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Correlation of Ultrasound and histopathology for diagnosis of endometrial cancer in post-menopausal women

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ABSTRACT

Objective: To determine the usefulness of trans-vaginal ultrasonography for diagnosis of endometrial carcinoma as screening tool by comparing sonographic thickness of endometrium and histopathology in post-menopausal women.
Study Design: Quasi-experimental study.
Place and Duration of Study: Pak Emirates Military Hospital, Rawalpindi Pakistan, from Jan 2024 to Jan 2025.
Methodology: After seeking approval of ethical commission, we recruited two Groups of post-menopausal ladies presented with abnormal uterine bleeding, one with normal endometrial thickness and another with abnormal endometrial thickness. We did transvaginal ultrasonography on all patients and performed histopathology of their endometrial tissue taken on biopsy. We compared the frequency of positive cases on histopathology and correlated it to their sonographic findings by calculating sensitivity and specificity to establish diagnostic yield of trans-vaginal ultrasonography in endometrial carcinoma.
Results: The sensitivity of trans-vaginal ultrasonography in diagnosis of carcinoma of endometrium was 64.1%, specificity was 92.0%, positive predictive value was 58.6% and negative predictive value was 79.8%. The frequency of carcinoma was 23(35.9%) in Group-A and it was 2(3.3%) in Group-B with *p*-value of <0.001.
Conclusion: We came to conclusion that trans-vaginal ultrasonography can be utilized as consistent screening tool for detection of carcinoma endometrium

Keywords: Biopsy, Endometrium, Hemorrhage, Menopause, Neoplasm, Sensitivity, Specificity, Ultrasonography and Uterus.

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INTRODUCTION

The endometrial carcinoma is 8.4% in Pakistani women.[1] In Europe, more than one in every twenty females has endometrial carcinoma (CA) and this frequency is raising in several nations specially developing countries.[2] Endometrial carcinoma mostly affects postmenopausal women in their sixth and seventh decade of life. In industrialized nations, the disease classically affects ladies between the age threshold of 55 and and peaks in sixth decade of life. If an early diagnosis and effective therapy are obtained, most cases of endometrial cancer have a positive prognosis and a greater survival rate. Only the uterus is affected by the disease in 75% of patients at the time of diagnosis which hold a good prognostic value.[3]

About eighty percent cases of endometrial carcinoma occur after menopause and ninety percent of ladies have abnormal uterine bleeding (AUB) at diagnosis, Abnormal uterine bleeding, is a common gynecological issue that has a substantial impact on the patient's social, family, and personal life. There isn't a universally accepted screening protocol for endometrial cancer, controlling the risk factors may help avoid the disease. Transvaginal ultrasonography or endometrial biopsies have been suggested as diagnostic methods for endometrial cancer by guidelines.[4,5] Transvaginal ultrasonography is the preferred method of investigation because to its affordability and excellent sensitivity. Endometrial biopsies, however, are used for conclusive diagnosis. Hysteroscopy and magnetic resonance imaging are easily available diagnostic modalities that can be used to evaluate endometrial thickness and/or uterine structural abnormalities. Surgery is the cornerstone of treatment which always include radical hysterectomy.[6]

There are many ladies who report to Pak Emirates Military Hospital (PEMH) with abnormal uterine bleeding in all age Groups and ultrasound is done routinely in all patients to see endometrial thickness. Therefore, ultrasound is the first line tool that can be of substantial importance in diagnosis of endometrial CA in resource limited setups. There are studies done who correlated the sonographic morphology to histopathological finding in known cases[7,8] but there are no screening studies done so far

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in Pakistan. The rationale of our study is correlate sonography with histopathology to establish the significance of ultrasonography which is a non-invasive and easily accessible test to diagnose endometrial cancer in vulnerable population that is women post menopause.

METHODOLOGY

We performed our Quasi-experimental study after obtaining ethical approval from hospitals ethical committee with IERB number: A/28/ERC/111/24 dated 11.6.2023. The study was carried out at Gynecology and Obstetrics Department of Pak Emirates Military Hospital, Rawalpindi Pakistan, from July 2023 to July 2024. Sample size was calculated with help of WHO sample size calculator keeping power of test 90%, significance level 5%, the anticipated population proportion with abnormal thickness of endometrium to have CA endometrium to be 19%[9] and the anticipated population proportion with normal thickness of endometrium not to have CA endometrium to be 47%.[9] The sample came out to be 58. We collected a sample of 128 patients (64 in each Group) through non-probability consecutive sampling.

Inclusion Criteria: Post-menopausal married ladies of age 55-75 years who had abnormal uterine bleeding.[10]

Exclusion Criteria: Patients with adenomyosis, fibroids, cervical or vaginal fibroids or polyps or any other pathology and blood dyscrasia were excluded. The sample was collected through non-probability consecutive sampling technique and randomized according to endometrial thickness. Patients who had endometrial thickness greater than 5mm were considered to have abnormal endometrial thickness and were included in Group A and Patients who had normal endometrial thickness on transvaginal ultrasound that is less than 5mm[11] were included in Group-B.

The patients with irregular uterine bleeding were identified after systematic history taking and detailed physical examination. The patients who fulfilled the inclusion criteria were subjected to transvaginal ultrasound. The transvaginal ultrasound was performed with the help of 10 hz Transvaginal probe (GE Ultrasound machine). All the patients were booked for elective dilatation and curettage for endometrial biopsy. The patients who followed up were subjected to dilatation and curettage under monitored anesthesia care and biopsy was taken. The biopsy sample was sent for histopathology. The patients were asked to follow-up with histopathology report. The histopathology report was generated by consultant histopathologist and report with indication of endometrial carcinoma was considered positive report. The demographic characteristics were recorded for all patients including age, weight, parity, menopause age and co-morbid (hypertension, diabetes mellitus and smoking). The primary outcome was sensitivity, specificity, positive predictive value, and negative predictive value of sonography in screening for endometrial carcinoma. The frequency of positive histopathology was also calculated as secondary outcome.

The data was analyzed using the Statistical Package for the Social Sciences (SPSS) version 26. The values of quantitative study variables were calculated along with standard deviation for quantitative variables and the frequencies with percentages were calculated for qualitative parameters. Chi-square analysis and independent samples t-Test were the statistical tests used to find significance. The *p*-value ≦0.05 was considered important. The study protocol is displayed in Figure.

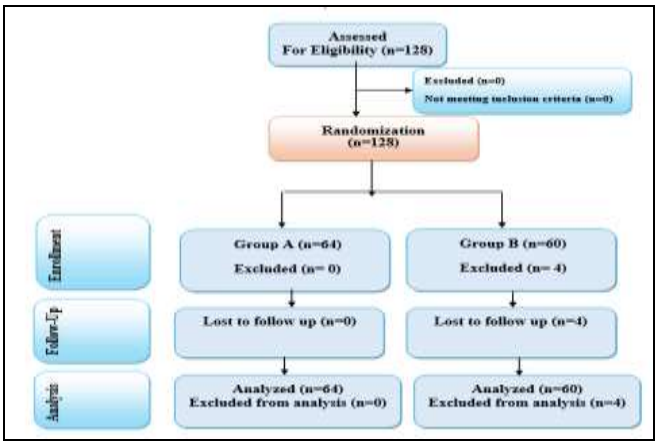

Figure: Flow Diagram of Study

RESULTS

A total of 128 patients (64 in each Group) completed the study protocol. The patients were Grouped equally into two Groups on basis of sonographic findings appreciated on transvaginal ultrasound. Four patients in Group B failed to follow up therefore they were dropped from result. There were 64 females in Group-A and 60 females in Group-B. The mean age of post-menopausal women in Group-A was 65.95±5.42 years, their mean weight was 66.87±4.95 kilograms and mean age at time of menopause was 45.45±3.69 years. There were 60 patients in Group B with mean age of 68.05±6.29 years,

mean weight of 69.48±5.89 kilograms and mean age at menopause was 45.25±3.69 years. There were 39(60.9%) diabetic patients in Group A and 35(58.9%) diabetics in Group B. Twenty (31.3%) patients in Group A were smokers and 14(23.3%) patients in Group B were smokers. There were 26(40.6%) hypertensive patients in Group A and 19(31.7%) hypertensive patients in Group B. The demographic features were similar in both Groups and presented in Table-I. The parity was compared through chi-square test with Monte Carlo simulation and showed no significant difference in parity distribution between Groups (Monte Carlo p=0.212).

Table-I: The Comparison of Demographic Features of study Groups (n=124)

Parameter		Group A n=64	Group B n=60	*p*-value
Mean Age (years)		65.95±5.42	68.05±6.29	0.411
Mean weight (Kg)		68.87±4.95	69.48±5.89	0.079
Mean age of menopause (Years)		44.34±3.96	45.25±3.69	0.318
		Frequency (%)	Frequency (%)	
Parity	0	1(1.6)	1(1.7)	0.212
	1	(7.8)	0(0)	
	2	15(23.4)	13(21.7)	
	3	4(18.3)	12(19.4)	
	4	14(21.9)	16(26.7)	
	5	6(9.4)	8(13.3)	
	6	10(7.6)	3(5.0)	
	7	6(9.4)	2(3.3)	
	8	1(1.6)	0(0)	
Diabetes Mellitus	Yes	25(39.1)	25(41.7)	0.198
	No	39(60.9)	35(58.3)	
Hypertension	Yes	26(40.6)	19(31.7)	0.216
	No	38(59.4)	41(68.3)	
Smoking	Yes	20(31.3)	14(23.3)	0.216
	No	44(68.8)	46(76.7)	

Table-II: The Frequency of Positive Histopathology in both Groups A (Abnormal Thickness) and Group B (normal thickness) (n=124)

		Group A n=64 Frequency (%)	Group B n=60 Frequency (%)	*p*-value
Frequency of endometrial CA on histopathology	Yes	23(35.9)	2(3.3)	<0.001
	No	41(64.1)	58(96.7)	

Table-III: The Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value of Trans-Vaginal Ultrasonography for the diagnosis of Endometrial Carcinoma (n=124)

Sensitivity	64.1%
Specificity	92.0%
Positive predictive value (PPV)	58.6%
Negative predictive value (NPV)	79.8%

The sensitivity of sonographic evidence was as 64.1% in diagnosing of CA endometrium. The specificity of sonographic evidence was 92.0% in diagnosis of endometrial carcinoma. The positive predictive value came out to be 58.6% and negative predictive value came out to be 79.8%. The Frequency of positive histopathology for endometrial carcinoma was 23(35.9%) in Group-A and it was 2(3.3%) in Group-B with p-value of <0.001. The results are displayed in Table-II and Table-III.

DISCUSSION

Our study provided substantial evidence on the reliability of trans-vaginal ultrasonography in the diagnosis of endometrial carcinoma, and it can be employed as screening tool. In our study we performed diagnostic dilatation and curettage of patients with abnormal uterine bleeding who had normal thickness on transvaginal ultrasound to find the negative predictive value of ultrasonography and it came out be reasonably good that is 79.8%. A few studies have been performed to correlate sonological findings to histopathology but most of these are retrospective studies and systematic reviews. We performed prospective study and compared two Groups of similar demographic characteristics of patient with same symptom that is abnormal uterine bleeding. The Group with abnormal endometrial thickness had the larger number of patients with positive histopathology which showed that ultrasonography has high sensitivity and negative predictive value.

Muhammad Kaleem Akhter *et al.*,[12] performed systemic analysis of six articles who tried to correlate endometrial thickness to endometrial histopathology. They concluded that transvaginal ultrasound proved to be a promising screening tool. There study included data mainly from retrospective research and they did not perform comparisons. We performed prospective experimental study and compared two Groups. We did not comment on long term survival as longer duration study is required for that. According to a single center retrospective study by Hyen Chul Jo *et al.*,[13] on South Korean populace, the endometrial thickness greater than 5mm in post-menopausal women proved to be an independent feature that correlated with CA endometrium. In our patients two patients with normal thickness had positive histopathology otherwise most patients with abnormal thickness had positive histopathology.

According to Shalini Mahapatra[14] the endometrial thickness between six to twelve millimeter correlates with positive histopathology. They performed hysteroscopy and took hysteroscopy guided biopsy to reduce the risk of false negative

results. They presented the sensitivity of TVS to be approximately 83 percent. However, in our patients' sensitivity was 64.1% which was slightly lower. The difference in our and their results is probably due to the use of hysteroscope while we performed only blind dilatation and curettage. They included the patients with fibroids in their study and used TVS to diagnose fibroid. We excluded the patients with fibroids and only focused on endometrial thickness.

In a prospective cohort study performed by Mohamed Ahmed *et al.*,[15] it was established that abnormal endometrial thickness and presence of obesity was correlated to endometrial carcinoma confirmed on histopathology. They implied that obese post-menopausal women should be screened for CA endometrium. We screened all women with both abnormal and normal looking endometrial thickness with abnormal uterine bleeding and did not include obesity in our inclusion criteria. Despite this, we came up with low false negatives that are 3.3%. Therefore, we recommend that we should perform transvaginal ultrasound of all patients with abnormal uterine bleeding irrespective of their risk factors and weight as the endometrial thickness seems to be an independent factor or sign of CA endometrium. Moreover, obesity is very prevalent in Pakistani females of post-menopausal age and its incidence is as high as twenty nine percent.[16] We did not focus on risk factors as there already well-established risk factors for endometrial CA and our aim was to verify screening tool.

The dysfunctional uterine bleeding develops early in course of endometrial carcinoma therefore the screening of all women with abnormal bleeding is important for screening purpose.[17] An Asian origin study by Beeresh CS[18] *et al.*, advocated against the endometrial biopsy of all patients with increased endometrial thickness. They suggested that homogenous thickness with regular borders should not be subjected to biopsy. We subjected all patients with abnormal uterine bleeding to biopsy as a routine practice in vogue as per hospitals standing operating instructions. We performed the biopsy of all patients with abnormal uterine bleeding including those who did not have sonographic evidence of CA endometrium and identified two positive cases who had normal thickness. We can safely suggest that ultrasound and endometrial biopsy together can be employed for screening but in that case, biopsy should be taken through less invasive means.

CONCLUSION

We came to conclusion that trans-vaginal ultrasonography can be utilized as consistent screening tool for detection of carcinoma endometrium.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

VA & AI: Data acquisition, data analysis, critical review, approval of the final version to be published.

UY & SFC: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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