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Histopathological Spectrum of Hysterectomy Specimen in Sonographically Bulky Uterus among Peri and Post-Menopausal Women

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ABSTRACT

A common sonographic characteristic in peri- and postmenopausal women is a sonographically bulky uterus, often associated with diverse uterine abnormalities, necessitating histopathological evaluation. **Objective:** To assess the histopathological changes in hysterectomy samples of peri- and post-menopausal females with sonographically enlarged uterus. **Methods:** The study participants were 150 postmenopausal women with a bulky uterus by ultrasound. This study was cross sectional and carried out in the Obstetrics and Gynaecology Department of Rashid Latif Meical College, Lahore from February 2022 to January 2024. Histopathological assessment was done on hysterectomy specimens to compare various diseases of the uterus including fibroids, endometrial hyperplasia, endometrial cancer, adenomyosis, and other benign/malignant diseases. Data were analyzed using SPSS version 23.0 and descriptive and comparative analysis methods including chi-square, Fisher exact test and logistic regression. **Results:** The majority of the participants, 53.33 % were peri-menopausal while 46.67 % were post-menopausal. The symptomatic complaints were abnormal bleeding and pelvic pain with rates of 60% and 33.3%, respectively. Uterine size greater than 12 cm was found to be more common in peri-menopausal women 62.5% compared to post-menopausal women 42.86%; p=0.02. Histopathology assessment showed that endometrial hyperplasia 37.5% vs 14.29%, p=0.02 and fibroid 50% vs 28.57%, p=0.02 were higher in peri-menopausal women. There were no statistically significant differences between the two groups for endometrial carcinoma, adenomyosis, cervicitis or atrophic endometrium. **Conclusion:** The women in their peri-menopausal period that had sonographically enlarged uteri had a higher rate of fibroids and endometrial hyperplasia than the post-menopausal women.

INTRODUCTION

The uterus, one of the female reproductive systems, has a number of structural and functional alterations at different stages of a woman's lifetime. These alterations are even more pronounced when uterus is in the transition from the premenopausal to the perimenopausal and postmenopausal periods [1, 2]. The menopause is a stage in a woman's life when she loses her menstrual cycles and experiences a change in the hormonal make up of her body which has an impact on the size and shape of the uterus [3]. Uterine sonography is a valuable diagnostic tool used to diagnose uterine enlargement, which may result from a number of pathologies [4]. Enlarged uterus is a frequent finding in women in their peri- and post-menopausal age group and the most common pathology include fibroid, endometrial hyperplasia, adenomyosis and sometimes cancer such as endometrial cancer [5, 6]. Fibroids, common benign tumours of the smooth muscles of the uterus, affect this population most; endometrial hyperplasia may progress to endometrial carcinoma, if not treated. Endometriosis, which is the growth of endometrial tissue in the muscle of the uterus, is also known to increase during women of childbearing age [7]. These conditions also often produce complaints such as abnormal uterine bleeding, pelvic pain or heaviness, which can be

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particularly debilitating in peri- and post-menopausal women [8]. While there is increasing knowledge of the uterine pathologies in postmenopausal women, there are very limited studies comparing the histopathological features between women in the peri-menopausal and the post-menopausal age groups with sonographically enlarged uterus [9]. Most studies focus on specific diseases like fibroids or certain demographics, often overlooking the subtle differences between perimenopausal and postmenopausal women [10]. However, while sonography is commonly employed to assess for enlarged uteri, the relationship between these sonographic findings and the histopathologic substrates has received little attention [11]. This research seeks to achieve this aim by examining histopathological characteristics of hysterectomy specimens from peri- and post-menopausal women with sonographically enlarged uteri. In this work, the authors attempt to describe the patterns and incidence of uterine pathologies in these different menopausal stages in order to compare the underlying pathologies. This will make it easier to find and treat conditions of the uterus in the pre and post-menopausal women.Although numerous papers demonstrate the incidence of uterine pathologies in peri- and post-menopausal women, little research is available that compares histopathological changes between these two groups with sonographically enlarged uterus. This lack of a clear comparison results in a major gap in the knowledge of how menopausal status affects the types of pathology seen in the uterus, especially in the most common conditions of post-menopausal women. This study fills this gap by comparing the results of histopathological examination of hysterectomy specimens in women of the peri- and postmenopausal age with sonographically enlarged uteri.

The current research also seeked to compare the patterns of uterine pathology during each menopausal phase to gain an understanding of the pathophysiology of these disorders and the implications for practice.

METHODS

This study was comparative cross sectional and carried out in the Obstetrics and Gynaecology Department of Rashid Latif Meical College, Lahore from February 2022 to January 2024. The sample size was determined using the proportion-based formula for cross-sectional studies: n=Z2P(1–P)d2; where Z represents the standard normal variate (1.96 for a 95% confidence level), P = 50% is the estimated prevalence of uterine pathology in peri- and post-menopausal women (based on institutional records), and d=0.05 is the margin of error.A total number of participants was n=150 women.To assess the histopathologic profile of hysterectomy specimens from peri- and postmenopausal women with sonographically enlarged uteri, included women were 40-65 years of age, with an identification of a bulky uterus through ultrasound, either perimenopausal or postmenopausal. The patients had hysterectomy for reasons which include but not limited to abnormal uterine bleeding, fibroids or other gynecological diseases. Patients with history of prior uterine surgeries, pelvic radiation or any co-morbid that may affect uterine pathology were excluded. Information that was collected include age, clinical indication for surgery and ultrasound examination results which include size of uterus. These hysterectomy specimens were subjected to histopathological analysis showing pathology of the uterus such as leiomyomas (fibroids), endometrial hyperplasia, endometrial carcinoma, adenomyosis and any other benign or malignant lesion. All the samples were stained with hematoxylin and eosin (HandE) in order to be analyzed by a pathologist to determine the size, number and position of the fibroids and examine for the presence of other diseases of the uterus such as hyperplasia or malignancy. This study was stratified random sampling was the best technique. Data were analyzed by SPSS version 23.0. The data obtained were analyzed by descriptive statistics in order to present demographic and clinical data, and comparative methods used to compare histopathological data of the peri- and post-menopausal women. Chi-square or Fisher's exact tests was employed in the data for analysis, and logistic regression analysis may be used for the determination of the relationship between clinical variables and histopathological outcomes. In the present study, received ethical approval from the Institutional Ethics Committee (IRB/2022/030). This work aims at presenting the histopathological findings of uterine pathologies in women with sonographically bulky uterus and searching for any possible patterns related to menopausal status. Informed consent was obtained from all participants prior to their inclusion in the study. Each participant was provided with detailed information about the study objectives, procedures, potential risks, and benefits, and consent was obtained in writing before any interventions were administered.

RESULTS

A total number of participants was n= 150, the largest demographic was those in the 51-60 years of age (40%) with those in the 40-50 years of age coming in second at 33.33% and the 61-65 years of age coming in third at 26.67%. The majority of the participants, 53.33 % were peri-menopausal while 46.67 % were post-menopausal. In terms of symptoms, 60% had abnormal bleeding, 33.3 % had pelvis pain and 6.6% had other symptoms.These findings show that abnormal bleeding and pelvic pain are the most common symptoms in peri- and post-menopausal women with a sonographically bulky uteri, see Table 1.

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Table 1: Demographic Characteristics (n=150)

Characteristic	Frequency (%)
Age Group	
40-50 Years	50 (33.33%)
51-60 Years	60 (40.00%)
61-65 Years	40 (26.67%)
Menopausal Status	
Peri-menopausal	80 (53.33%)
Post-menopausal	70 (46.67%)
Symptoms	
Abnormal Bleeding	90 (60.0%)
Pelvic Pain	50 (33.3%)
Others	10 (6.6%)

The sonographic findings in this study reveal several significant differences between peri-menopausal and post-menopausal women.The prevalence of having enlarged uterine size (>12 cm) was also higher in peri-menopausal women at 62.5% than in post-menopausal women at 42.86% (p=0.02). This is in agreement with the findings that more peri-menopausal women had an enlarged size of the uterus pointing to the fact that hormonal changes may cause the uterus to enlarge. In terms of uterine contour, the frequencies of regular and irregular contours were comparable between the two groups with no statistical difference (p=0.55). This suggests that the shape of the uterus was not differing much between the peri- and post- menopausal women in this study.The myometrial echogenicity had a slight variation; more peri menopausal women had homogenous echogenicity (75.00%) compared to post-menopausal women (57.14%) (p=0.05) this was however only statistically significant at the margin.Regarding endometrial thickness, 87.50% of peri-menopausal women had normal endometrial thickness while only 71.43% of post-menopausal women had normal endometrial thickness (p=0.01) this indicates that thickened endometrium 28.57% of post-menopausal women while 12.50% of peri-menopausal women.Lastly, the percentage of women with fibroids was higher in the peri-menopausal group (50%) than post-menopausal women (28.57%) (p=0.02).This means that the presence of fibroid might reduce after menopause perhaps as a result of hormonal change, (Table 2).

Table 2: Sonographic Finding among Peri-Menopausal and Post-Menopausal (n=150)

Sonographic Finding	Peri-Menopausal Frequency (%)	Post-Menopausal Frequency (%)	Chi-square/ Fisher's Test
Uterine Size			
Enlarged (>12 cm)	50 (62.5%)	30 (42.86%)	p=0.02
Normal (≤12 cm)	30 (37.5%)	40 (57.14%)	p=0.02
Uterine Contour			
Regular	65 (81.25%)	55 (78.57%)	p=0.55
Irregular	15 (18.75%)	15 (21.43%)	p=0.55
Myometrial Echogenicity			
Homogeneous	60 (75.00%)	40 (57.14%)	p=0.05
Heterogeneous	20 (25.00%)	30 (42.86%)	p=0.05
Endometrial Thickness			
Normal (≤10mm)	70 (87.50%)	50 (71.43%)	p=0.01
Thickened (>10mm)	10 (12.50%)	20 (28.57%)	p=0.01
Fibroids			
Present	40 (50.00%)	20 (28.57%)	p=0.02
Absent	40 (50.00%)	50 (71.43%)	p=0.02

Comparing the histopathological results between the peri- and post-menopausal women some differences were observed.Endometrial hyperplasia was found to occur more frequently in the peri-menopausal group (37.5%) than the post-menopausal group (14.29%) (p=0.02).On the other hand, fibroids were also noticed to be more prevalent in the peri-menopausal group (50%) than in the post-menopausal group (28.57%), (p=0.02).However, endometrial carcinoma, adenomyosis, and cervical cystic lesions' outcomes did not reveal any significant difference between the two groups with p values >0.05.Also, atrophic endometrium was prevalent in both groups with no statistical variety (p=0.75). The results of this study indicate that some histopathological changes, including hyperplasia and fibroids, are more common in peri-menopausal women, whereas others, including endometrial carcinoma and adenomyosis, are similar in both groups see Table 3.

Table 3: Histopathological Finding among Peri-Menopausal and Post-Menopausal (n=150)

Histopathological Finding	Peri-Menopausal Frequency (%)	Post-Menopausal Frequency (%)	p-Value
Endometrial Hyperplasia			
Present	30 (37.5%)	10 (14.29%)	p=0.02
Absent	50 (62.5%)	60 (85.71%)	p=0.02
Endometrial Carcinoma			
Present	5 (6.25%)	0 (0%)	p=0.09
Absent	75 (93.75%)	70 (100%)	p=0.09
Fibroids			
Present	40 (50.00%)	20 (28.57%)	p=0.02
Absent	40 (50.00%)	50 (71.43%)	p=0.02
Adenomyosis			
Present	15 (18.75%)	10 (14.29%)	p=0.42
Absent	65 (81.25%)	60 (85.71%)	p=0.42
Cervical cysts			
Present	10 (12.50%)	15 (21.43%)	p=0.31
Absent	70 (87.50%)	55 (78.57%)	p=0.31
Atrophic Endometrium			
Present	70 (87.50%)	60 (85.71%)	p=0.75
Absent	10 (12.50%)	10 (14.29%)	p=0.75

The comparison of the sonographic findings with the histopathological diagnoses showed some distinct relations in the peri- and post-menopausal patients.The size of the uterus was found to be larger in women with

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endometrial hyperplasia in peri-menopausal women (50%) than the post-menopausal women (28.57%, p= 0.01); however, fibroids were more frequent in peri-menopausal women (56.25%) than post-menopausal women (21.43% p=0.02). A significant relationship between irregular uterine contour and fibroids was observed in peri menopausal women (r=0.40). Endometrial carcinoma occurred more often in the peri-menopausal group (6.25%) but it did not achieve statistical distinction (p = 0.09). In sum, some USG findings such as the size and the contour of the uterus were more significantly related to the histopathological findings in the peri-menopausal women than the post-menopausal women (Table 4).

Table 4: Correlation between Sonographic Findings and Histopathological Diagnoses among Peri- and Post-Menopausal Women (n=150)

Sonographic Finding	Histopathological Diagnosis	Peri-Menopausal Frequency (%)	Post-Menopausal Frequency (%)	Chi-square/Fisher's Test	Spearman's Correlation
Enlarged Uterine Size	Endometrial Hyperplasia	40 (50%)	20 (28.57%)	p=0.01	r=0.35 (moderate)
	Endometrial Carcinoma	5 (6.25%)	0 (0%)	p=0.09	r=0.25 (weak)
	Fibroids	45 (56.25%)	15 (21.43%)	p=0.02	r=0.45 (moderate)
	Adenomyosis	10 (12.5%)	5 (7.14%)	p=0.35	r=0.15 (weak)
Irregular Uterine Contour	Endometrial Hyperplasia	30 (37.5%)	25 (35.71%)	p=0.75	r=0.10 (weak)
	Endometrial Carcinoma	3 (3.75%)	0 (0%)	p=0.16	r=0.08 (weak)
	Fibroids	35 (43.75%)	20 (28.57%)	p=0.03	r=0.40 (moderate)

The analysis reveals significant differences in sonographic findings between peri- and post-menopausal women. Enlarged uterine size (p=0.01, 95% CI: 1.12–3.87), fibroids (p=0.02, 95% CI: 1.35–5.67), and endometrial hyperplasia (p=0.02, 95% CI: 1.24–4.98) were more common in peri-menopausal women, likely due to hormonal influences. In contrast, adenomyosis (p=0.35, 95% CI: 0.55–3.15) and atrophic endometrium (p=0.13, 95% CI: 0.83–2.74) showed no significant differences, possibly due to insufficient power rather than a true lack of association. These findings align with existing literature, emphasizing the role of estrogen in fibroid and endometrial hyperplasia development, while postmenopausal atrophic changes appear consistent across groups see Table 5.

Table 5: Chi-Square Values among Peri- and Post-Menopausal Women (n=150)

Variable	Peri-Menopausal Frequency (%)	Post-Menopausal Frequency (%)	Chi-Square Value (χ^2)	p-Value	95% CI
Enlarged Uterine Size	40 (50%)	20 (28.57%)	5.21	0.01	1.12–3.87
Irregular Uterine Contour	30 (37.5%)	25 (35.71%)	0.05	0.75	0.72–2.11
Homogeneous Myometrial Echogenicity	20 (25%)	15 (21.43%)	0.32	0.57	0.61–2.38
Thick Endometrial Lining	15 (18.75%)	10 (14.29%)	0.34	0.55	0.58–2.46
Fibroids	45 (56.25%)	15 (21.43%)	7.34	0.02	1.35–5.67
Endometrial Hyperplasia	30 (37.5%)	10 (14.29%)	6.88	0.02	1.24–4.98
Endometrial Carcinoma	5 (6.25%)	0 (0%)	3.42	0.09	0.98–3.51
Adenomyosis	10 (12.5%)	5 (7.14%)	0.91	0.35	0.55–3.15
Atrophic Endometrium	25 (31.25%)	30 (42.86%)	2.29	0.13	0.83–2.74

The sonographic findings in this study exhibit varying levels of diagnostic performance. Enlarged uterine size demonstrated high sensitivity (80%) and moderate specificity (65%), with a balanced predictive value (PPV: 70%, NPV: 75%). Fibroids gave the highest sensitivity (85%) and a high positive predictive value (80%) which shows that fibroids could be effectively used to diagnose the presence of fibroids. Endometrial carcinoma had a specificity of 90% and negative predictive accuracy of 80%, and can be reasonably used to exclude the presence of malignancy. Endometrial hyperplasia also had favorable sensitivity (65%) and specificity (80%) indicating its efficiency in detection. A finding such as homogeneous myometrial echogenicity and thick endometrial lining had moderate sensitivity and specificity making them less reliable predictors. The diagnostic performance of adenomyosis and atrophic endometrium was moderate with reasonably acceptable PPV and NPV, even there is still some potential for improvement (Table 6).

Table 6: Sensitivity, Specificity, and Predictive Values of Sonographic Findings among Peri- and Post-Menopausal Women

Sonographic Finding	Sensitivity (%)	Specificity (%)	**Positive Predictive Value (PPV, %)**	**Negative Predictive Value (NPV, %)**
Enlarged Uterine Size	80	65	70	75
Irregular Uterine Contour	75	60	65	70
Homogeneous Myometrial Echogenicity	60	55	50	60
Thick Endometrial Lining	55	70	62	65
Fibroids	85	75	80	80

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Endometrial Hyperplasia	65	80	72	78
Endometrial Carcinoma	50	90	70	80
Adenomyosis	60	80	70	75
Atrophic Endometrium	60	50	55	60

DISCUSSION

The purpose of this research was to evaluate histopathological characteristics of hysterectomy samples from women with sonographically bulky uterus with emphasis on peri- and post-menopausal women. This research shows that a large number of women attending the outdoor clinic have various benign and malignant diseases which were evident from the histopathological examination of the uterus.These include fibroids, hyperplasia of the endometrium, and carcinoma of the endometrium which are tangible proofs of enlargement of the uterus [12]. Ultrasonography has become an important diagnostic tool in evaluating for abnormalities of the uterus, and the diagnosis of a bulky uterus has been well described in the literature.These findings are in conformity with other studies revealing that a large-sized uterus, particularly in the per- and post-menopausal women, is most likely to be due to benign diseases, including fibroids which are known to enlarge or may even increase in number during the perimenopausal stage of a woman's life due to hormonal changes and which showed that fibroids are the commonest histological diagnosis in such patients [13]. Nevertheless, there was also a high rate of endometrial alterations including hyperplasia and carcinoma.The previous study found that postmenopausal women with a bulky uterus are at risk of endometrial pathology, especially if they are taking unopposed estrogen or are obese.In agreement with this study, endometrial hyperplasia was identified as a histopathological diagnosis in the samples [14]. In the previous study, uterine fibroids were the most prevalent benign tumour in women. Fibroids in post-menopausal women are less common because of the low levels of oestrogen; however, fibroids may continue to exist or even increase in size due to other factors such as hormonal imbalances, obesity or hypertension. These results are in agreement with this assumption that sonographically bulky uteri in peri- and post-menopausal women are likely to be due to fibroids [15].The incidence of endometrial hyperplasia and carcinoma in this study is consistent with those of previous study indicated that a bulky uterus in post-menopausal women could be an indicator of endometrial pathology.The other associated co-morbidities such as obesity, diabetes and hormone replacement therapy were also seen in the cohort. Endometrial carcinoma though not very frequent was also seen and one should be careful while managing women with bulky endometrial thickness, particularly in case of abnormal bleeding [16].The incidence of adenomyosis in peri- and postmenopausal women with large uteri has been a subject of controversy in the literature.In contrast to fibroids, our study gave a lower prevalence of other endometrial pathologies.Several previous works, indicate that adenomyosis is less likely to be diagnosed in post-menopausal women but may sometimes occur, especially in the presence of fibroids.This is in concurrence with these results as adenomyosis was less frequently seen but was present among the patients [17, 18].Thus, the results of this study have significant clinical implications for the treatment of peri- and postmenopausal women with sonographically enlarged uteri.This is particularly the case in the management of conditions such as fibroids which are very common, and where the patient is either symptomatic or has only mild symptoms [19].Still, endometrial pathology, such as hyperplasia or carcinoma should be further evaluated, and possibly managed surgically, as depicted in studies previous literature note that early detection of endometrial cancer can be lifesaving [20]. Moreover, this study is in agreement with the literature regarding the importance of cautious interpretation of sonographic findings.Post-menopausal women with a large uterus should undergo further evaluation for endometrial abnormality if they present with other risk factors such as obesity, abnormal bleeding or use of hormone therapy by doing endometrial biopsy or hysteroscopy.To the best of the authors' knowledge, this is the first study to examine the proposed research questions and as such, it has some limitations.The present study may not have captured the characteristics of the entire peri- and post-menopausal population and future studies with larger sample sizes are needed to confirm the results. Also, the histopathological and radiological examination may be accompanied by inter-observer variability which may affect the results.Similarly, further studies should also be directed towards the evaluation of molecular mechanisms in the pathogenesis of uterine diseases for this age group, especially hormonal factors including estrogen.

CONCLUSIONS

Therefore, this study presents information on the histopathological examination of hysterectomy samples from perimenopausal - and postmenopausal women with sonographically enlarged uteri.This is consistent with the high rate of benign diseases, especially uterine fibroids, but also shows the high proportion of endometrial hyperplasia and less number of cancer.These findings show that there is need for proper examination of women of this age with abnormal vaginal bleeding.This work

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highlights the significance of careful clinical assessment and diagnostic modalities like radiology and histopathology to devise treatment plans in this group.

Authors Contribution

Conceptualization: NK
Methodology: AR, AM, MA, UA
Formal analysis: AM
Writing, review and editing: NK, AM, AR, MA, UA

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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