings: Neoplastic lesions were divided into four groups, namely, surface epithelial tumors, germ cell tumors, sex-cord-stromal tumors and metastatic tumors. Out of 31(62%) neoplastic lesions, surface epithelial tumors constituted majority of ovarian neoplasm (51.61%) followed by germ cell tumors (32.25%) and tumors metastatic to ovary (9.67%). Sex cord stromal tumors were least common and constituted (6.45%). Among surface epithelial stromal tumors & germ cell tumors, benign tumors were more frequent than malignant tumors.

Table 6: Histological Types (Neoplastic) Based On Cell Of Origin.

TYPES	BENIGN	MALIGNANT	TOTAL (n=31)	% Age
Surface Epithelial Tumors	13	03	16	51.61%
Germ Cell Tumors	09	01	10	32.25%
Sex Cord Stromal Tumors	0	02	02	06.45%
Metastatic	0	03	03	09.67%

In neoplastic tumors, majority of surface epithelial tumors were serous (38.70%) ie serous cystadenomas(29.03%), serous cystadenofibromas (03.22%), and papillary serous cystadenocarcinoma (06.45%) respectively(Figure-2). Other types was mucinous tumor(12.90%) being mucinous cystadenomas (09.67%) and mucinous cystadenocarcinoma (22%). (Figure-3).Benign surface epithelial tumors were more common among serous subtypes (32.25%) than mucinous tumors (09.67%). Mature cystic teratoma (29.03%) was the commonest histological subtype among germ cell tumors. In all cases, cysts were lined by stratified squamous epithelium along with adnexal structures, (cartilage and bone) as mesodermal derivatives. The endodermal derivatives were digestive tract mucosa & thyroid follicles. One case of mixed germ cell tumor showed both yolk sac tumor & dysgerminoma components (Figure-6). Among Sex-cord stromal tumors (SCST), we had one case of sertoli leydig cell tumor (Figure-5) & other case of granulosa cell tumor (Figure-4) Sertoli leydig cell tumor showed variable sized tubules & cords with edematous stroma and infiltration by lymphocytes. Under metastatic group, genital tract was primary site of metastasis. Among 3 metastatic tumors, one case each of leiomyosarcoma, endometrial stromal sarcoma (Figure-7) & squamous cell carcinoma from cervix were noted.

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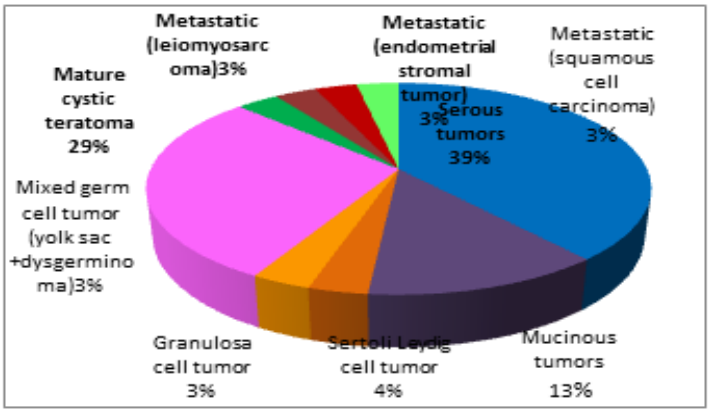
Table 7: Histological Typing Of Tumors (Based On WHO Classification)

Types of tumors	Nature of tumors	Total	Percentage
SURFACE EPITHELIAL TUMORS	Serous Tumors	12	38.70%
	Benign	10	32.25%
	Malignant	02	06.45%
	Mucinous Tumors	04	12.90%
	Benign	03	09.67%
	Malignant	01	03.22%
SEX CORD STROMAL TUMORS	Granulosa Cell Tumor	01	03.22%
	Sertoli Leydig Cell Tumor	01	03.22%
GERM CELL TUMORS	Mature Cystic Teratoma	09	29.03%
	MixedGermCellTumor(Yolk Sac + Dysgerminoma)	01	03.22%
METASTATIC	Myometrium(leiomyosarcoma)	03	09.67%
	Endometrium (Endometrial Stromal Sarcoma)		
	Cervix (Squamous Cell Carcinoma)		

DISCUSSION

We observed 62% cases of ovarian neoplasms and 38% as non-neoplastic lesions showing concordance with study by Ashraf et al[17] & Patel K et Al[19].Another study by Gupta et al[20] observed different results ie (neoplastic 41.20% and non-neoplastic 58.80%) .Zaman S et al[14] encountered 68.87% (non neoplastic) and 31.12% (neoplastic) lesions. More recently Bodal VK et al reported 60% non-neoplastic and 40% as neoplastic lesions. Makwana HH et al, noted higher incidence of non-neoplastic (58.46%) than neoplastic(41.54%) lesions.

Figure 1: Pie Chart showing Histological Typing of Tumors (Based on WHO Classification)



In our study, majority of ovarian neoplasms were benign (70.96%) and malignant constituted (29.03%). No tumor with borderline malignancy seen. This is again in concordance with study by Ashraf et al showing (64.57%) benign and (35.43%) malignant tumors, while other author's study gave different results. Yasmin S et al [13], in their study showed similar results indicating more incidence of benign tumors (89.71%) than malignant tumors (10.29%). Our study also correlated with study carried out by Bukhari U et al [15],indicating 80% benign and 20% malignant tumors with No tumor border line malignancy. This observation contrasts with study of Bhagyalakshmi et al [18] showing (benign 78.03%, border line 3.74% and malignant 18%), while Bodal VK et al reported 75% benign, 1.66% border line and 23.34% malignant tumors respectively. Our study indicated majority of ovarian tumors as surface epithelial stromal category (51.61%). Study by Makwana HH et al, Bhagyalakshmi et al, Bodal VK and Ashraf A et al also showed similar results, as highest percentage of surface epithelial stromal tumors ie 65.71%, 80.02%, 71.67%, and 52.76% respectively. Pradhan A et al16 documented lower incidence as 46.9% in comparison. Second common neoplasm was germ cell tumors constituting 32.25%, similar to studies by other authors. Third common tumor was sex cord stromal tumors (SCST) 6.45%. Incidence was relatively lower than those observed by Makwana HH et al as (9.29%).

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Next common ovarian tumors was metastatic tumors (2.14%), comparable to study by Makwana HH et al. However other workers documented lower incidence.

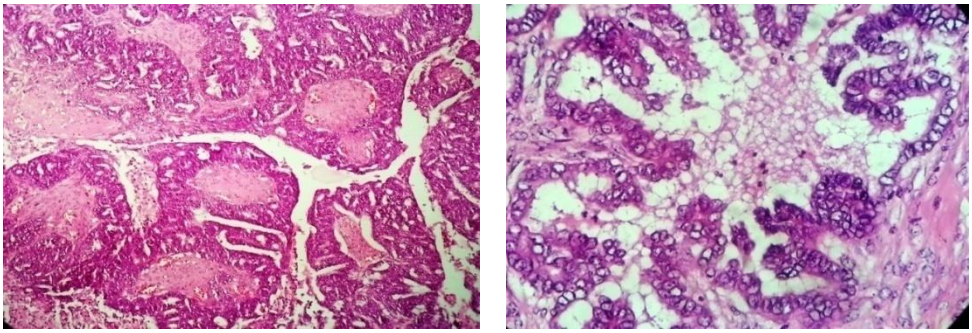

Figure 2: Papillary serous cystadenocarcinoma showing papillary architecture with thick fibrovascular core. (100x, H&E) &(400x) with high nuclear grading.

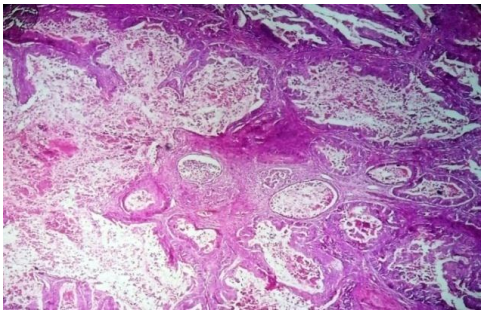

Figure 3: Mucinous cystadenocarcinoma showing complex glandular architecture with minimal intervening stroma. (100x, H&E)

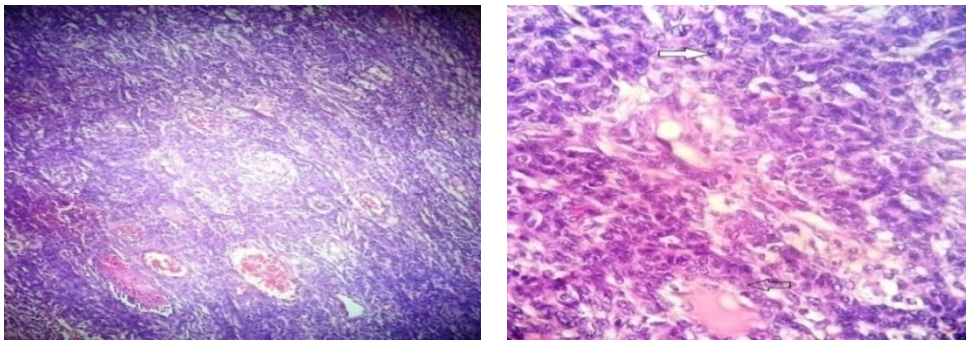

Figure 4: Granulosa cell tumor showing solid sheets & microfollicular pattern of tumor cells. (100x, H&E) & tumor cells showing coffee-bean nuclei (white arrow). (400x, H&E)

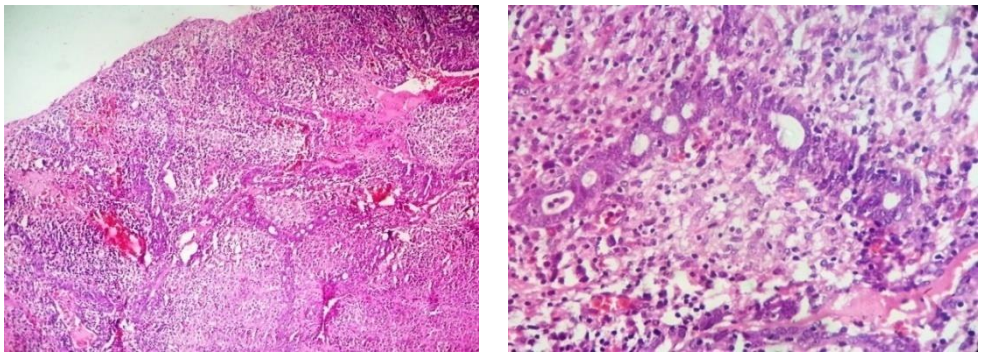

Figure 5: Sertoli-leydig cell tumor showing tubules lined by sertoli cells and separate sheet of leydig cells. (100x, H&E).and (400x, H&E)

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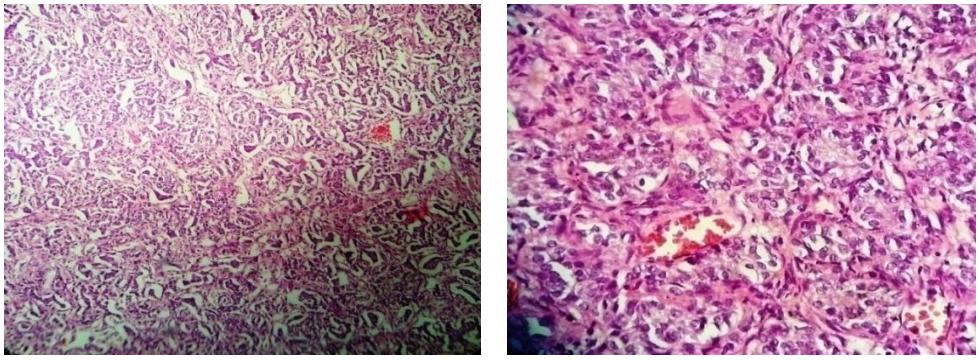

Figure 6: Mixed germ cell tumor showing yolk sac component exhibiting microcystic pattern. (100x, H&E) & dysgerminoma component showing tumor cells having round nuclei arranged in nests and separated by septa.(400x,H&E).

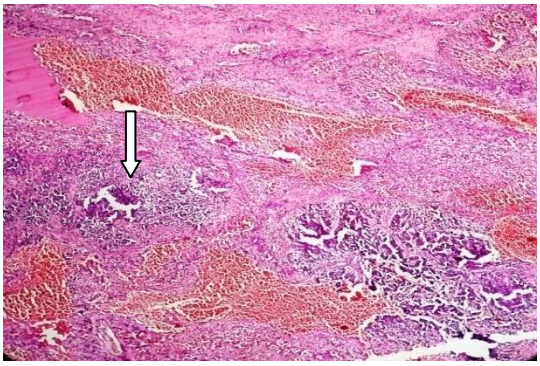

Figure 7: Ovarian stroma shows deposits of endometrial stromal sarcoma. (100 x,H& E).

CONCLUSION

Ovarian neoplasms were more common than non- neoplastic lesions and found mainly, unilaterally in women aged between 31- 50 yrs. A secondary tumor from endometrium was seen at younger age of 35 yrs. All 6% cases were known cases of extra ovarian carcinomas at the time of presentation indicating genital tract, as commonest primary site. 37.5% of cases showed raised CA-125 levels (>35 IU/ml). Commonest non-neoplastic lesion was follicular cyst followed by endometriosis. Among ovarian neoplasms, surface epithelial tumors constituted maximum numbers, followed by germ cell tumors and metastatic tumors respectively. Benign tumors were more commonly seen than malignant tumors, with no borderline malignancy. Serous cystadenomas, mature cystic teratomas & mucinous cystadenomas were common benign tumors, while serous cystadenocarcinomas were commonest primary malignancy. Mature cystic teratoma was commonest histological type among germ cell tumours. Malignant germ cell tumors, constituting 3.22% of all ovarian malignancies, were much less common than epithelial ovarian cancers. Primary malignancies were found to be more common than secondary tumors. In developing countries like India, cost effective histological assessment of ovarian lesions remains mainstay of final diagnosis till date. Assessment of CA-125 levels for ovarian lesions/or tumors is a nonspecific serological test, and is also used as screening test for ovarian cancers in some countries. A specific screening test for ovarian malignancies is the need of time. Regular Pelvic Ultrasound examination yearly in high risk population can be helpful to see structural changes. So early detection and proper histological categorization in conjunction with advanced diagnostic modalities, a more accurate diagnosis can be made, that may be helpful for proper management and thus improving overall prognosis of ovarian malignancies.

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