

Sonography and Magnetic Resonance Imaging for the Diagnosis of Adenomyosis: Comparison with Histopathology

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ABSTRACT

Objectives: To assess the accuracy of sonography and MRI in identifying adenomyosis, with histopathology serving as the reference standard for comparison i.e., the gold standard.

Methodology: The study was done at the Department of Diagnostic Radiology/ Pathology, POF Hospital / Wah Medical College, Wah Cantt from August, 2018, to August, 2019.

The patients who underwent surgical treatment in the relevant department were included in the study. Tissue samples obtained from these patients were subjected to histopathological analysis, which was interpreted by a consultant pathologist. The sonographic and MRI findings were subsequently compared to the histopathology report for each patient.

Results: The mean age of the enrolled patients in the study was 38.3±5.5 years. Specificity, Sensitivity, negative predictive value, positive predictive value, and diagnostic accuracy of sonography and MRI was calculated by taking histopathology as gold standard and found to be 92.1%, 88.0%, 95.8%, 78.5%, and 91.0% respectively for sonography and 96.0%, 84.0%, 94.8%, 87.5%, and 93.0% respectively for MRI.

Conclusion: Sensitivity of sonography remained to be high as compared to MRI in present study while specificity and accuracy of MRI remained to be high from sonography. It is necessary to observe the unusual and usual characteristics of adenomyosis for further improvements in diagnostic outcomes.

Keywords: Adenomyosis; endometriosis; internal adenomyosis; transvaginal sonography

Authors' Contribution:

^{1,2}Conception; Literature research; manuscript design and drafting; ^{3,4}Critical analysis and manuscript review; ^{5,6}Data analysis; Manuscript Editing.

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Introduction

Adenomyosis is a common gynecological condition where non-cancerous endometrial tissue grows within the myometrium, causing thickening and enlargement of the smooth muscle layer. Progresses in imaging procedures nowadays allow for the diagnosis of adenomyosis in patients not only during hysterectomy but also in those visiting gynecology units for routine ultrasound exams. Studies show

that imaging detects adenomyosis in about 30% of women under the age of 40.^{1,2} This condition commonly affects women in their later reproductive years and is linked to risk factors such as uterine trauma from childbirth or surgery, multiple pregnancies, age, smoking, chronic endometriosis, and high estrogen levels.

It manifests in two primary forms: diffuse and focal. Focal form of adenomyosis is also named

adenomyoma, involves ectopic endometrial tissue and nodules of hypertrophic myometrium, whereas diffuse adenomyosis has scattered adenomyotic foci throughout the myometrium.⁴

The exact cause of adenomyosis remains unclear, though two primary theories have been proposed. One theory proposes that adenomyosis may develop when the endometrial basal layer penetrates into the myometrium. Another theory proposes that it may arise from pluripotent Müllerian remnants that are situated abnormally due to irregularities during embryonic development. Despite these hypotheses, the exact mechanisms underlying the onset of adenomyosis remain unclear. While some individuals remain asymptomatic, others may experience general symptoms, including pelvic pain, dysmenorrhea, and menometrorrhagia. Adenomyosis commonly co-occurs with other uterine conditions, such as endometrial polyps, endometriosis, and leiomyomas. Because adenomyosis is linked to other conditions and has nonspecific symptoms, clinical criteria alone are usually inadequate for an accurate diagnosis.⁴

The Morphological Uterus Sonographic Assessment (MUSA) group, an international authority on uterine imaging in 2015, released a consensus outlining preferred terms for defining myometrial lesions observed on ultrasound.⁵ In 2021, skilled gynecologists concentrating in ultrasound diagnosis of adenomyosis issued an updated consensus, refining the MUSA criteria for adenomyosis and introducing a classification system that differentiates between direct and indirect signs⁶. Direct features of adenomyosis include echogenic sub-endometrial lines, hyper-echogenic islands, myometrial cysts, and buds. Indirect features include a globular uterine shape, asymmetrical myometrial thickening, fan-shaped shadowing, translesional vascularity, and disrupted or irregular junctional zone. This consensus has significantly advanced the non-invasive diagnostic accuracy for

adenomyosis.⁷ While histopathological examination of a hysterectomy specimen is required for a definitive diagnosis of adenomyosis, non-invasive methods like transvaginal ultrasound (TVUS) and magnetic resonance imaging (MRI) have enabled diagnosis before surgery. A recent systematic review and meta-analysis assessed imaging techniques for diagnosing adenomyosis, revealing sensitivities of 78% for MRI, 74% for 2D-TVS, and 84% for 3D-TVS⁸. The respective specificity values were 88% for MRI, 76% for 2D-TVS, and 84% for 3D-TVS. MRI is generally considered to be more accurate than TVUS; however, due to limited MRI accessibility in many hospitals in Pakistan, ultrasound remains the primary diagnostic tool for its effectiveness, non-invasive nature, and availability.

MRI has recently become the preferred imaging method for confirming suspected adenomyosis cases due to its high sensitivity, specificity, and diagnostic accuracy. MRI also offers detailed insights into the extent and characteristics of the disease, as well as any related uterine lesions. However, given the limited research on adenomyosis in Pakistan, this study intended to review existing literature and evaluate the diagnostic features of both MRI and ultrasonography for identifying adenomyosis within the local population. This study designed to measure the diagnostic accuracy of MRI and sonography for identifying adenomyosis, using histopathological analysis as the gold standard for comparison.

Methodology

This cross-sectional validation study was conducted at the Diagnostic Radiology Department, Pakistan Ordnance Factories Hospital / Wah Medical College, Wah Cantt, from August 5, 2018, to August 4, 2019, following approval from the institutional ethics review board. With a 95% confidence level and an assumed adenomyosis prevalence of 30%, the required sample size was calculated as 101 cases using the WHO sample size calculator. The reported

sensitivity for ultrasound was 89% and specificity was 90%, and for MRI sensitivity was 86% and specificity was 95%. Non-probability purposive sampling was employed, including women aged 15 to 45 with symptoms such as chronic pelvic pain, dysmenorrhea, heavy menstrual bleeding, and uterine enlargement. Exclusions included postmenopausal women, pregnant women, those with malignancies, pelvic organ prolapse, those on hormone replacement therapy, those unfit for surgery, and individuals contraindicated for MRI (e.g., with pacemakers, claustrophobia, or contrast hypersensitivity).

The study adhered to the guidelines outlined by the institutional ethics committee. Patients meeting the inclusion criteria were recruited after obtaining their informed consent. A detailed questionnaire was administered to collect the relevant medical history of the selected patients. All patients underwent pelvic scans with a 3.5 MHz curvilinear probe after optimal bladder filling, followed by a TVS examination using a 7.5 MHz probe. Patients were diagnosed for adenomyosis on sonography with features of bulky uterus, myometrial cyst, asymmetrical myometrial thickening, hyperechoic striations and junctional zone alterations and were subjected to contrast enhanced MRI of the pelvis. MRI examination was done on SIEMENS MAGNETOM AERA 1.5 TESLA with 6-8 hours fasting with full bladder and empty bowel by a technologist. Supine position was maintained during image acquisition. The imaging protocols included sagittal and axial T1, T2, and STIR sequences, along with coronal T2 spin echo and STIR sequences. MRI diagnosis of adenomyosis was based on findings such as junctional zone thickening greater than 12 mm, asymmetrical thickening of the myometrial wall, and foci with high T2 signal intensity and high T1 FS signal intensity. All imaging findings were reviewed by a consultant radiologist. Patients then underwent surgery, and tissue samples were sent

for histopathological analysis by a consultant pathologist. The results from sonography and MRI were compared with the histopathology findings. Data analysis was performed using SPSS 23 version. Descriptive statistics were generated for qualitative variables, including enlarged uterus, myometrial cysts, heterogeneous echotexture, hyperechoic striations, altered junctional zone, and regions with high T2 and T1 FS signal intensity. Sensitivity, specificity, NPV, and PPV for MRI and ultrasound were assessed using a 2x2 contingency table, with histopathology as the gold standard.

Results

The study included 101 women of reproductive age, with a mean age of 38.3 ± 5.5 years. Among them, 10 participants (9.9%) were between 20 and 30 years old, while the majority, 91 participants (90.1%), were aged 31 to 45 years.

Sonographic findings revealed that an enlarged bulky uterus was the most prevalent observation in nearly all patients, succeeded by asymmetrical myometrium, myometrial cysts, the junctional zone alterations, and hyperechoic striations. It's crucial to acknowledge that there might be overlaps in various characteristics, and each case could manifest with more than one finding. A comprehensive breakdown of the results is outlined in Table I.

The MRI findings distribution showed that the highest number of cases presented with asymptomatic thickening of the myometrial wall followed by foci of high T2 and T1 FS signal intensity, while 24.8% cases presented with the junctional zone thickening of more than 12mm. These findings are outlined in Table II.

The diagnostic performance of ultrasound and MRI was assessed by calculating their sensitivity, specificity, PPV, NPV, and overall accuracy, with histopathology serving as the reference standard. Comprehensive results are presented in Tables III and IV.

| Sonographic findings | Number | Percentage |
|------------------------------------|--------|------------|
| Myometrial cyst | 45 | 44.6 |
| Asymmetric myometrium | 51 | 50.5 |
| Bulky enlarged uterus | 99 | 98.0 |
| Hyper-echoic striations | 21 | 20.8 |
| Alterations of the Junctional zone | 25 | 24.8 |

| MRI findings | Number | Percentage |
|---|--------|------------|
| Thickening of junctional zone > 12mm | 25 | 24.8 |
| Asymmetric thickening of myometrial wall | 86 | 85.1 |
| Foci of high T2 signal intensity +high T1 FS signal intensity | 33 | 32.7 |

| Sonography | Histopathology (Gold Standard) | | Total |
|-----------------|--------------------------------|----------------------------|------------|
| | Positive | Negative | |
| Positive | a 22 (True Positive) | b 6 (False Positive) | 28 |
| Negative | c 3 (False Negative) | d 70 (True Negative) | 73 |
| Total | 25 | 76 | 101 |

| Sonography | Histopathology (Gold Standard) | | Total |
|-----------------|--------------------------------|----------------------------|------------|
| | Positive | Negative | |
| Positive | a 22 (True Positive) | b 6 (False Positive) | 28 |
| Negative | c 3 (False Negative) | d 70 (True Negative) | 73 |
| Total | 25 | 76 | 101 |

Sensitivity: $a/a+c \times 100 = 88.0\%$
Specificity: $d/d+b \times 100 = 92.1\%$
Positive Predictive Value (PPV): $a/a+b \times 100 = 78.5\%$
Negative Predictive Value (NPV): $d/c+dx100=95.8\%$
Diagnostic accuracy: $a+d/a+d+b+c \times 100 = 91.0\%$

The total does not equal 100% due to the presence of compound responses

Discussion

Non-invasive diagnostic techniques, like ultrasound, are essential for identifying various conditions, including adenomyosis. In this study, ultrasound achieved 88.0% sensitivity, 92.1% specificity, 78.5% PPV, 95.8% NPV, and an overall diagnostic accuracy of 91.0%, with histopathology as the gold standard. These results, however, differ from those reported in previous studies. Hussein NAM et al.⁹ reported that transvaginal ultrasound (TVUS) had 83.3% sensitivity, 86.8% specificity, 66.7% PPV, 93.4% NPV, and 85.4% overall diagnostic accuracy for diagnosing adenomyosis. These findings align with our study, which highlights the superior diagnostic performance of ultrasound, characterized by strong sensitivity and specificity. Sadek et al. reported that 3D-TVS demonstrated 97.9% sensitivity, 66.7%

specificity, 93.18% PPV, 40% NPV and 92.5% diagnostic accuracy in the diagnosis of adenomyosis¹⁰. While the observed sensitivity was similar to our findings, there was a notable difference in specificity. Nonetheless, both studies agreed that sub-endometrial linear striations were the most reliable indicator for identifying leiomyomas and diagnosing both adenomyosis and leiomyomas with TVUS^{9, 10}. This underscores the importance of utilizing standardized ultrasound protocols and expert interpretation to enhance diagnostic accuracy. Additionally, our findings suggest that specific sonographic features can contribute to the accurate identification of adenomyosis.

The accuracy of non-invasive methods for diagnosing adenomyosis varies significantly across studies. Eisenberg et al.¹¹, for example, reported that sonography had 100% sensitivity, 25% specificity, 89.5% PPV, and 100% NPV for adenomyosis diagnosis, although histological confirmation was only available for 15% of cases in their study. Cunningham et al.¹² found that transvaginal ultrasound (TVUS) achieved 86% sensitivity, 86% specificity, 71% PPV, and 94% NPV, with the most frequent finding being a heterogeneous, hypoechoic myometrium. Additionally, Chapron et al.² reported 83.8% sensitivity and 63.9% specificity for TVUS in detecting adenomyosis and noted that confirmatory MRI was deemed unnecessary in their research.

Sonography faces notable limitations in accurately diagnosing adenomyosis, as it often shares overlapping features with leiomyomas, making differentiation challenging in certain cases. This distinction is critical, as treatment approaches and prognosis differ for each condition. For isolated adenomyosis, gynecologists generally favor conservative medical management, whereas surgical options are more frequently chosen for leiomyomas (fibroids) or cases involving both

adenomyosis and leiomyomas, especially when the uterus is enlarged. There is a recognized need in the gynecological community for an accurate, non-invasive diagnostic method to clearly identify adenomyosis, leiomyoma, or both conditions together. Săsăran et al.⁷ demonstrated that 3D ultrasonography, qualitative elastography, and contrast-enhanced ultrasound, all using the endovaginal approach, exhibited high diagnostic accuracy for adenomyosis. Zannoni et al.¹³ reported that transvaginal ultrasound (TVUS) had 77% sensitivity, 96% specificity, 91% PPV, 89% NPV, and 90% overall diagnostic accuracy for diagnosing adenomyosis. Liu et al.¹⁴ in a systemic review and meta-analysis, found that TVUS was equivalent to MRI in diagnosing adenomyosis. Similarly, Shah et al.¹⁵ reported that ultrasonography achieved 100% sensitivity, 98.5% specificity, and 98.75% diagnostic accuracy, recommending it as the prime diagnostic method for uterine pathologies, including adenomyosis.

Maudot et al.¹⁶ reported that pelvic sonography for diagnosing adenomyosis had 52% sensitivity, 85% specificity, 77% PPV, 86% NPV, and 38.1% diagnostic accuracy. The results were comparable to MRI in diagnosing the condition. The researchers suggested that adopting a standardized sonographic classification system could enhance and standardize the accuracy of adenomyosis diagnosis.

In our current study, MRI demonstrated 84% sensitivity, 96% specificity, 87.5% PPV, 94.8% NPV and 93% overall diagnostic accuracy diagnosing adenomyosis, using histopathology as the gold standard. Salem et al.¹⁷ highlighted MRI as a reliable noninvasive method for diagnosing adenomyosis and related conditions, reporting 92.3% sensitivity, 75% specificity, and 90% diagnostic accuracy. These results are consistent with our findings, supporting MRI as an effective tool for evaluating adenomyosis, identifying associated abnormalities, and distinguishing it from similar conditions.

Krentel et al.¹⁸ examined the risks, challenges, and complications in diagnosing and treating adenomyosis and myomas. They suggested that a reliable adenomyosis diagnosis can be achieved through a combination of gynecological examination, clinical history, and 2D and 3D transvaginal ultrasound, with Doppler sonography and MRI offering added insights, especially when fibroids are present. Chapron et al.² revealed that 2D and 3D TVUS, along with MRI, are effective in accurately identifying the various phenotypes of adenomyosis, including diffuse and focal types. Based on their findings, they advocated for a comprehensive, non-invasive diagnostic approach that integrates the patient's risk factors, clinical symptoms, examination, and imaging results.

Rubab et al.¹⁹ equated the diagnostic performance of TVUS and MRI for adenomyosis. Their results indicated comparable diagnostic accuracy between the two methods. They recommended TVUS as the preferred initial diagnostic tool for adenomyosis, citing its accessibility, cost-effectiveness, and high patient tolerance.

MRI is a key non-invasive diagnostic tool, with 84% sensitivity, 96% specificity, 87.5% PPV, 94.8% NPV, and 93% diagnostic accuracy, in this study. However, when compared to sonography, MRI demonstrated lower sensitivity and PPV in our findings. Bazot et al.²⁰ reported a pooled sensitivity for transvaginal ultrasound (TVUS) ranging from 0.72 to 0.82, specificity between 0.85 and 0.81, and a positive likelihood ratio of 4.67 to 3.7 for all adenomyosis subtypes. In contrast, MRI showed 0.77 pooled sensitivity, 0.89 pooled specificity, 6.5 positive likelihood ratio, and 0.2 negative likelihood ratio, for diagnosing adenomyosis. They concluded that MRI is more valuable than TVUS in diagnosing adenomyosis. Tellum et al.⁸ in their systematic review and meta-analysis, found that both MRI and TVUS provided reliable and accurate diagnostic performance in detecting adenomyosis, with no

significant difference in diagnostic capability between the two methods. They recommended TVUS as the primary diagnostic imaging method.

Tariq et al.²¹, equated the diagnostic accuracy of MRI and ultrasound in detecting adenomyosis among 162 patients and concluded that MRI exhibited superior diagnostic accuracy compared to TVUS. The reported diagnostic accuracy for MRI and TVUS was 78.4% and 60.5%, respectively, which aligns with the findings of this study.

In our study, sonography revealed bulky and enlarged uterus in 99 cases. Additional features included asymmetrical myometrium in 51 cases, myometrial cysts in 45 cases, junctional zone alterations in 25 cases, and hyperechoic striations in 21 cases. These findings are consistent with results from previous studies^{12, 13, and 17}. Common gray-scale ultrasound characteristics associated with adenomyosis include an asymmetrically thickened and globular uterus, indistinct endometrial boundaries, and heterogeneous myometrium with thin "venetian blind" shadowing within areas of increased echogenicity, echogenic linear striations, and the presence of myometrial nodules and cysts extending from the endometrium into the myometrium.

In this study, MRI findings indicated that the most common presentation of adenomyosis was asymptomatic thickening of the myometrial wall, followed by foci with high T2 and T1 FS signal intensity and junctional zone thickening greater than 12 mm. These findings are consistent with previous research, identifying 12 mm or more junctional zone thickness as a primary MRI criterion for diagnosing adenomyosis.²² Andersson et al.²³ observed that inter-rater agreement for diagnosing adenomyosis was higher with TVUS than with MRI. However, MRI demonstrated greater reliability between raters across most variables, especially in assessing the junctional zone. In a meta-analysis, Alcazar et al.²⁴ found statistically insignificant difference ($P=0.7509$)

between MRI and TVUS in accurately diagnosing adenomyosis. In a current study by Shaikh et al.²⁵, transvaginal ultrasound revealed 74.36% sensitivity and 96.15% specificity for detecting adenomyosis, with MRI serving as the reference standard. The PPV was 98.31%, and the NPV was 55.56%. They recommended transvaginal ultrasound as the preferred initial diagnostic tool due to its strong sensitivity and specificity, aiding in diagnosis and individualized treatment planning. They suggested reserving MRI for cases with high clinical suspicion, particularly when ultrasound results are inconclusive or ambiguous.

Careful assessment of both typical and atypical characteristics of adenomyosis is essential for accurate diagnosis, which in turn supports informed management decisions and can improve patient outcomes. Future research should prioritize standardizing imaging protocols and exploring the combined use of multiple imaging modalities to enhance diagnostic precision in adenomyosis. Although MRI has limitations, including longer examination times, higher costs, and minor examiner variability, it remains a dependable diagnostic method for adenomyosis⁷. MRI continues to hold a strong reputation for accuracy and effectiveness in the non-invasive diagnosis of this condition.

Conclusion

In conclusion, both sonography and MRI are effective for accurately diagnosing adenomyosis. In this study, sonography demonstrated higher sensitivity, whereas MRI showed greater specificity and overall diagnostic accuracy compared to sonography.

Disclaimer

The current manuscript is a part of dissertation presented to College of Physicians and Surgeons of Pakistan to fulfill FCPS Part II requirement by Dr. Afreen Anjum.

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