Diagnostic Accuracy of Transvaginal Ultrasound in Adenomyosis Taking MRI as a Gold Standard

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ABSTRACT

Objective: To evaluate the accuracy of transvaginal ultrasound in the diagnosis of adenomyosis using MRI as the gold standard, and to characterise the most commonly seen and accurate ultrasonographic features and their combination.

Study Design: Cross-sectional, descriptive study.

Place and Duration of the Study: Department of Radiology, The Aga Khan University Hospital, Karachi, from January 2018 to July 2021.

Methodology: Transvaginal ultrasound examination was performed on patients (n = 208) who presented with symptoms related to menstrual cycles and pelvic abnormalities. Additionally, patients who sought infertility evaluation were also included in the study. The findings from the ultrasound examinations were assessed and tabulated alongside the results of the MRI scans. All examinations were conducted by senior radiologists / sonographers. The sensitivity, specificity, positive and negative predictive values (PPV and NPV, respectively) of ultrasound features were calculated individually and in combination, taking MRI as the gold standard. To enhance the accuracy of ultrasound findings, various variables were combined, and their sensitivities and specificities were calculated.

Results: Overall, transvaginal ultrasound had a high specificity of 96.15% (95% CI: 85.67 - 99.33), a relatively low sensitivity of 74.36% (95% CI: 66.63 - 80.85), PPV of 98.31 (95% CI: 93.40 - 99.70) and NPV of 55.56 (95% CI: 44.73 - 65.90). The most sensitive dual variable used was a bulky uterus combined with altered myometrial echotexture, with a sensitivity of 72.97% (95% CI: 64.95 - 79.78) and specificity of 95.83% (95% CI: 84.57-99.27). The best combined triple variable was a bulky uterus with altered echotexture and streaky myometrium, with a sensitivity of 71.85% (95% CI: 63.35 - 79.10) and a specificity of 95.46% (95% CI: 83.30 - 99.21).

Conclusion: Transvaginal ultrasound features can identify adenomyosis characteristics in most of the patients. This could reduce the number of pelvic MRIs performed for the detection of adenomyosis.

Key Words: *Adenomyosis, Diagnosis, Magnetic resonance imaging, Bulky uterus, Altered myometrial, Echotexture, Ultrasound.*

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INTRODUCTION

Adenomyosis is a common nonmalignant condition in females of the reproductive group that usually occurs between adolescence and menopause. Patients usually present with pelvic pain, menorrhagia, dysmenorrhea, and dyspareunia.[1,2] It is a disease of the myometrium in which endometrium invades the myometrium, giving it a bulky and heterogeneous appearance. It is usually generalised, affecting a large portion of myometrium, or it can be focal, which usually affects the posterior uterine wall.

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MRI is the gold standard in the diagnosis of adenomyosis; however, due to its high cost and limited availability, its use is limited.[3] Trans-abdominal pelvic ultrasound as a modality is less sensitive in the detection of adenomyosis.[4] Patients with normal transvaginal ultrasound and symptoms suggestive of adenomyosis require further evaluation with an MRI of pelvis, as adenomyosis can be mild or focal and hence undetectable on ultrasound. An enlarged uterus on examination with pelvic symptoms raises the clinical suspicion of adenomyosis. The exact diagnosis of adenomyosis is made after hysterectomy on histopathological grounds.[5-7]

Transvaginal ultrasound is currently considered the primary investigation of choice. It has shown comparable sensitivity to MRI with easy accessibility and cost-effectiveness.[8] The most common ultrasonographic features are an enlarged uterus, myometrial heterogeneity, echogenic nodules or striations, myometrial cysts, cystic striations, a thickened and indistinct junctional zone, and increased vascularity.[8-10]

With adenomyosis, the uterus is usually enlarged, giving it a globular appearance. Despite a marked enlargement of the uterus, the overall contour is usually preserved.[11-13] There is diffusely heterogeneous or coarse echotexture of the uterine myometrium with multiple echogenic nodules and linear striations; additionally, multiple tiny cysts may be seen. The junctional zone cannot be separately delineated and has an indistinct and shaggy appearance.[12,14] Vascularity may appear to be increased in colour and power doppler because of uterine hypertrophy and hyperplasia.[15,16]

MRI is an important tool in understanding the exact extent of disease, which helps to individualise treatment options. The most sensitive MRI feature is thickening of the junctional zone by more than 12 mm and the presence of T1 hyperintense foci within the myometrium that are suggestive of haemorrhage within the ectopic endometrial tissue. The most sensitive sequence is the T2WI sagittal image (Figure 1). Post-contrast images usually do not add much to the diagnosis of adenomyosis.[14,17,18]

The purpose of this study was to determine the most common ultrasonographic findings used in the diagnosis of adenomyosis and to compare their sensitivity and specificity using MRI as the gold standard.

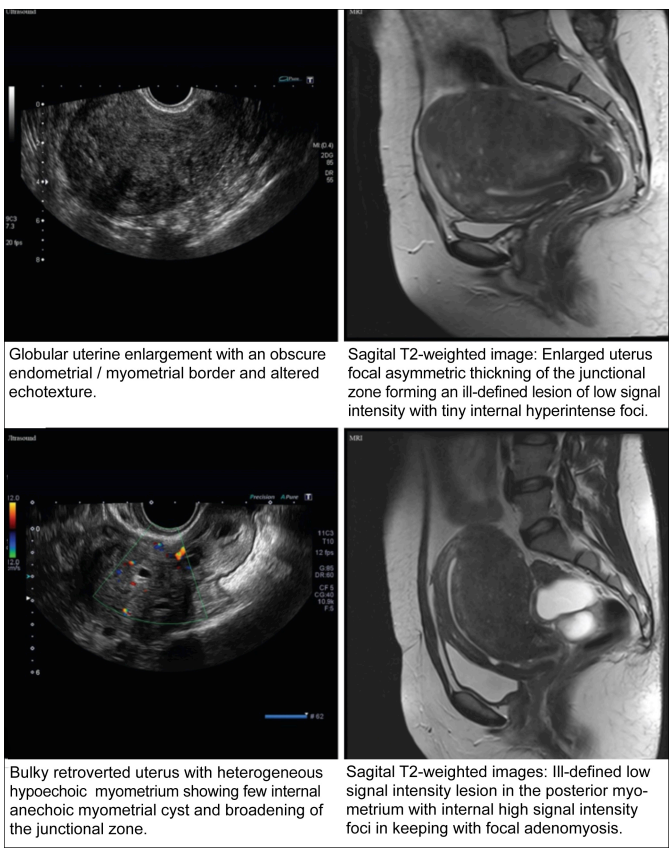

Figure 1: Transvaginal ultrasonography features and corresponding magnetic resonance imaging (MRI) findings for the diagnosis of adenomyosis.

METHODOLOGY

This was a cross-sectional study including 208 patients in the final analysis, recruited consecutively. The sample size was calculated using the formula for estimating sample size for studies determining diagnostic accuracy. Transvaginal ultrasound diagnostic accuracy in adenomyosis: assuming MRI as the reference standard, the following factors were considered: the desired level of precision (3.9%), the anticipated prevalence of adenomyosis (8.80%),[2] the desired confidence level (95%), corresponding to a significance level (α) of 0.05, and the expected sensitivity and specificity of the transvaginal ultrasound, which were assumed to be 75% and 96%, respectively and the calculated sample size was 208 patients. Patients aged ≥18 years, who presented with symptoms related to menstrual cycles, and pelvic abnormalities were included. Additionally, patients who sought infertility evaluation were also included in the study. Cases in which MRI was not evaluable due to the technical limitations or having an equivocal diagnosis of adenomyosis on pelvic MRI were excluded from the study. Moreover, cases where adenomyosis was detected incidentally during the imaging work-up of an unrelated pelvic pathology were also excluded.

The Picture Archiving and Communication System (PACS) was searched for all consecutive pelvic MRI performed at The Aga Khan University Hospital, between January 2018 and July 2021 for the evaluation of menorrhagia, dysmenorrhea, pelvic pathology, and infertility evaluation. All patients had a corresponding antecedent pelvic ultrasound performed within the 12 months prior to the pelvic MRI.

The findings from transvaginal ultrasound examination were assessed and tabulated alongside the results of the MRI scans. All examinations were conducted by senior radiologists/sonographers at the radiology department. The presence or absence of six sonographic parameters namely bulky uterus, pseudo-widening of the junctional zone, ultrasound echotexture, myometrial cyst, echogenic nodule /streaky myometrium, and relative absence of mass effect were assessed. All responses were recorded as 'yes' or 'no'. Results were documented on a structured format.

The imaging protocol for the MRI pelvis included axial T1-weighted sequences with fat saturation, axial, sagittal and coronal T2-weighted sequences, and T1WI post-contrast images. The slice thickness was 4 to 6 mm. Sequences were performed on 1.5 - 3 T clinical MRI systems.

The imaging protocol for the transvaginal ultrasound examination was performed using endovaginal curved array (5–12 MHz) transducers. This involved acquiring grayscale and colour Doppler sonograms of the uterus, ovaries, and adnexae, and these were recorded as still images and cine clips. The images were retrospectively reviewed on PACS. This study was conducted after receiving exemption from the institutional ethical review committee. The requirement of informed consent was, therefore, waived.

Table I: Ultrasound findings and single characteristics.

Findings	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	p-value
Overall ultrasound findings	74.36(66.63-80.85)	96.15(85.67-99.33)	98.31(93.40-99.70)	55.56(44.73-65.90)	<0.001
Bulky uterus	71.80(62.60-78.56)	88.46(75.87-95.22)	94.92(88.80-97.92)	51.11(40.42-61.71)	<0.001
Ultrasound echotexture	71.80(63.94-78.56)	96.15(85.67-99.33)	98.25(93.18-99.70)	53.19(42.66-63.46)	<0.001
Myometrial cyst	37.18(29.69-45.31)	100.0(91.43-100.0)	100.0(92.26-100.0)	34.67(27.21-42.92)	<0.001
Pseudo-widening of junctional zone (PWJZ)	62.82(54.69-70.31)	84.62(71.37-92.66)	92.45(85.22-96.45)	43.14(33.49-53.31)	<0.001
Echogenic nodule / Streaky myometrium	67.95(59.94-75.10)	88.46(75.87-95.22)	94.64(88.22-97.21)	47.92(37.70-58.30)	<0.001
Relative absence of mass effect	72.44(64.61-79.13)	98.08(88.42-99.90)	99.12(94.50-99.95)	54.26(43.70-64.46)	<0.001

Table II: Dual ultrasound characteristics.

Dual characteristics	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	p-value
Bulky uterus + US echotexture	72.97(64.95-79.78)	95.83(84.57-99.27)	98.18(92.94-99.68)	53.49(42.46-64.20)	<0.001
Bulky uterus + Myometrial cyst	57.29(46.79-67.20)	100.0(90.40-100.0)	100.0(91.86-100.0)	52.87(41.93-63.64)	<0.001
Bulky uterus + PWJZ	70.15(61.54-77.58)	93.18(80.29-98.22)	96.90(90.58-99.20)	50.62(39.36-61.82)	<0.001
Bulky uterus + Streaky	72.46(64.10-80.00)	95.46(83.30-99.81)	98.00(92.41-99.66)	52.50(41.10-63.46)	<0.001
Bulky uterus + Relative absence of mass effect	73.47(65.44-80.25)	97.87(87.28-99.89)	99.09(94.26-99.95)	54.12(43.00-64.86)	<0.001
US echotexture+ Myometrial cyst	57.14(46.75-66.97)	100.0(91.11-100.0)	100.0(92.00-100.0)	54.35(43.67-64.66)	<0.001
US echotexture + PWJZ	70.46(61.79-77.91)	95.65(83.96-99.24)	97.90(91.87-99.64)	53.01(41.80-63.94)	<0.001
US echotexture + Streaky	72.14(63.83-79.22)	95.83(84.57-99.28)	98.10(92.48-99.66)	54.12(43.00-64.86)	<0.001
US echotexture + Relative absence of mass effect	73.15(65.17-79.92)	98.04(88.21-99.90)	99.09(94.31-99.95)	55.56(44.73-65.91)	<0.001
Myometrial cyst + PWJZ	50.00(40.54-59.45)	100.0(90.00-100.0)	100.0(92.13-100.0)	43.56(33.84-53.78)	<0.001
Myometrial cyst + Streaky	53.70(43.38-63.26)	100.0(90.40-100.0)	100.0(92.26-100.0)	47.92(37.70-58.30)	<0.001
Myometrial cyst + Relative absence of mass effect	57.43(47.20-67.09)	98.08(88.42-99.90)	98.31(89.70-99.91)	54.26(73.70-64.46)	<0.001
PWJZ + Streaky	68.75(59.87-76.49)	95.24(82.58-99.17)	97.78(91.44-99.61)	50.00(38.30-61.30)	<0.001
PWJZ + Relative absence of mass effect	70.37(61.80-77.76)	97.78(86.77-99.88)	98.96(93.51-99.95)	52.38(41.26-63.28)	<0.001
Streaky+ Relative absence of mass effect	72.03(63.80-79.05)	97.87(87.28-99.89)	99.04(93.99-99.95)	53.49(42.46-64.20)	<0.001

The Statistical Package for Social Science (SPSS) version 21® was used for the data analysis. Data normality was assessed using the Kolmogorov-Simirnov test. Nominal variables were computed as numbers and percentages. The mean [(standard deviation (SD)] or median [(interquartile range (IQR)] were used for variables with continuous nature. The association between age and clinical and ultrasonographic characteristics of adenomyosis was ascertained using the Chi-square test or Fisher's exact test, where appropriate. The sensitivity, specificity, positive predictive, and negative predictive values of ultrasonographic characteristics were assessed one by one and in the form of various possible sets (dual or triplet match) for the finding of adenomyosis where appropriate. Mann-Whitney statistics were used for the calculation of the median difference. The significance level was set at <0.05.

RESULTS

The mean (SD) age of the study sample was 40.68 ±11.46 years. The most common indication documented was menorrhagia in 18.75% (n = 39) of the patients followed by pelvic pathology and infertility in 16.35% (n = 34) and 15.38% (n = 32) of the patients, respectively. Moreover, dysmenorrhoea was documented in 8.65% (n = 18) of the patients, whereas the clinical indication was not known in 40.87% of the patients. Of the total 208 patients, 75% (n = 156) of the patients had adenomyosis on MRI as the standard of reference, and 25% (n = 52) of the patients had no sign of adenomyosis. Positive ultrasound findings for adenomyosis were found in 56.73% (n = 118) of the patients. The remaining 90 patients showed no finding for adenomyosis.

Table III: Triple ultrasound characteristics.

Triple characteristics	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	p-value
Bulky + US echotexture + Myometrial cyst	58.06(47.38-68.08)	100.0(90.40-100.0)	100.0(91.73-100.0)	54.12(43.00-64.86)	<0.001
Bulky + US echotexture + PWJZ	69.77(60.96-77.38)	95.35(82.94-99.19)	97.83(91.62-99.62)	51.25(40.00-62.49)	<0.001
Bulky + US echotexture + Streaky	71.85(63.35-79.10)	95.46(83.30-99.21)	97.98(92.19-99.65)	52.50(41.10-63.66)	<0.001
Bulky + US echotexture + Relative absence of mass effect	72.92(64.77-79.82)	97.87(87.28-99.89)	99.06(94.01-99.95)	54.12(43.05-64.86)	<0.001
Bulky + Myometrial cyst + PWJZ	57.44(46.83-67.45)	100.0(89.33-100.0)	100.0(91.73-100.0)	50.62(39.36-61.82)	<0.001
Bulky + Myometrial cyst + Streaky	59.14(48.45-69.10)	100.0(90.00-100.0)	100.0(91.87-100.0)	52.50(41.10-63.66)	<0.001
Bulky + Myometrial cyst + Relative absence of mass effect	58.51(47.88-68.44)	100.0(90.40-100.0)	100.0(91.87-100.0)	54.12(43.00-64.86)	<0.001
Bulky + PWJZ + Streaky	68.85(59.74-76.76)	94.87(81.37-99.11)	97.67(91.10-99.60)	49.33(37.70-61.03)	<0.001
Bulky + PWJZ + Relative absence of mass effect	70.00(61.24-77.56)	97.62(85.91-99.88)	98.91(93.24-99.94)	51.25(40.90-62.49)	<0.001
Bulky + streaky + Relative absence of mass effect	70.06(63.61-79.24)	97.67(86.20-99.88)	98.99(93.70-99.95)	52.50(41.09-63.66)	<0.001
US echotexture + Myometrial cyst + PWJZ	58.51(47.88-68.44)	100.0(90.00-100.0)	100.0(91.87-100.0)	53.01(41.80-63.94)	<0.001
US echotexture + Myometrial cyst + Streaky	58.95(48.37-68.79)	100.0(90.40-100.0)	100.0(92.03-100.0)	54.12(43.05-64.86)	<0.001
US echotexture + Myometrial cyst + Relative absence of mass effect	58.33(47.82-68.17)	100.0(91.11-100.0)	100.0(92.00-100.0)	55.56(44.73-65.90)	<0.001
US echotexture + PWJZ + Streaky	68.85(59.74-76.76)	95.24(82.58-99.17)	97.67(91.10-99.60)	51.28(39.77-62.66)	<0.001
US echotexture + PWJZ + Relative absence of mass effect	70.00(61.24-77.56)	97.78(86.77-99.88)	98.91(93.24-99.94)	53.01(41.80-63.94)	<0.001
US echotexture + Streaky + Relative absence of mass effect	72.46(64.10-79.56)	97.87(87.28-99.89	99.09(93.82-99.95)	54.76(43.56-65.52)	<0.001
Myometrial cyst + PWJZ + Streaky	58.76(48.30-68.52)	100.0(89.00-100.0)	100.0(92.13-100.0)	50.00(38.70-61.30)	<0.001
Myometrial cyst + PWJZ + Relative absence of mass effect	58.76(48.30-68.52)	100.0(89.99-100.0)	100.0(92.13-100.0)	52.38(41.26-63.28)	<0.001
Myometrial cyst + Streaky + Relative absence of mass effect	59.18(48.77-68.86)	100.0(90.40-100.0)	100.0(92.26-100.0)	53.49(42.46-64.20)	<0.001
PWJZ + Streaky + Relative absence of mass effect	68.80 (59.81-76.62)	97.56(85.60-99.87)	98.85(92.87-99.94)	50.63(39.23-61.97)	<0.001

A comparative analysis was conducted between patients with and without adenomyosis, as determined by MRI findings, with respect to age and clinical indications. Patients with adenomyosis had a median age greater than those without adenomyosis (35.5 *vs.* 41.0, p = 0.019). Similarly, those with adenomyosis had higher proportions of menorrhagia and infertility, and the association was statistically significant (p<0.001).

Transvaginal ultrasound as a modality was found to be highly specific when compared to MRI, with specificity of 96.15% (95% CI: 85.67 - 99.33) but relatively low sensitivity of 74.36% (95% CI: 66.63-80.85) with a PPV of 98.31% (95% CI: 93.40 - 99.70) and a NPV of 55.56% (95% CI: 44.73 - 65.90).

Six sonographic parameters were assessed in each patient (Table I). All the variables were more commonly found in patients with adenomyosis than those without adenomyosis (p<0.001). The most common characteristics that were present included a bulky uterus with a sensitivity of 71.80% (95% CI: 62.60 - 78.56) and specificity of 88.46% (95% CI: 75.87 - 95.22), altered echotexture with a sensitivity 71.80% (95% CI: 63.94 - 78.56) and a specificity of 96.15% (95% CI: 85.67 - 99.33), and the pseudo-widening of the junctional zone and streaky myometrium had a sensitivity more than 62% and a specificity >84%. The different variables were combined to see their combined sensitivity and specificity. Around 15 dual (Table II) and 20 triple (Table III) variables were acquired, and individual and combined sensitivity were checked. The preponderance of dual and triple matching was more commonly observed in patients with adenomyosis than in those without adenomyosis (p<0.001).

On ultrasound, two characteristics that showed high sensitivity and specificity were a bulky uterus with altered echotexture and a bulky uterus with a streaky echotexture. The details are depicted in Table II. The best triple characteristics that showed high sensitivity and specificity were a bulky uterus with altered echotexture and streaky myometrium, a bulky uterus with altered echotexture and pseudo-widening of the junctional zone, and ultrasound echotexture with pseudo-widening of the junctional zone and streaky myometrium (Figure 1). The high specificity of transvaginal ultrasound made it a reliable investigation for the detection of adenomyosis.

DISCUSSION

Adenomyosis is a benign gynaecological condition defined by the infiltration of basal endometrium into the myometrium. The patient usually presents with menorrhagia, dysmenorrhea, and pelvic pain. The clinical diagnosis usually remains difficult because of its clinical resemblance to other gynaecological conditions, such as uterine fibroids, endometriosis, and endometrial polyps; therefore, radiology plays an important role in the detection.[2] MRI is the modality of choice, however recent meta-analysis showed comparable sensitivity and specificity of transvaginal ultrasound in the diagnosis of adenomyosis.[2,8,11] The 2D transvaginal ultrasound had comparable accuracy to the MRI in the diagnosis of adenomyosis with a pooled sensitivity of 72% and a pooled specificity of 81% as compared to the MRI which had a sensitivity of 77% and specificity of 89%.[8] Considering the emerging role of transvaginal ultrasound, radiologists must know the exact ultrasonographic features that can help in making a diagnosis of adenomyosis.[8] These included a bulky uterus, myometrial heterogeneity, myometrial cysts, streaky myometrium, pseudo-widening of the junctional zone, and a relative absence of mass effect.[4,9,10] Individual as well as combined sensitivity and specificity of each variable were calculated to further specify the most common variables that lead to the diagnosis of adenomyosis.

Among the six variables, a bulky uterus and heterogeneous myometrium had a sensitivity >70% and specificity >90%. Pseudo-widening of the junctional zone and echogenic nodules had a sensitivity >60% and specificity >80%.

To further improve the accuracy of transvaginal ultrasound, different variables were combined and the combined accuracy was calculated. The most sensitive dual variables were a bulky uterus with altered echotexture, a bulky uterus with pseudo-widening of the junctional zone, and a bulky uterus with streaky myometrium. All these dual variables had a sensitivity >70% and a specificity >90%. The presence of any of the combinations of triple variables had a specificity of >95%. The greatest sensitivity of 72.92% amongst triple variables was found in a combination of a bulky uterus with altered echotexture and a relative absence of mass effect.

In this study, transvaginal ultrasound showed a relatively low sensitivity, 74.36% (95% CI: 66.63-80.85) but high specificity, 96.15% (95% CI: 85.67-99.33) in the detection of adenomyosis. The PPV was 98.31% (95% CI: 93.40-99.70) and the NPV was 55.56% (95% CI: 44.73-65.90). This was compared with the studies done by other investigators to see the sensitivities and specificities of transvaginal ultrasound in the diagnosis of adenomyosis. One study found a specificity of 91.8% and a sensitivity of 36.8% of transvaginal ultrasound as compared to MRI in the detection of adenomyosis.[8] Another study showed a sensitivity of 72%, a specificity of 81%, a positive likelihood ratio of 3.7 (95% CI: 2.1-6.4) and negative likelihood ratio of 0.3 (95% CI: 0.1-0.5).[8] The variability in sensitivity and specificity between the studies was due to the patients' selection criteria, as this study included normal subjects in which myometrial cysts were not seen, so it had reached a specificity of almost 100%, however, sensitivity was 37.18 % (95% CI: 29.69-70.31). Another misleading variable in this study was the absence of a mass effect with a specificity of 98.08% (95% CI: 88.42-99.90) which was also not observed in the normal subjects.

This study had limitations, such as the fact that ultrasound examinations were operator-dependent and the accuracy of detection of ultrasound findings varied with sonographer's experience. Another limitation was the presence of concomitant intramural fibroids, which limited the detection of adenomyosis.

CONCLUSION

Transvaginal ultrasound is sensitive and specific initial method of choice to evaluate adenomyosis, that can help in making the diagnosis and individualising the treatment plan. MRI examination can be restricted to those patients in whom clinical suspicion is strong and ultrasound shows inconclusive or equivocal findings.

ETHICAL APPROVAL:
The study was conducted after receiving exemption from the Institutional Ethical Committee of The Agha Khan University Hospital.

PATIENTS' CONSENT:
Informed consent was waived due to the retrospective design of the study.

COMPETING INTEREST:
The authors declared no competing interest.

AUTHORS' CONTRIBUTION:
AS: Conception of the work, acquisition, analysis, interpretation of data, literature search, drafting of the initial version.
IM: Conception, data analysis, review and editing.
AM: Language editing, design of the work, data analysis.
SAS: Organisation, review, and proofreading of the manuscript.
All authors approved the final version of the manuscript to be published.

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