Correlation between Ultrasound Features and Histopathological Findings in Adnexal Masses – A Study in a Tertiary Care Center in Central India

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Abstract

Background: Ovarian cancer has emerged as one of the most common malignancies affecting women in India. A multidisciplinary approach is needed for the optimal management of patients presenting with adnexal mass wherein the radiologist and the pathologist play an important role in assisting in clinical decision-making. The present study is done to correlate the ultrasound findings with the histopathological findings and to study the whole spectrum of adnexal masses.

Methods: This is a prospective observational study carried out on 60 patients with adnexal masses and pre-operative ultrasound assessment and who underwent surgical resection of their masses in a tertiary care center.

Results: The pre-menopausal age group was more frequently affected than post-menopausal age group. A large number of adnexal masses were of ovarian origin. The incidence of neoplastic adnexal masses is much higher than the non-neoplastic masses. Among the neoplastic adnexal masses majority were ovarian tumors. The incidence of benign ovarian tumors is higher than malignant tumors. Among the malignant tumors, serous cystadenocarcinoma was the most common tumor. Majority of the ovarian tumors diagnosed by ultrasonography (USG) as purely cystic in architecture were proven benign tumors on histopathology. Of the solid-cystic tumors, 50% were benign, and 50% malignant on histopathology solid architecture of the tumors was the least common, and the majority were malignant. USG diagnosis of adnexal masses revealed a sensitivity of 94.4%, specificity of 83.3%, positive predictive value of 70.8%, and negative predictive value of 97.2%.

Conclusions: USG is a sensitive and specific modality in pre-operative diagnosis of the malignant nature of lesions. The presence of solid component in an ovarian mass was a highly accurate predictor of malignancy.

Key words: Adnexal masses, Histopathology, Ovarian tumors, Ultrasound

INTRODUCTION

The adnexal mass may be benign or malignant, but most of these are benign. Most common adnexal mass is of ovarian origin and presents with a diverse range from the functional ovarian cyst to benign tumors or malignant tumors of the

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ovary. The most critical step after identification of the mass is the determination of the degree of suspicion for malignancy, which has a profound effect on patient survival.

Patients are subjected to thorough clinical examination, transvaginal, or transabdominal ultrasonography (USG) and measurement of CA-125, also called the three-pronged evaluation. The role of a gynecologist and radiologist is of paramount importance in the initial assessment of the patient. A revolutionary change has occurred in the pre-operative detection of adnexal masses with the use of grayscale transvaginal and transabdominal USG. It has emerged as a sensitive modality in the diagnosis of malignant masses. The main reason to discriminate

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preoperatively between benign and malignant mass is to promote more conservative management for benign disease and optimize referrals to gynecologic oncologists in cases of suspected ovarian malignancies. A multidisciplinary approach is needed for the optimal management of patients presenting with adnexal mass wherein the radiologist and the pathologist play an important role in assisting in clinical decision-making.

Of all the adnexal masses, ovarian tumors alone account for nearly two-third of all the cases. Ovarian cancer has emerged as one of the most common malignancies affecting women in India. The age-specific incidence rate for ovarian cancer revealed that the disease increases from 35 years of age and reaches a peak between the ages of 55 and 64 years. In India, during the period 2004–2005, the proportion of ovarian cancer varied from 1.7% to 8.7% of all female cancers in various urban and rural population. [1]

The present study is done to correlate the radiological findings with the histopathological findings and to study the whole spectrum of adnexal masses. Ovarian tumors contribute to a large number of cases and an important cause of morbidity and mortality in women of reproductive age group. The ovarian tumors are studied with special emphasis.

Aims and Objectives

The aims and objectives of the study are as follows:

- To study the correlation between "Radiological and histopathological findings in various adnexal masses in a tertiary care center of central India."
- Frequency distribution of various adnexal masses by age, anatomic region, and type.
- To study the sensitivity and specificity of the threepronged approach to clinical diagnosis, ultrasound, and serum CA-125 levels individually in the diagnosis of malignant ovarian tumors.
- To correlate between histopathological and immunohistochemistry findings where ever possible.

MATERIALS AND METHOD

This is a prospective observational study carried out on 60 patients with adnexal masses and pre-operative ultrasound assessment and who underwent surgical resection of their masses from March 2017 to August 2018. Patients with radiological diagnosis and no histopathological reports or vice versa or patients who did not give consent were excluded from the study. The relevant data of the patients including age, parity, clinical presentation, menstrual status, ultrasound

Table 1: Histopathological diagnosis				
Histopathological diagnosis	Nature of tumor	Types	Histopathological diagnosis	n (%)
Surface epithelial - tumors	Serous	Benign	Serous cystadenoma	14 (23.3)
		Borderline	•	0 (0)
		Malignant	Serous cystadenocarcinoma	5 (8.3)
	Mucinous	Benign	Mucinous cystadenoma	10 (16.7)
		Borderline		0 (0)
		Malignant	Mucinous carcinoma	2 (3.3)
	Endometrioid	Benign		0 (0)
		Borderline		0 (0)
		malignant	Endometrioid adenocarcinoma	1 (1.7)
	Clear cell tumors	Benign		0 (0)
		Borderline		0 (0)
		malignant		0 (0)
	Brenner (transitional cell) tumors			0 (0)
Sex cord - stromal tumor	Granulosa - cell tumor			2 (3.3)
	Juvenile granulosa cell tumor			1 (1.7)
	Fibroma the comas			0 (0)
	Sertoli-Leydig cell tumor			0 (0)
	Other sex cord-stromal tumors			0 (0)
Germ cell tumor	Immature teratoma			0 (0)
	Mature teratoma			6 (10)
	Teratoma with malignant transforma	tion		1 (1.7)
	Dysgerminoma			1 (1.7)
	Yolk sac tumor			2 (3.3)
	Mixed germ cell tumor			0 (0)
Metastatic tumors	Krukenberg tumor			1 (1.7)
Nonovarian lesions	Leiomyoma	Benign		7 (11.7)
	Leiomyosarcoma	Malignant		2 (3.3)
	Ectopic pregnancy			3 (5)
Non neoplastic ovarian lesion	Endometriotic cyst			2 (3.3)

findings, and serum CA-125 levels were recorded in a pro forma.

The surgically resected adnexal masses included:

- Ovarian/oophorectomy specimens, either with an attached fallopian tube or in isolation
- Fallopian tube specimens
- Subserosal fibroid along with uterus cervix or as myomectomy specimen
- Broad ligament fibroid.

RESULTS

Analysis of clinical and histopathological diagnosis was done [Table 2], 38 cases were classified clinically as benign of these 36 were proven benign on histopathology. Two cases, however, were malignant on histopathology similarly, 22 cases were classified clinically as malignant of these 16 were proven malignant on histopathology and 6 were benign on histopathology. Thus, 6 cases were false positive on clinical examination and two cases were false negative on clinical examination.

The sensitivity, specificity, and positive and negative predictive value of clinical diagnosis in diagnosing the malignant nature of lesions:

- Sensitivity of clinical diagnosis: 88.9%
- Specificity of clinical diagnosis: 85.7%
- Positive predictive value of clinical diagnosis: 72.7%
- Negative predictive value of clinical diagnosis: 94.7%.

Analysis of radiological and histopathology diagnosis was done [Table 3]. On radiological USG assessment, 24 cases

Table 2: Clinical diagnosis versus histopathology report for malignant tumors

Clinical	Histopathology report		
diagnosis	Malignancy present	Malignancy absent	
Malignancy present	16	6	22
Malignancy absent	2	36	38
Total	18	42	60

Table 3: Ultrasound diagnosis versus histopathological report for malignant tumors

Ultrasound	Histopathol	Total	
diagnosis	Malignancy present	Malignancy absent	
Malignancy present	17	7	24
Malignancy absent	1	35	36
Total	18	42	60

x²=31.76, P<0.0001

x²=30.20, P<0.0001

were classified as malignant of these 17 were proven malignant on histopathology. Thus, seven false positive cases were identified by the radiological assessment. Out of 36 cases classified as benign on USG, 35 proven benign on histopathology. Thus, one case was identified as false negative by USG assessment.

- Sensitivity of ultrasound diagnosis 94.4%
- Specificity of ultrasound diagnosis 83.3%
- Positive predictive value of ultrasound diagnosis 70.8%
- Negative predictive value of ultrasound diagnosis 97.2%

Analysis of ultrasound features with the gross characteristics of adnexal masses [Table 4]: Majority of the tumors diagnosed by USG as cystic masses were proven benign tumors on histopathology. The tumors classified as solid cystic on USG, 50% were benign and 50% malignant on histopathology. Out of 4 tumors classified as solid on USG three were proven malignant on histopathology and one was a benign tumor.

Analyses of CA - 125 assays levels and benign versus malignant nature of ovarian masses [Table 5]. A total of 24 patients had their serum levels checked for CA - 125. Twelve cases had CA - 125 assays levels raised >35 IU/ml and 12 cases had normal levels of CA - 125. Of the 12 cases of raised CA - 125 levels, ten cases were proven malignant on histopathology, and two cases benign thus, two cases were a false positive. Of the 12 cases of normal levels of CA - 125 assays, ten were proven benign and two malignant on histopathology. Thus, two cases were false negative.

The sensitivity, specificity, and positive and negative predictive value of CA – 125 in ascertaining benign or malignant nature of ovarian neoplasms:

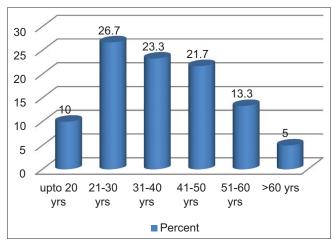
Table 4: Ultrasonography echo pattern versus histopathological gross features of ovarian tumors

Ultrasonography	Histop	Total (%)	
consistency	Benign (%)	Malignant (%)	
Cystic	17 (56.67)	1 (6.25)	18 (39.13)
Solid	1 (3.33)	3 (18.75)	4 (8.70)
Solid Cystic	12 (40.00)	12 (75.00)	24 (52.17)
Total	30 (100)	16 (100)	46 (100)

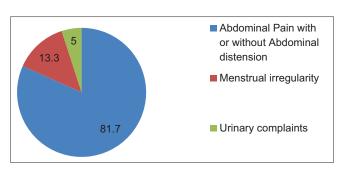
x²=10.14, P<0.006

Table 5: CA – 125 assays versus histopathology report for malignant tumors

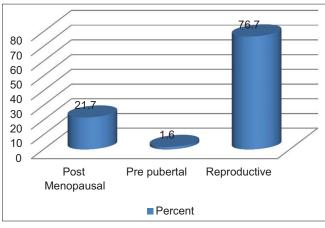
CA - 125 Assays	Histopathology report		Total
	Malignant	Benign	
>35 IU/ml	10	2	12
≤35 IU/mI	2	10	12
Total	12	12	24



Graph 1: Age-wise distribution of cases



Graph 2: Presenting complaints



Graph 3: Menstrual status

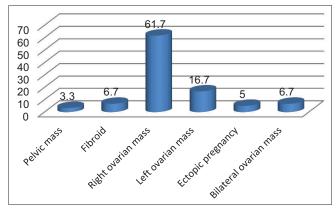
Sensitivity: 83.3%Specificity: 83.3%

Positive predictive value: 83%Negative predictive value: 83%

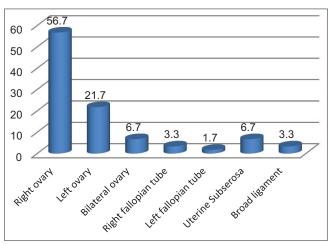
DISCUSSION

Age-Wise Distribution of Adnexal Mass

In the present study, the age range of patients is from 31 to 66 years [See Graph 1]. The mean age of patients is 38.3



Graph 4: Clinical diagnosis



Graph 5: Radiologically confirmed site of lesion

 \pm 13.2. About 71.6% of patients were in the reproductive age group and at the extreme of ages that is below 20 years, and above 60 years, the number of cases was less. The youngest patient in the present study is a 13-year-old girl, belonging to prepubertal age group, presented with pain in abdomen since 2–3 months, she was diagnosed with yolk sac carcinoma measuring 16 cm \times 8.1 cm \times 6 cm. Germ cell tumor is common in children and young adults. The oldest patient is 66-year-old female with leiomyosarcoma measuring 15 cm \times 14 cm \times 10 cm.

Presenting Complaints

In the present study, the most frequenting presenting symptom was abdominal pain with or without abdominal distension and was present in 81.7% of patients. The second most common symptom was menstrual irregularities, present in 13.3% of patients. Urinary complaints were reported in 5% of patients [See Graph 2].

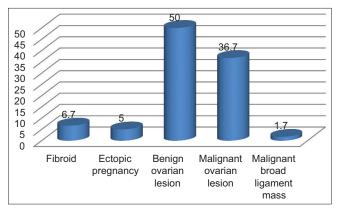
Menstrual Status of the Patients

In our study, 21.7% of patients were postmenopausal and 76.7% of patients belong to the reproductive age group. There is one patient belonging to prepubertal age group [See Graph

3]. Similar findings were reported in a study by Dalia *et al.* (2017)^[2] in which 56% of patient belongs to the reproductive age group and 12% were in the menopausal age group. Study Priya and Kirubamani (2017)^[3] revealed similar findings with 62.83% of women belonging to the reproductive age group and 10.6% of women were postmenopausal.

Site of Lesion

In the present study, 85% of adnexal masses are of ovarian origin. About 6.7% of masses are originated from uterine subserosa. About 5% were of fallopian tube origin and only 3% of the masses were of broad ligament origin [See Graphs 4-6].



Graph 6: Ultrasound diagnosis

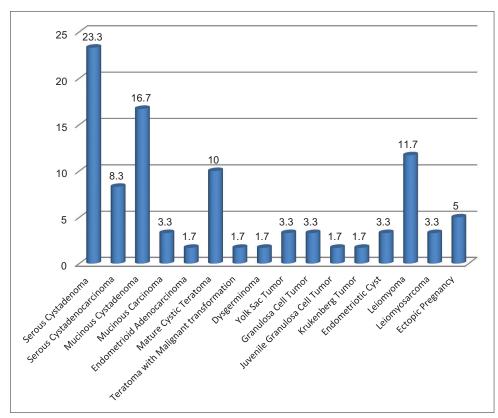
The findings are in concordance with other past studies [Table 6]:

Analysis of Clinical and Histopathological Diagnosis in Determining Malignant Nature of Adnexal Masses Studied

A total of 60 cases of adnexal mass were analyzed out of which 22 cases were diagnosed clinically as malignant, and 38 cases were diagnosed as benign. Out of 22 malignant cases, six cases proved to be benign on histopathology. Hence, six cases were diagnosed with false positive on clinical examination. Out of 38 benign cases, 36 were proven benign on histopathology and two cases were malignant. Hence, two cases were diagnosed with false negative on clinical examination. The sensitivity of clinical diagnosis is 88.9%, specificity of clinical diagnosis is 85.7%, positive predictive value

Table 6: Site (organ of origin) of adnexal mass – comparison with other studies

Study name	Ovary (%)	Fallopian tube (%)	Other causes (%)
Radhamani <i>et al.</i> (2017) ^[5]	93	-	-
Prasad et al. (2017)[4]	96	4	-
Dalia et al. (2017)[2]	84	14	2
Bhagde (2016)[168]	78	16	6
Present study	85	5	10



Graph 7: Histopathological diagnosis [Table 1]

is 72.7%, and negative predictive value is 94.7% in our study.

A study by Priya and Kirubamani (2017),^[3] a total of 113 cases were analyzed and 39 cases were diagnosed malignant on clinical assessment out of which 25 were proven benign on histopathology and 14 as malignant. Hence, 25 false positive cases were diagnosed on clinical examination. Out of 74 cases classified as benign on clinical examination, 72 cases were benign and two cases were malignant. Hence, two cases were diagnosed with false negative on clinical examination.

The findings of the study are concordant with our study with regard to the specificity of clinical examination. The higher degree of sensitivity of clinical examination in our study was due to a thorough preoperative assessment of the patients presenting with adnexal masses which included bimanual pelvic examination, radiological assessment, and measurement of CA-125 assays. All the modalities of pre-operative diagnosis combined together increases the overall sensitivity of clinical diagnosis of adnexal masses.

Diagnostic Accuracy of USG in Differentiating benign from Malignant Lesions

Analysis of the 60 adnexal masses revealed that 17 cases were identified true positive and 35 cases were identified as truly negative. Seven cases were identified as false positive and one was identified as a false negative. The sensitivity was 94.4%, specificity was 83.3%, positive predictive value was 70.8%, and negative predictive value was 97.2%. The findings of our study were concordant with the study by Praad et al.[4] in which USG showed the sensitivity of 92%, specificity of 89%, positive predictive value of 92%, and negative predictive value of 89% in differentiating benign from malignant lesions. A study by Priya and Kirubamani^[3] showed USG sensitivity of 88% and specificity of 80.68% in prediction of ovarian cancer. The findings are similar to our study. A study done by Radhamani and Akhila^[5] revealed that USG had sensitivity of 87.5% and specificity of 95.65% with an accuracy of 95% for predicting ovarian cancer. In a study by Rathore et al., [6] USG showed sensitivity of 100%, specificity of 88.4%, and accuracy of 90.3% in diagnosing malignancy in adnexal masses [Table 7].

Histopathological Distribution of the Adnexal Masses

In our study, the most common histologically confirmed ovarian tumor is serous cystadenoma followed by mucinous cystadenoma and germ cell tumors [See Graph 7]. Majority of the studies conducted showed similar findings as our study.

In a study by Prakash *et al.* (2017),^[7] serous cystadenomas were the most common ovarian tumors diagnosed, accounting for 64.5%. Mucinous cystadenomas were the second most common benign tumor diagnosed, accounting for 24.2%.

A study conducted by Fatima *et al.* (2017),^[8] serous cystadenomas was the most common ovarian tumor diagnosed accounting for 54% of cases. Mucinous cystadenomas were the second most common tumor diagnosed.

In a study by Patel *et al.* (2018),^[9] serous cystadenomas accounted for 57.4% of ovarian tumors and were the most common benign tumor reported. Mucinous cystadenomas accounted for 16% and were the second most common benign tumor reported.

Incidence of Ovarian Tumors as benign Malignant

In our study, 46 cases of the ovarian tumor were reported out of the 46 tumors, 30 were benign tumors, and 16 were malignant. Similar incidence was recorded in many different studies where the incidence of benign tumors was more than malignant [Table 8].

As the study was conducted in medical college, which is a tertiary care center we have a higher incidence of malignant cases as compared to other studies.

CA – 125 Values in Diagnosis of Benign and Malignant Tumors

Serum CA – 125 assays is a valuable preoperative parameter for both diagnosis and monitoring of ovarian epithelial carcinoma.

In our study, serum CA - 125 assays were done in 24 patients of ovarian neoplasms. The analysis was done to assess the role of CA - 125 values in the diagnosis of benign and malignant tumors. Out of 24 patients,

Table 7: Sensitivity, specificity, positive predictive value, and negative predictive value of ultrasound – comparison with past studies

Study name	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Prasad et al.[4]	92	89	92	89
Rathore et al.[6]	100	88.4	-	-
Dalia et al.[2]	71	73.33	71	73
Radhamani et al.[5]	87.5	95.65	-	-
Priya et al.[3]	88	80.68	-	-
Present study	94.4	83.3	70.8	97.2

Table 8: Incidence of benign and malignant nature of adnexal mass

Study name	Benign (%)	Malignant (%)
Patel et al. (2018)[9]	93.2	6.2
Dalia et al.[178]	90	10
Fatima et al.[172]	72	13
Priya et al.[175]	78	21
Radhamani et al.[167]	90.46	9.5
Present study	66	34

12 patients had raised levels (>35 U/ml) in serum and 12 had normal levels (<35 U/ml).

Of the 12 patients with raised CA – 125 level 10 cases were proven malignant on histopathology and two were benign. Of the 12 patients with normal levels of CA – 125, ten were proven benign, and two were malignant on histopathology. The overall sensitivity was 83.3%, specificity was 83.3%, positive predictive value of 83%, and negative predictive value of 83% with the confidence interval of 51.6–97.9.

The overall sensitivity of CA - 125 screening in distinguishing benign from malignant adnexal masses reportedly ranges from 61% to 90%, specificity ranges from 71% to 93%, positive predictive value ranges from 35% to 91%, and negative predictive value ranges from 67% to 90%. [10] The values are similar to our study. Thus, in our study, CA - 125 levels were sensitive and specific in ascertaining the malignant nature of ovarian neoplasms.

A study by Radhamani and Akhila (2017)^[5] showed a sensitivity of 62.5% and specificity of 84.25% in ascertaining the malignant nature of ovarian neoplasms.

Ultrasound Echo Pattern of Ovarian Masses in Relation to Histopathology

In our study, the majority of the ovarian tumors diagnosed by USG as purely cystic in architecture were proven benign tumors on histopathology. The tumors classified as solid-cystic in architecture on USG, 50% were diagnosed as benign and 50% malignant on histopathology. Out of the four tumors classified as solid on USG, three were proven malignant and one was benign on histopathology.

The findings were similar to a study by Hassan *et al.*^[11] In our study, the majority of the cystic masses diagnosed by USG were proven benign 64.04% on histopathology. Out of 6 solid masses, four were proven malignant on histopathology. Moreover, out of eight solid-cystic masses, seven were benign and one was malignant on histopathology.

In a study by Priya and Kirubamani (2017), [3] similar findings were recorded. Out of the cystic masses, majority

were benign on histopathology. Solid tumors turned out to be malignant. Among solid-cystic tumors majority were malignant on histopathology.

Cases

- Case 1 A 48 years old with metastatic adenocarcinoma signet ring cell type (Krukenberg Tumor) [Figure 1a-e].
- Case 2 Leiomyosarcoma [Figure 2a-e].
- Case 3—Low grade papillary serous cystadenocarcinoma ovary in 27 years old [Figure 3a-e].

USG revealed the presence of a large ill-defined multilocular cystic mass of size approximately 13.6 cm × 8 cm in the pelvic region. Uterus displaced anteriorly with the minimum endometrial collection. Bilateral ovaries are not visualized.

Computed tomography findings revealed multiseptated mass-like lesion in the pelvic region with septations and gross ascites suggestive of cystic ovarian growth.

CA - 125 level - 802 U/ml.

On gross examination a creamish color mass measuring $10 \text{ cm} \times 4 \text{ cm} \times 3 \text{ cm}$ partially capsulated showing papillary projections on a surface measuring $1.5 \text{ cm} \times 1.5 \text{ cm}$. On cut section, multilocular, cystic area, and few cysts filled with thick mucoid material. Cystic area measuring $1.5 \text{ cm} \times 1.5 \text{ cm}$. One cyst showing papillary projections measuring $3 \text{ cm} \times 1 \text{ cm}$. Wall thickness varies from 0.2 cm to 0.4 cm.

The IHC penal of markers with showed immunoreactivity is Cytokeratin 7, KI 67 (Positive 10–20%), P53 (weak positive). Cytokeratin 20, Vimentin, and WT1 were negative. A diagnosis of low-grade serous cystadenocarcinoma was made.

- Case 4 Dysgerminoma [Figure 4]
- Case 5 Mature cystic teratoma [Figure 5]
- Case 6 Serous cystadenoma [Figure 6].

SUMMARY

Adnexal masses were found to be more common in the reproductive age group. The premenopausal age group was more frequently affected than post-menopausal age group. Majority of the patients presented with abdominal pain associated with or without abdominal distension as the most frequent presenting symptom. Majority of the patients were clinically diagnosed as ovarian masses. A large number of adnexal masses were of ovarian origin. There were cases of fallopian tube origin and also broad ligament origin masses. USG diagnosis of adnexal masses revealed a sensitivity of 94.4%, specificity of

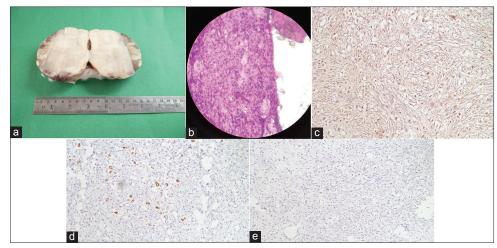


Figure 1: (a) A 48 years old with metastatic adenocarcinoma signet ring cell type (Krukenberg Tumor). Cut section showing solid homogenous tan white and fleshy appearance. (b) Microscopic image showing signet ring cells infiltrating within the cellular and fibrotic stroma. (c) ×20 low power view cytoplasmic positivity for CK7. (d) ×20 low power view CK 20 positivity. Tumor cell shows focal positivity for CK20. (e) ×20 low power view negative for CA125

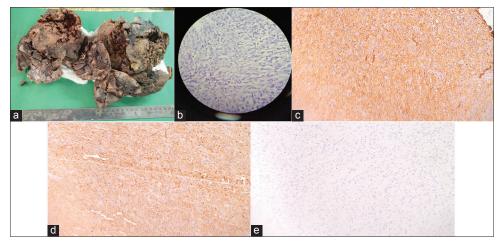


Figure 2: (a) A case of leiomyosarcoma in a 66 years old. Cut section large variegated mass with solid cystic areas and foci of hemorrhage and necrosis. (b) Microscopic image showing hypercellularity pleomorphism, atypical mitoses. (c) ×20 low power view showing positivity for vimentin. (d) View ×20 low power showing positivity for CD117. (e) View ×20 low power negative for desmin

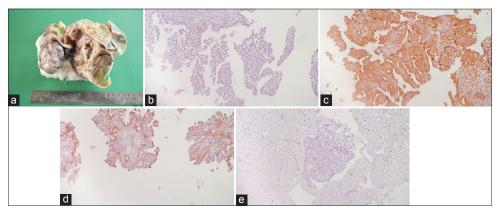


Figure 3: (a) Papillary serous cystadenocarcinoma in a 27 year old. On cut section the tumor is solid cystic with necrotic areas and papillary projections. (b) ×20 low power view showing weak positivity for P-53. (c) ×20 low power view negative for WT1. (d) ×20 low power view positive for CK7. (e) ×20 low power view negative for CK20



Figure 4: Gross image of dysgerminoma. Cut section shows solid homogenous tan color



Figure 5: Gross image of mature cystic teratoma. Cut section cyst filled with greasy material, composed of keratin and sebum



Figure 6: Gross image of serous cystadenoma. Cut section unilocular smooth outer and inner surfaces

83.3%, positive predictive value of 70.8%, and negative predictive value of 97.2%. USG is a sensitive and specific

modality in pre-operative diagnosis of the malignant nature of lesions. The clinical diagnosis of adnexal masses revealed a sensitivity of 88.9%, specificity of 85.7%, positive predictive value of 72.7%, and negative predictive value of 94.7%. Although the clinical diagnosis is a less sensitive in predicting pre-operative diagnosis of the malignant nature of lesions, our study showed the clinical diagnosis is sensitive in pre-operative diagnosis of the malignant nature of masses. The incidence of neoplastic adnexal masses is much higher than the non-neoplastic masses. Among the neoplastic adnexal masses majority were ovarian tumors. The incidence of benign ovarian tumors is higher than malignant tumors. Surface epithelial ovarian tumors were the most common category followed by germs cell tumors. Benign serous cystadenoma was the most common ovarian tumor followed by benign mucinous cystadenoma. Among the malignant tumors, serous cystadenocarcinoma was the most common tumor followed by granulosa cell tumor. Mature cystic teratoma was the most common germ cell tumor. Majority of the ovarian tumors diagnosed by USG as purely cystic in architecture were proven benign tumors on histopathology. Of the solid-cystic tumors, 50% were benign and 50% malignant on histopathology solid architecture of the tumors was the least common, and majority were malignant. CA - 125 is an important tumor marker in preoperative evaluation and ascertaining the malignant nature of ovarian neoplasms.

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