



Comparative Evaluation of Ultrasonography and Doppler with Histopathological Findings in Adnexal Masses Amongst Perimenopausal Women

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Citation of this Article: Dr. Kazi Rokeya Rahaman, Dr. (Prof) Rehana Najam, Dr. Astha Lalwani, “Comparative Evaluation of Ultrasonography and Doppler with Histopathological Findings in Adnexal Masses Amongst Perimenopausal Women,” IJMSAR – September – 2021, Vol. – 4, Issue - 5, P. No. 23-34.

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Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Introduction

Ovaries and the fallopian tubes are collectively referred to as adnexa. Adnexal masses are found frequently in all age groups including perimenopausal females and its diagnosis remains a prevalent issue. The initiation of use of Ultrasonography has changed the range of diagnostic tactic of adnexal masses, specially combined with Doppler. Although, CA125 in combination with other novel biomarkers like CA 19–9, HE4, EGFR, IL-2R, G-CSF, MIF, Eotaxin, cVCAM have enhanced sensitivity as well as specificity in early

stage diagnosis of ovarian carcinoma, except CA-125, no other screening test is widely used due to availability and cost issues. Even with proper history, clinical examination, laboratory tests etc diagnosing and treating adnexal masses can be challenging. Also, the literature regarding this topic in particularly perimenopausal age group has been limited. Hence we did this study to appraise the diagnostic accuracy of ultrasonography and doppler, also to establish its correlation through per-operative findings and

histological diagnosis in adnexal masses in perimenopausal women.

Aims & Objectives

This study was done to assess the spectrum of adnexal masses and to compare the ultrasound/doppler studies with histopathological findings in adnexal masses amongst perimenopausal women, thus evaluating the diagnostic accuracy of ultrasonography and Doppler.

Methodology

Medical archives of 192 patients of adnexal masses who met the eligibility criteria were assessed for the retrospective study conducted in the OBG department of TMMC. Detailed history, findings of clinical examination and the investigations were recorded on predesigned proforma. Then the findings were correlated with ultrasonographic, laboratory tests and histopathologic evaluation. The statistical data were analysed using the SPSS software version 26.0. Association between groups was calculated using Pearson's correlation coefficient.

Observation and Results

Out of 192 cases, 37.5% were benign and 62.5% were malignant. Majority of malignancy cases were found in nulliparas. Most common coexisting factor in case of malignant lesions was Assisted reproductive therapy/ovulation induction (36.67%) followed by infertility (30.00%) and obesity (23.33%) whereas in case of benign lesions it was endometriosis (44.44%). Commonest clinical symptom was found to be pain abdomen (60.42%) trailed by mass abdomen (33.33%). The most common type of benign lesion was Simple Cystic lesion (33.33%) and most common type of malignant lesion was Solid lesion (43.34%). On colour Doppler study, neovascularization was discovered in 93.33% of malignant masses in

contrast to 0% of benign masses. Out of 68 carcinoma cases where Histopathological examination was done, 56 had been correctly diagnosed by Ultrasonography, 12 cases were misdiagnosed. Correlation between sonographic and histopathological diagnosis was found to be significant (p value < 0.05) as per Pearson Correlation.

Conclusion

Although histopathology remains gold standard, Ultrasonography with Doppler study is comparable, specially in poor resource settings and was proved to be an extremely useful and dependable diagnostic method in establishing the preoperative diagnosis of adnexal masses.

Keywords

Adnexal mass, Ultrasonography, Doppler, histopathology (HPE)

Introduction

Ovaries and the fallopian tubes are collectively referred to as adnexa.[1] Adnexal masses denote the ovarian cysts or masses, fallopian tube masses, broad ligament pathology and Para tubal cysts. Adnexal masses might be discovered in females of all age groups with significantly capricious prevalence, may it be childhood, reproductive age group or perimenopausal age group. These masses may vary from benign lesions like functional cysts to malignant lesions such as ovarian carcinoma.[2]

Adnexal mass is a common place medical presentation in gynaecological field and might be from gynaecological or non-gynaecological source. Most commonly adnexal mass term represents masses concerning the ovaries because of the increased proclivity of the ovary for neoplasia. [3,4] Adnexal masses are found frequently in perimenopausal

females and their diagnosis remains a prevalent issue.[5]

The initiation of use of Ultrasonography has changed the range of diagnostic tactic of adnexal masses, specially combined with Doppler.[6] Ovarian carcinoma records for 6% of all malignancies in females. It is the 8th foremost source of malignancy in females and the 5th commonest form of carcinoma related demise with highest number of fatalities amongst the gynaecological malignancies.[7,8]

Pelvic ultrasonography is commonly performed to envision the uterus and the adnexa in both asymptomatic and symptomatic patients. Although pelvic ultrasound has high sensitivity in detection of adnexal lesions, its specificity in determining malignant lesion is lesser. Moreover, the distinction amongst functional ovarian lesions which mostly heal spontaneously over time and non-functional lesions has notable inferences for the counselling and management of patients. Other categories of adnexal lesions (for example para-ovarian cysts, mature cystic teratoma, endometrioma etc) are equally important to identify correctly and promptly as they might hinder fertility of the patients, may be accompanying other noteworthy pelvic disease, or even lead to ovarian torsion.[9,10] Therefore, the precise usage of pelvic ultrasonography has turned out to be a fundamental part of the gynaecological assessment.

Although, CA125 in combination with other novel biomarkers like CA 19-9, HE4, EGFR, IL-2R, G-CSF, MIF, Eotaxin, cVCAM have enhanced sensitivity as well as specificity in early stage diagnosis of ovarian carcinoma, except CA-125, no other screening test is widely used for screening purpose, specially in developing countries due to availability and

cost issues.[11] Even with proper detailed history, thorough clinical examination, laboratory tests etc diagnosing and treating adnexal masses can be extremely challenging.

To advance the sensitivity and specificity of the ultrasonography, doppler flow measurement was introduced as a diagnostic tool. This technique is based on the contemplation that all neoplasms, including ovarian ones, brings a modification of the vascularization pattern that occurs due to angiogenesis phenomenon. [12,13]

The combination of transvaginal ultrasonography and use of Colour Doppler for the diagnosis of malignant lesions like ovarian cancers by the detection of low resistance in intratumor blood vessels resulting from angiogenesis and neovascularization in malignant neoplasms opens up new horizons in gynaecological ultrasound, especially for diagnosis of adnexal mass lesions in pelvis.[14] Histopathology is still considered to be the Gold standard for the assessment of benign and malignant adnexal lesions.[3]

Hence, this study was conducted to assess the diagnostic precision of ultrasound and doppler and to evaluate its correlation with per-operative findings and histological diagnosis of adnexal masses amongst perimenopausal women.

Aims & Objectives

To study the spectrum, presentation and associated risk factors of adnexal masses amongst perimenopausal women.

To study the ultrasonography / Doppler findings in patients with adnexal masses.

To study the Histopathological findings of adnexal mass which were operated upon.

To compare the ultrasound /doppler findings with the histopathological findings in patients who underwent surgery.

Materials. and Method

A retrospective study was carried out in the Obstetrics & Gynaecology Department in Teerthanker Mahaveer Medical College, Moradabad over 18 months. Medical records of 192 patients with adnexal masses who met the eligibility criteria i.e. women aged 45-55 years who got admitted in the department of Obstetrics and Gynaecology for the diagnostic evaluation of a clinically suspected (patients with symptoms indicative of a tumour like irregular cycles, pain, and fullness and pressure symptoms of abdomen) or palpable adnexal mass or incidentally detected adnexal mass were assessed. The study excluded ongoing viable intrauterine pregnancies, malignancies secondarily infiltrating adnexa, non-gynaecological masses. Detailed history, findings of clinical examination, specific investigations and histopathological findings (of the patients who underwent surgery) were recorded on predesigned proforma from the medical archives of eligible patients. Afterwards, correlation was made between ultrasonographic, laboratory tests and histopathological findings. It is notable that on the patients grayscale ultrasound and colour doppler were performed with a ultrasound and Doppler scanner unit (Siemens S2000 USG) while they had undergone treatment. Transabdominal sonography (TAS) of lower abdomen and pelvis was conducted using a 3.5-MHz convex transducer and transvaginal examination was performed after putting the patient in dorsal position with empty bladder using a wideband 5–9

MHz endocavitary transducer. For Colour Doppler parameters, the same presets were used for all the patients. Pulsatility index (PI) and resistive index (RI) findings were Documented. Whenever the PI was <1.0 or RI was <0.4, the masses were categorised to be indicative of malignancy. Finally, correlation between these indices, ultrasonographical and histopathological findings was assessed.

Statistical Analysis

The Microsoft excel was used to create the database and to produce graphs. Data were calculated by appropriate statistical formula and was assessed via statistical package for social sciences [SPSS inc. Version 23.0, Chicago, IL]. Percentages and frequencies were estimated for categorical data and association among different categories was evaluated by Pearson's correlation coefficient. P-value < 0.05 at 95% confidence interval was contemplated to be statistically significant.

Results

From records of 218 patients aged 45-55 years who presented with adnexal masses during the study period, 192 patients were considered eligible for the study depending on the selection criteria. 21 women who had neoplasms of non-gynaecological source and 5 women who had ongoing viable intrauterine pregnancies were excluded from the study.

Out of selected 192 cases, 72 (37.5%) were benign and 120 (62.5%) were malignant. Majority of malignancy cases were found in nulliparas (43.75%). (Table 1)

Table 1: Distribution of type of Lesion and parity among study population

		Number	Percentage
Type of Lesion	Benign	72	37.50%
	Malignant	120	62.50%
Parity	Nullipara	84	43.75%
	Primipara	48	25.00%
	Multipara	60	31.25%

Most common coexisting factor in case of malignant lesions was Assisted reproductive therapy/ovulation induction (36.67%) followed by infertility (30.00%) and obesity (23.33%) whereas in case of benign lesions it was endometriosis (44.44%). (Table 2)

Table 2: Distribution of associated risk factors among study population

	Benign		Malignant	
Pelvic infection	12	16.67%	12	10.00%
Endometriosis	32	44.44%	0	0.00%
Infertility	12	16.67%	36	30.00%
ART/ IVF	12	16.67%	44	36.67%
Obesity	4	5.55%	28	23.33%

The most common presenting complaint was pain abdomen (60.42%) followed by mass abdomen (33.33%), weight loss (14.58%), pressure symptoms (10.42%), abnormal bleeding per vaginum (8.33%) and ascites (8.33%). (Table 3)

Table 3: Distribution of symptoms among study population

Symptom	Number	Percentage
Pain abdomen	116	60.42%
Mass abdomen	64	33.33%
Weight loss	28	14.58%
Pressure symptoms	20	10.42%
Abnormal bleeding pervaginum	16	8.33%
Ascites	16	8.33%

The most common benign lesion type was Simple Cystic lesion (33.33%) followed by Solid Cystic (27.78%), predominantly Solid (22.22%), Complex Cystic (16.67%) and Ascites (5.56%). The most common finding in malignant lesion was Increased Vascularity [Low RI & PI] (93.33%), omental deposits (60.00%), Ascites (53.33%) followed by predominantly Solid (43.34%), Complex Cystic (33.33%) and Solid Cystic (23.33%). (Table 4)

Table 4: Radiological findings in Benign & Malignant ovarian tumors

USG Features	Benign (72)		Malignant (120)	
	Count	Percentage	Count	Percentage
Simple Cystic	24	33.33%	0	0%
Solid Cystic	20	27.78%	28	23.33%
Complex Cystic	12	16.67%	40	33.33%
Predominantly Solid	16	22.22%	52	43.34%
Ascites	4	5.56%	64	53.33%
Increased Vascularity [Low RI & PI]	0	0%	112	93.33%
Omental Caking/Deposits	0	0%	72	60.00%

CA-125 value was found to be elevated (>35 IU/ml) more among Malignant lesions. (Table 5) Neovascularity was also found to be significantly more in malignant lesions.(Table 6).

Table 5: CA-125 value in detection of benign and malignant tumor

CA-125	Benign(72)	Malignant(120)	Total (%)
>35 IU/ml	8	116	124 (64.58%)
<35 IU/ml	20	4	24 (12.5%)
Total	28	120	148 (77.08%)

Table 6: Distribution of Neovascularity on color Doppler and doppler indices

Type of lesion	Pulsatility Index			Resistive Index			Presence of neovascularity
	PI<0.8	PI = 0.8-1.0	PI >1.0	RI <0.4	RI = 0.4-0.6	RI >0.6	
Benign (72)	8	12	52	0	20	52	0 (0%)
Malignant (120)	96	20	4	36	84	0	112 (93.33%)

Out of 92 operated cases where Histopathological examination was done, amongst 68 malignancy cases 56 had been correctly diagnosed by Ultrasonography, 12 cases were misdiagnosed. Amongst these cases, ultrasonographical diagnosis were 8 simple ovarian cyst cases, 4 cases of hydrosalpinx, 4 tubo-ovarian mass, 4 endometriosis and 56 cases of possible malignancy. Correlation between sonographic and histopathological diagnosis was observed as statistically significant (p value = 0.02) as per Pearson Correlation. (Table 7)

Table 7: Correlation between histopathology and USG findings

HPE report (92)	Sonological findings				
	Hydrosalpinx/ Infective pathology	Endometriosis	TO mass	Benign	Malignant
Infectious pathology (4)	4	0	0	0	0
Endometrioma (4)	0	4	0	0	0
Broad ligament fibroid (4)	0	0	4	0	0
Fallopian tube carcinoma (4)	4	0	0	0	0
Benign cystadenoma(12)	0	0	0	12	0
Malignant cyst adenocarcinoma (64)	0	0	0	8	56

Discussion.

Owing to wide assemblage of varieties and origin, anatomical position in female pelvis as well as proximity of structures of various systems, insidious onset, atypical presenting symptoms and recurring physiological changes within, timely diagnosis and depiction of adnexal lesions is every so often extremely difficult. Ultrasound is contemplated to be the keyimagery tool for the evaluation of the type and derivation of mass and account of character of the lesion as benign or malignant.

USG Findings and Symptoms

In the current study, there were 37.5% benign and 62.5% malignant lesions. Whereas, in the study by *Das et al*, [15] 20.68% were malignant and 51.04% were benign neoplasms. Our study is also in agreement with studies conducted by *Ganga P et al*, *Sharma I et al* and *Yogambal M et al*, who found the frequency of benign and malignant lesions to be similar. [16-18]

Dasgupta et al [19] in their study noted that on histopathological examination, 61% tumours were found to be benign and 39% were malignant. Similarly *Badge et al*. reported 76% of ovarian tumours to be benign and the rest (24%) to be malignant. [20] It is notable that the study population in the above mentioned studies mostly belonged to reproductive age group whereas our study was conducted on perimenopausal women.

In present study, the commonest complaint happened to be abdominal pain (60.42%) followed by mass abdomen (33.33%), weight loss (14.58%), pressure symptoms (10.42%), abnormal bleeding per vaginum (8.33%) and ascites (8.33%) respectively. Similar to our study, *Das et al* [15] revealed that pain abdomen was found to be in 72.41% cases. This was also comparable to other studies by *Radhamani S et al*, *Al shukri et al*

and *Bhagde AD et al* in all of which pain abdomen was the commonest presenting symptom and found to be present in 98%, 92% and 82% cases respectively. [21,22,3] *Das et al*¹⁵ in their study showed that second most common symptom was lump abdomen which was likewise in our study. Other symptoms included infertility, menstrual irregularities, urinary complaints, alimentary symptoms etc.

*Dasgupta et al*¹⁹ also affirmed that abdominal pain was the commonest symptom (found in 55% cases) followed by abdominal swelling (32% cases) and menstrual irregularities (31%) respectively. These findings were alike to those recorded in studies by *Pillai and Anuranjani & Patil*. [23,24]

*Das et al*¹⁵ noted that mostly found benign neoplasm was serous cystadenoma (41.89%) which was similar to the findings recorded in the current study where the commonest type of benign lesion was of simple cystic type in ultrasonography. Similar results were observed by *Kanthikar SN et al*, here serous cyst adenoma was noted in 35.71% cases. [25] Also *Sharma I et al* [17] in their study discovered serous cystadenoma as most frequently occurring tumor (34%). Among malignant tumours commonest type to be found was serous cyst adenocarcinoma (21.35%) that is alike to studies done by *Kanthikar SN et al*, (8.57%), *Sharma I et al*, (12.74%) where they also found serous adenocarcinoma to be the commonest malignant tumor. [25,17]

Serum CA125 level

Serum CA125 level is a significant factor for diagnostic purpose as well as prognosis of epithelial carcinomas. Reportedly the general sensitivity of CA125 screening in separating malignant from benign adnexal neoplasms varies from 61% to 90%, whereas specificity spans from 71% to 93%,

negative predictive value from 67% to 90% and positive predictive value from 35% to 91%.[18]

These parameters are found to be comparable with those in the present study. Wide range of variations in these figures take place due to differences in prevalence of carcinomas in the study populations, the proportion of perimenopausal and postmenopausal patients, and the threshold level of CA125, which is considered abnormal. An interesting notable fact is that majority of the medical disorders with raised CA125 ensue in the perimenopausal patients while maximum epithelial ovarian carcinomas happen in the postmenopausal age group. Hence, the sensitivity and specificity of an increased CA125 level which accompanies an adnexal mass are highest after menopause.[19]

In our study, CA-125 value >35 IU/ml was found more among malignant lesions. (Table 5) Neovascularity was also found to be significantly more in malignant lesions. *Dasgupta et al*[19] found that 58% patients presented with raised CA125 level (>35 U/ml). *Medeiros et al.* reported better specificity than that found in the present study while using the same cut-offs, and they concluded that CA125 is a useful screening test for predicting the benign or malignant nature of ovarian tumours.[26] Sensitivity found in the current study was almost similar to that found by *Radhamani and Akhila*.[3]

Colour Doppler Findings

In our study, neovascularity was observed more in malignant lesions. $PI < 0.8$ and $RI = 0.4-0.6$ was found to be significantly more among malignant lesions. *Vijay et al*[4] stated that out of 26 histopathologically proven malignant cases, 61.54% had $RI < 0.43$ and 38.46% cases had $RI > 0.43$. Our observations were in agreement with *Madan et al.*,[27]*Khurana et al.*,[28]

and *Priya et al.*[29] The observation of present study was also in close agreement with findings in trials of *Salemet al.*,[30]*Sehgalet al.*,[31] as well as *Shyamala et al.*[32]

Radhamani and Akhila (2017)[3] in their study established that clinical examination findings, ultrasound findings and RMI values associate positively with HPE findings which is extremely useful in early detection of malignancy and its appropriate management which corroborates with our study.

Pillai (2017)[23] studied the varied medical spectrum of gynaecological adnexal lesions and correlated the potential diagnosis depending on clinical evaluation as well as USG findings with intra-operative surgical finding and HPE results, he concluded that methodological advancement encompassing a detailed history, thorough clinical evaluation, use of apt imaging tools and accurate clarification of diagnostic measures imperative for ideal managing of gynaecological pelvic lesions.

Ormsby et al (2017)[33] reviewed ultrasonographic assessment of adnexal lesions in the age of type 1 and type 2 ovarian carcinomas and concluded that USG is inexpensive, non-invasive, combined with having wide availability, low morbidity, high sensitivity in identifying anomalies in adnexal lesions and also risk-free in image procurement.

Pal Kedarnath (2016)[34] in his study concluded that USG can be extremely helpful in detection & specific regarding diagnosis of an adnexal mass. Moreover, inclusion of TVS supplied new information in many cases as it can detect the fine internal sonomorphological characteristics, thus making combined approach with both TVS and TAS most handy.

MA Shukri et al (2014)[21] concluded that acute abdominal pain, nausea and vomiting is commonest presentation of adnexal pathology, and its timely diagnosis can improve the outcome, which was a similar conclusion found in our study.

Dotlic et al (2011)[35] in their study scrutinised the preoperative as well as postoperative findings of women having adnexal masses to detect predicting features of nature and stage of the tumour preoperatively. In the study they concluded that the post menopausal patients, specially of older age group, having elevated Body Mass Index and Risk of Malignancy Index must instantly be transferred to a tertiary center so that necessary surgery can be carried out.

McDonald et al (2010)[36] assessed the accuracy of preoperative patient demographics, USG findings and serum CA125 level to predict risk of malignancy in patients with adnexal mass and after comparison with HPE findings concluded that patients with solid or complex ovarian neoplasms with elevated CA125 are at higher risk which corroborates with our study.

Brown (2007)[37] found that majority of ovarian malignancies are composed of a solid element which has visible flow in colour doppler, thus strongly indicating the diagnosis.

Geomini et al (2006)[38] stated that visualisation of blood vessels predominantly in the central part of an adnexal mass by 3D ultrasound and 3D power Doppler as well as the flow index and the mean gray index are substantially significant factors to differentiate benign and malignant lesions.

The addition of colour Doppler imaging was found to improve the depiction of adnexal masses by identifying vascularization in tumour and by measuring

blood flow parameters of tumour vessels. By this, the possibilities of making a correct diagnosis of malignancy or benignity are increased.[31] The use of colour Doppler to differentiate a benign from a malignant tumour is based on the observation of the remarkable the vascularization in the malignant masses with low resistance flows and high velocity. Resistance index < 0.4 and pulsatility index < 1.0 generally indicate malignancy.[28]

Moreover, it is known that the vascularization of the tumor is heterogeneous. This is not only related to the type of tumor, but also to its rate of growth and its localization.[31,28] Thus, it is essential, in order to improve the diagnostic accuracy of ovarian masses, to combine the morphological score with a flow score.[31,39]

The limitations of this study were this study had a retrospective study, the small sample size of the study, more multicentric trials are needed to come to a definitive conclusion and non-selection study.

Conclusion

Our findings conclude that proper methodological use of imaging techniques serve to produce comparable results as blood-based screening methods using multiple biomarker panel such as CA-125/HE4 combination for the discrimination of benign and malignant adnexal masses.

This study displayed a noteworthy rise in the specificity, sensitivity, negative predictive value and positive predictive value on combining colour doppler with grayscale ultrasound in comparison with ultrasonography solo in determining the prospective diagnosis of adnexal masses, especially whether they are benign or malignant, and this conclusion is in consensus with previously done studies.

Although histopathology remains gold standard, Ultrasonography with Doppler study is comparable, especially in poor resource settings and was established as an extremely useful and dependable diagnostic technique.

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