

# ADDIS ABABA UNIVERSITY



## SCHOOL OF MEDICINE

**Ultrasonography and its correlation with histopathologic diagnosis in adnexal masses at Tikur Anbessa Specialized Hospital, 2020, Addis Ababa, Ethiopia**

**(A Retrospective Cross Sectional Study)**

**A research paper to be submitted to Addis Ababa University College of health science department of Radiology, for partial fulfillment of the requirement for postgraduate certificate in Radiology.**

**Prepared by: Tesfa Yilma (MD, Radiology Resident)**

**Advisor: Wondim Getnet (MD, Body Imaging Subspecialist)**

November, 2020 Addis Ababa

## **ABBREVIATIONS**

AAU	Addis Ababa University
CT	Computed Tomography
IOTA	International Ovarian Tumor analysis
MRI	Magnetic Resonance Imaging
PET-CT	Positron Emission Tomography –Computed Tomography
SPSS	Statistical Package for social Science
TASH	Tikur Anbessa Specialized Hospital
USG	Ultrasonography

## **ACKNOWLEDGEMENT**

I would like to thank Addis Ababa University, Department of Radiology for being the reason to know more and providing the opportunity to develop this research proposal. My Deepest and heartfelt appreciation goes to my advisor Dr. Wondim Getnet for his valuable support and his humble advice, starting from topic selection until the end of the project. I take this opportunity to extend my thanks for other staff and residents for their support when I was in need.

## Table of Contents

ABBREVIATIONS .....	b
ACKNOWLEDGEMENT .....	3
List of figures.....	5
List of tables .....	5
Abstract .....	6
1. Introduction.....	7
1.1. Background.....	7
1.2. Statement of the problem.....	8
1.3. Significance of the study .....	9
2. Literature review .....	9
3. Research Questions.....	11
4. Objectives.....	11
4.1. General objectives .....	11
4.2. Specific objectives .....	11
5. Methods and Materials.....	12
5.1. Study area and Period.....	12
5.2. Study design .....	12
5.3. Source and study population.....	12
5.4. Inclusion and exclusion criteria .....	12
5.5. Sample size determination and sampling procedures .....	13
5.6. Data processing and analysis .....	14
5.7. Ethical consideration .....	14
5.8. Dissemination of results .....	14
Result.....	14
Discussion .....	21
Limitations .....	24
Conclusion and Recommendation .....	24
References.....	25

## List of figures

Figure 1: Age distribution of 75 patients with adnexal masses at TASH, 2016-2020.....	15
Figure 2: Characteristics of septation in cystic adnexal lesions on USG findings (n=50) at TASH, 2016-2020.....	18

## List of tables

Table 1. 1: Proportion of benign and malignant mass according to age group as diagnosed by USG and histopathology at TASH, 2016-2020 .....	16
table 1. 2: laterality of masses among benign and malignant groups according to USG findings at TASH, 2016-2020.....	17
table 1. 3: Composition of the mass/lesion among benign and malignant groups according to USG findings at TASH, 2016-2020.....	17
table 1. 4: Presence or absence of papillary projection among benign and malignant group on USG finding at TASH, 2016-2020 .....	18
table 1. 5: Peritoneal/omental deposits among benign and malignant group based on USG findings at TASH, 2016-2020.....	19
table 1. 6: Presence or absence of ascites among benign and malignant group based on USG findings at TASH, 2016-2020.....	19
table 1. 7: Diagnosis of histopathology of adnexal masses at TASH, 2016-2020.....	20
table 1. 8: Sensitivity, specificity, PPV, PNV, accuracy and kappa value of USG compared with histopathology of adnexal masses at TASH, 2016-2020 .....	21
table 1. 9: Comparison of current study with published data .....	22

## **Abstract**

**Background:** Adnexal mass is a common gynecologic problem. The role of imaging is differentiating malignant and benign adnexal masses with intention of guiding patient management. Ultrasonography is the initial imaging modality used in the evaluation of adnexal masses and histopathology is the gold standard in confirming the diagnosis.

**Objective:** Correlation of ultrasound findings with histopathologic diagnosis of adnexal masses at Tikur Anbessa Specialized Hospital.

**Methods:** A cross-sectional retrospective study was analyzed from a period of July 1<sup>st</sup> 2016 to June 30 2020 G.C (4-year period) at Tikur Anbessa Specialized Hospital. Medical records of all patients operated for adnexal pathologies were retrieved. Ultrasonographic findings and examiner's final diagnosis of the mass as to benign or malignant was recorded and its histopathologic correlation was done using kappa statistical method.

**Result:** In this study, of 75 patients with adnexal masses, 41 were malignant and 36 were correctly predicted with ultrasonography. The sensitivity, specificity and accuracy of ultrasound in diagnosing adnexal masses were 87.5%, 70.6% and 80% respectively. We found a positive predictive value (PPV) of 78.3% and a negative predictive value (NPV) of 82.8%. Moderate level of agreement was found between ultrasonography and histopathologic diagnosis with kappa value 0.59.

**Conclusion and recommendation:** USG showed excellent sensitivity with reduced specificity in diagnosing malignant adnexal masses. The lower specificity of USG in predicting benign or malignant adnexal pathologies could lead to unnecessary surgical intervention. However, its inherent advantage of wide availability, inexpensive, lack of radiation and acceptable sensitivity in diagnosing benign and malignant adnexal masses make an USG an important tool in guiding further patient management. Establishing standardized reporting protocol using ovarian-adnexal reporting lexicon for USG and further multicenter prospective studies with strict application of IOTA simple rules for benign and malignant adnexal masses with different level of operator experience are recommended to make good use of USG in optimizing patient treatment in our setting

# **1. Introduction**

## **1.1. Background**

Adnexal mass is a common gynecologic problem with a wide range of masses, which comprise mass of the ovary, fallopian tube, or surrounding connective tissues. It may be found in females of all ages. It may also be secondarily involved from pathologies of adjacent structures, or metastatic deposits from other sites, such as breast and gastrointestinal tract[1]. Commonly, adnexal masses are classified as cystic, complex or solid masses. Follicular cysts, corpus luteum cyst, cystic teratomas, paraovarian cyst, and hydrosalpinx are the commonest cystic masses. Cystadenomas, hemorrhagic cyst, endometrioma, ectopic pregnancy, teratoma (dermoid), abscess, hydrosalpinx are among the main complex masses. Whereas solid teratomas, Adenocarcinomas, fibromas, arrhenoblastomas and dysgerminomas are solid masses[2].

The Primary goal of imaging in the evaluation of an adnexal mass is to differentiate malignant and benign lesions [3]. Ultrasound is the first-line imaging modality in evaluation of patients with suspected pelvic pathology[4]. Gray-scale US is useful for evaluating the morphology of adnexal masses, such as differentiating between cystic and solid masses, assessing internal complexity, and identifying mural nodules. Color or power Doppler imaging is used to detect vascular flow within any solid components. Once the patient has a known malignancy, US is insensitive for initial staging and follow up imaging, for which CT, MRI or PET-CT should be used. Aside from identifying calcifications or macroscopic fat in mature cystic teratomas, CT has limited role in the primary diagnosis of adnexal masses due to poor soft-tissue discrimination. It is primarily utilized in patients with known ovarian malignancy, to assess extent of disease before surgery or evaluate for recurrence. MRI provides excellent tissue contrast resolution and characterization. The major limitations of MRI are accessibility, cost, and the need for the patient to lie still for the examination[4].

Ultrasound is considered as the best diagnostic instrument in finding of adnexal masses[5, 6]. The differentiation between functional ovarian masses that will resolve over time and

nonfunctional masses has tremendous implications for patients' counseling and management. Other types of adnexal cysts (such as endometrioma, mature cystic teratoma, and paraovarian cysts) are also important to diagnose correctly since they may affect patients' fertility and other indirect problems[7].

Ultrasound along with color Doppler imaging are excellent modalities in describing the nature of adnexal pathologies; more over they are cheap, non-invasive and less time consuming. [8].

### **1.2.Statement of the problem**

Adnexal masses are considered one of the most common disorders in gynecology. The lesions of adnexal origin constitute one of the leading cause of female morbidity, a less common cause of mortality and a frequent reason for gynecologic surgery. They can have a variety of causes, including simple ovarian cysts, benign and malignant ovarian tumors, inflammation of the fallopian tubes, and many other causes. The incidence of adnexal malignancy ranks after the carcinoma of the cervix and endometrium. In 2008, the worldwide incidence of adnexal malignancy making the disease as the sixth most common malignancy among women. Ovarian cancer is the third most common malignancy diagnosed in Sub-Saharan and Ethiopian women[9]. In spite of diagnostic and therapeutic advances in the care of women with adnexal malignancy, the overall 5-year survival rate has been changed a little. The adnexal masses often remain undiagnosed until they are large or spread to the pelvis. It is almost difficult to distinguish a benign lesion from its malignant counterpart based on the clinical presentation of adnexal mass[10].

The prevalence of adnexal lesions in the general population of an Indian study is 0.17% -5.9% in asymptomatic women and 7.1% -12% in a symptomatic women[3].

The key task of the radiologist is to distinguish benign from malignant adnexal lesions in order to direct patients to proper management algorithm. Determining whether a clinically detected adnexal lesion is benign or malignant on imaging is often impossible till surgical exploration and histological examination are performed[11]. This may occur with a technically suboptimal examination, as a result of overlapping US features between some types of lesions, or with rare lesions[2]And the field of view is limited and also sometimes the presence of bowel gas obscures proper visualization of the pelvic organs[11].

Although pelvic ultrasound is highly sensitive in detecting adnexal masses, its specificity in detecting malignancy is lower[7]. Histopathology examination is considered as the gold standard[3, 8].

Researches have been conducted to discover method to detect, analyze, and deal with adnexal masses in other parts of the world. When it comes to our country, Ethiopia, no published studies were found. Thus, this research provided sensitivity, specificity and diagnostic accuracy of ultrasound in our setting by evaluating the level of diagnostic strength of USG in differentiating benign from malignant adnexal masses and its degree of agreement with histopathologic findings. Furthermore, it would be used as a basis for further prospective studies.

### **1.3. Significance of the study**

Distinguishing malignant from benign adnexal pathologies and their description based on imaging offers major help in patient management. Histopathologic reports are considered the gold standards for evaluating the accuracy of imaging findings. Although CT and MRI can be used in the diagnosis of adnexal masses, US is the primary choice of imaging for it is cost effective and readily available. Although there are numerous published studies done at global level assessing the diagnostic sensitivity, specificity and accuracy of US for benign and malignant adnexal masses and its histopathologic correlation, there are no published reports done locally. Thus, findings from this study give latest information on the sensitivity, specificity and accuracy of ultrasound in differentiating benign and malignant adnexal masses by comparing with histopathological findings. Furthermore, in low resource settings like ours, where further imaging with CT or MRI is limited, decision on patient management could be made on USG findings.

## **2. Literature review**

The name adnexal mass is most often used for masses involving the ovary because of the high tendency of the ovary for neoplasia which represent two third of these cases[12, 13]. Fewer neoplasms occur in the fallopian tube, which are generally involved in the inflammatory process. Differential diagnosis of adnexal mass is complex and includes functional cysts, benign and

malignant ovarian tumors, paraovarian cysts, tuboovarian abscesses, hydrosalpinx, ectopic pregnancies, tubal malignancy, broad ligament fibroid, fimbrial cysts, sigmoid colon or colon distended with gasses or feces, pelvic kidney, and pregnancy in bicornuate uterus. These masses pose both a diagnostic and management dilemma. Ultrasonography is the primary modality used for detection and characterization of the mass[13]. The benign adnexal pathologies are more common than malignant. Prevalence of malignancy is higher in older ages. The sensitivity & specificity of ultrasound was proved to be very high in detection of adnexal pathologies. Even twisted ovarian cyst & ruptured ectopic pregnancy was correctly diagnosed on ultrasound & Doppler study, which was confirmed preoperatively[11]. The International Ovarian Tumor Analysis (IOTA) group has developed a Simple Rules approach to the sonographic evaluation of an ovarian lesion. These Simple Rules were initially developed from a population of women who all had surgery for an adnexal mass to help less-experienced operators distinguish between benign and malignant adnexal masses. These Simple Rules permit ultrasound practitioners of varying degrees of expertise and background to quickly use uniform terminology and arrive at similar results. The IOTA Simple Rules are comprised of 5 features that are indicative of malignant lesions (M rules) and 5 features that are indicative of benign lesions (B rules). If 1 or more M features apply in the absence of a B feature, the mass is classified as malignant. If 1 or more B features apply in the absence of M features, the mass is classified as benign. If both M features and B features apply, or if no rule applies, the mass cannot be categorized. In the original study, the rules could be applied in 76% (937 of 1233) of tumors, and in these, the masses were correctly classified as benign or malignant with sensitivity of 93% (259 of 278) and specificity of 90% (594 of 659). The positive and negative predictive values were 80% (259 of 324) and 97% (594 of 613), respectively[14]. A prospective study done in 2017, India also reported high level of agreement between USG and histopathologic diagnosis using IOTA simple rules [15].

Transvaginal ultrasonography is the first choice for imaging to differentiate between a benign and a malignant adnexal mass, with a sensitivity of 93.5% and a specificity of 91.5% [16]. The addition of Doppler to ultrasonography can also aid in differentiation[16]. If disease is suspected outside of the ovary, computed tomography may be indicated, whereas magnetic resonance imaging may show malignant characteristics in the ovary more clearly [16]. A retrospective study done in Romania observed a strong correlation between the ultrasound finding and the

pathological result for adnexal tumors ( $p < 0.001$ ) [17]. Various more recent researches done in India reported high sensitivity, specificity, and accuracy of USG in diagnosing benign and malignant adnexal masses [3, 13, 18]. In a cross-sectional study done in 2018 which included eighty four women with different ages having adnexal masses, diagnosed by ultrasonographic evaluations found that USG enabled correct diagnosis of 63 of the 68 benign masses (92.65%) and all 16 malignant masses (100%) [10]. Sensitivity, specificity, accuracy, positive predictive value and negative predictive value of ultrasonography were determined by comparing with final histopathological diagnosis [10]. Ultrasonography in evaluation of nature and type of adnexal masses had sensitivity-88%, specificity-91%, accuracy-94%, positive predictive value-83% and negative predictive value-96% [10].

### **3. Research Questions**

1. What is sensitivity of USG in diagnosing adnexal masses?
2. What is specificity of USG in diagnosing adnexal masses?
3. What is diagnostic accuracy of USG in diagnosing adnexal masses?
4. How do USG findings of adnexal masses correlate with histopathologic diagnosis

### **4. Objectives**

#### **4.1. General objectives**

Correlation of ultrasound diagnosis with histopathologic findings of adnexal masses at Tikur Anbessa Specialized Hospital

#### **4.2. Specific objectives**

Describe the sonographic features benign and malignant adnexal masses

Correlation of ultrasound diagnosis of benign and malignant adnexal masses with histopathologic report

## **5. Methods and Materials**

### **5.1. Study area and Period**

This study was conducted at Tikur Anbessa Specialized Hospital (TASH), Addis Ababa Ethiopia.

TASH is under college of health sciences campus of Addis Ababa University (AAU), which is one of the pioneer universities in the country. The hospital is a tertiary level referral and teaching hospital providing service to people from all corners of the country in its various departments. It gives undergraduate, post graduate and several subspecialty training programs in medical and health sciences. The radiology department is equipped with high-tech radiologic devices including two x-ray machines, around ten ultrasound machines; two CT scan machines and a 1.5T MRI machine. This study was conducted from July 1<sup>st</sup> 2016 to June 30<sup>th</sup> 2020 GC

### **5.2. Study design**

This was an institutional based retrospective cross-sectional study of patients with adnexal masses having both histopathologic report and preoperative USG.

### **5.3. Source and study population**

Source population: All patients with adnexal masses having histopathologic diagnosis and pre-operative US report.

Study population: All patients with adnexal masses having histopathologic diagnosis during the study period were included if prior pre-operative US had been performed.

### **5.4. Inclusion and exclusion criteria**

Inclusion criteria

- ✓ All patients who have both pre-operative ultrasound report and subsequent histopathologic report.

Exclusion Criteria:

- ✓ Patients who have known adnexal pathology prior to current US study
- ✓ Only description without specific histopathologic diagnosis
- ✓ Descriptions with mixed DDx (benign and malignant)

### 5.5. Sample size determination and sampling procedures

A minimum sample size sufficient to demonstrate an agreement of  $k=0.7$  between USG and histopathology in diagnosing benign and malignant adnexal masses was 174 patients. The study was powered at 80% with 95% level of confidence. The hypothesized agreement between USG and histopathology was based on a study conducted by Guerriero et al. that demonstrated an agreement of 0.71. The sample size calculation assumed a lower limit of the kappa co-efficient of  $k=0.6$  and a 50% occurrence of adnexal masses among patients who were served in the study site. The table below indicates derived sample sizes based on the following [19].

$K_0$ = Hypothesized kappa co-efficient (0.7)

$k_L$ = Lower confidence limit of the hypothesized kappa co-efficient (0.6)

$\pi$ = prevalence of adnexal masses (50%)

$n$  = number of raters. In this case, it was 2; USG and histopathology

$\kappa_0$	$\kappa_L$	$\pi$	Number of Raters ( $n$ )			
			2	3	4	5
0.50	0.40	0.10	559	373	301	255
		0.30	264	146	112	95
		0.50	228	120	89	76
0.60	0.40	0.10	140	94	76	64
		0.30	66	37	28	24
		0.50	57	30	23	19
0.70	0.60	0.10	463	311	247	207
		0.30	205	124	99	87
		0.50	174	102	81	73
0.80	0.60	0.10	116	78	62	52
		0.30	52	31	25	22
		0.50	44	26	21	19

All patients with pelvic surgery for ovary(ies), tube(s) and adnexae were searched for from operation room logbook and then patients' medical records were traced and accessed. Patients were recruited into the study when they had both pre-operative USG report and histopathologic diagnosis. The imaging details were extracted from all USG reports including the impression of benign versus malignant category and the favored histologic diagnosis, if offered. The corresponding histopathologic diagnosis were recorded for each patient. Data collection was conducted after receiving ethical clearance to conduct this study from the Ethical Review Committee of Radiology department. Data was collected by the Principal Investigator and was filled into an SPSS software.

## **5.6.Data processing and analysis**

The data collection instruments were coded and data was checked and entered using Epi-data version 3.1 software. It was cleaned and edited accordingly and was exported to SPSS version 21.0 statistical package for analysis and was checked for missing values before analysis. Some descriptive statistics were computed. The sonographic findings were matched with the results of histopathology tests to confirm the sonographic diagnoses. The chi- squared ( $\chi^2$ ) and/or Fisher exact test were used to analyze the data and to test if there were any significant difference between variables. All statistical analysis were performed using SPSS (Version 21), and statistical significance was set at  $P < 0.05$ .

## **5.7.Ethical consideration**

Permission to undertake the study was obtained from Ethical Review Committee of Radiology department to access the medical records of the patients.

## **5.8.Dissemination of results**

Results of the study will be submitted to the department of radiology of TASH as part of dissertation requirement for the postgraduate certificate program and will be presented on a seminar prepared by the research committee for all staff and residents in the department. It will also be submitted for medical journals for possible publication.

## **Result**

There were 212 lists of patients on logbook that underwent USG and surgery for adnexal mass but only 113 of them were available on charts. Out of 113 cases available on chart, only 75 of them were eligible for this study for having full data. Thus, 75 patients who underwent surgery & transabdominal US over the last 4 years (mid 2016-mid 2020) were included and statistically analyzed. The median age of the patients was 45 (mean=43.57) with the minimum and maximum age of 16 and 75 years respectively. The following histogram shows the age distribution of patients.

Figure 1: Age distribution of 75 patients with adnexal masses at TASH, 2016-2020

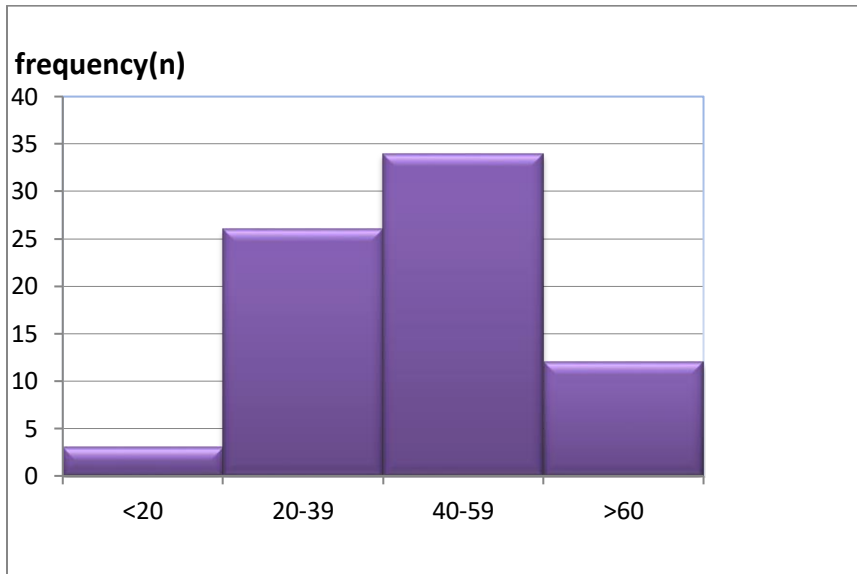


Fig 1: Histogram showing the age distribution of patients

USG diagnosed 29(38.67%) as likely benign and 46(61.33%) as likely malignant whereas, histopathology identified 34(45.33) as benign and 41(54.67) as malignant. The most common age group was 40-59(45.3%). Most of the benign adnexal masses were seen in age group of 20-39 years in both USG and pathology finding whereas most of the malignant masses were seen in age group of over 40 years. It was found that 75% of adnexal masses diagnosed in over 60 years of age were malignant.

Table 1.1 below shows the distribution of benign and malignant adnexal masses based on USG and histopathology diagnosis at TASH, 2016-2020.

Table 1. 1: Proportion of benign and malignant mass according to age group as diagnosed by USG and histopathology at TASH, 2016-2020

Final diagnosis of USG				Histopathologic diagnosis		
Age	Likely benign	Likely malignant	Total & (%)	Benign	Malignant	Total & (%)
<20	2	1	3(4.00)	2	1	3(4.00)
20-39	16	10	26(34.70)	17	9	26(34.70)
40-59	10	24	34(45.30)	12	22	34(45.30)
>60	1	11	12(16.00)	3	9	12(16.00)
<b>Total (%)</b>	29(38.67)	46(61.33)	75(100)	34(45.33)	41(54.67)	75(100)
P<0.005 on Fisher exact test, significant						

## USG Features

On USG finding the characteristics of mass (lesion) including laterality, size and composition was assessed and most patients were found to have unilateral lesions comprising of 48(64%). Almost all lesions were large (>4cm). The majority of cases were cystic (66.7%) and 21 of them were found to have papillary projection of which 17 were malignant. Completely solid tumors were found in Only 4 patients of which three were malignant and one was benign. In addition to sonomorphologic features of the masses, the presence or absence of ascites as well as peritoneal deposits were also evaluated. Of 29 patients found to have ascites, 26 were having malignant lesions. Peritoneal deposit was detected with USG only in 10 patients and all patients were classified as having malignant lesions. Three patients reported to have peritoneal deposits with USG but found to be benign with histopathology were granulomatous inflammation, mature cystic teratoma and mucinous cystadenoma. The following table shows characteristics of masses on USG.

table 1. 2: laterality of masses among benign and malignant groups according to USG findings at TASH, 2016-2020

Laterality	Benign	Malignant	Total (%)
Unilateral	20	28	48(64%)
Bilateral	3	6	9(12.00)
not mentioned	6	12	18(24.00)
Total	29(38.67)	46(61.33)	75(100)

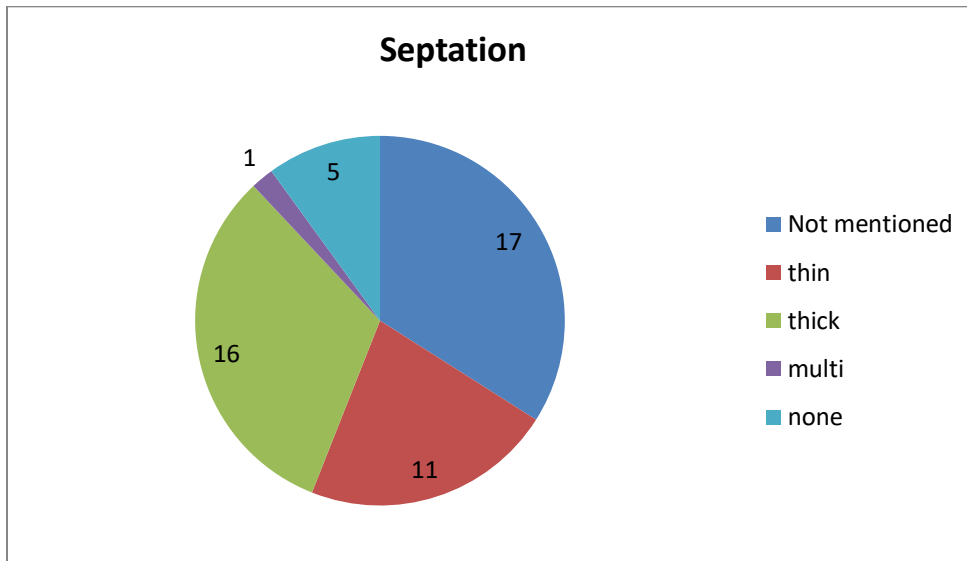
table 1. 3: Composition of the mass/lesion among benign and malignant groups according to USG findings at TASH, 2016-2020

Composition	Benign	Malignant	Total (%)
Cystic	22	28	50(66.70)
Solid-cystic(mixed)	6	15	21(28.00)
Solid	1	3	4(5.30)
Total	29(38.67)	46(61.33)	75(100)

$p > 0.05$  on Fisher exact test, not significant

The cystic lesion was further characterized by the thickness of the wall and septation as well as the presence or absence of papillary projection. Hence, out of 50 cystic lesions, there were 3(6%) thin and 11(22%) thick walled lesions, but wall thickness was not mentioned in 36(72%) of them. There were also 11(22%) lesions with thin septations and 1 multiseptated lesion. The following pie chart illustrates septation characteristics in adnexal masses of cystic lesions on USG.

Figure 2: Characteristics of septation in cystic adnexal lesions on USG findings (n=50) at TASH, 2016-2020



The presence or absence of papillary projection was also evaluated on USG and 21(44%) of cystic lesions had papillary projection and the majority of them 17(34%) were in malignant group (table 1.4).

table 1. 4: Presence or absence of papillary projection among benign and malignant group on USG finding at TASH, 2016-2020

Papillary projection	Benign	Malignant	Total (%)
Absent	9	7	16(32)
Present	4	17	21(44)
Not mentioned	9	4	13(26)
Total	22	28	50(100)

Additionally, presence of extra-lesional findings like peritoneal deposits and ascites was also detected by USG. Thus, the presence of peritoneal deposits was 13.3% among malignant group but not any in benign group. The difference was significant at  $p < 0.05$  (table 1.5).

table 1. 5: Peritoneal/omental deposits among benign and malignant group based on USG findings at TASH, 2016-2020

Peritoneal deposit	Likely benign	Likely malignant	Total (%)
Present	0	10	10(13.30)
Absent	29	36	65(86.70)
Total	29	46	75(100)
P <0.005 on Fisher exact test, significant			

USG also diagnosed 61.3% of cases with ascites amongst that 26 of them were in malignant group. However, there were only 3 patients from benign group which were found to have ascites out of 29 patients and the differences were significant (p<0.0001).

table 1. 6: Presence or absence of ascites among benign and malignant group based on USG findings at TASH, 2016-2020

Ascites	Likely benign	Likely malignant	Total (%)
Absent	26	20	46(61.30)
Present	3	26	29(38.70)
Total	29	46	75(100)
P<0.0001, fisher exact test, significant			

#### Histopathology findings of adnexal mass

Histopathology found out that 41 (54.67%) out of 75 adnexal mass cases were malignant and most of them 35(85.37%) were epithelial ovarian cancer among which 31 of them were serous (seven borderline). Whereas, there were 4 non-epithelial malignant tumors, 3 granulosa cell tumors and one immature teratoma. There was only one metastatic case of GI origin. Out of 34 benign pathologies, 9 of them were serous cystadenoma/fibroma, 4 mature teratoma and 5 of them were inflammatory or infectious diseases. The following table shows benign and malignant diagnosis of histopathology.

table 1. 7: Diagnosis of histopathology of adnexal masses at TASH, 2016-2020

Benign lesions	N (%)	Malignant lesions	N (%)
Serous cystadenoma/fibroma	9(26.47)	Epithelial ovarian cancer	
Mucinous cystadenoma/fibroma	2(5.88)	▪ Serous	24(58.54)
Endometrioma	1(2.94)	▪ Mucinous	1(2.44)
Follicular functional cyst	2(5.88)	▪ Endometrioid	1(2.44)
Corpus luteal cyst	2(5.88)	▪ Undifferentiated	1(2.44)
Simple cyst	2(5.88)	Borderline epithelial tumor	
Mature teratoma	4(11.77)	▪ Serous	7(17.07 )
Ovarian fibroma	3(8.83)	▪ Low grade pseudomyxoma peritonei	1(2.44)
Serous cystadenoma &TB oophoritis	1(2.94)	Non-epithelial ovarian cancer	
Ectopic pregnancy	1(2.94)	▪ Adult granulosa cell tumor	2(4.87)
Pedunculated myoma	2(5.88)	▪ Juvenile granulosa cell tumor	1(2.44)
Infectious or inflammatory	5(14.71)	▪ Immature teratoma	1(2.44)
Serouscystadenoma &TB oophoritis	1(2.94)	Metastasis	1(2.44)
		Borderline malignant Brenner tumor	1(2.44)
Total	34(100)	Total	41(100)

Compared with histopathology (gold standard), USG diagnosed 36 cases as malignant correctly (TP) and 10 incorrectly (FP), it also diagnosed 24 cases as benign correctly (TN) and 5 cases incorrectly (FN). Thus, sensitivity and specificity of USG in diagnosing adnexal mass as malignant and benign was 87.8% and 70.6% respectively with diagnostic accuracy of 80%. Its positive and negative predictive values were 78.3% and 82.3% respectively, and kappa value as 0.59. Table 8 below shows the sensitivity, specificity, PPV, NPV and kappa value of USG compared with histopathology in diagnosing adnexal masses as benign and malignant.

table 1. 8: Sensitivity, specificity, PPV, PNV, accuracy and kappa value of USG compared with histopathology of adnexal masses at TASH, 2016-2020

USG	Histopathology		Total
	Malignant	Benign	
Malignant	36 Sensitivity=87.8% PPV= 78.3%	10	46
Benign	5	24 Specificity= 70.6% NPV=82.8%	29
Total	41	34	75
Accuracy = 80%		K= 0.59 P= 0. 0001, significant	

### Discussion

Ovarian cancer is among the leading causes of cancer deaths in women globally [11].

It is known that some patients with benign adnexal lesions might undergo unnecessary extensive surgery whereas patients with potentially malignant mass might inadvertently be triaged into expectant management. Pre-operative prediction of adnexal masses as benign and malignant using USG, which is widely available and inexpensive help optimize patient management[20].

The mean age of patients in this study was 43.57 years ranging from 16 years to 75 years which is comparable to other studies[13, 15, 18]. There was significant differences among age group on incidence of benign and malignant masses on US findings in the current study ( $p < 0.005$  on fisher exact test) suggesting that there is an increased chance for an adnexal mass to be malignant with increasing age of the patient. Most of the malignant adnexal masses were found in patients aged more than 40 years and benign masses were most common in patients between 20-39 years of age consistent with findings in most literatures [11, 13, 15, 18]. The highest incidence of adnexal pathologies reported in study done by MM Roshed et al. was in women between 21-40 years of age which is a younger age group than the present study (40-59 years). This is because the former study was done in a majority of younger population.

Among 75 patients with adnexal masses, 45.33% were benign and 54.67% were malignant in contrast to findings in some prospective studies, in which benign adnexal pathologies were more

common than malignant [10, 13, 15, 21]. This is probably due to the greater proportion of women in post-menopausal age group in this study. The other reason is the fact that the data was obtained from operation room logbook, might have higher number of patients with malignant adnexal pathologies, which are more likely to be operated on.

In this study, of 41 patients with malignant adnexal neoplasms confirmed with histopathology, 36 patients were correctly labeled as malignant on preoperative gray scale USG using sonomorphologic criteria as predictors of malignancy and benignity of adnexal masses with a sensitivity, specificity and accuracy of 87.8, 70.6% and 80% respectively. Our present study has similar sensitivity, specificity and accuracy with observational prospective study done by Priya MHF et al [18]. However, the specificity and accuracy of the present study were lower than the specificity and accuracy reported by other authors [10, 13]. The lower specificity and accuracy in this study is due to the limited number of patients and the lack of use of additional tumor characteristics (tumor vascularity) which were used in those studies. Another prospective study authored by Sugandha gaRg et al., which used sonomorphologic features of adnexal masses to classify them as benign and malignant reported comparable sensitivity and accuracy with slightly lower specificity. The positive predictive value (PPV) of USG for malignant adnexal masses in the current research was 78.3%. The degree of agreement (kappa value 0.59) is also in the range of moderate to high level of agreement reported in most literatures [15, 22-24]. The following table summarizes the comparison of sensitivities, specificities and accuracy of the current study with the published data

table 1. 9: Comparison of current study with published data

	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV	NPV
Current study	88.7	70.6	80	78.3	82.8
Priya et al.	88	80.7	82.3	56.4	95.9
Roshed et al.	88	91	94	83	96
Radhamani et al.	87.5	95.7	95	63.6	98.9
Sugandha et al.	91.6	84.8	88.9	68.8	96.6
Grab et al.	92	60	63	23	98

The current study found no significance difference among benign and malignant adnexal masses concerning consistency, a similar report with a research authored by Yashi et al. In this study, 23 (46%) of 50 cystic, 15 (71%) of 21 mixed solid-cystic, and 3(75%) of 4 solid masses were found to be malignant at histopathologic examination consistent with findings in other literatures that reported completely solid adnexal masses were found to have highest rate of malignancy. However, there are also solid adnexal masses such as ovarian fibroid and pedunculated myoma which are benign in nature [14]. There were five unilocular cystic masses with papillary projection. Two were borderline serous cystadenocarcinoma in reproductive age group and 3 were high grade serous cystadenocarcinoma in postmenopausal women. All were classified as malignant on USG. There are some literatures [14, 20] which reported the presence of papillary

projection in unilocular cysts are associated with low malignant potential or full blown malignant tumors.

The presence of ascites was another USG criterion to predict the malignant nature of adnexal masses. Of 29 patients with ascites in this research, 26 were classified as malignant on USG with six false positive cases. These were 2 ovarian fibromas, 1 case of serous cystadenofibroma, 1 mature cystic teratoma, 1 mucinous cystadenoma and a case of granulomatous inflammation. Ovarian fibromas were described as cystic lesions with papillary projection and ascites. Although classic sonographic appearance of ovarian fibromas are solid mass with posterior acoustic shadowing which may be associated with ascites and pleural effusion, cystic appearance are also described making them difficult to accurately diagnose on USG with such atypical presentation in which it is recommended to have MRI to define their fibrous nature [14]. MRI was not done in our case. The case of mucinous cystadenoma was seen as large pelvic cystic mass with thick septation, papillary projection, ascites and peritoneal nodules. It is rare to find mucinous cystadenoma with papillary projection and there were no literatures reporting isolated benign mucinous cystadenoma with peritoneal nodules. However, there are few researches which mentioned intermixed mass composed of a mucinous cystic tumor and mural nodules of pleomorphic undifferentiated sarcoma and benign Brenner tumor and associated with multifocal nodular histiocytic aggregates on the surface of the greater omentum [25]. With all these sonographic features suggestive of malignancy it is prudent to consider the possibility of areas of frank malignant tumor and make repeat histopathologic review in this case.

In the current study there were five (5) cases reported as benign on USG but turned out to be malignant on histopathologic examination. These were three (3) cases of serous cystadenocarcinomas: one in 26 years old woman, which was described as unilateral thin-walled cystic adnexal lesion with thin septation and no papillations or ascites. The other was unilateral mixed cystic-solid lesion measuring 6.7cm in its largest dimension with no ascites in a 40-year-old woman and the third case was unilateral cystic lesion with thin septation and papillary projection in 57 years old woman measuring 6.4cm in its maximum dimension. Opinions vary among existing literatures regarding the predictive power of mixed cystic-solid adnexal masses for malignancy. IOTA simple rules required size of  $\geq 10$ cm to be considered malignant for such masses when other criteria for malignancy were not present[15]; whereas Brown et al. described cystic mass with solid component as the strongest feature of malignancy without mentioning the cut off point for size[2]. Septal thickness and number of papillary projection are also important predictors of malignancy. In our study, although subjective assessments might play a role, inconsistent application of USG simple rules by the sonologist can be deduced from failure to mention the size and number of papillary projection as well as septal thickness in the description. Given the time interval from USG examination to surgery was 8 months with no follow up imaging of the lesion just described in the 57 years old patient, it was difficult to rule out the possibility of malignant transformation. The other two were adult and juvenile granulosa cell tumors. One was 12cm \* 7cm measuring mixed solid-cystic unilateral mass with no ascites or

peritoneal deposit in a 61-year-old woman reported to be adult granulosa cell tumor at histopathologic examination; the juvenile granulosa cell tumor was described as huge abdominopelvic cystic mass with thin septation but no papillary projection, ascites or peritoneal deposit in 23 years old patient. Although granulosa cell tumors can have any consistency, from purely solid to purely cystic, and difficult to apply sonographic simple rules because of their rarity, the large size and mixed solid-cystic nature of the mass in this 61 years old woman would have helped the sonologist conclude as malignant, underscoring the importance of IOTA simple rules. The period from the time of USG examination to the time of surgery was less than 6 months in both cases.

There were also two patients with infectious and inflammatory lesions, which mimicked malignancy on USG. One was described as bilateral thick-walled cystic adnexal lesion with thick septation and papillary projection in a 22-year-old patient confirmed to be tuberculous salpingitis at histopathologic examination. The second was a 56-year-old woman with bilateral multiseptated cystic adnexal lesion with ascites and peritoneal nodules but found to be granulomatous inflammation at biopsy. Infectious and inflammatory adnexal pathologies are among the difficult lesions to classify as benign and malignant based on sonomorphologic features [14].

### **Limitations**

Its retrospective nature and small number of patients limited this study. Additionally, non-electronic medical record keeping made retrieving patient files difficult. Many patient files were with incomplete records due to poor chart keeping and use of a different record number in the pathology department. The other limitation was that USG descriptions were not detail to the standard.

### **Conclusion and Recommendation**

USG showed excellent sensitivity with reduced specificity in diagnosing malignant adnexal masses. The lower specificity of USG in predicting benign or malignant adnexal pathologies could lead to unnecessary surgical intervention. However, its inherent advantage of wide availability, inexpensive, lack of radiation and acceptable sensitivity in diagnosing benign and malignant adnexal masses make an USG an important tool in guiding further patient management. Establishing standardized report using ovarian-adnexal reporting lexicon for USG and further multicenter prospective studies with strict application of IOTA simple rules for benign and malignant adnexal masses with different level of operator experience are recommended to make good use of USG in optimizing patient treatment in our setting.

## References

1. and N.I.o.H.C.D.C. Statement, *Ovarian cancer: screening, treatment, and follow-up*. Gynecol Oncol, 1994.
2. Douglas.L. , B.K.M., Dudiak , F.C., Laing, M, *Adnexal Masses: Ultrasound Characterization and Reporting*. . Radiology, 2010: p. 254: 342-354.
3. Om Prakash Rathore, K.R., R. N. Gehlot *Radiopathological Correlation of Adnexal Lesions: Our experience*. JMSCR, 2017.
4. Dinushi S. Perera, H.B.P., *Imaging of the adnexal mass*. Clinical obstetrics and gynecology, 2015. **58**: p. 28-46.
5. Van Gorp T, V.J., Van Calster B, Cadron I, Leunen K, Amant F, Timmerman D, Vergote I., *Subjective assessment by ultrasound is superior to the risk of malignancy index (RMI) or the risk of ovarian malignancy algorithm (ROMA) in discriminating benign from malignant adnexal masses*. Eur J Cancer, 2011: p. 48:1649–1656.
6. Meys EM, K.J., Kruitwagen RF, Slangen BF, Van Calster B, Aertgeerts B, Verbakel JY, Timmerman D, Van Gorp T, *Subjective assessment versus ultrasound models to diagnose ovarian cancer: a systematic review and meta-analysis* Eur J Cancer, 2016: p. 58:17–29.
7. MD, P., *Pitfalls in the sonographic evaluation of adnexal masses*. Ultrasound Q, 2012.
8. Elizabeth Asch, D.L., Young Kim, Jonathan L. Hecht, *Histologic,Surgical,and Imaging Correlations of Adnexal Masses* Ultrasound Med, 2008: p. 27:327–342.
9. SWANTJE PISZCZAN, D.D., HEZKIEL PETROS, MENGISTU GURMU, ERIC SVEN KROEBER, ADAMU ADDISSIE, RAFAEL MIKOLAJCZYK, and A.M. RAHEL G. GHEBRE, CHRISTOPH THOMSEN, AHMEDIN JEMAL, EVA JOHANNA KANTELHARDT, *Clinical Characteristics and Survival of Patients with Malignant Ovarian Tumors in Addis Ababa, Ethiopia*. The oncologist, 2019. **24**: p. e303-e311.
10. MM Roshed, M.A., SM Hossain, *A comparative study of nature of adnexal masses by ultrasonography and histopathology* Bang Med J Khulna 2018. **5**(1): p. 7-11.
11. Jagruti Kalola<sup>1</sup>, H.H., Anjana Trivedi, Jay Thakkar *Ultrasound Evaluation of Adnexal Pathologies*. Scholars Journal of Applied Medical Sciences (SJAMS), 2014. **2**(6G): p. 3324-3330.
12. Hassan AY, E.a.A., Darweesh FF, *Two dimensional ultrasound and doppler in assessment of adnexal masses in correlation to histopathological analysis*. Academic J Cancer Res. , 2014: p. 7(1):8-18.
13. S Radhamani, M.V.A., *Evaluation of Adnexal Masses - Correlation of Clinical, Sonological and Histopathological Findings in Adnexal Masses*. International Journal of Scientific Study, February 2017. **4**(11).
14. Phyllis Glanc, B.B., Tom Bourne et al, *FirstInternationalConsensusReporton Adnexal Masses* J Ultra sound Med, 2017: p. 0278-4297
15. Sugandha gaRg, a.K., jaSwindeR KauR mohi, PReet Kanwal Sibia, navKiRan KauR *Evaluation of IOTA Simple Ultrasound Rules to Distinguish Benign and Malignant Ovarian Tumours*. Journal of Clinical and Diagnostic Research, 2017.
16. Wendy S. Biggs, S.T.M., *Diagnosis and management of adnexal masses*. American family physician, 2016. **96**.
17. Liana Pleş, R.-M.S., Anca Burnei, *The experience of our Clinic in laparoscopy for adnexal masses and the correlation between ultrasound findings and pathological results*. Rom J Morphol Embryol 2016: p. 1337–1341

18. Margaret Harriet Priya F.\*, V., N. Hephzibah Kirubamani, *Clinical correlation of ovarian mass with ultrasound findings and histopathology report*. International Journal of Reproduction, Contraception, Obstetrics and Gynecology, 2017. **6**(12): p. 5230-5234.
19. Donner, A.a.R., Michael A. , *Sample Size Requirements for Interval Estimation of the Kappa Statistic for Interobserver Agreement Studies with a Binary Outcome and Multiple Raters*. The International Journal of Biostatistics, 2010. **6**(1).
20. Brentj Wagner, M., USAFMC .James L Buck, CDR, MC, USNR and M.K.M.M. Jeffrey D. Seidman, Major, USAF MC, *Ovarian Epithelial Neoplasms: Radiologic-Pathologic Correlation*. Radiographics, 1994. **14**: p. 1351-1374.
21. Dieter Grab, M.D., Felix Flock, M.D.,\* Iris Sto"hr, M.D.,\* Karin Nu"ssle, M.D., Andrea Rieber, M.D., and M.D. Sabine Fenchel, Hans-Ju"rgen Brambs, M.D., Sven N. Reske, M.D., and Rolf Kreienberg, M.D, *Classification of Asymptomatic Adnexal Masses by Ultrasound, Magnetic Resonance Imaging, and Positron Emission Tomography*. Academic Press, 2000. **77** p. 454–459.
22. Bhawna Sharma, N.A.R.A.e.a., *Evaluation of simple International ovarian tumor analysis ultrasound rules in differentiating between benign and malignant ovarian tumors and their histopathological correlation*. International Journal of Reproduction, Contraception, Obstetrics and Gynecology, Feb 2020 **9**(2): p. 652-658.
23. Dr. Yashi, S.S., *Correlation of Ultrasound Findings with Histopathology of Pelvic Masses in a Tertiary Care Hospital*. International Journal of Health Sciences & Research, 2019. **9**(1).
24. Guerriero, S.A.e.a., *Past, present and future ultrasonographic techniques for analyzing ovarian masses*. Womens Health 2015. **11**(3): p. 369–383.
25. Shaolong Yang, M., Li Wang, MD, Kai Sun, MD, *Ovarian mucinous cystic tumor associated with sarcomatous mural nodule and benign Brenner tumor*. Medicine, 2019. **98**(3).