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REVIEW ARTICLE

Peri- and Postmenopausal Uterine Bleeding Transvaginal Ultrasound with Hysterosonography and Diagnostic Correlation with Hysteroscopy

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ABSTRACT

The recent years have seen medical science and technology expand by leaps and bounds. We have shifted focus from correction of the problem to prevention of the problem. Abnormal uterine bleeding is an important cause of ill health in perimenopausal women.In the perimenopausal years, there is an increase in the incidence of bleeding irregularities. This is because of an increase in the prevalence of benign and malignant uterine lesions. There has also been a significant increase in the number of women presenting with postmenopausal bleeding. At transvaginal ultrasonography (TVS), the finding of a thickened central endometrial complex, with or without cystic changes, is often nonspecific and may be caused by an endometrial polyp, submucosal fibroid, endometrial hyperplasia, carcinoma or cystic atrophy. In addition, because of an increased prevalence of adenomyosis or adenomyosis-like changes in women around this age group, proper transvaginal sonographic assessment of endometrial thickness and abnormalities is of utmost importance but maybe difficult in some women.

When TVS cannot accurately measure the endometrial thickness or when there is a nonspecific thickened central endometrial complex, hysterosonography can provide additional information and can help in the diagnosis and final treatment. Hysterosonography, as an adjunct to TVS, allows identification of intracavitary lesions and focal and diffuse endometrial abnormalities and helps determine the abnormality. Final diagnosis confirmed by hysteroscopy. In this review, we discuss these common abnormalities and the correlation of TVS and hysterosonographic findings with hysteroscopic evaluation.

Keywords: Abnormal uterine bleeding, Transvaginal sonography (TVS), Hysterosonography, Hysteroscopy.

INTRODUCTION

The recent years have seen medical science and technology expand by leaps and bounds. We have shifted focus from correction of the problem to prevention of the problem. Abnormal uterine bleeding is an important cause of ill health in peri- and postmenopausal women. In these women there is an increased number of uterine lesions, including endometrial polyps, leiomyomas, endometrial hyperplasia, endometrial carcinoma and adenomyosis, which all contribute to the abnomral uterine bleeding seen in this age group.

The Extent of the Problem

Abnormal uterine bleeding is defined subjectively as excessive menstrual loss or objectively as menstrual blood loss of more than 80 ml per menses. Twelve percent of all gynecological referrals are due to excessive blood loss. One-third of all patients attending gynecological outpatient department are for abnormal and excessive bleeding patterns. However, 40% of these women referred for opinion have a menstrual loss which, if measured, will be less than 80 ml per menses. But, of equal importance is the impact of the blood loss on the quality of woman's life. This is why many women opt for a hysterectomy by the time they are 50 years of age. What is important to remember is that many of these could have been managed by conservative methods of management. The same holds true for women presenting with postmenopausal bleeding. All women do not need a hysterectomy as method of treatment.[1-5]

Transvaginal ultrasonography (TVS) is frequently used for endometrial assessment. A thin, atrophic endometrium normally requires no further work-up. However, a thickened central endometrial complex, with or without cystic changes, is often nonspecific.[5,6] Hysterosonography is a useful adjunct to TVS when the findings are very conclusive on TVS alone. The procedure involves the instillation of sterile saline solution into the endometrial cavity through a small catheter, under continuous US guidance. It allows identification of intracavitary lesions and focal and diffuse endometrial abnormalities, and can be used to determine whether an abnormality is endometrial or subendometrial.[6,7] In this article, we review the spectrum of uterine and endometrial findings at and hysterosonography in peri- and postmenopausal women in the form of cases and

discuss the correlation between the TVS findings and the final hysetroscopic diagnosis.

Patient Population

Our patient population consisted of perimenopausal and postmenopausal women with presentation of excessive vaginal bleeding or postmenopausal vaginal bleeding. The patients were aged between 40 and 65 years. They were subjected to a thorough medical and physical examination, all routine investigations which included CBC with platelet count, LFT, RFT, stool routine, fasting and postlunch blood sugar, urine routine and microscopy, abdominal and transvaginal sonography (TVS), and ECG. The patients were asked to undergo a hysterosonography, if results of TVS were equivocal or unclear. When indicated hysteroscopy with corrective surgery was performed and material sent for histopathological examination (HPE). In patients with postmenopausal bleeding, a diagnostic hysteroscopy was performed even if TVS findings were within normal range and corrective surgery done when indicated.

Normal Appearance of Endometrium on TVS

The normal postmenopausal endometrium is atrophic. It should appear thin, homogeneous and echogenic (Fig. 1A) at TVS. At hysterosonography (Fig. 1B), a smooth, thin endometrium surrounds the anechoic, saline solution-distended endometrial cavity. Sometimes fluid can be seen in the endometrial cavity at TVS. As an isolated finding, fluid in the endometrial cavity is usually due to cervical stenosis (Fig. 2). In one prospective study of asymptomatic postmenopausal women, 6% had intracavitary fluid at TVS without a mass in the cervix or endometrial cavity at hysteroscopy.[8] Hysteroscopic and histopathologic findings confirmed atrophic endometrium.

Endometrial thickening at TVS is an important finding, often indicative of endometrial pathologic conditions. In women with postmenopausal bleeding, a recent meta-analysis by Smith-Bindman et al[9] recommended that a double-layer endometrial thickness of > 5 mm be considered abnormal and reported a sensitivity of 92% and a specificity of 81% in the detection of any endometrial disease (cancer, hyperplasia, polyp).[9] However, there is no clear definition of what constitutes an abnormal endometrial thickness for perimenopausal. If such women present with bleeding and their endometrial thickness is > 5 mm, further investigation is necessary. In asymptomatic women, the upper limit for normal endometrial thickness and the usefulness of TVS screening remain controversial. Various authors[8-11] have reported transvaginal sonographic endometrial thicknesses of 5, 9, and 10 mm as abnormal cut-off values for the identification of endometrial disease in asymptomatic perimenopausal women. However, the results of these studies[9,11] are limited by verification bias and by small sample size.[9-11] Recent study studying women on tamoxifen suggested that the optimal endometrial thickness cut-off for identification of abnormalities (polyps and submucosal fibroids) was > 6 mm, if maximal test accuracy (sensitivity and specificity) is desired. With this cut-off value, the sensitivity was 84.1% and specificity 58.2%.[10,12,13]

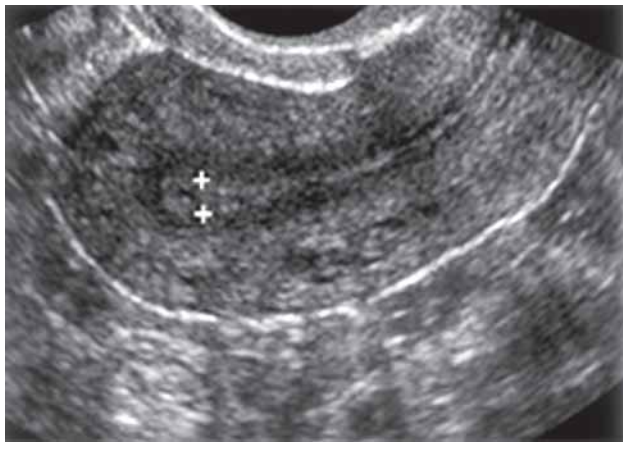


Fig. 1A: A 44-year-old woman presented with 11 months amenorrhea followed by bleeding. TVS image shows a thin endometrium suggestive of atrophic changes

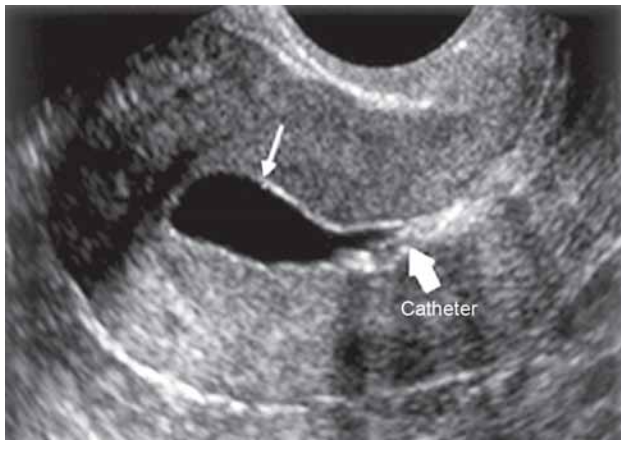


Fig. 1B: Hysterosonography in the same woman showing fluid in the endometrial cavity with thin walls. A catheter is seen in the lower portion of the uterus

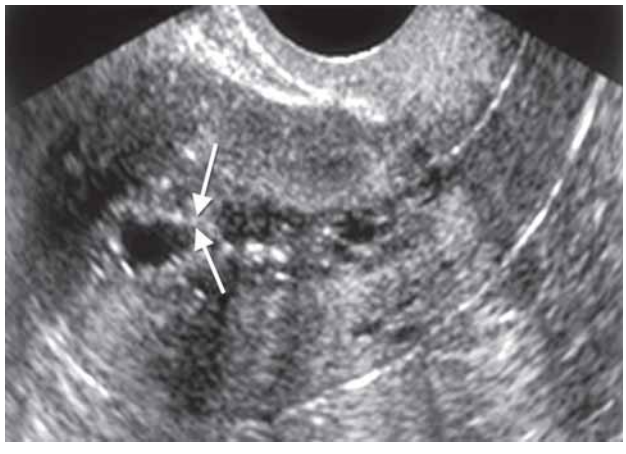
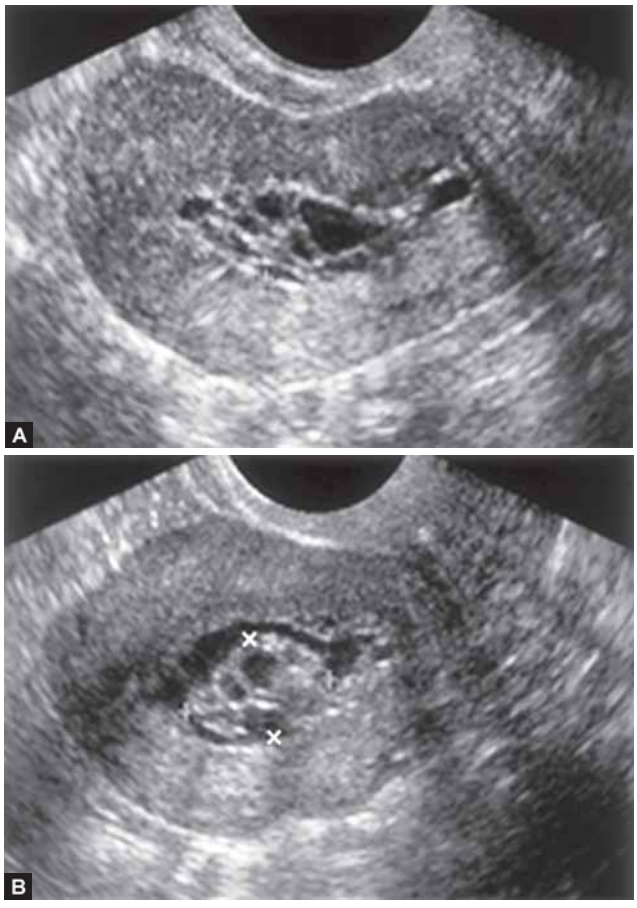


Fig. 2: A 58-year-old asymptomatic woman who came for a routine health check-up. TVS shows fluid in the endometrial cavity with thin but irregular endometrium. Hysteroscopic and histopathologic findings confirmed atrophic endometrium. The fluid was due to cervical stenosis

ENDOMETRIAL POLYP

In peri- and postmenopausal women, endometrial polyps are the commonest abnormality found. They are often seen in asymptomatic women. In fact, they are present in 39% of



Figs 3A and B: TVS in a 40-year-old woman who presented with menorrhagia. Findings suggest a benign endometrial cystic polyp. (A) Thickened central endometrial complex with cystic spaces. It is the presence of a hyperechoic line which favors the diagnosis of a polyp, (B) hysterosonogram shows fluid outlining a smooth margins which again suggests a benign polyp

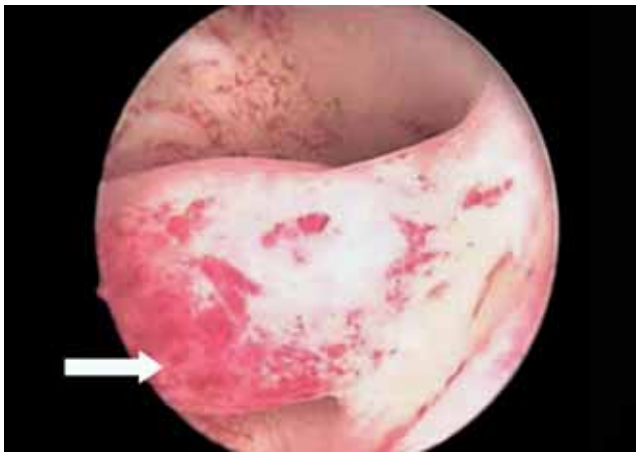
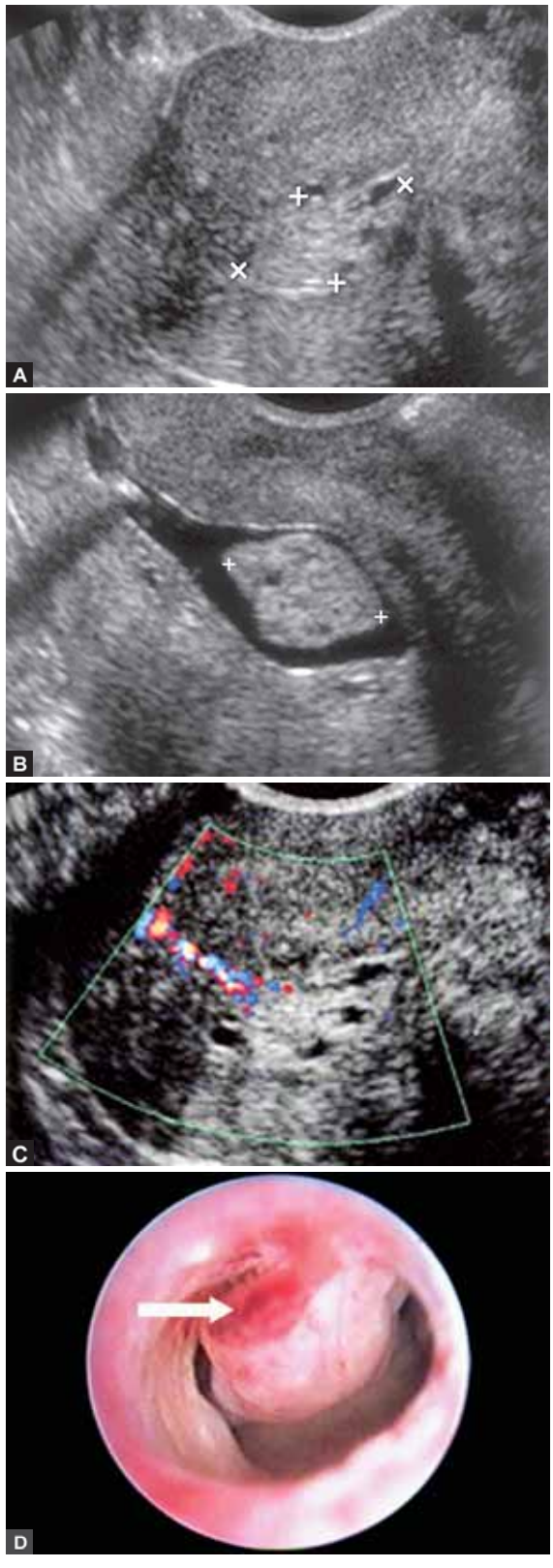
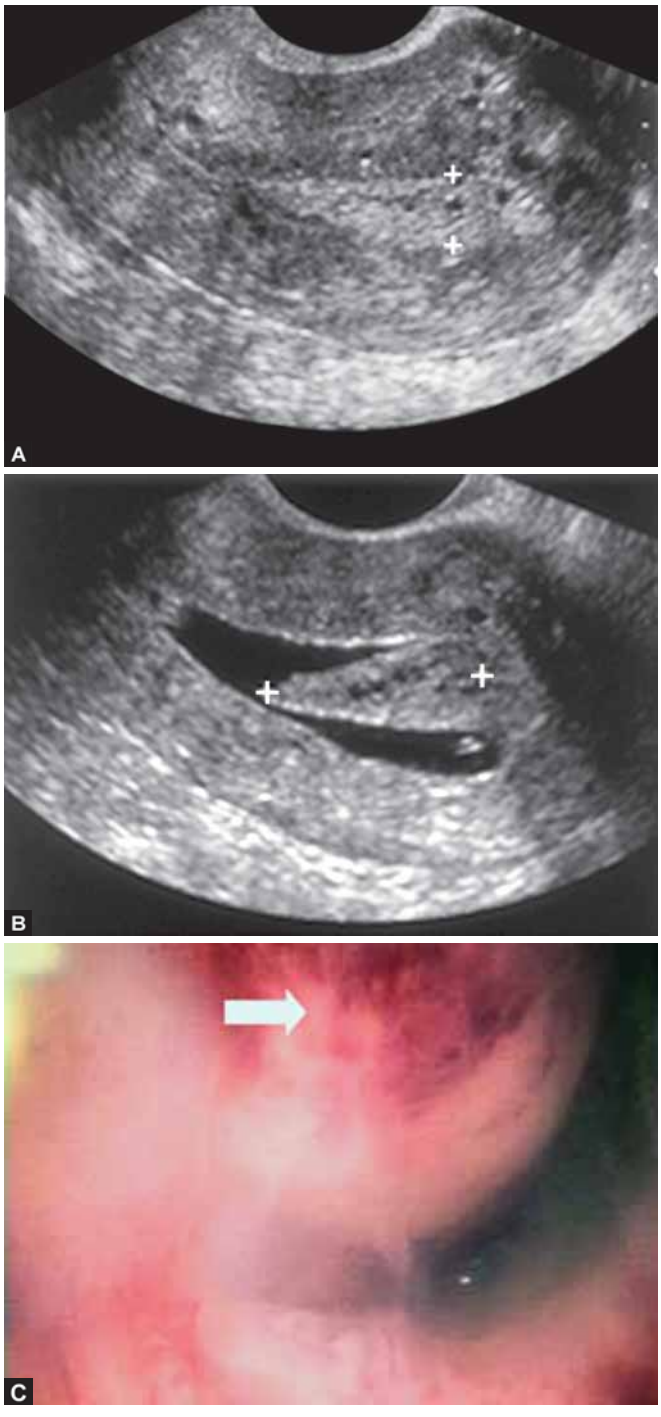


Fig. 3C: Hysteroscopy shows a polyp with a broad base and HPE confirmed it as a benign polyp. Also, note that the hemorrhagic areas on the undersurface of the polyp



Figs 4A to D: TVS along with hysterosonogram and a color Doppler and the hysteroscopic picture of the polyp of a 49-year-old peri-menopausal woman who presented with heavy bleeding. (A) TVS image showing a thickened endometrium, 22 mm, with evidence of echogenic outline, suggestive of a polyp. There are small cystic spaces within the thickened endometrial echoes, (B) hysterosonogram with the fluid in the cavity clearly defines the thickened endometrium is actually an intracavitary polyp. A balloon catheter tip can be also seen in the cervix, (C) color Doppler showing a single feeding artery in the pedicle of the polyp, (D) hysteroscopic picture showing the vascular base of a sessile polyp (arrow)

asymptomatic women and picked up only on routine screening or health check-up. TVS often shows nonspecific thickening of the central endometrial complex, with or without cystic changes (Figs 3A, 4A, 5A and 6A).[12,13] The presence of a distinct hyperechoic line partially or completely surrounding the



Figs 5A to C: A 45-year-old perimenopausal woman who presented with irregular and heavy bleeding. She had been bleeding for 20 days and still had a 9 mm thick endometrium. (A) TVS image shows a 9 mm thick endometrium with small cystic areas which is suggestive of a polyp. The myometrium also shows presence of adenomyosis though the uterus is not bulky, (B) hysterosonogram shows fluid outlining—a broad-based intracavitary polyp occupying most of the cavity, (C) hysteroscopic view of the polyp. Note that the slight area of hemorrhage at the tip of the polyp (arrow)

abnormal endometrial complex favors a focal intracavitary process, such as a polyp, a submucosal fibroid that protrudes into the cavity, or focal endometrial hyperplasia[14] (Figs 3A and 4A). Applying color at this time may help in identifying the feeding artery in the pedicle of the polyp and is a helpful diagnostic feature (Fig. 4C). So often, we get patients coming

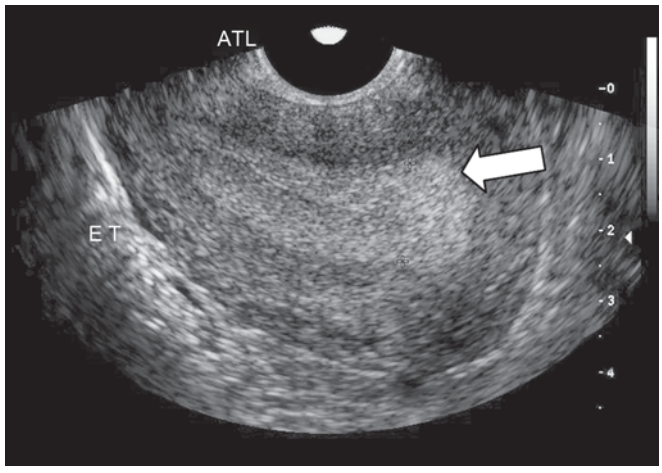


Fig. 6A: A homogeneous, echogenic thickened endometrium with focal echogenicity near the fundus, suggestive of a endometrial polyp in a 56-year-old woman who presented with heavy bout of postmenopausal bleeding. ET = 13.9 mm

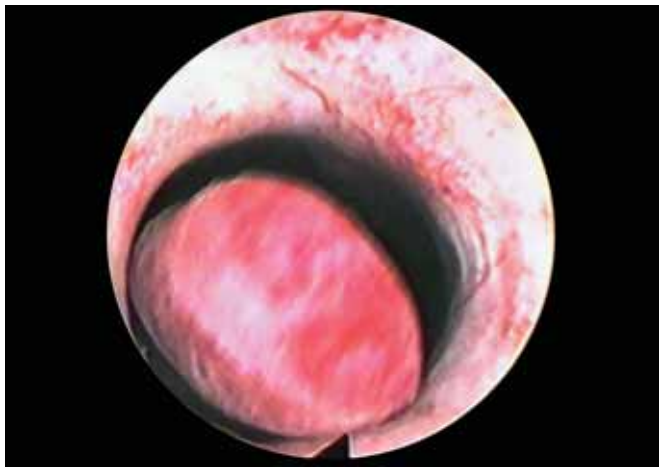


Fig. 6B: Hysteroscopy shows a large polyp occupying the cavity. But smooth appearance suggests it is benign. Hysterosonography was attempted but not done as patient was very uncomfortable and hence the procedure was abandoned. HPE findings confirmed the diagnosis of a benign polyp

for a second opinion because a routine health check-up showed presence of thickened endometrium and the patients were advised a hysterectomy for fear of endometrial carcinoma. Appropriate imaging will ensure proper diagnosis and counseling, thereby avoiding many such hysterectomies. When in doubt, hysterosonogrpahy can help in identifying the pathology.[7,8,13]

At hysterosonography,[15] a polyp appears as an echogenic mass with smooth margins. It usually has a narrow attachment to the endometrial wall, but some polyps can be sessile (Fig. 5B) and have a broad base. However, it will be completely surrounded by the saline solution (Figs 3B and 4B). Polyps can either have a homogeneous echotexture or show small cystic areas (see Figs 3B and 4B).

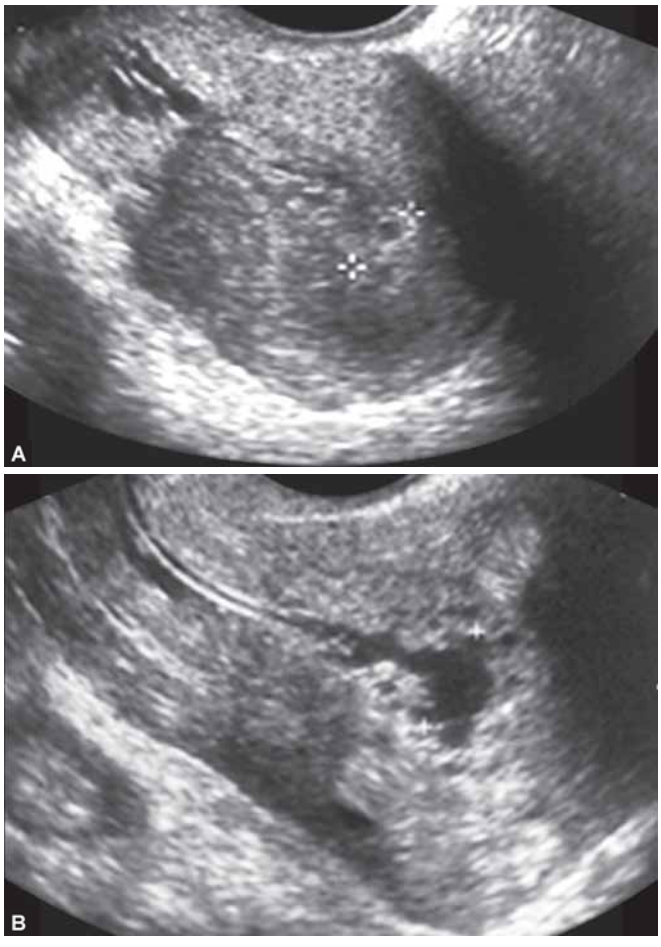
At hysteroscopy (Figs 3C, 4D, 5C, 6B), most polyps are pink-gray to white with smooth, glistening surfaces, beneath which small cysts may be visible. The polyps can be pedunculated with a narrow stalk or sessile with a broad base. Unlike carcinoma, they do not bleed easily though some polyps are hemorrhagic or infarcted. On histopathologic examination

HPE—a typical benign polyp shows fibrotic stroma, irregular endometrial glands and thick-walled blood vessels.[16,17]

Endometrial Hyperplasia

Commonly in the perimenopausal years there is unopposed estrogen stimulation which leads to hyperplasia of the endometrium and, if unattended, it can lead to endometrial carcinoma. History of irregular cycles, PCOS are risk factors in development of hyperplasia which can lead to endometrial carcinoma. Excessive menstrual bleeding can be ovulatory as well as anovulatory. It is the latter which has a higher incidence of progression to endometrial hyperplasia. Endometrial hyperplasia can be divided into two broad categories at histopathologic examination: Hyperplasia without cytologic atypia and hyperplasia with cytologic atypia. The risk of development of endometrial carcinoma is 23% in patients with atypical hyperplasia *vs* 2% in patients with hyperplasia without atypia.[8,18]

TVS is an important tool in the diagnosis of these patients and endometrial hyperplasia can be very easily picked up. Typically, there is a well-defined endometrial thickening with or without cysts. At hysterosonography, diffuse, smooth thickening of the endometrium suggests endometrial hyperplasia. However, focal or asymmetric endometrial thickening with surface irregularity has also been described for hyperplasia. As there is a potential risk of development of endometrial carcinoma, all patients with evidence of endometrial hyperplasia must have an endometrial biopsy[16,18] (Figs 7A and B).



Figs 7A and B: A 45-year-old woman presented with menorrhagia and a continuous bout of bleeding since 14 days. (A) The endometrium was ill-defined with some areas of irregularity at the fundus and measured 12 mm after 14 days of heavy bleeding, (B) the irregular endometrial outline on hysterosonography shows small cystic spaces. HPE showed complex endometrial hyperplasia

It is always advisable to take a hysteroscopic directed biopsy with full visualization of the uterine cavity and blind endometrial biopsy/sampling should be discouraged. It is also recommended that a complete curettage with evaluation of the entire endometirum should be done. In fact, such curettage can be therapeutic in some cases. Many clinics now offer a diagnostic office hysteroscopy with pipelle sampling of endometrium, if there is no evidence of hyperplasia. At hysteroscopy, endometrial hyperplasia is seen as unusually thicker endometrium compared with the normal pink-gray glistening, mucoid appearance. It may also appear polypoidal. Small cysts may be visible, and dilated congested sinusoids may be seen just beneath the surface.[19-21]

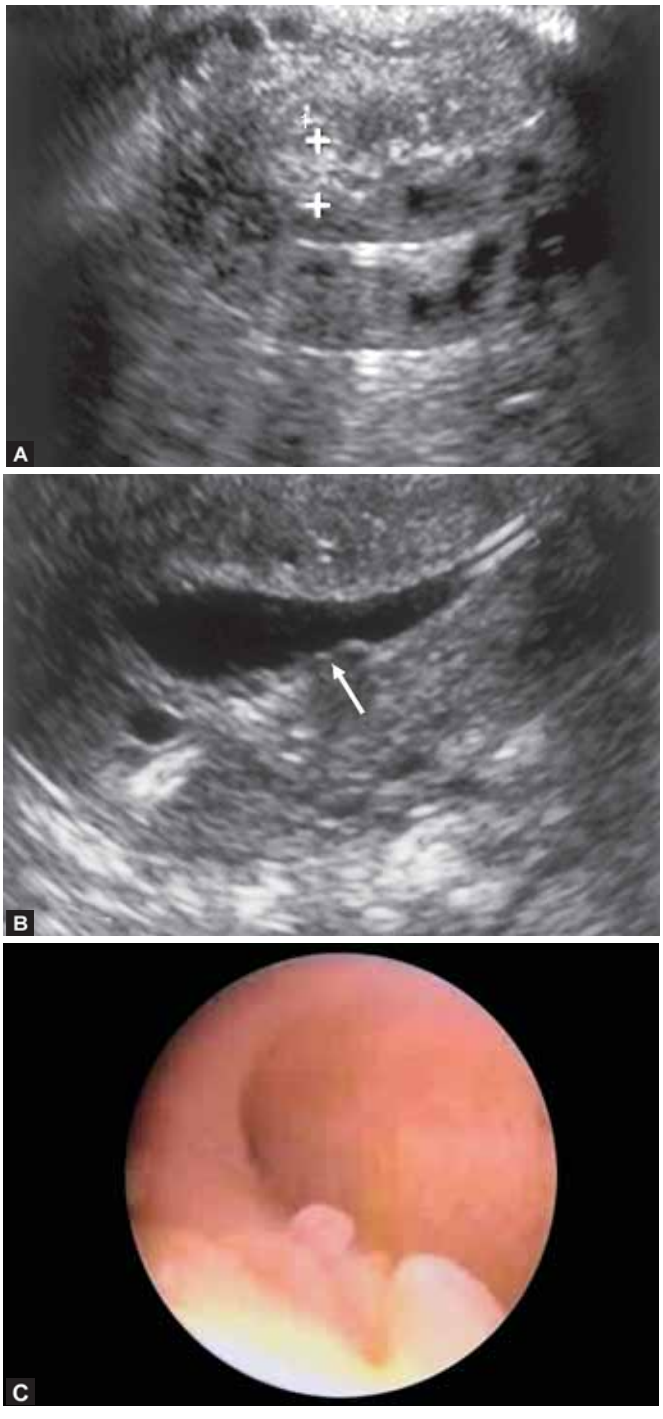
Histopathologic examination will show architecturally complex, closely packed endometrial glands, which are lined by cells. It is these cells which show evidence of cytologic atypia and must be closely examined to rule out *in situ* carcinoma. The diagnosis is usually one of simple hyperplasia (without atypia) or complex hyperplasia (with atypia). Depending on the age of the patient and the presenting symptoms the decision for treatment must be taken.[21,22]

Endometrial Cystic Atrophy

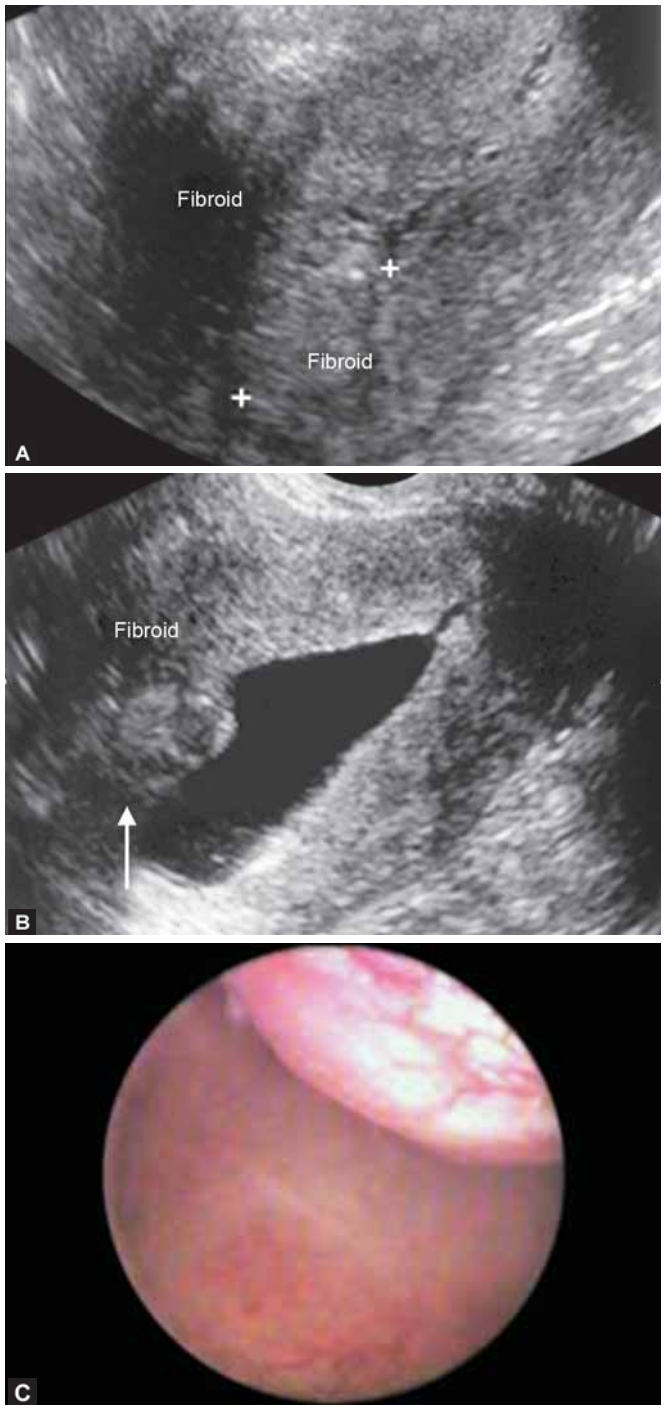
A rare variety of benign endometrial thickening is seen in postmenopausal women, called endometrial cystic atrophy. This is a benign process but the diagnosis is histological. Typically there is evidence of multiple cystic spaces (dilated glands) lined with atrophic epithelium, present within a dense fibrous stroma.[21] At histopathologic examination, these thickened protuberances are identified as cystic glandular dilatation. Sometimes, the changes of endometrial cystic atrophy are so extensive that the appearance of a cystic endometrium may be mistaken for diffuse or focal areas of endometrial thickening even at hysterosonography. Ideally, atrophic endometrium appears very thin. However, the presence of endometrial cysts may lead to a spuriously widened endometrial measurement (Fig. 8A). At hysterosonography (Fig. 8B), endometrial cysts can be seen clearly. At hysteroscopy, the endometrium appears flat but has hypervascularized, scattered protuberances.[22,23]

Submucosal Leiomyoma

Fibroids are the commonest gynecological pathology found in the perimenopausal years. However, 50% of fibroids are asymptomatic and do not need any treatment unless causing problems for the patient.[24] Leiomyomas, or fibroids, are seen in perimenopausal women and sometimes even in postmenopausal women. The symptoms are due to enlargement and



Figs 8A to C: (A) A 69-year-old postmenopausal woman with bleeding. TVS shows a 7 mm thick endometrial echo with a few cystic areas, (B) hysterosonography shows a slightly thickened endometrium with irregular posterior wall (solid straight arrow). A catheter is seen in the cervix. Hysteroscopy showed this irregularity to be due to presence of small endometrial cysts which were benign, (C) hysteroscopic view showing the small cysts on the posterior endometrium



Figs 9A to C: (A) Submucosal leiomyoma in a 41-year-old asymptomatic woman. TVS shows an enlarged uterus with multiple fibroids and displaced endometrial cavity, (B) hysterosonogram shows intramural myoma impinging in the cavity and a thin layer of endometrium overlying it, (C) hysteroscopic picture of the myoma prior to resection

patient may present with bleeding, pain or both. Submucosal fibroids are most likely to cause menstrual problems in these women. As they enlarge, submucosal fibroids may protrude into the endometrial cavity, causing menorrhagia. They are easily detected at sonography. On TVS, a submucosal fibroid may appear hypoechoic or show heterogeneous echogenicity and often demonstrate acoustic attenuation (Fig. 9A). The fibroid may displace or distort the endometrium or cause false endometrial thickening. They can be single or multiple.

At hysterosonography, a submucosal fibroid is seen as a round structure arising from the myometrium (Fig. 9B). The thin, overlying echogenic endometrium usually can be identified.

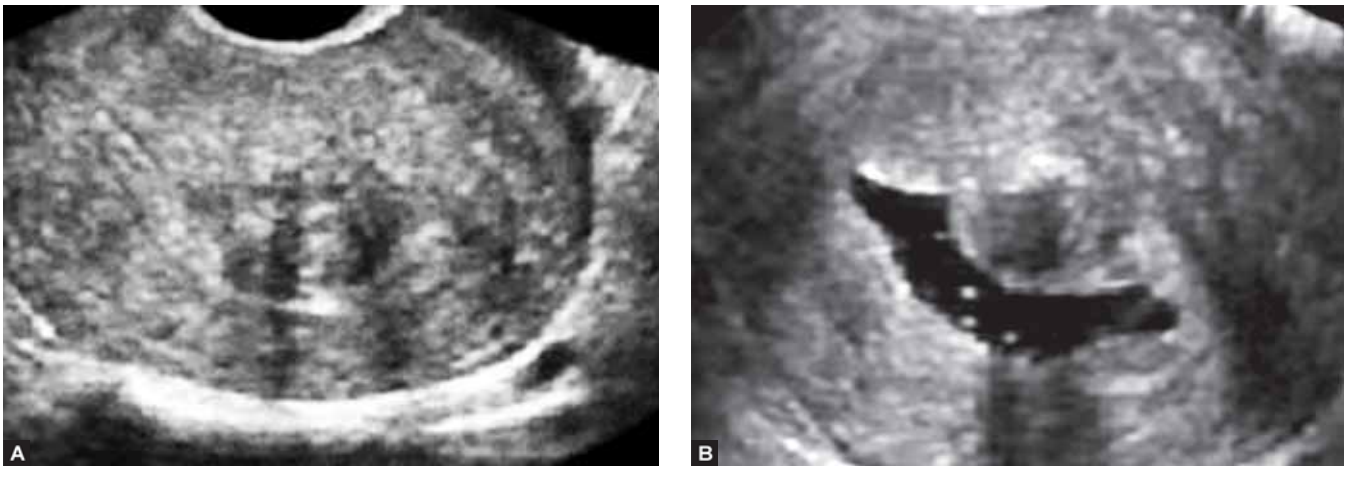
It usually appears with a wide attachment to the myometrium but may be pedunculated. Sometimes it may also be possible to gauge the depth of the myometrial invasion.[24] This is important as it helps in planning the definitive surgery for the patient. If not very clear, color Doppler or MRI can be advised to get the depth of invasion.

At hysteroscopy, submucosal fibroids (Fig. 9C) appear as rounded masses that bulge to varying extents into the endometrial cavity. The mucosal surface tends to be smooth and relatively flat, although it may also be congested, ulcerated or hemorrhagic. The fibroid may be vascular but tends to be of a firmer consistency than an endometrial polyp. Upon resection of the fibroid, it has a typical appearance similar to that of intramural fibroids with crisscross fibers of myometrium.[25] At times, the fibroid may also form pedunculated tumors that appear as soft or firm polypoid masses protruding through the external cervical os or, rarely, through the vaginal introitus.

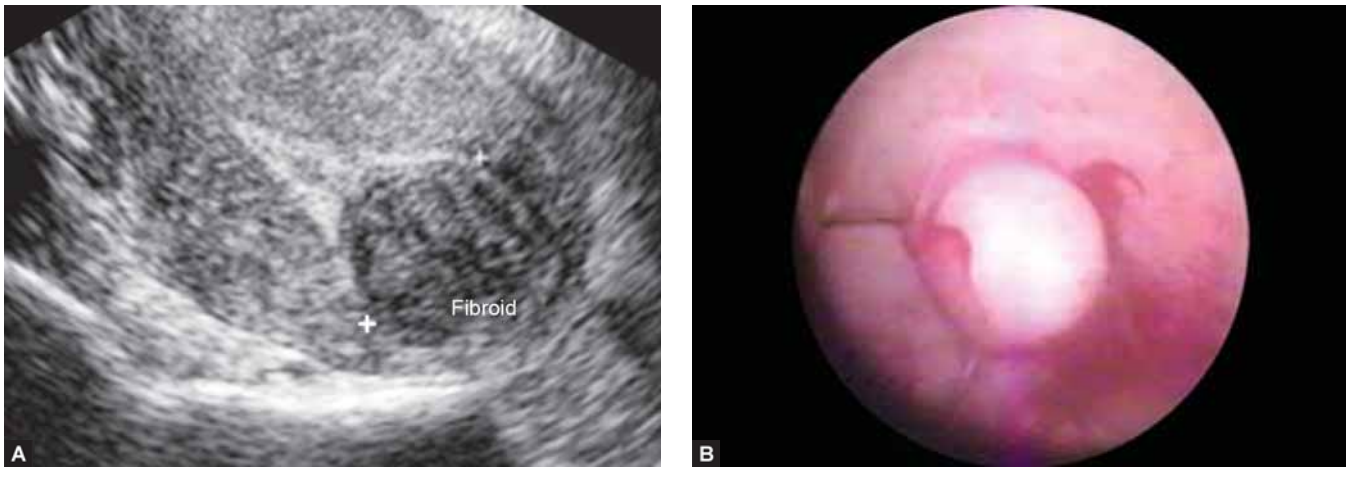
It is important to evaluate the endometrium completely, as there may be coexisting pathologies in women who presented with menorrhagia (Figs 10A and B).

Adenomyosis

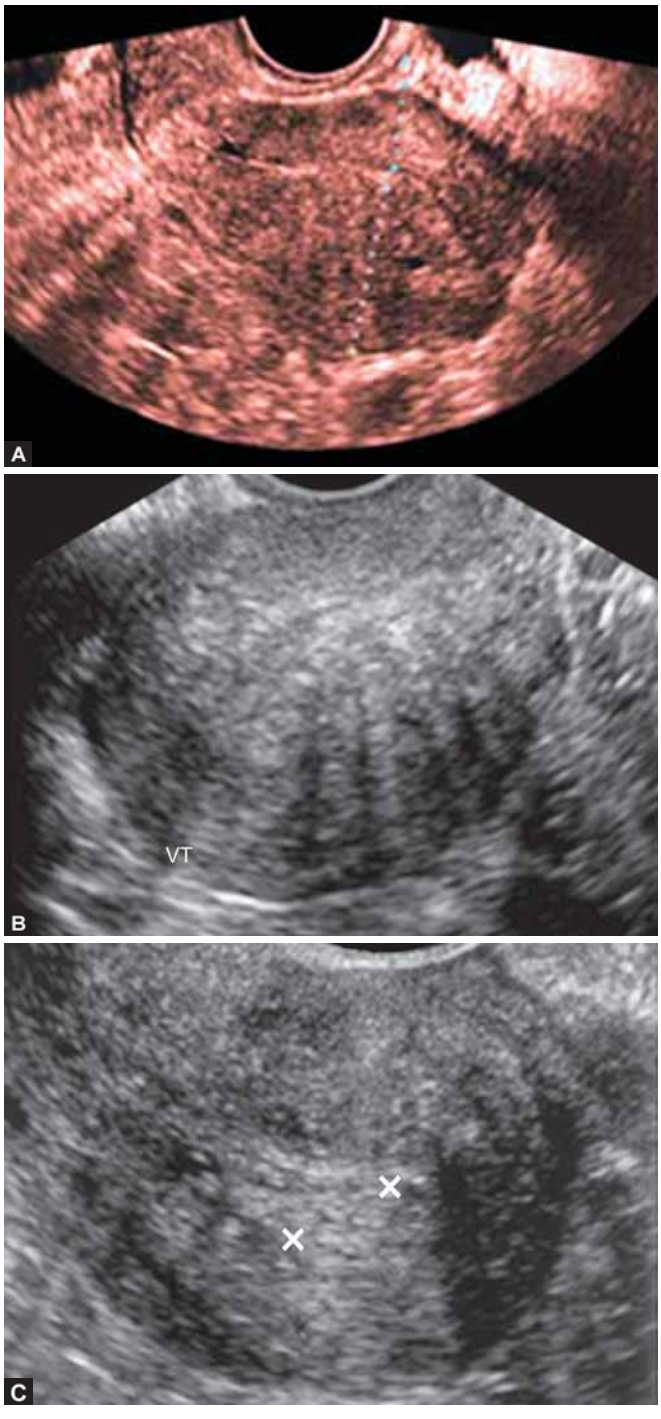
Adenomyosis is characterized pathologically by the presence of ectopic endometrial glands and stroma within the myometrium. It causes uniform uterine enlargement and abnormal uterine bleeding along with dysmenorrhea. Sometimes there can be focal or asymmetric thickeneing of the uterine wall with increased myometrial echotexture.[26] This is often seen on TVS as heterogeneous and poorly circumscribed areas within the myometrium with myometrial or subendometrial cysts. Frequently also seen are subendometrial echogenic linear striations and subendometrial echogenic nodules along with poor definition of the endometrial-myometrial junction. Adenomyosis may give a false-positive appearance of a thickened endometrium at TVS[27-29] (Figs 12A to C). MRI is a useful tool for confirming the presence of subendometrial or myometrial location of cysts and a thin endometrium and give the correct diagnosis. Diffuse thickening of the junctional zone greater than or equal to 12 mm accurately confirms the diagnosis of adenomyosis at MRI.[27,28]



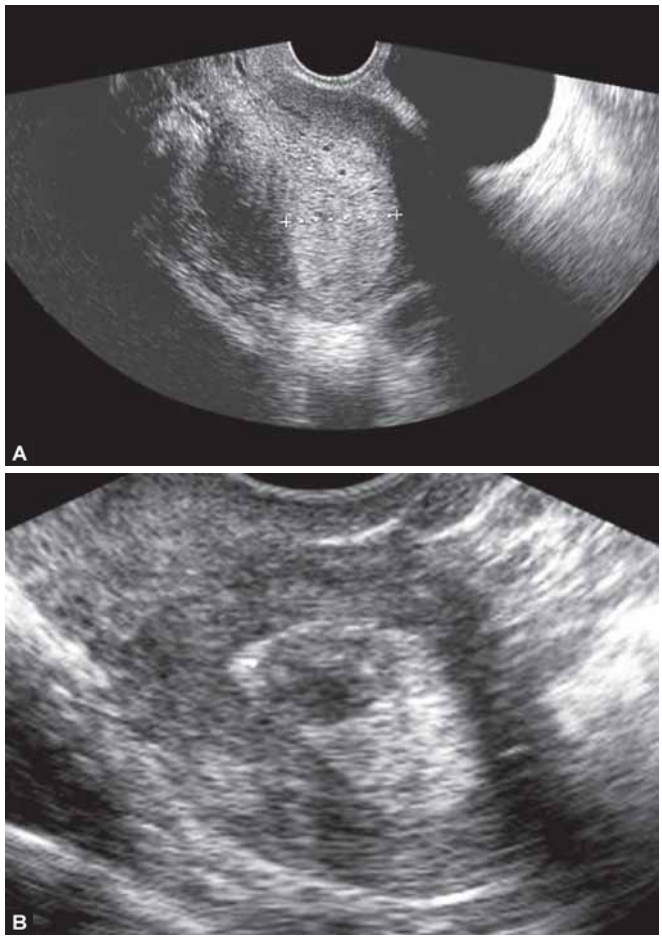
Figs 10A and B: (A) A 51-year-old woman presented with menorrhagia. TVS sonography shows presence of an ill-defined intracavitory mass, probably a submucous fibroid, (B) hysterosonography shows a submucous fibroid but the endometrial edges are irregular. This patient choose to undergo a hysterectomy. Histopathologic findings of the uterus showed a benign endometrial fibroid as well as microscopic foci of endometrial carcinoma in the fibroid base as well as the adjacent endometrium



Figs 11A and B: (A) Fibroid impinging in the endometrial cavity in a 48-year-old lady who presented with menorrhagia, (B) hysteroscopic view of the myoma prior to resection



Figs 12A to C: Different women who presented with menorrhagia with adenomyosis. (A) Sonography showing adenomyosis in a 46-year-old woman. TVS showing a poorly defined, irregular endometrial echo, thickened myometrium with presence of cysts are suggestive of adenomyosis, (B) false-positive appearance of thickened endometrium at TVS showing a thick, poorly defined central endometrial complex with cystic areas in the myometrium suggestive of adenomyosis in a 49-year-old woman who presented with menorrhagia, (C) a 48-year-old woman who presented with heavy and prolonged bleeding. TVS shows a ill-defined 20 mm endometrium with thickened myometrium showing small cystic spaces



Figs 13A and B: Endometrial carcinoma. (A) TVS shows a well-defined irregular thickening of the endometrium in a 58-year-old postmenopausal woman who presented with bleeding. The ET is 29.1 mm, (B) a 63-year-old woman with foul-smelling discharge with postmenopausal bleeding. TVS sonography shows presence of an irregular endometrial thickening with degenerative cystic spaces within

Endometrial Carcinoma

There is an increase in the number of cases reported each year with endometrial cancer. There are two reasons behind this, one is a more aggressive screening program which has resulted in many early cases of abnormalities being identified.[29] And, the other is a higher incidence of hyperestrogenic status in women with early menarche and late menopause. Many asymptomatic women opt for health check-ups which results in identifying an abnormal enodmetrial pattern on ultrasound. On TVS exam, an irregular, patchy and partially echogenic endometrium should alert the operator on the possibility of endometrial carcinoma, even in an asymptomatic woman. Many women present as postmenopausal bleeding but there is an increased incidence of endometrial carcinoma in premenstrual women, especially with PCOS (Figs 13 and 14). The endometrial thickening may be well defined at times, but more frequently it is irregular or poorly defined thickening.[29,30]

At hysterosonography, an irregular inhomogeneous mass or irregular, focally thickened endometrium is highly suggestive of endometrial carcinoma. Frequently there is presence of fluid in the cavity and hysterosonography may not be needed for confirmation (Figs 13 and 15A). Also, commonly found is associated with cervical stenosis making distensibility of the endometrial cavity difficult. Here too, MRI imaging gives valuable information in the endometrial evaluation as well as staging of the malignancy if present.[29-31]

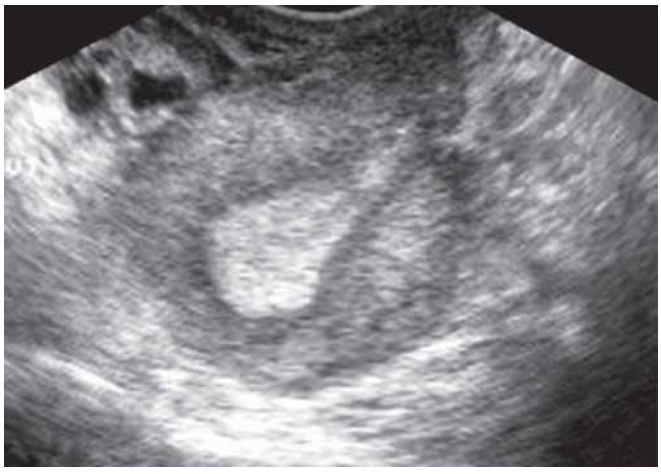
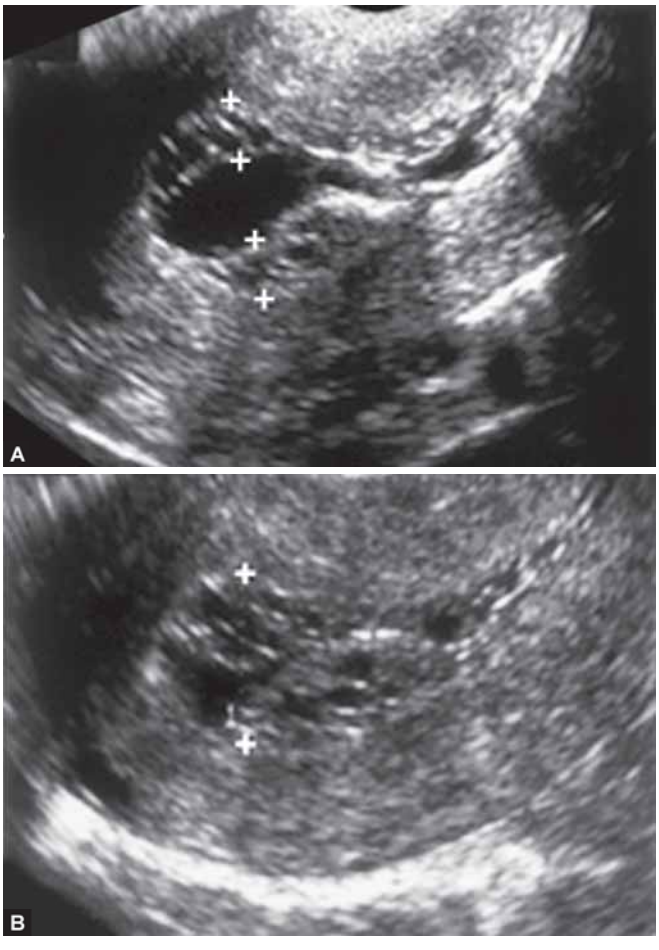


Fig. 14: A 40-year-old woman who presented with irregular uterine bleeding



Figs 15A and B: (A) A 60-year-old woman came with postmenopausal bleeding. TVS showing fluid in the endometrial cavity which has a lobulated outline irregular margins. The thickness of the ET along with fluid is 21 mm, (B) a 39-year-old woman who presented with irregular and prolonged bleeding. TVS shows the presence of thickened ET 13 mm with cystic spaces and small areas of fluid collection

At hysteroscopy, appearance can vary from a flat, sessile or pedunculated, irregular, polypoidal growth.[31-33] It consists of irregularly heaped-up tissue with a granular or at times necrotic appearance. It appears opaque, dry, pale yellow or white and friable. Hemorrhage and ulceration are common, particularly when the tumor is poorly differentiated, and abnormal vascular patterns may be seen on the surface of the tumor. Dark yellow areas are often conspicuous as a result of necrosis or the accumulation of lipid-filled cells of stromal origin between the neoplastic glands. At HPE study, confluent, fused endometrial glands exhibit cribriform architecture and nuclear atypia.

TVS showing a 18 mm heterogeneous endometrial echo with small cystic areas HPE showed presence of adenocarcinoma of the endometrium.

CONCLUSION

TVS may not depict the true endometrial thickness or may give a false-positive appearance of thick endometrium owing to adenomyosis or endometrial cystic changes. The evidence suggests low specificity of TVS (56.6%) in the identification of endometrial abnormalities in asymptomatic women, whereas hysterosonography has a higher specificity (79.2%). TVS is the first imaging test undertaken for evaluation of the uterus in women presenting with abnormal uterine bleeding. However, when TVS is not conclusive or when there is nonspecific thickening of the central endometrial complex, hysterosonography can provide additional information and can help in appropriate diagnosis. This will help in planning the hysterosocpic evaluation and treatment planning for peri- and postmenopausal women presenting with abnormal uterine bleeding.

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