Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/jptcp.v31i1.4001

DIAGNOSTIC ACCURACY OF ULTRASOUND IN DIFFERENTIATING OVARIAN NEOPLASM, BY TAKING HISTOPATHOLOGY AS GOLD STANDARD

Rabail Hameer[1], Shafaq Aijaz[2*], Abid Hussain[3], Sualeha Usman[4], Radha[5], Ekta Raj[6], Iqra Mustafa[7]

[1]FCPS Diagnostic Radiology, WMO BPS17, Liaquat University of Medical and Health Sciences, Jamshoro - Pakistan
[2*]Consultant FCPS Radiology, WMO BPS 17, Diagnostic Radiology, People University of Medical and Health Sciences, Nawabshah - Pakistan
[3]Senior Registrar Radiology, Indus Medical College, Tando Muhammad Khan - Pakistan
[4]FCPS-II Trainee Diagnostic Radiology, Liaquat University of Medical and Health Sciences Jamshoro - Pakistan
[5]FCPS Diagnostic Radiology, Consultant Radiologist, Jinnah Postgraduate Medical Centre, Karachi, - Pakistan
[6] FCPS Radiology, Diagnostic Radiology Department, Civil Hospital, Hyderabad - Pakistan
[7]Postgraduate Trainee Radiology, Diagnostic Radiology Department, Liaquat University of Medical and Health Sciences, Jamshoro - Pakistan

***Corresponding author:** Shafaq Aijaz
*Consultant FCPS Radiology, WMO BPS 17, Diagnostic Radiology, People University of Medical and Health Sciences, Nawabshah – Pakistan Email: memonshafaq@rocketmail.com

Abstract:

Introduction: Ovarian neoplasms are common gynecological problems. Ultrasound is the primary imaging of choice for evaluation of ovarian lesions. Moreover, it is a cost-effective modality and used to characterize mass on the basis of features initially.

Objective: "To determine the diagnostic accuracy of ultrasound in differentiating ovarian neoplasm, by taking histopathology as gold standard

Study design: Cross-sectional study

Setting: Department of radiology, Liaquat University of Medical and Health Sciences, Jamshoro - Pakistan

Study duration: 10th November 2021 till 10th may 2022

Methods:

Women aged 20-45 years presenting with ovarian lesions >8 cm on ultrasound were included. Patients underwent laparotomy after ultrasound. Diagnostic accuracy including sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of ultrasound was calculated using 2 x 2 tables keeping histopathological findings as gold standard.

Results: Mean age of the patients was 36.01 ± 6.44 years. Mean duration of symptoms was 27.75 ± 17.2 months. Total 25 (11.50%) had 1 parity and 192 (88.50%) had >1 parity. Diagnostic accuracy of ultrasound in cases of malignancy showed sensitivity, specificity, positive predicted value (PPV), negative predicted value (NPV) and overall diagnostic accuracy as 82.68%, 73.68%, 93.67%, 47.46% and 81.11% taking histopathology as gold standard.

Conclusion: Ultrasound has high sensitivity, moderate specificity, and high diagnostic accuracy in diagnosing malignant ovarian masses taking histopathology as gold standard.

Keywords: Ovarian masses; ultrasound; ovarian cancer; sensitivity; specificity

Introduction:

Ovarian cancer is now the fourth leading cause of cancer death in the United States, with more than 14,000 deaths being reported each year.[1] adnexal lesion characterization (benign vs malignant) is essential for proper patient evaluation and treatment decisions. Among women in the United States, ovarian cancer is the eighth most common cancer and the fifth leading cause of cancer death, after lung and bronchus, breast, colorectal and pancreatic cancers.[2] Cancer data reported by an institutional study conducted in Pakistan, show that female breast cancer was the most common cancer accounting for 38.5% of female malignancies followed by ovarian cancer 13.6% [3]. Ovarian cancer has highest mortality rate among all gynecological malignancy due to late diagnosis. Due to lack of early clinical symptoms around 60%-70% of women have advance disease (stage III or IV) at the time of diagnosis.[4] Ultrasonography is the primary modality used for detection and characterization of the mass.[5] It plays an important role in the initial evaluation of an adnexal mass as well as in screening of high-risk patients.[6] Ultrasound relies on morphologic features to distinguish between benign and malignant lesions; features such as thick irregular walls, papillary projections, and solid echogenic locules are considered signs of malignancy.[7] A morphologic scoring system using endovaginal ultrasound was suggested to distinguish benign from malignant ovarian lesions. Funt SA et al., showed in their study that ultrasound is the primary imaging modality for the ovaries, with accuracy of up to 94% for diagnosis of malignancy.[8,9] an study conducted by Gentry-Maharaj et al evaluated the sensitivity and specificity of ultrasound and its efficacy for diagnosing ovarian cancer in comparison with CA-125, they showed the specificity of Ultrasound to be around 74.4% and specificity to be around 90%.[10] Early and accurate differential diagnosis of adnexal masses, including their benign or malignant nature is important to decide early intervention among ovarian mass women. Ultrasound is the most basic, non-invasive technique which can be used for diagnosis. Apart from that, in our economically challenged country ultrasound is one of the most cheaply diagnostic measures which can be availed easily at any basic health unit of our society[2,9]. A study to predict diagnostic accuracy only using ultrasound hasn't been conducted in our setup on our objective, so this study has been planned to assess the sensitivity, specificity, and positive and negative predictive values of abdominal sonographic imaging for discriminating ovarian masses."

Material and methods:

Setting: The study will be conducted in the department of radiology Liaquat University Hospital, Hyderabad - Pakistan

Duration of study: 10th November 2021 till 10th May 2022

Study design: Cross sectional

Sample size: Sample size is estimated using diagnostic accuracy sample size calculator by using sensitivity 74%,specificity 90%[10],prevalenace 53[11]% margin error of about 8% for sensitivity, 5.8% for specificity, the estimated sample size is 217.

Sampling technique: Non-probability consecutive sampling

Inclusion criteria:
• Women will undergo laparotomy for ovarian masses
• Age between 20-45 years
• Ovarian lesion measuring >8 cm

Exclusion criteria:
• Patients already known with ovarian neoplasm
• Pregnant women showing ovarian lesions on routine ultrasound
• Patients with known bleeding disorders, diagnosed before.
• Patients don't want to participate in the study

Data Collection Procedure:
Patients presented in gynecology and radiology departments and those fulfill the inclusion criteria as per approval of ethical committee letter no (lumhs/rec/-901) will be enrolled in this study after taking informed consent. Complete medical history and clinical examination will be done. All the selected patients will undergo fresh ultrasound and finding related to ovarian neoplasm, will take their biopsy for histopathology after laparotomy. Ultrasound will be taken by senior sonologist having experience more than 5 years. During laparotomy specimen will be taken and kept in 10% formalin and sent immediately to the diagnostic laboratory for the histopathology. All the findings of study variables such as age, place of residence, parity, findings of ovarian neoplasm on ultrasound and histopathology was noted on the performa.

Data analysis:
The data will be entered and analyzed in statistical program spss version 21.0. Mean and standard deviation or median was be estimated for quantitative variables like age, parity, duration of disease. Simple frequency and percentage was calculated for place of residence, ultrasound findings and biopsy findings. 2 x 2 table was used to calculate the sensitivity (se), specificity (sp) "positive predictive value (ppv), negative predictive value (npv) and accuracy of "ultrasound findings" by taking histopathology as gold standard. Effect modifier like age, place of residence, duration of disease and parity will be addressed through post stratification 2 x 2 table and was computed to calculate the sensitivity, specificity, ppv, npv and diagnostic accuracy of ultrasound."

Results:
Mean age of the patients was 36.01 ± 6.44 years. (Table 1)
There were 49 (22.60%) patients with ≤30 years of age and 168 (77.40%) with >30 years of age. (Figure 4)
Mean duration of symptoms was 27.75 ± 17.2 months. (Table 2)
There were 112 (51.60%) patients with ≤25 months of duration of symptoms and 105 (48.40%) patients with >25 months of duration of symptoms. (Figure 5)

Total 25 (11.50%) had 1 parity and 192 (88.50%) had >1 parity. (Figure 6)
Total 118 (54.40%) patients in urban areas and 99 (45.60%) patients in rural areas. (Figure 7)
Positive findings for malignancy on ultrasound were found in 158 (72.80%) patients while on Histopathology malignancy was observed in 179 (82.50%) patients. (Figures 8 and 9)
Diagnostic accuracy of ultrasound in cases of malignancy showed sensitivity, specificity, positive predicted value (PPV), negative predicted value (NPV) and overall diagnostic accuracy as 82.68%, 73.68%, 93.67%, 47.46% and 81.11% taking histopathology as gold standard. (Table 3)
Stratification was done with respect to age, duration of symptoms, parity and place of residence. Results are shown in detailed in tables 4-11.

Table 1: Mean age of the patients (n=217)		
Mean ± SD	Minimum	Maximum
36.01 ± 6.44	20	45

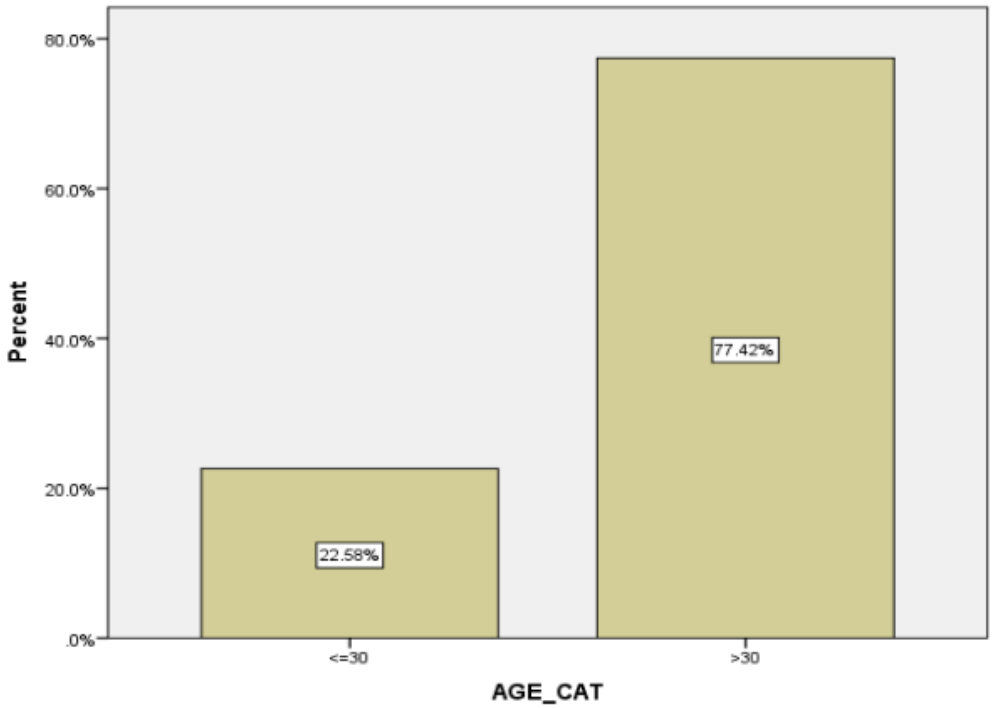

Figure 4: Age group of patients in years

Table 2: Mean duration of symptoms in months (n=217)		
Mean ± SD	**Minimum**	**Maximum**
27.75 ± 17.2	1	69

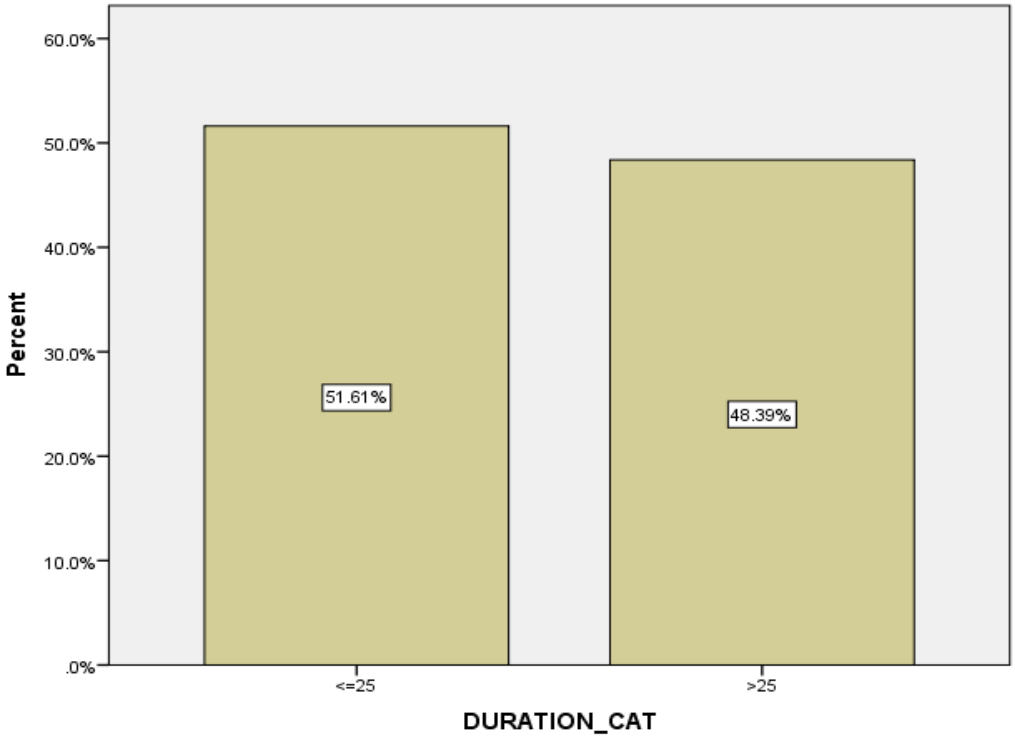

Figure 5: Duration of symptoms in months

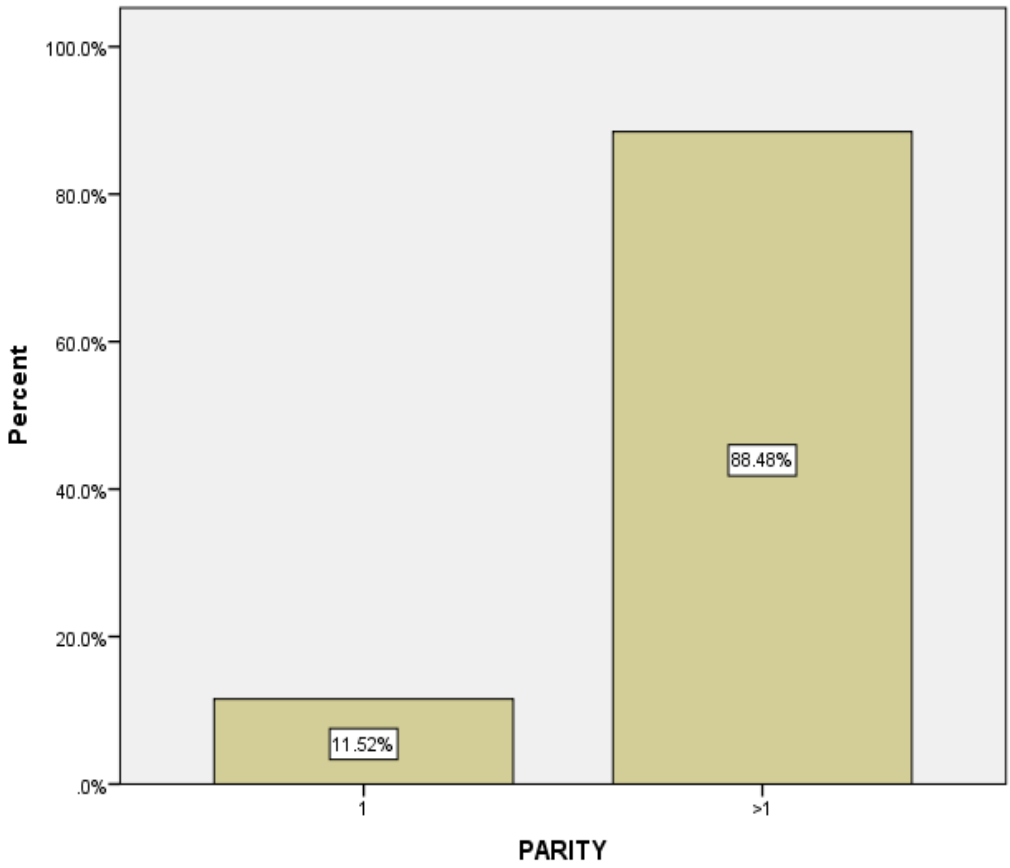

Figure 6: Parity

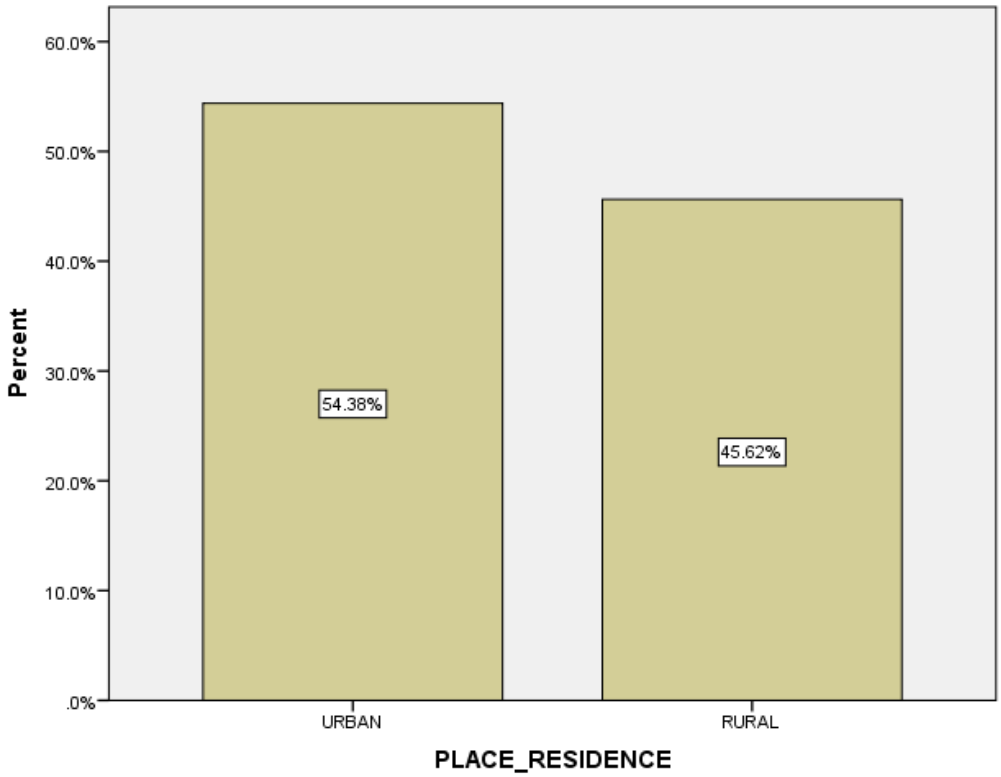

Figure 7: Place of residence

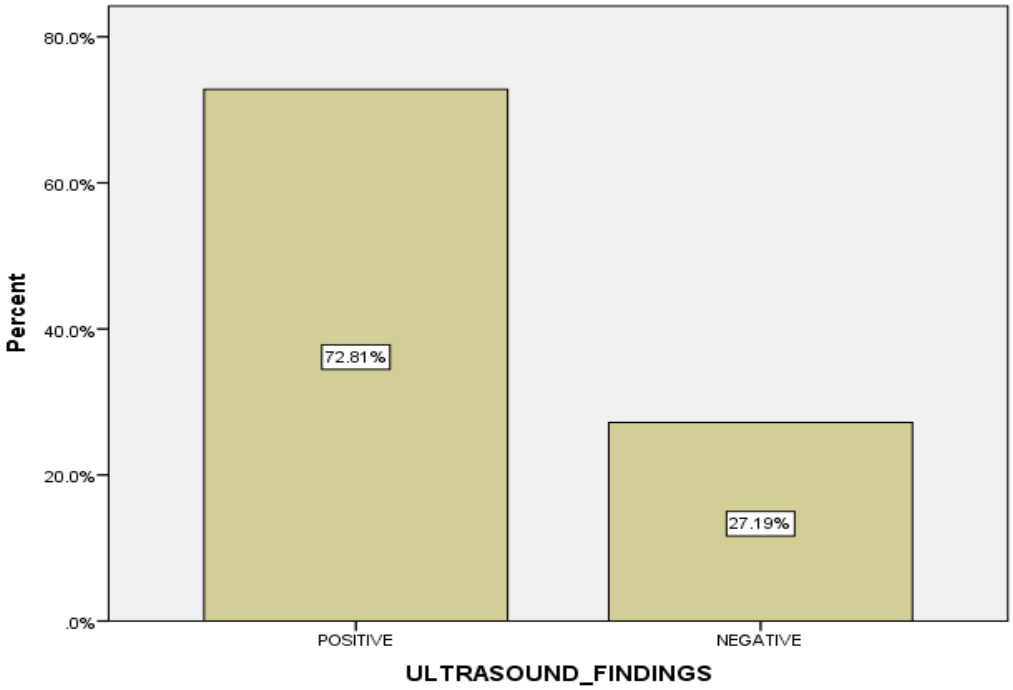

Figure 8: Ultrasound findings

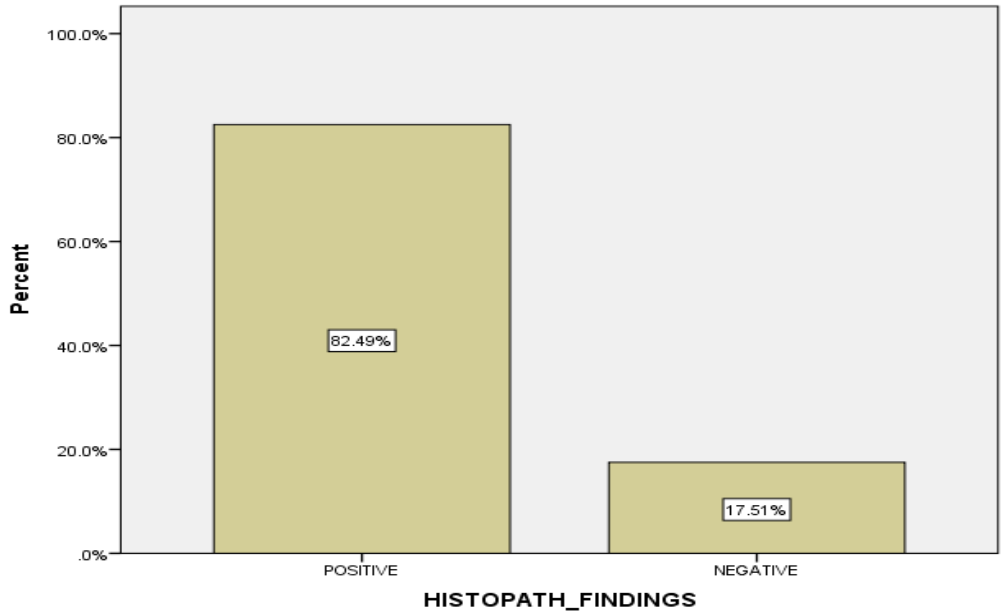

Figure 9: Histopathology findings

Table 3: Diagnostic accuracy of Ultrasound taking Histopathology as gold standard (n=217)			
Ultrasound	**Histopathology**		
	Positive	**Negative**	**Total**
Positive	148	10	158
Negative	31	28	59
Total	179	38	217

Sensitivity: 82.68%
Specificity: 73.68%
PPV: 93.67%
NPV: 47.46%
Diagnostic accuracy: 81.11%

Table 4: Age ≤30 years and Diagnostic accuracy of Ultrasound taking Histopathology as gold standard (n=49)			
Ultrasound	**Histopathology**		
	Positive	**Negative**	**Total**
Positive	28	4	32
Negative	9	8	17
Total	37	12	49

Sensitivity: 75.68%
Specificity: 66.67%
PPV: 87.50%
NPV: 47.06%
Diagnostic accuracy: 73.47%

Table 5: Age >30 years and Diagnostic accuracy of Ultrasound taking Histopathology as gold standard (n=168)			
Ultrasound	**Histopathology**		
	Positive	**Negative**	**Total**
Positive	120	6	126
Negative	22	20	42
Total	142	26	168

Sensitivity: 84.51%
Specificity: 76.92%
PPV: 95.24%
NPV: 47.62%
Diagnostic accuracy: 83.33%

Table 6: Duration of symptoms ≤25 months and Diagnostic accuracy of Ultrasound taking Histopathology as gold standard (n=112)			
Ultrasound	**Histopathology**		
	Positive	**Negative**	**Total**
Positive	78	8	86
Negative	14	12	26
Total	92	20	112

Sensitivity: 84.78%
Specificity: 60.00%
PPV: 90.70%
NPV: 46.15%
Diagnostic accuracy: 80.36%

Table 7: Duration of symptoms >25 months and Diagnostic accuracy of Ultrasound taking Histopathology as gold standard (n=105)			
Ultrasound	**Histopathology**		
	Positive	**Negative**	**Total**
Positive	70	2	72
Negative	17	16	33
Total	87	18	105

Sensitivity: 80.46%
Specificity: 88.89%
PPV: 97.22%
NPV: 48.48%
Diagnostic accuracy: 81.90%

Table 8: Parity 1 and Diagnostic accuracy of Ultrasound taking Histopathology as gold standard (n=25)			
Ultrasound	**Histopathology**		
	Positive	**Negative**	**Total**
Positive	16	2	18
Negative	5	2	7
Total	21	4	25

Sensitivity: 76.19%
Specificity: 50.00%
PPV: 88.89%
NPV: 28.57%
Diagnostic accuracy: 72.00%

Table 9: Parity >1 and Diagnostic accuracy of Ultrasound taking Histopathology as gold standard (n=192)			
Ultrasound	**Histopathology**		
	Positive	**Negative**	**Total**
Positive	132	8	140
Negative	26	26	52
Total	158	34	192

Sensitivity: 83.54%
Specificity: 76.47%
PPV: 94.29%
NPV: 50.00%
Diagnostic accuracy: 82.29%

Table 10: Urban place of residence and Diagnostic accuracy of Ultrasound taking Histopathology as gold standard (n=118)			
Ultrasound	**Histopathology**		
	Positive	**Negative**	**Total**
Positive	82	4	86
Negative	13	19	32
Total	95	23	118

Sensitivity: 86.32%
Specificity: 82.61%
PPV: 95.35%
NPV: 59.38%
Diagnostic accuracy: 85.59%

Table 11: Rural place of residence and Diagnostic accuracy of Ultrasound taking Histopathology as gold standard (n=99)			
Ultrasound	**Histopathology**		
	Positive	**Negative**	**Total**
Positive	66	6	72
Negative	18	9	27
Total	84	15	99

Sensitivity: 78.57%
Specificity: 60.00%
PPV: 91.67%
NPV: 33.33%
Diagnostic accuracy: 75.76%

Discussion

Our study was conducted on a large sample size of 217 and showed sensitivity, specificity, positive predicted value (PPV), negative predicted value (NPV) and overall diagnostic accuracy of ultrasound in cases of malignancy as 82.68%, 73.68%, 93.67%, 47.46% and 81.11% taking histopathology as gold standard.

A study done on 620 women showed 64.8% having benign ovarian tumour and 218 (35.2%) having malignant ovarian tumour. The AUC of the ultrasound model to differentiate benign and malignant adnexal masses was 0.97 (95% CI, 0.96-0.98). Performance was excellent for the discrimination between benign and stage II-IV OC and between benign and ovarian metastasis, with AUCs of 0.99 (95% CI, 0.99-1.00) and 0.99 (95% CI, 0.98-1.00), respectively.[45] The model was less effective at distinguishing between BOT and stage I OC and between BOT and ovarian metastasis, with AUCs of 0.54 (95% CI, 0.45-0.64) and 0.66 (95% CI, 0.56-0.77), respectively. When including CA125 in the model, the performance in discriminating between stage II-IV OC and stage I OC and between stage II-IV OC ovarian metastasis was improved (AUC increased from 0.88 to 0.94, P = 0.01, and from 0.86 to 0.97, p = 0.01).[12]

Another study showed that US-based radiomics models performed satisfactorily in showing higher accuracy by successfully discriminating borderline and malignant ovarian serous tumors compared to the evaluations by senior sonographers (AUC = 0.789 for seniors and 0.877 for radiomics models in task one; AUC = 0.612 for senior and 0.839 for radiomics model in task 2). The study showed that the CCR model, comprising CA125 level, lesion location, ascites, and radiomics signatures, performed the best (AUC = 0.937, 95%CI 0.905-0.969 in task 1, AUC = 0.924, 95%CI 0.876-0.971 in task 2) in the training as well as in the validation cohorts (AUC = 0.914, 95%CI 0.851-0.976 in task 1, AUC = 0.890, 95%CI 0.794-0.987 in task 2). The calibration curve and DCA analysis of the CCR model more accurately predicted the classification of the tumors than the clinical features alone.[13]

Another ultrasound study on 224 patients showed that 119 (53.1%) developed benign tumors and 105 (46.9%) had malignant tumors. When the cut-off value for malignancy risk was 10%, the ADNEX model including CA 125 achieved a sensitivity of 94.3% (95% CI: 88.0-97.9%), specificity of 74.0% (95% CI: 65.1-81.6%), positive predictive value of 76.2% (95% CI: 70.2-81.3%), negative predictive value of 93.6% (95% CI: 87.0-97.0%), diagnostic odds ratio of 45.25, and an AUC of 0.94 (95% CI: 0.90-0.97) for differentiating between benign and malignant ovarian tumors. The AUC in the model excluding CA 125 was 0.93 (95% CI: 0.89-0.96), but the difference was not statistically significant (P=0.20). The accuracy of the ADNEX model for the diagnosis of ovarian tumors of all subtypes exceeds 80% when CA 125 measurements were included in the application, but the sensitivity for diagnosing borderline, stage I, and metastatic ovarian tumors was only 60.0%.[14]

Another recent study was undertaken to assess the accuracy of ultrasound guided fine needle aspiration cytology (FNAC) and cell-block immunocytochemistry, and to estimate the risk of malignancy, using a categorical reporting system, in the diagnosis of ovarian masses. The overall sensitivity, specificity, positive and negative predictive values and diagnostic accuracy for diagnosing ovarian malignancy were 88.4%, 85.7%, 96.8%, 60.0% and 88% respectively. Risk of malignancy for each category was 80%, 0%, 4.5%, 66.7%, 88.5% and 98.5% respectively.[15]The study concluded that ultrasound-guided FNAC has high specificity and diagnostic accuracy for preoperative diagnosis of ovarian malignancies and hence is a valid diagnostic procedure in certain clinical situations. Reporting using a categorical system imparts uniformity and also provides the clinicians with an associated risk of malignancy to guide further management.

The ability of Gynecological Imaging Reporting and Data System (GI-RADS) combined with 3D-CEUS scoring system to distinguish benign and malignant ovarian tumors is superior to conventional ultrasound GI-RADS classification. The sensitivity, specificity, and accuracy of GI-

RADS combined with 3D-CEUS scoring system were 96.2% and 98.1%, 87.10%, whereas those of MRI were 87.10%, 91.23%, and 92.11% respectively, indicating that there was high concordance in ovarian tumors assessment between the 2 diagnostic methods. The new scoring system has a good correlation with microvessel density (P = 0.000, r = 0.73), estrogen receptor (P = 0.000, r = 0.59), progesterone receptor (P = 0.000, r = 0.56), and matrix metalloproteinase-9 (P = 0.000, r = 0.61). The GI-RADS combined with 3D-CEUS scoring system was valuable in clinical diagnosis and differential diagnosis of ovarian tumor and show good agreement with MRI.[16]

Clinical application value was investigated of transvaginal color Doppler ultrasound (TV-CDS) combined with serum tumor markers carbohydrate antigen 125 (CA125), vascular endothelial growth factor (VEGF) and osteopontin (OPN) in the diagnosis of ovarian cancer (OC).[17] 106 patients with OC and fifty patients with benign ovarian diseases were selected. Both groups of patients underwent TV-CDS examination. The lesion morphology and internal structure were observed, and the tumor blood flow signal, resistance index (RI) and pulsability index (PI) under ultrasound were determined. Serum CA125 was detected by electrochemiluminescence, and VEGF and OPN levels were detected by enzyme-linked immunosorbent assay. The incidence of irregular lesion morphology, unclear boundary, uneven internal echo, microcalcification and side-acoustic images in OC group (OCG) was significantly higher than that in BCG (P<0.01). As for blood flow grading, most patients in the MTG were in grade II and III, while most patients in the BCG were in grade 0. Compared with BCG, the flow RI and PI in the OCG were significantly reduced (P<0.01). The levels of serum CA125, VEGF and OPN in OCG were significantly higher than those in BCG. The expression levels of serum CA125, VEGF and OPN in OC patients with clinical high stage (stage III and IV), poorly differentiated, ascites, recurrence and metastasis were significantly higher than those in patients with clinical low stage (stage I and II), well differentiated, no ascites and no recurrence and metastasis (P<0.05). With the disappearance of the tumor or the decrease of tumor load, the serum marker levels after treatment were significantly lower than that before treatment (P<0.05). The sensitivity and accuracy of the combined examination in the diagnosis of OC were obviously improved compared with the single and partial combined examinations (P<0.05). In conclusion, combined examination can significantly improve the sensitivity and accuracy of OC, which is conducive to early diagnosis and clinical intervention of OC.[17]"

Conclusion:

The sensitivity, specificity, positive predicted value (PPV), negative predicted value (NPV) and overall diagnostic accuracy of ultrasound in differentiating ovarian neoplasm malignancy was 82.68%, 73.68%, 93.67%, 47.46% and 81.11% taking histopathology as gold standard.

References:

1. M. Pourissa, S. Refahi, Moghangard MD. The diagnostic accuracy of abdominal ultrasound imaging for detection of ovarian masses. Iranian Journal of Radiology. 2007 Jan 1; 4(2):103-7.
2. Goyal M, Agarwal VK. Diagnostic accuracy of B-mode USG and Doppler scan for ovarian lesions. Journal of clinical and diagnostic research: JCDR. 2016 Sep; 10(9):TC01.
3. Salwar CM, Siddiqui N, Khichari RA, Bandar F. Epithelial ovarian cancer at a cancer hospital in a developing country. Asian Pac J Cancer Prev. 2006 Oct 1; 7(4):595-8.
4. Salem S, Wilson SR. Gynaecological ultrasound In Rumack Carol M. Diagnostic Ultrasound. 3rd edition. volume 1. Missouri: Elsevier Inc; 2005. p. 563
5. Radhamani S, Akhila MV. Evaluation of Adnexal Masses-Correlation of clinical, sonological and histopathological findings in adnexal masses. Int J Sci Stud. 2017 Feb 1;4(11):88-92.
6. Brown DL. A practical approach to the ultrasound characterization of adnexal masses. Ultrasound Q. 2007; 23:87–105
7. Javadi S, Ganeshan DM, Qayyum A, Iyer RB, Bhosale P. Ovarian cancer, the revised FIGO staging system, and the role of imaging. Am J Roentgenol.2016Jun;206(6):1351-60.
8. Funt SA, Hricak H. Ovarian malignancie. Top MagnReson Imaging. 2003;14(4):329–37.

9. Zaka-ur-Rab Z. Evaluation of laboratory markers of sepsis screen in the diagnosis of early onset neonatal septicemia. Int J ContempPediatr. 2016 Nov;3(4):1144-1149
10. Gentry-Maharaj A, Burnell M, Dilley J, Ryan A, Karpinskyj C, Gunu R, et al. Serum HE4
11. Kalsoom U, Arooj S, Raja R, Mushtaq R, Masood M. Diagnostic accuracy of transvaginal doppler ultrasound in differentiating malignant and benign ovarian masses. Ann King Edward Med Uni. 2020 Sep 30;26(2):359-63.
12. He P, Wang JJ, Duan W, Song C, Yang Y, Wu QQ. Estimating the risk of malignancy of adnexal masses: validation of the ADNEX model in the hands of nonexpert ultrasonographers in a gynaecological oncology centre in China. J Ovarian Res. 2021 Dec 2;14(1):169.
13. Qi L, Chen D, Li C, Li J, Wang J, Zhang C, et al. Diagnosis of Ovarian Neoplasms Using Nomogram in Combination With Ultrasound Image-Based Radiomics Signature and Clinical Factors. Front Genet. 2021 Sep 28;12:753948.
14. Peng XS, Ma Y, Wang LL, Li HX, Zheng XL, Liu Y. Evaluation of the Diagnostic Value of the Ultrasound ADNEX Model for Benign and Malignant Ovarian Tumors. Int J Gen Med. 2021 Sep 16;14:5665-5673.
15. Gupta P, Velamala P, Gupta N, Suri V, Lal A, Rohilla M, et al. Ultrasound-guided fine needle aspiration of ovarian masses: Assessment of diagnostic accuracy and risk stratification using a categorical reporting system. Cytopathology. 2021 Jul;32(4):441-458.
16. Yang L, Lv G, Chen H, Yang S, Liao J, Zhang W, et al. Diagnostic Efficiency of Gynecologic Imaging Reporting and Data System Combined With 3-dimensional Contrast-enhanced Ultrasound Scoring System in Evaluating Ovarian Tumor. Ultrasound Q. 2020 Dec;36(4):375-381.
17. Yu C, Dou T, Liu Y, Liu R. Clinical value of TV-CDS combined with serum tumor markers in diagnosis of ovarian cancer. Oncol Lett. 2020 Aug;20(2):2028-2034.