

# Role of 3D Ultrasound and Doppler in Differentiating Clinically Suspected Cases of Leiomyoma and Adenomyosis of Uterus

KAVERI SHARMA<sup>1</sup>, MANASH KUMAR BORA<sup>2</sup>, B.P VENKATESH<sup>3</sup>, PARTHO BARMAN<sup>4</sup>, SUMIT KUMAR ROY<sup>5</sup>,  
USHA JAYAGURUNATHAN<sup>6</sup>, ESWARAMOORTHY SELLAMUTHU<sup>7</sup>, FAZIL MOIDU<sup>8</sup>

## ABSTRACT

**Introduction:** Adenomyosis and Leiomyoma are common disorders affecting females in their reproductive age. They mimic each other in clinical presentation. Due to similarities in clinical symptoms and signs, missing one diagnosis in favour of the other is not very uncommon. Accurate diagnosis of these two conditions is important for their management. In this study we evaluated role of 3D Ultrasound and Doppler in differentiating clinically suspected cases of leiomyoma and adenomyosis of uterus.

**Materials and Methods:** A total of 100 patients with symptoms of abnormal uterine bleeding (with or without dysmenorrhoea), lump abdomen, chronic pelvic pain or dyspareunia who were clinically diagnosed as leiomyoma of uterus and/or adenomyosis were enrolled in to the study. These patients underwent transvaginal sonography (TVS), trans abdominal sonography (TAS) along with color and spectral Doppler sonography. Scanning was done in follicular phase of the menstrual cycle to avoid bias due high vascularity of endometrium in secretory phase. The morphology of the lesion, its vascularity, and Pulsatility Index (PI), Resistive Index (RI) and Vmax (maximum velocity) were measured. Only those patients who were chosen for operative treatment were included in the study.

Radiological diagnosis was then correlated with intra-operative and histopathological diagnosis.

**Results:** On imaging, while using morphological criteria and Doppler for diagnosing leiomyoma, it was found that “peripheral vascularity” was seen in 52 (89%) cases, which was the highest. Similarly while diagnosing adenomyosis it was, the criteria “central vascularity” was seen in 28 cases (93%) and “ill defined junctional zone in 3D ultrasound” was seen in 26 cases (86%), which was also observed to be highest.

With the cut off values taken for PI,RI and Vmax, diagnosis of leiomyoma was found to be 93.4% sensitive, 95.6% specific and with a positive predictive value of 97.6% and negative predictive value of 88.6%. Diagnosis of adenomyosis showed a sensitivity of 95.6%, specificity of 93.4% and a positive predictive value of 88.6% and negative predictive value of 97.6%. Imaging diagnosed the co-existence of both the conditions correctly in 8 (66%) cases.

**Conclusion:** The parameters of blood flow impedance (that is PI, RI, and Vmax) of arteries within or around the uterine lesions revealed a consistent and significant difference between leiomyoma and adenomyosis. So apart from morphological criteria used in 3D TAS and TVS, aid of color Doppler can more accurately differentiate and diagnose these conditions.

**Keywords:** Myometrium, Pulsatility Index (PI), Resistive Index (RI)

## INTRODUCTION

Adenomyosis is a common disorder affecting women in reproductive years commonly presenting as menorrhagia, dysmenorrhoea, chronic pelvic pain, dyspareunia and adverse effects on fertility [1].

Due to similarities in clinical symptoms and signs, missing one diagnosis in favour of the other is not very uncommon [2]. Leiomyomas are well-defined benign masses of uterine smooth muscles, sharply demarcated from the surrounding myometrium by a pseudocapsule which can be easily removed surgically [3]. Adenomyosis are ill-defined lesions where myometrium is interspersed with endometrial glands and stroma. Their complete removal through surgery is difficult or even impossible where only hysterectomy remains as the definitive treatment. So accurate preoperative diagnosis of these two conditions is vital for those patients wishing to retain their fertility or to those for whom a myomectomy would be an appropriate treatment. To date, however, postsurgical histopathology is the only definitive way to make an accurate diagnosis.

In our study we found that 3D ultrasonography can better depict the morphology of uterine lesion and provide accurate evaluation of the junctional zone of uterus. We observed that Doppler can reveal differences in the haemodynamics with respect to RI,PI and Vmax

in leiomyoma and adenomyosis and provide an important parameter to differentiate them. It can also help in more accurate assessment of the prevalence of co-existence of adenomyosis with leiomyoma of uterus as noted in our study.

## MATERIALS AND METHODS

The study was performed by the Departments of Obstetrics & Gynaecology, Department of Radiology and Department of Pathology in Aarupadai Veedu Medical College and Hospital, Pondicherry, India. The aim of this study was to evaluate whether 3D Ultrasound and Colour Doppler ultrasonography are capable of accurately differentiating uterine leiomyoma from adenomyosis and also to assess the prevalence of co-existence of both these conditions in the uterus.

**Study type:** Observational (Validity of diagnostic test).

**Study design:** Hospital based study.

**Sample size:** Hundred patients were evaluated over a period of one year.

The mean age among patients with leiomyoma was  $38.1 \pm 3.9$  y, compared to  $40.5 \pm 5.3$  y among patients with adenomyosis.

**Inclusion criteria:** All patients admitted with clinical symptoms of

abnormal uterine bleeding with or without dysmenorrhoea, lump abdomen, chronic pelvic pain and who were diagnosed as leiomyoma of uterus and/or adenomyosis based on clinical examination.

### Exclusion criteria

- **Following patients were excluded from the study**-Diagnosed cases of leiomyoma and adenomyosis of uterus that were managed conservatively.
- Diagnosed cases of abnormal uterine bleeding and chronic pelvic pain due to other causes like CA Cervix, DUB, endometriosis, endometrial carcinoma and endometrial polyps.

Patients underwent a detailed clinical examination including per speculum examination, bimanual examination (per vaginal, per rectal) along with Pap smear, endometrial biopsy (after fractional curettage) and cervical biopsy if indicated.

The equipments used for imaging were Esoate My Lab 40 with multi frequency (3.5 Mhz to 5 Mhz) curvilinear probe and TVS probe (6 Mhz to 9 Mhz). The other machine was Volusion S6 4D Colour Doppler machine from GE with multi frequency (3.5 Mhz to 5.5 Mhz) curvilinear probe and TVS probe (8 Mhz to 12 Mhz).

The referred patient was asked to void urine and a TVS was performed first. The lesion was evaluated with respect to its morphology, number, size and echotexture. Colour Doppler evaluation of the lesion was done to assess its vascularity, TVP (tumour vascular pattern). Simultaneously, spectral Doppler was done to record the PI, RI and Vmax of the lesions.

If the uterus and both adnexa could not be visualized entirely with TVS, patient was asked to drink water to fill the bladder. Pelvis was then scanned trans abdominally with the same protocol. In suspected cases of leiomyoma, imaging was done to look for morphological criteria like well-defined margins, heterogeneous structure and variable echogenicity [1] presence of recurrent shadows, absence of anechogenic or cystic areas in the lesion unless suggestive of necrosis, sharp contour bulge of the uterus and a well-defined junctional zone in 3D coronal view of uterus.

With colour and Doppler imaging, TVP was assessed to see if the vessels were located at the periphery of the lesion [4] with high Vmax (as compared to adenomyosis). A low PI of less than 1.2 and low RI of less than 0.7 was considered positive for leiomyoma.

Similarly in suspected cases of adenomyosis, imaging was done to look for heterogeneous myometrial area with ill-defined boundaries, intra-myometrial cysts of 1 to 3 mm in diameter [1], asymmetric wall thickening, ill-defined junctional zone in 3D coronal view of uterus [5].

With colour Doppler imaging, TVP was assessed to see if the vessels were centrally located with low Vmax (as compared to leiomyoma). A high PI of more than 1.2 and high RI of more than 0.7 was considered positive for adenomyosis. Patients diagnosed with ultrasound as leiomyoma or adenomyosis or both and who had indication for surgery were operated with standard surgical protocols and intra operative findings were recorded. Post-operatively, specimens were sent for histopathology.

## RESULTS

A total of 100 patients were enrolled in to the study with different signs and symptoms suggesting a clinical diagnosis of either leiomyoma or adenomyosis [Table/Fig-1].

Out of 100 cases studied, 62 cases were clinically diagnosed as leiomyoma and 38 cases were suspected to have adenomyosis. None of the cases were clinically suspected to be having both. No positive finding was given with ultrasound and Doppler imaging in 1 case of dyspareunia and 3 cases of dysmenorrhoea. Out of 96 cases, 58 cases (60%) were diagnosed as leiomyoma, 30 cases (31%) as adenomyosis and 8 cases (8%) had both the conditions in imaging.

Clinical symptom	No.of.Cases	Percentage
AUB	10	10%
AUB with Dysmenorrhoea	12	12%
AUB with lump	30	30%
Dysmenorrhoea	12	12%
Lump abdomen	18	18%
Chronic pelvic pain	6	6%
Dyspareunia	12	12%

**[Table/Fig-1]:** Table showing clinical symptoms and their percentage in suspected cases of leiomyoma and adenomyosis of uterus n= 100  
AUB: Abnormal uterine bleeding

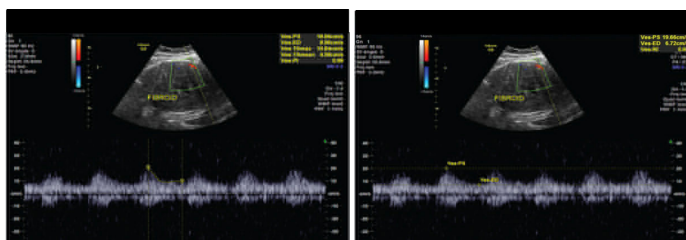
Morphological criteria for Leiomyoma	No.of.Cases and percentage (n=58)	Morphological criteria for Adenomyosis	No.of.Cases and percentage (n=30)
Well-defined margins	40, (68%)	ill-defined margins	24, (80%)
Variable echogenicity	20, (34%)	Heterogeneous myometrial area	22, (73%)
Absence of cystic areas	45, (77%)	Intra-myometrial cysts of 1 to 3 mm in diameter	25, (83%)
Presence of recurrent shadows	38, (65%)	Asymmetric wall thickening,	18, (60%)
Sharp contour bulge of the uterus	30, (51%)	Diffuse enlargement of uterus	22, (73%)
Well-defined defined junctional zone in 3D ultrasound	48, (82%)	ill-defined junctional zone in 3D ultrasound	26, (86%)
Peripheral vascularity	52, (89%)	Central vascularity	28, (93%)

**[Table/Fig-2]:** Table showing use of morphological criteria by ultrasound and Doppler to diagnose leiomyoma and adenomyosis of uterus

Doppler Indices	TP	TN	FP	FN	Ss	Sp	PPV	NPV
no of cases and "%"	50	26	4	8	93.4	95.6	97.6	88.6

Overall diagnostic accuracy of the test is : 93.8%

**[Table/Fig-3]:** Accuracy of spectral Doppler PI and RI in diagnosing leiomyoma of uterus  
Ss: Sensitivity, Sp: Specificity, PPV: Positive predictive value, NPV: Negative predictive value TP: True positive, TN: True Negative, FP: False positive, FN: False Negative



**[Table/Fig-4]:** Image showing PI<1.0 in a case of fibroid in colour and spectral Doppler  
**[Table/Fig-5]:** Image showing RI<0.7 in a case of fibroid in colour and spectral Doppler

[Table/Fig-2] Shows the distribution of sonographic morphological and doppler criteria's seen in the cases.

While imaging patients of leiomyoma, it was found that "peripheral vascularity" was seen in 52 (89%) of cases and was the criterion having the highest prevalence. It was followed by "well-defined junctional zone in 3D ultrasound" in 48 cases (82%), "absence of cystic areas" in 45 cases (77%), "well-defined margins" in 40 cases (68%), "presence of recurrent shadows" in 38 cases (65%), and "sharp contour bulge" in 30 cases (51%). The criterion observed least was "variable echogenicity", seen only in 20 cases (34%).

Similarly while imaging adenomyosis, the criterion "central vascularity" was seen in 28 cases (93%) and was the most frequently observed parameter. "Ill-defined junctional zone in 3D ultrasound" was seen in 26 cases (86%). Other criteria observed

were "intra-myometrial cysts of 1 to 3 mm" 25 of cases (83%), "ill defined margins" in 24 cases (80%), and "heterogenous myometrial area with diffuse enlargement of uterus" in 22 cases (73%). The criterion least observed was "asymmetrical wall thickening" noted in only 18 (60%) cases. The Doppler criteria used for diagnosing leiomyoma was a  $PI < 1.2$  and  $RI < 0.7$  [Table/Fig-3].

[Table/Fig-4,5] of leiomyoma of uterus with colour and spectral Doppler showing decreased PI and RI. With this criteria it was found to be true positive in 50 cases, true negative in 26 cases, false positive in 4 cases and false negative in 8 cases giving a sensitivity of 93.4%, specificity of 95.6%, positive predictive value of 97.6% and negative predictive value of 88.6%. Overall diagnostic accuracy of the test was 94%.

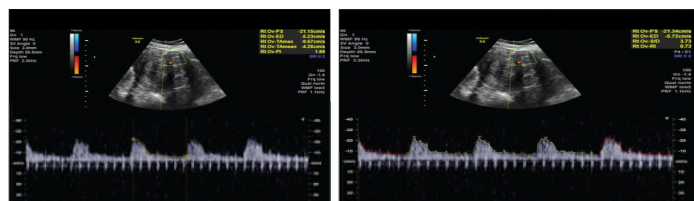
Similarly, Doppler criteria used for diagnosing adenomyosis were a  $PI > 1.2$  and  $RI > 0.7$  [Table/Fig-6].

[Table/Fig-7,8] of adenomyosis of uterus with colour and spectral Doppler showing increased PI and RI. With these criteria, it was found to be true positive in 26 cases, true negative in 50 cases, false positive in 8 cases and false negative in 4 cases giving a sensitivity of 95.6%, specificity of 93.4%, positive predictive value of 88.6% and negative predictive value of 97.6%. Overall diagnostic accuracy of the test was 93.8%. [Table/Fig-9] shows the Doppler indices and Vmax in leiomyoma and adenomyosis.

The parameters of blood flow impedance that is PI, RI, and Vmax of arteries within or around the uterine lesions revealed a consistent and significant difference in between the two groups. The imaging diagnosis of co-existence of both the lesions was noted in 8 cases.

Doppler Indices	TP	TN	FP	FN	Ss	Sp	PPV	NPV
no of cases and "%"	26	50	8	4	95.6	93.4	88.6	97.6
Overall diagnostic accuracy of the test is : 93.8%								

**[Table/Fig-6]:** Accuracy of spectral Doppler PI and RI in diagnosing adenomyosis of uterus  
Ss: Sensitivity, Sp: Specificity, PPV: Positive predictive value, NPV: Negative predictive value  
TP: True positive, TN: True Negative, FP: False positive, FN: False Negative



**[Table/Fig-7]:** Image showing  $PI > 1.0$  in a case of adenomyosis in colour and spectral doppler

**[Table/Fig-8]:** Image showing  $RI > 0.7$  in a case of adenomyosis in colour and spectral doppler

S.no	Examination	PI	RI	Vmax cm/sec
1.	Leiomyoma	$0.9 \pm 0.20$	$0.50 \pm 0.15$	$12.0 \pm 2.5$
2.	Adenomyosis	$1.5 \pm 0.20$	$0.9 \pm 0.15$	$7.0 \pm 2.5$

**[Table/Fig-9]:** PI, RI and Vmax of arteries in and/ or around the uterine lesion

Clinical symptom	No.of.Cases	Operative Procedure	
		Myomectomy	Hysterectomy
AUB	10	4	6
AUB with Dysmenorrhoea	12	4	8
AUB with lump	30	10	20
Dysmenorrhoea	12	4	5
Lump abdomen	18	10	8
Chronic pelvic pain	6	2	4
Dysparaunia	12	1	10
Total	100	35	61

**[Table/Fig-10]:** Table showing operative procedure carried out in the study population  
AUB: Abnormal uterine bleeding There was no uterine lesion seen in imaging in 3 cases of dysmenorrhoea and 1 case of dysparaunia, so no operative procedure was done

S.no	Examination	Leiomyoma	Adenomyosis	Both
1.	Clinical	62	38	None
2.	USG and Doppler	58	30	8
3.	Histopathology	53	28	12

**[Table/Fig-11]:** Table showing clinical, imaging and histopathological diagnosis of leiomyoma, adenomyosis and coexistence of both in the study

Standard operative procedures and management protocols were carried out in patients. Out of 96 patients operated myomectomy was done in 35 cases (36%) and hysterectomy was done in 61 cases (63%) [Table/Fig-10].

Histopathological examination of the operative specimens was done. It was found that three cases had indeterminate results due lack of sufficient material for biopsy. Out of 93 cases biopsied, 53 cases (60%) were leiomyoma, 28 cases (30%) were adenomyosis and 12 cases (13%) showed coexistence of both the conditions.

[Table/Fig-11] shows clinical diagnosis, imaging diagnosis and final outcome of cases with respect to histopathology. Referring to [Table/Fig-11], it was noted that by using various sonographic morphological and Doppler criteria, imaging was able to correctly diagnose 53 cases (85%) of leiomyoma and 28 cases (73%) of adenomyosis.

Although none of the cases were suspected to be having both the conditions clinically, it was diagnosed in 8 cases by imaging. However, 12 cases were subsequently diagnosed in biopsy with both conditions coexisting. Retrospectively, the reasons found were probably due to small size lesions, one lesion much larger than the other as was seen in one case and presence of small lesions near the cornua of the uterus. However imaging diagnosed the co-existence correctly upto 66% of cases (8 out of 12 cases).

## DISCUSSION

Abnormal uterine bleeding is a very common symptom in gynecological practice, especially in premenopausal women. Two commonly encountered aetiologies of abnormal uterine bleeding are leiomyomas and adenomyosis.

Uterine leiomyomas are benign tumours of smooth muscle origin, with varying amounts of fibrous connective tissue usually arising in the myometrium but may be found uncommonly in the cervix, broad ligament or ovaries [6] Leiomyomas have been reported to occur in up to 70% of women by the age of 50 y [7] and multiple lesions can be found in up to 84% of women [7]. These benign hormone dependent lesions respond to both estrogen and progesterone, often increase in size during pregnancy and usually decrease in size after menopause. Early menarche and obesity predispose to development of leiomyomas due to be increased exposure to estrogen in such conditions [8]. Majority of women with leiomyomas are asymptomatic; but up to 20–50% of patients can have symptoms such as lump abdomen, menorrhagia, pelvic pain, infertility and complications during pregnancy [9].

Up to 30% of hysterectomies are performed in cases with symptomatic leiomyoma [9]. Other treatment options includes myomectomy or administration of gonadotrophin-releasing hormone (GnRH) analogs [9]. Recently, a non invasive technique for treating leiomyoma has been introduced. Known as MRI-HIFU which is MRI guided high intensity focussed ultrasound, focussed high energy ultrasound waves are used to cause localized heating and cell death in uterine leiomyomas.

In adenomyosis endometrial glands and stroma traverse deep into the myometrium and are associated with surrounding myometrial hypertrophy [9]. The typical clinical symptom with adenomyosis is excessive uterine bleeding accompanied by worsening dysmenorrhoea. However, these findings are also being seen in other conditions such as leiomyoma, endometriosis, or endometrial polyps that commonly accompany adenomyosis [1,10]. Lesions

may be characterized as diffuse or focal. The highest prevalence occurs in parous women, 30-50 years old, and half of the remain asymptomatic [10]

The prevalence of adenomyosis, according to literature, varies from 5% to 70% [10]. The rate of preoperative diagnosis of adenomyosis on the basis of clinical findings is poor, ranging from 2.6% to 26% [9].

Adenomyosis as such is not treatable by conservative surgery and usually mandates hysterectomy whereas several studies have shown promising results of the conception rate among infertile patients following myomectomy [1,11]. So it is imperative to arrive at a proper diagnosis for appropriate treatment of the patient.

Imaging modalities commonly used to diagnose these two conditions are TAS, TVS magnetic resonance imaging (MRI) and hysterosalpingography (HSG) under special circumstances.

Going through previous literature, it is observed that HSG criteria of cavitory lesions, spiculated patterns, and lollipop-like diverticuli or TAS criteria in grey scale imaging of 5- to 7-mm cystic spaces that disrupted the normal echo patterns of the uterus have been less effective due to its lack of diagnostic sensitivity and specificity [1].

Reinhold et al., [12] and Dueholm et al., [13] in their earlier studies have illustrated that the sensitivity and specificity of 2D-TVS in diagnosing adenomyosis was quite high.

But 3D ultrasound imaging shows the anatomy of junctional zone even more clearly than the usual 2D imaging and helps in diagnosis adenomyosis more accurately as illustrated by Exacoustos et al., [5].

In their study Exacoustos et al., [5] found that with 3D ultrasound the JZ infiltration and distortion had high sensitivity (88%) and the best accuracy (85% and 82%, respectively).

In the present study it was found "ill defined junctional zone in 3D ultrasound" in 26 cases or 86% of the adenomyosis cases diagnosed in imaging.

Other notable features of their study in diagnosing adenomyosis was the presence of myometrial cysts was the most specific 2D-TVS feature (specificity,98%; accuracy, 78%) and heterogeneous myometrium was the most sensitive parameter (sensitivity, 88%; accuracy, 75%). We found presence of intra myometrial cysts in 83% of cases and heterogenous myometrial areas 73% of the cases.

In the same study they found that localized adenomyosis and adenomyoma were characterized by the presence of diffuse vessels, while fibroids had flow aligned along the external myoma capsule, appearing on imaging as a vascular ring.

In our study similar findings were note, central or diffuse vascularity in 93% cases of adenomyosis and peripheral vascularity in 89% cases of fibroid. This was a vital sign to differentiate the two in colour Doppler.

In another study by Al Ahmed et al., [14], while comparing the efficacy of 2D and 3D USG in diagnosing adenomyosis, they found that highest sensitivity rate was for the non-homogenous or heterogeneous myometrial areas with ill-defined boundaries seen in 90% of cases in their study and was seen in 73 % of cases in our study. The highest positive predictive value (PPV) was for intra-myometrial cysts seen in 97.2% in their study and was seen in 83% of cases in our study. In their study, while using 3D coronal view in USG they found that heterogeneous or non-homogenous ill-defined myometrial areas were seen in 95.7% cases, asymmetric wall thickness was seen in 95.4% and ill-defined endometrial myometrial junction was seen in 95.2% cases. We observed that in 80%, 60% and 86% of cases respectively.

With respect to leiomyoma, morphological criteria of "peripheral vascularity" were seen in 52 (89%) cases which was the criterion showing highest prevalence. Doppler USG typically shows circumferential vascularity; however, fibroids which are necrotic or have undergone torsion will show absence of flow [5]

Uterine myomas can be very well assessed by 3D US as described by Raine et al., in their study [15]. The Multiplanar display, especially the coronal view allows precise localization of a fibroid with respect to the endometrial canal.

Spectral Doppler criteria used in similar earlier studies have revealed that adenomyosis had a higher PI and RI and a lower Vmax of intratumoral vessels than the outer feeding vessels of leiomyoma.

In one study, Kurjak et al., have shown that increased blood velocity and decreased RI and PI in both uterine arteries occurred in patients with uterine fibroids [16]. Sladkevicius et al., found that uterine myomas substantially affect blood flow velocity in the uterine arteries and that PI values < 1.0 are common in uterine myomas [17].

In the present study we found similar results. In leiomyoma comparatively high velocity flow was found in the periphery of the lesion in 52 (89%) cases, with PI <1.2 and RI<0.7, giving a sensitivity of 93.4%, specificity of 95.6%, positive predictive value of 97.6% and negative predictive value of 88.6%. Overall diagnostic accuracy of the test was 94%.

Further, in adenomyosis comparatively low velocity flow was found in the central part of the lesion in 28 cases (93%) , with PI >1.2 and RI>0.7, giving a sensitivity of 95.6%, specificity of 93.4%, positive predictive value of 88.6% and negative predictive value of 97.6%. Overall diagnostic accuracy of the test was 93.8%.

Reinhold et al., [12] showed that the application of TVS in diagnosing adenomyosis was as good as that of MRI. The sensitivity and specificity were 89% for TVS and 86% for MRI. The positive predictive value was 71% for TVS and 65% for MRI. The negative predictive value was 96% for TVS and 95% for MRI.

The cost of MRI examination and long scan acquisition times are the inhibiting factors to use it as a screening examination in practice. Therefore TVS, especially 3D TVS with higher resolution, can be used as an effective screening tool. Moreover the use of Doppler with respect to vascularity and blood flow impedance by studying PI,RI and Vmax of the lesions provides additional parameters to differentiate and diagnose leiomyoma from adenomyosis.

## CONCLUSION

The clinical signs and symptoms in leiomyoma and adenomyosis overlap substantially, making a definite clinical diagnosis difficult many a times. As the treatment protocols are very different, accurate preoperative diagnosis is vital for proper management. Apart from grey scale imaging, morphological criteria in 3D TAS or TVS, the patterns and distribution of blood flow in colour Doppler and the PI,RI and Vmax in spectral Doppler can increase the accuracy of imaging in diagnosing and differentiating leiomyoma of uterus from adenomyosis. The examination is quick, accurate and reproducible with high diagnostic accuracy which makes differential diagnosis between these conditions easy, avoiding more time consuming and costlier investigations like MRI.

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**PARTICULARS OF CONTRIBUTORS:**

1. Assistant Professor, Department of Obstetrics and Gynecology, AVMCH, Pondicherry, India.
2. Associate Professor, Department of Radiology, AVMCH, Pondicherry, India.
3. Professor, Department of Radiology, AVMCH, Pondicherry, India.
4. Professor and HOD, Department of Pathology, AVMCH, Pondicherry, India.
5. Associate Professor, Department of Pathology, AVMCH, Pondicherry, India.
6. Assistant Professor, Department of Radiology, AVMCH, Pondicherry, India.
7. Assistant Professor, Department of Radiology, AVMCH, Pondicherry, India.
8. PG Student, Department of Radiology, AVMCH, Pondicherry, India.

**NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:**

Dr. Manash Kumar Bora,  
Second Floor, Vishram Apatment, Door No.4, S.V.Patel Salai, Pondicherry-605001, India.  
E-mail : drmanashbora@yahoo.com

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