Sonographic evaluation of Endometrial Hyperplasia in perimenopausal & postmenopausal women- A systematic review

Aqsa Hafeez, Syyeda Khadija Prof Dr Syed Amir Gillani, Zobia Saleem, Mehwish Rauf, Tayyaba Aslam, Summan Hameed, Dr Gull Zaman

Abstract- Endometrial hyperplasia refers to thel thickening of the endometrial lining of uterus causing l uterine bleeding. This condition frequently occur during or after menopause. It increases the risk of endometrial cancer. Simple hyperplasia is the most common type of endometrial hyperplasia having smaller risk of becoming cancerous. The databases searched were Google Scholar, Pubmed, Embase and Science direct. The studies were screened and data analysis performed by using content analysis. We identified 15 studies comprising of ultrasound evaluation of endometrial hyperplasia.In the analysis 15 studies including 11935 perimenopausal and postmenopausal women, ultrasound reported endometrial hyperplasia in 744 cases (6.2%) including simple endometrial hyperplasia in 658 cases (5.5%), complex endometrial hyperplasia in 86 cases (0.7%) and endometrial focal lesion & carcinoma in 60 cases (0.5%). In this systematic review of 15 studies, including perimenopausal and postmenopausal women ultrasound is utilized to investigate the endometrial lesion. Sonography has high positive predictive value for diagnosing endometrial hyperplasia but does not adequately define focal and cancerous endometrial lesion. Transvaginal ultrasonography is significantly better in defining intrauterine abnormalities due to high sensitivity (100%) and specificity (63.7%).In the view of the results obtained from studies included in this systematic review, we conclude that ultrasound is an appropriate diagnostic tool in detecting EH. The objective of this study was to evaluate the sonographic findings of endometrial hyperplasia in perimenopausal & postmenopausal women.

Index Terms— Endometrial hyperplasia, ultrasound of endometrium, perimenopausal and postmenopausal bleeding

1 INTRODUCTION

Endometrial hyperplasia is an abnormal proliferation of the endometrial glands and stromal tissue, defined as diffuse smooth thickening >10 mm. It is the thickening of endometrial lining causing heavy or abnormal uterine bleeding. Endometriall hyperplasia tends to occur during or after menopause so, it affects both perimenopausal and postmenopausal women. It rarely occurs in younger age of about 35 years. It is not cancer but raises the chances of developing endometrial carcinoma, a type of uterine carcinoma.[1] In perimenopausal women normal endometrial thickness depends on the stage of the menstrual cycle, but thickness >15 mm is considered the upper limit of normal in the secretory phase. In postmenopausal women the thickness of endometrium >5 mm is considered abnormal.[2] Hyperplasia can be excluded in patients when the endometrial thickness measures < 8 mm.[3] In women with endometrial hyperplasia secretion of estrogen is more and progesterone is not enough. These hormones play an important role in menstrual cycle and pregnancy. During ovulatory phase the estrogen cause the thickening of endometrium while progesterone prepares the uterus for pregnancy. When no pregnancy takes place, progesterone level drops. The decreasing progesterone level shed the lining of uterus. Women with endometrial hyperplasia secrete more estrogen & less progesterone, so the uterus does not shed the endometrial lining and it continues to grow & thicken. Instead of this, obesity contributes to elevated levels of circulating estrogen as a result of which risk of endometrial hyperplasia increases.[4] Risk factors for EH include diabetes mellitus, breast cancer treatments (tamoxifen), obesity, hormone therapy, polycystic ovarian syndrome, early age for menstruation and late onset of menopause.[5] Signs & symptoms of endometrial hyperplasia include abnormal menstruation (short menstrual periods uncommonly long periods or missed periods), heavy menstrual bleeding, postmenopausal bleeding. [6] The endometrial hyperplasia is divided into two broad categories. Simple endometrial hyperplasia has normal looking cells that usually will not convert to cancerous cells. This condition does not require treatment. Simple or complex atypical endometrial hyperplasia results in the

overgrowth of abnormal cells causes this to become precancerous condition. Without treatment the risk of cancer increases.[7]

Many conditions can cause uterine bleeding in perimenopausal and postmenopausal women. To identify the cause of uterine bleeding clinician may suggest these investigations. A transvaginal ultrasound produces high frequency sound waves to produce images of the uterus. Ultrasound is the first line investigative modality to evaluate the endometrial thickness in perimenopausal & postmenopausal women presents with abnormal uterine bleeding. Imaging the endometrium on 5-10 day of reproductive cycle reduces the variability in endometrial thickness.[8] There is homogenous smooth increase in endometrial thickness but EH may also result in focal thickening & surface irregularity that is suspicious for carcinoma. **E**ndometrial biopsy removes tissue samples from the uterus lining. Pathologists study the cells to confirm endometrial cancer. About one-third of endometrial carcinoma thought to be preceded by endometrial hyperplasia, therefore a biopsy is required for a accurate diagnosis. **Hysteroscopy** uses a thin, lighted tool called a hysteroscope to examine the cervix and the uterus. This procedure can be performed along with a dilation and curettage (D&C). With hysteroscopy, the clinician can see abnormalities within the endometrial cavity and take a targeted biopsy of any suspicious area.[9].In high risk perimenopausal women (ET> 15mm) and postmenopausal women (ET > 5 mm), the evaluation of morphology and vascularity of endometrium is performed by using Gray scale and Doppler ultrasound.[10] Endometrial hyperplasia is rare. It affects approximately 133 out of 100,000 women[11]. All types of hyperplasia can cause abnormal and heavy menstrual bleeding that can make the woman anemic.[12] The objective of this systematic review was to identify the sonographic evaluation of endometrial hyperplasia in perimenopausal & postmenopausal women presenting with abnormal uterine bleeding.

(Table 1 included the difference between perimenopausal and postmenopausal women) [13, 31, 32]

Table 1

Parameter	Perimenopausal women	Postmenopausal women
Definition	The time marking the end of reproductive years	The time when women experiences no menstrual bleeding
Uterine size	A parity related enlargement in the uterine size in multiparous women	There is significant reduction in uterine size. The reduction in uterine size was related to years since menopause.
Clinical presentation	Irregular heavy menstrual bleeding	Postmenopausal bleeding
Endometrial thickness cut off value	15mm	>5mm
Appearance of endometrium in simple endometrial hyperplasia	Characteristic triple layer or five line appearance with homogenous endometrial thickening in the secretory phase.	No characteristic three & five line appearance Endometrial thickening is focal or diffuse
Appearance of endometrium in complex endometrial hyperplasia	Focal endometrial thickening with surface irregularity, heterogeneous echogenicity and focal lesions with regular surface. Cystic changes also seen.	Heterogeneous endometrial thickness & echogenicity with intrauterine fluid collection

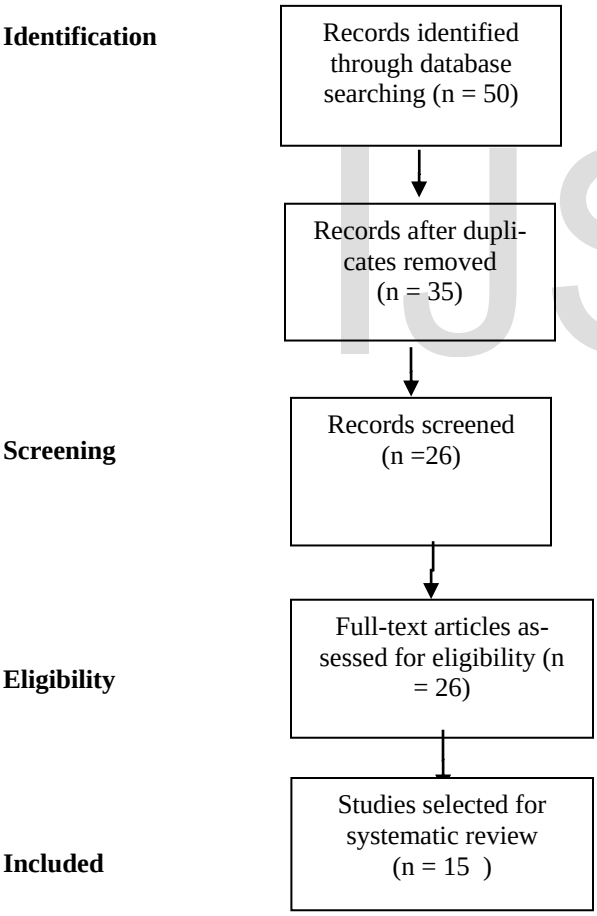
2. **Methodology:**

Literature Search: The literature search was conducted in the following databases: Google Scholar, PubMed, Science Direct and Embase. Search terms used for retrieving the articles were: Endometrial hyperplasia, Ultrasound imaging of endometrium,

perimenopausal and postmenopausal bleeding. All types of articles published in the last 15 years like reviews, commentary, correspondence, journals, and original research article relevant to the subject of the review were searched.

Selection of articles: From all the articles that were relevant to the topic of the review, only original research articles and 1 systematic review that sonographically assessed the endometrial hyperplasia in perimenopausal & postmenopausal women, were included. Total 26 articles were selected by initial screening that included perimenopausal and postmenopausal women presenting with AUB. Further, 11 articles were excluded because they either require subscription, copyright permission or they contain non-English literature. The final number of articles included was 15.

(Prisma flow chart representing study selection process)



3. Results:

In this review of 15 studies, including 11935 perimenopausal and postmenopausal women presenting with abnormal uterine bleeing ultrasound is utilized to investigate the endometrial lesion. In the content analysis of these studies, ultrasound reported endometrial hyperplasia in 744 cases (6.2%) including simple endometrial hyperplasia in 658 cases (5.5%), complex endometrial hyperplasia in 86 cases (0.7%) and endometrial focal lesion & carcinoma in 60 cases (0.5%). Sonography has high positive predictive value for diagnosing endometrial hyperplasia but does not adequately define focal and cancerous endometrial lesion. Transvaginal ultrasonography is significantly better in defining intrauterine abnormalities. The sensitivity and specificity of TVS was 100.0% and 63.7% respectively.
Hari Kishor Shrestha (2020) conducted cross sectional study included359 postmenopausal women presenting with history of at least three months amenorrhea were undergone transvaginal ultrasonography with measurement of endometrial thickness and uterine size. TVS reported EH in 69 cases (19.2%). Endometrial biopsies were taken in 69 cases (19.2%) only. [12]
Yu Ran Park (2019) conducted retrospective cohort study included perimenopausal & postmenopausal women who underwent transvaginal ultrasonography (TVS) for an incidental finding of a thickened endometrium. 92 patients were included in this study. Of the 92 patients, 78 (84.8%) had normal pathology, while 14 (15.2%) had endometrial pathology (EH+), including 5 patients (35.7%) with simple hyperplasia without atypia, 3 (21.4%) with complex hyperplasia, and 6 (42.9%) with endometrial carcinoma. [13]
Samreen Afzal & Sidra Afzal (2018) conducted a cross-sectional observational study. A total 200 postmenopausal women presenting with abnormal uterine bleeding were included in this study.. Among 200 participants 118 (59%) patients were diagnosed with endometrial hyperplasia on TVS (screen positive) and 82(41%) were screened negative. TVS has 84% diagnostic accuracy for detecting endometrial hyperplasia. (14) (15)

Juan Luis Alcázar (2018) conducted systematic review and included the review of nine articles comprising data from 4751 women (postmenopausal women, endometrial thickness ≥11 mm). The prevalence of endometrial hyperplasia with atypia was 2.4%. The relative risk of endometrial cancer and/or endometrial hyperplasia with atypia in the group with ≥11 mm endometrial thickness was 2.59%.[16]

A research was published in the journal of American College of Obstetricians and Gynecologists (2018). The study is a retrospective cohort study included 4,383 postmenopausal women to assess endometrial cancer detection rates based on different cut-off levels. Using a 4 mm endometrial echo as a cut-off value, transvaginal ultrasonography has an extremely high negative predictive value (greater than 99%).[17]

L Jokubkiene (2016) included 510 postmenopausal women in his study and this was a cross-sectional observational study.

12% of patients had sonographic endometrial thickness ≥ 5.0 mm, 67% of these with an endometrial thickness ≥ 5.0 mm had intrauterine focal lesions (EH).[18]

B Gultekin (2016) conducted cross-sectional observational study and included 106 women with a sonographic finding of thickened endometrium in his study. All patients underwent B-mode scanning and elastosonography. After sonographic evaluation, all patients underwent endometrial tissue sampling via dilatation and curettage. Histopathological results indicated that 22 patients had endometrial hyperplasia, 20 patients had endometrial polyps, and 64 patients had normal ultrasound results, with or without abnormal uterine bleeding..[19]

M.R. Metin (2016) study is prospective study included 61 women with either postmenopausal bleed or normal TSE. 32 women had endometrial hyperplasia, 14 had endometrial carcinoma and 15 were normal who served as a control group. Endometrial hyperplasia group showed average SI values of 1.8 while endometrial carcinoma group had SI value of 1.00. [20]

Behrooz Shokouhi (2015) prospective study enrolled 68 premenopausal and 52 postmenopausal women (total=120). TVS reported EH in 85 cases (70.83%).Simple cystic hyperplasia was the commonest seen in 22% of patients. The diagnostic accuracy of TVS for endometrial hyperplasia in this study was 75.6%.[21]

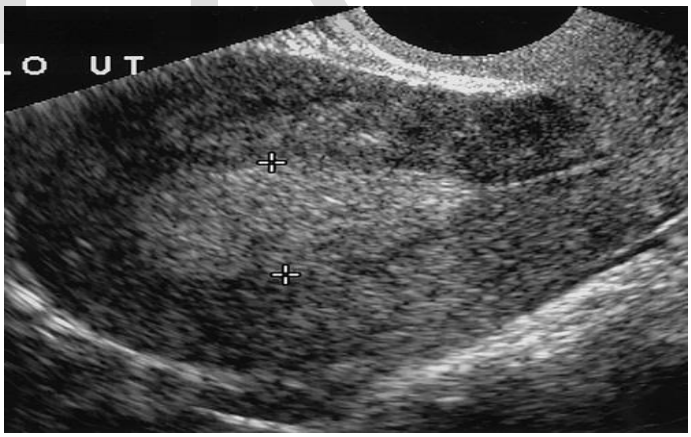
S Ates (2014) conducted a retrospective cohort study to find out the value of TVS in finding pathologies of endometrium in postmenopausal women with or without bleeding. Patients were divided into two groups. Group A comprised of 91 patients who presented with postmenopausal bleeding and endometrial thickness of equal to or greater than 5mm. Group B consisted of 44 women who were asymptomatic and had incidental finding of thickened endometrium (more than 5mm). 7 cases of endometrial hyperplasia and 6 cases of endometrial carcinoma were detected in group A while only 2 cases of endometrial hyperplasia and no case of endometrial carcinoma were detected in group B. [22]

Fatima Nazim (2013) carried out cross sectional observational study in 263 women presented with abnormal uterine bleeding. Diagnostic accuracy of TVS in identifying endometrial hyperplasia using histopathology as gold standard was found to be 75.6%TVS has a moderate diagnostic accuracy in detecting endometrial hyperplasia. Due to the fact that transvaginal ultrasound is safe, acceptable and easily available is non-invasive in nature. TVS is to be used as a 1st line diagnostic tool in patients who present with abnormal uterine bleeding. [23]

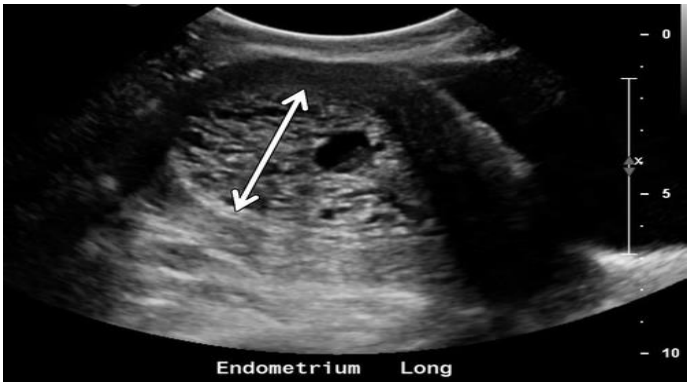
Wojciech Pieta (2009) comparative study included 182 patients in which endometrium sample was obtained for analysis. Correlation between thickness of endometrium and histological diagnostic was sought. A value of cut down ultrasound measured endometrial thickness to exclude endometrial cancer was 9 mm. [24]

Paçarada Myrvete (2007) conducted a prospective study which comprised of 150 women who underwent TVS. Endometrial biopsy was taken and sent for biopsy in 82 patients. More than 1/3 of patients who had endometrial thickenss between 3 to 10mm showed no evidence of pathology while patients with endometrial thickness of more than 10mm had hyperplasia, polyposis or carcinoma.[25]

Andrzej Starczewsk (2005) comparative study included 659 postmenopausal women aged 41-85 (mean 61.5). They were divided into three groups. The first one counted 186 women (28.22%) with metrorrhagia and normal endometrial ultrasound image. The second one counted 293 women (44.46%) with only changes in ultrasound examination and the third one counted 180 women (27.31%) with metrorrhagia and incorrect ultrasound image of endometrium (images the endometrial thickness above 5 mm). The endometrial cancer is the frequent in women with postmenopausal bleeding and endometrial hypertrophy in ultrasound examination, especially when endometrial image is non-homogenous and irregular. [26]



(Figure 1 shows normal premenopausal endometrium. Sagittal US image of the uterus obtained during the secretory phase of the menstrual cycle shows a thickened, echogenic endometrium.)[1-4]



(Figure 2 shows sagittal gray-scale transvaginal US image in a 64-year-old woman demonstrates a thickened endometrium (double-headed arrow) that is hyperechoic and contains cystic spaces. This patient was receiving tamoxifen therapy, and the imaging findings are secondary to a medication-induced proestrogenic state) [1-4]

4. Discussion

This review suggests that sonography has been proposed as a mean for the non invasive identification of endometrial thickness in perimenopausal and postmenopausal women who present with abnormal uterine bleeding. Endometrial hyperplasia is the precancerous lesion of type I endometrial lesion, so identification of the type of pathology and better diagnostic accuracy is crucial to improve the prognosis of women with EH. Sonographic features suggestive of simple hyperplasia include focal endometrial thickening with surface irregularity, homogenous echogenic endometrium and focal lesions (subendometrial polyp & carcinoma).. Heterogeneous endometrial thickening & echogenicity with intrauterine fluid collection is seen in precancerous lesion and complex hyperplasia. [2]

In the review of 15 studies, 11935 perimenopausal and postmenopausal women ultrasound was utilized to investigate the endometrial lesion. In the content analysis of these studies, ultrasound reported EH in 744 cases (6.2%) including simple EH in 658 cases (5.5%), complex EH in 86 cases (0.7%) and endometrial focal lesion & carcinoma in 60 cases (0.5%). Numerous studies have shown that sonography has high positive predictive value for endometrial hyperplasia but does not adequately define focal and cancerous endometrial lesion. Several small studies reported that transvaginal ultrasonography is significantly better in defining intrauterine abnormalities. The sensitivity and specificity of TVS was 100.0% and 63.7% respectively. The review showed TVUS was in near perfect agreement (86%) with hysteroscopy in the diagnosis of complex EH. However, some authors found hysteroscopy is superior to conventional ultrasound in discriminating simple and complex EH. Histopathology is gold standard for diagnosing complex EH in both perimenopausal and postmenopausal women.[16]

Dilatation & curettage method for diagnosing EH may miss the endometrial cancer due to examination blindness. TVS has the advantage of being non invasive, easily available, reproducible and cost effective. It can show the abnormal endometrial thickness, heterogeneous endometrial echogenicity and the features suggestive of endometrial lesion.[9]

A number of studies proposed that postmenopausal women with the endometrial thickness greater than the cut off value (> 5mm) and also perimenopausal women in which the endometrial thickness of 15 mm is considered as upper limit of the normal value should be recommended to receive endometrial biopsy.[5]

Nevertheless there were limitations in this study: the quality of the studies included in the review was not high that affected the reliability of the conclusion. Some features that may have affected the sonographic evaluation such as menstrual phase were potentially causing bias in the conclusion. Moreover this systematic review only included English literature so it did not rule out the possibility of language bias.

Hence, further studies are needed in the future for validation of these conclusions.

5. Conclusion:

In our conclusion, we suggest that transvaginal ultrasound is the first line investigation for the assessment of endometrial hyperplasia in perimenopausal and postmenopausal women due to the non invasive nature and potentially high diagnostic accuracy that allow more accurate decisions for future investigation and planning. So, ultrasound can act as multipurpose investigative modality in cases where endometrial lesion (EH) is detected. In the view of the results obtained from studies included in this systematic review, we conclude that ultrasound is an appropriate diagnostic tool in perimenopause and postmenopause women presenting with AUB, especially in detecting simple EH.

6. Acknowledgments

First of all, utmost thanks to the Almighty ALLAH for the divine intervention in this academic endeavor. Sincere gratitude is hereby extended to the all those who never ceased in helping until this paper was structured especially the Research Supervisor, Dr. Syeda Khadija and Prof. Dr.Syed Amir Gilani Dean Faculty of Allied Health Sciences, Mehwish Rauf, Zobia Saleem contributed in conception of study design. Tayyaba Aslam and Summan Hameed, Gull Zaman drafted the work

Disclaimer:

I,Aqsa Hafeez the corresponding author of this manuscript, certify that the data collected, is purely for academic purpose and for this research only.

- *Aqsa Hafeez is currently pursuing masters degree program in Diagnostic Ultrasound in The University of Lahore, Pakistan, PH-03401761187. E-*

mail: aqsahafeez76@gmail.com
- *Syyeda Khadija is currently pursuing Phddegree program in diagnostic Ultrasound in The University of Lahore, Pakistan, PH-03351543555. E-mail: Syyedakhadija55@gmail.commail.com*
- *Prof Dr Syed Amir Gillani , The Dean faculty of Allied Health Sciences in The University of Lahore, Pakistan, PH-03008460876. E-mail: Profgillani@gmail.com.*
- *Zobia Saleem is currently pursuing master degree program in diagnostic Ultrasound in The University of Lahore, Pakistan, PH-03314842303. E-mail: zobiasaleem95@gmail.com*
- *Mehwish Rauf is currently pursuing master degree program in Health administration in The Punjab University, Pakistan, PH-03065342561. E-mail: mehwish rauf111@gmail.com*
- *Tayyaba Aslam is currently pursuing master degree program in diagnostic Ultrasound in The University of Lahore, Pakistan, PH-03474100534. E-mail: tayyabaaslam265@gmail.com*
- *Summan hameedis currently pursuing master degree program in diagnostic Ultrasound in The University of Lahore, Pakistan, PH-03064547362. E-mail: summanhameed@rsmi.uol.edu.pk*
- *Dr Gull Zaman is currently pursuing master degree program in diagnostic Ultrasound in The University of Lahore, Pakistan, PH-03007321004. E-mail: Gull@gullzaman.com.*

REFERENCES

1) Palmer J, Perunovic B, Tidy J. The Obstetrician & Gynaecologist. 2008;10 (4)
2) Jorizzo JR, Chen MY, Martin D et-al. Spectrum of endometrial hyperplasia and its mimics on saline hysterosonography. AJR Am J Roentgenol. 2002;179 (2): 385-9. AJR Am J Roentgenol (full text) - Pubmed citation
3) Tahmasebi F, Stewart S, Mitra A, Morje M, Sayasneh A. Transvaginal Saline Contrast Sonohystography to Investigate Postmenopausal Bleeding: A Systematic Review. Cureus. 2020 Aug 28;12(8):e10094. doi: 10.7759/cureus.10094. PMID: 33005515; PMCID: PMC7523543.
4) Smith-Bindman R, Kerlikowske K, Feldstein VA. Endovaginal ultrasound to exclude endometrial cancer and other endometrial abnormalities. JAMA. 1998, 280:1510-1517. 10.1001/jama.280.17.1510
5) American Cancer Society. Endometrial Cancer Risk Factors. Accessed 8/31/2020.https://my.clevelandclinic.org/health/diseases/16569-atypical-endometrial-hyperplasia/diagnosis-and-tests
6) National Cancer Institute. Endometrial Hyperplasia. Accessed 8/31/2020.https://my.clevelandclinic.org/health/diseases/16569-atypical-endometrial-hyperplasia/diagnosis-and-tests.
7) American College of Obstetricians and Gynecologists (ACOG). Endometrial Hyperplasia. Accessed 8/31/2020.https://my.clevelandclinic.org/health/diseases/16569-atypical-endometrial-hyperplasia/diagnosis-and-tests
8) Ferrazzi E, Torri V, Trio D, Zannoni E, Filiberto S, Dordoni D: Sonographic endometrial thickness: a useful test to predict atrophy in patients with postmenopausal bleeding. An Italian multicenter study. Ultrasound Obstet Gynecol. 1996, 7:315-321. 10.1046/j.1469-0705.1996.07050315.x
9) Opolskiene G, Sladkevicius P, Valentin L: Ultrasound assessment of endometrial morphology and vascularity to predict endometrial malignancy in women with postmenopausal bleeding and sonographic endometrial thickness > or = 4.5 mm. Ultrasound Obstet Gynecol. 2007, 30:332-340. 10.1002/uog.4104
10) Opolskiene G, Sladkevicius P, Valentin L: Two- and three-dimensional saline contrast sonohysterography: interobserver agreement, agreement with hysteroscopy and diagnosis of endometrial malignancy. Ultrasound Obstet Gynecol. 2009, 33:574-582. 10.1002/uog.6350
11) American Academy of Family Physicians. Endometrial Hyperplasia. Accessed 8/31/2020.https://my.clevelandclinic.org/health/diseases/16569-atypical-endometrial-hyperplasia/diagnosis-and-tests
12) Shrestha HK, Adhikari RC, Shrestha KB (2020). Endometrial assessment by transvaginal ultrasonography and correlation with histopathology among post menopausal women. Journal of pathology of Nepal. Vol 10(1), 1613-1617. Available at https://doi.org/10.3126/jpn.v10i1.26936
13) Park YR, Lee SW, Kim.Y, (2019) Endometrial thickness cut-off value by transvaginal ultrasonography for screening of endometrial pathology in premenopausal and postmenopausal women. 62(6): 445–453 Available at doi:10.5468/ogs.2019.62.6.445
14) S. Afzal, R. Manzoor, S. Tazion, M. Hafeez, N. Badar. (2018), Transvaginal ultrasound for diagnosing endometrial hyperplasia in perimenopausal women with abnormal uterine bleeding. Pakistan Journal of Medical and Health Sciences.12(1), 400-403. Available at https://www.researchgate.net/publication/325287951_Transvaginal_ultrasound_for_diagnosing_endometrial_hyperplasia_in_perimenopausal_women_with_abnormal_uterine_bleeding
15) S. Afzal , R. Manzoor , S. Tazion , M. Hafeez, N.Badar (2018), Transvaginal ultrasound for diagnosing endometrial hyperplasia in perimenopausal women with abnormal uterine bleeding. Pakistan Journal of Medical and Health Sciences.12(1), 400-403. Available at https://www.researchgate.net/publication/325287951_Transvaginal_ultrasound_for_diagnosing_endometrial

_hyperplasia_in_perimenopausal_women_with_abnormal_uterine_bleeding

16) Alcázar JL, Bonilla L, Marucco J, Padilla AI, Chacón E, Manzour N, Salas A. Risk of endometrial cancer and endometrial hyperplasia with atypia in asymptomatic postmenopausal women with endometrial thickness ≥11 mm: A systematic review and meta-analysis. J Clin Ultrasound. 2018 Nov;46(9):565-570. doi: 10.1002/jcu.22631. Epub 2018 Aug 16. PMID: 30113073.
17) The role of transvaginal ultrasonography in evaluating the endometrium of women with postmenopausal bleeding. ACOG Committee Opinion No. 734. American College of Obstetricians and Gynecologists. Obstet Gynecol 2018;131:e124–9. VOL. 131, NO. 5. https://www.acog.org/clinical/clinical-guidance/committee-opinion/articles/2018/05/the-role-of-transvaginal-ultrasonography-in-evaluating-the-endometrium-of-women-with-postmenopausal
18) L. Jokubkiene, P. Sladkevicius and L. Valentin. Transvaginal ultrasound examination of the endometrium in postmenopausal women without vaginal bleeding. UltrasoundObstetGynecol2016; 48: 390–396.https://doi.org/10.1002/uog.15841
19) Gultekin IB, Imamoglu GI, Turgal M, Gultekin S, Öcal FD, Alkan A, Kucukozkan T. Elastosonographic evaluation of patients with a sonographic finding of thickened endometrium. Eur J Obstet Gynecol Reprod Biol. 2016 Mar;198:105-109. doi: 10.1016/j.ejogrb.2016.01.017. Epub 2016 Jan 14. PMID: 26803388.
20) M.R.Metin·H.Aydin,Ö.Ünal,Y.Akçay·M.Duymuş·E .Türkyilmaz·S.Avcu·Differentiation between endometrial carcinoma and atypical endometrial hyperplasia with transvaginal sonographic elastography.Volume 97, Issue 4, April 2016, Pages 425-431https://doi.org/10.1016/j.diii.2015.11.007
21) Shokouhi B. Role of transvaginal ultrasonography in diagnosing endometrial hyperplasia in pre- and post-menopause women. Niger Med J. 2015 Sep-Oct;56(5):353-6.
    a. doi: 10.4103/0300-1652.170390. PMID: 26778888; PMCID: PMC4698852.
22) *Ates S, Sevket O, Sudolmus S, Ozel A, Molla T, Dane B, Dansuk R. The value of transvaginal sonography in detecting endometrial pathologies in postmenopausal women with or without bleeding. Minerva Ginecol. 2014 Aug;66(4):335-40. PMID: 25020052.*
23) *F. Nazim, Z. Hayat, A. Hannan. Role of transvaginal ultrasound in identifying endometrial hyperplasia. Vol 25, No 1-2 (2013). https://jamc.ayubmed.edu.pk/index.php/jamc/article/view/1863*
24) Pieta W, Radowicki S. Przydatność ultrasonograficznego pomiaru grubości endometrium w wykrywaniu patologii błony sluzowej macicy u kobiet z nieprawidłowymi krwawieniami macicznymi w okresie peri- i postmenopauzy [Usefulness of ultrasound endometrium thickness measurement in diagnosis of endometrium pathology in women with abnormal peri- and postmenopausal bleeding]. Ginekol Pol. 2009 Jul;80(7):503-7. Polish. PMID: 19697813.
25) Paçarada Myrvete, Lulaj Shefqet, Kongjeli Niltene, Kongjeli Gyltene, Obërtinca Bujar, Veliu Afrim. Correlation of postmenopausal endometrial changes determined by transvaginal sonography and histopathological analysis. March 2009, Journal of the Turkish German Gynecology Association 10(1). https://www.researchgate.net/publication/26601310_Correlation_of_postmenopausal_endometrial_changes_determined_by_transvaginal_sonography_and_histopathological_analysis
26) Starczewski A, Brodowska A, Strojny K, Puchalski A, Mieczkowska E, Szydłowska I. Znaczenie badania USG w rozpoznawaniu patologicznych rozrostów błony sluzowej macicy u kobiet po menopauzie [The value of ultrasonography in diagnosis of atypical endometrial hyperplasia in postmenopausal women]. Przegl Lek. 2005;62(4):227-9. Polish. PMID: 16229240.
27) Nalaboff KM, Pellerito JS, Ben-levi E. Imaging the endometrium: disease and normal variants. Radiographics. 21 (6): 1409-24. Radiographics (full text).
28) Williams PL, Laifer-narin SL, Ragavendra N. US of abnormal uterine bleeding. Radiographics. 23 (3): 703-18. doi:10.1148/rg.233025150
29) Sahdev A. Imaging the endometrium in postmenopausal bleeding. BMJ. 2007;334 (7594): 635-6. doi:10.1136/bmj.39126.628924.BE

30) Smith-bindman R, Weiss E, Feldstein V. How thick is too thick? When endometrial thickness should prompt biopsy in postmenopausal women without vaginal bleeding. Ultrasound Obstet Gynecol. 2004;24 (5): 558-65. doi:10.1002/uog.1704
31) Jorizzo JR, Chen MY, Martin D et-al. Spectrum of endometrial hyperplasia and its mimics on saline hysterosonography. AJR Am J Roentgenol. 2002;179 (2): 385-9. AJR Am J Roentgenol (full text).
32) Gupta A, Desai A, Bhatt S. Imaging of the Endometrium: Physiologic Changes and Diseases: Women's Imaging. (2017) Radiographics: a review publication of the Radiological Society of North America, Inc. 37 (7): 2206-2207. doi:10.1148/rg.2017170008.
33) Pennant.M, Mehta.R, Moody.P. Premenopausal abnormal uterine bleeding and risk of endometrial cancer (2016), An International Journal of Obstetrics & Gynaecology vol 124. Doi:10.1111/1471-0528.14385