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Endometriosis: Clinical, Magnetic Resonance Imaging and Pathologic Findings

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ABSTRACT

Background & Objective: Endometriosis is one of the most common diseases in the female population. The range of diagnostic delays in this disease is long and leads to adverse health-related consequences. The aim of this study was to evaluate diagnostic experiences in patients with endometriosis who are candidates for laparoscopic surgery.

Materials & Methods: This cross-sectional study was performed on 433 patients with endometriosis who were candidates for laparoscopic surgery referred to Shohada-Tajrish Hospital in Tehran, Iran, between January 2016 and December 2021. A questionnaire including demographic and clinical information, MRI, and pathology reports were collected from participants. The MRI lesions were segmented and the results were compared with pathology and clinical examination. For statistical analysis SPSS software, version 22 was used.

Results: A total of 433 participated in this study with a mean age of 34.18±7.99. The average estimated duration of disease symptoms (months) was 40.58±42.33. The predictive value of clinical symptoms is weak compared to MRI. However, the probability that the disease is not present when the clinical signs are negative is acceptable in most of the endometriosis sites. MRI considerably shows the true negative rate, but its sensitivity is only relatively acceptable for the diagnosis of ascites (67.66%). Calculating the accuracy of MRI reports probably shows the overall classification of the patients via MRI test.

Conclusion: despite extensive research, there are no suitable and accurate non-invasive methods for diagnosing endometriosis**.** MRI and clinical examination alone are not useful for definitive diagnosis and it is better to examine biomarkers and artificial intelligence for non-invasive and accurate diagnosis of this disease.

Keywords: Endometriosis, Magnetic Resonance Imaging, Pathology, MRI

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Introduction

The presence of endometrial-like tissue somewhere other than its original site, such as the pelvic peritoneum, rectovaginal septum, and ovaries, indicates a chronic inflammatory disease and is called endometriosis **(1, 2)**. According to studies, 5-10% of reproductive-aged women and up to 50% of the population of infertile women may have endometriosis **(3-6)**. Fatigue, chronic pelvic pain and stress are symptoms of endometriosis, so the disease can affect women's mental, physical and social wellbeing **(7)**. According to the mentioned symptoms, this disease can lead to a decrease in quality of life, infertility and disruption of daily activities **(8, 9)**. Although many patients with endometriosis are asymptomatic, the disease can cause pain during intercourse and during menstruation. Also, the need for medical treatments and extensive surgeries and their substantial risks and financial burden are other problems of this disease **(10-12)**. The nature and cause of this disease are not exactly known, but some factors such as genetics, ecology, immune system, angiogenesis and endocrinology can be involved in causing endometriosis **(13)**.

Reasons that endometriosis is difficult to diagnose include the overlap between endometriosis-related chronic pelvic pain and other chronic pain, and the possibility of normal clinical findings in women with endometriosis **(14, 15)**. Based on the results of studies, the diagnostic delay range of the disease in many women is about 4 to 11 years **(16-19)**. Delay in the diagnosis of this disease can lead to long-term chronic pain, reduced fertility and reduced quality of life in patients with endometriosis **(20)**. Therefore, due to the high prevalence and risks of this disease, appropriate

methods should be used by physicians for rapid and accurate diagnosis of the disease.

The aim of this study was to evaluate the characteristics, demographic information and diagnostic experiences (such as MRI, clinical and pathologic finding) in patients with endometriosis who are candidates for laparoscopic surgery in Shohada-Tajrish Hospital in Tehran. The use of appropriate clinical diagnostic techniques may reduce the delay in diagnosis time and thus lead to faster patient relief, prevention of disease progression and its consequences.

Methods

Study Design and Population

This cross-sectional study was performed on all patients with endometriosis which were candidates for laparoscopic surgery and referred to Shohada-e-Tajrish Hospital as a referral educational hospital in Tehran, the capital of Iran, between January 2016 and December 2021.

Questionnaire included age, weight, height, number of pregnancies, abortion, delivery, painful menstruation, pelvic pain, pain during intercourse, pain during defecation, intermenstrual spotting, and family history of Endometriosis, history of infertility, MRI and pathology report. The MRI lesions were segmented at the site of involvement and the extent and depth of the involvement, and the results were compared with pathology. The protocol of this study was approved by the Ethics committee of Shahid Beheshti University of Medical Sciences (code: IR.SBMU.RETECH.REC.1398.346). All principles of Helsinki's Declaration were met throughout the study processes.

Statistical Analysis

SPSS platform version 22 was used for statistical analysis. Frequency and mean and standard deviation were reported. Pearson correlation coefficient and t-test was used for data analyzing at the significance level of 0.05.

Results

A total of 433 women were participated in this study with a mean age of 34.18±7.99. The mean BMI of study participants was 24.76±4.30 (16-40). Family history of endometriosis was reported in 7.4% of patients. The average estimated duration of disease symptoms was 40.58±42.33 months. 72.1% of study population were married and 55% had at least 1 pregnancy. 24% of all had never experienced hormone therapy and 85.2% did not receive hormone therapy 3 months before the surgery (Table 1).

Findings of patients' evaluations via various diagnostic tests are reported in a supplementary file. The values are described using frequency and percentage or mean± standard deviation as well as the range. Part I reports the prevalence of clinical signs for the various locations interested by endometriosis, and Topographic laparoscopic data are summarized in part II. The data about the endometriosis lesions was collected for all the study patients who underwent laparoscopic procedures. The highest incidence was found in the peritoneum and ovaries. Finally, part III illustrates the diagnosis outcomes based on MRI. With this diagnostic technique, the most prevalent observations were cysts, followed by solid cystic tumors (52.7% of right cysts and 61.4% of left cysts) and based on MRI findings, 12% rectosigmoid involvement was diagnosed among patients.

In Table 2, the diagnostic value of MRI reports is compared with the pathologic findings, which is considered as the gold standard. Sensitivity declares the true positive rate that is relatively acceptable only for diagnosis of ascites (66.67%), while the specificity of MRI was high in all evaluated areas with values higher than 70%. It shows that MRI considerably shows the true negative rate. The probability that the disease be present when the MRI findings were positive was shown by positive predictive values which were lower than 50% in all areas. Whereas, the negative predictive values for MRI were higher than 70%. Finally, the accuracy of MRI reports was calculated, which shows the overall probability that a patient is correctly classified via MRI test.

The diagnostic value of clinical examination is compared with MRI reports in Table 3. Results show the weak predictive value of clinical signs in comparison with MRI. However, according to the negative predictive values in Table 3a, the probability that the disease is not present when the clinical signs be negative is acceptable in most of the endometriosis sites. The accuracy of clinical examination in classifying the endometriosis was low, except in the area of the vagina.

Table1. Characteristics of the patients included in the study

Variable		Frequency	Percent
Age		34.18±7.99 (14-55)	
BMI		24.76±4.30 (16-40)	
Family history of endometriosis	No	401	92.6
	Yes	32	7.4

Variable		Frequency	Percent
Age at disease onset		28.74±11.15 (0-53)	
Duration of symptoms (months)		40.58±42.33 (0-360)	
Marital status	single	86	19.8
	married	312	72.1
	divorced	24	5.5
	In relationship	11	2.3
Number of pregnancies	0	195	45.0
	1	93	21.5
	1<	145	33.4
Number of abortions	0	347	80.1
	1	52	12.0
	1<	34	7.8
Delivery type	None	219	50.6
	Natural	86	19.9
	CS	101	23.3
	both	27	6.2
History of hormone therapy	no	104	24.0
	yes	329	76.0
Hormone therapy 3 months before surgery	no	369	85.2
	yes	64	14.8

Table2. Diagnostic value of MRI in comparison with pathologic findings

	sensitivity	specificity	Positive Predictive Value	Negative Predictive Value	Accuracy
Hydrosalpinx	13.48% (7.17% to 22.37%)	89.53% (85.81% to 92.56%)	25.00% (15.33% to 38.03%)	80.00% (78.53% to 81.40%)	73.90% (69.50% to 77.98%)
Non-endometrioma cyst	20.34% (13.49% to 28.73%)	79.68% (74.81% to 83.99%)	27.27% (19.79% to 36.31%)	72.75% (70.58% to 74.82%)	63.51% (58.78% to 68.05%)
cul-de-sac involvement	33.33% (0.84% to 90.57%)	95.12% (92.63% to 96.95%)	4.55% (0.90% to 19.93%)	99.51 (98.92% to 99.78%)	94.69% (92.14% to 96.60%)
Ureteral involvement	5.26% (0.13% to 26.03%)	94.69% (92.06% to 96.64%)	4.35% (0.64% to 24.22%)	95.61% (95.13% to 96.04%)	90.76% (87.63% to 93.32%)
Uterine lesions	41.77% (33.99% to 49.87%)	73.82% (68.20% to 78.91%)	47.83% (41.15% to 54.58%)	68.81% (65.52% to 71.93%)	62.12% (57.37% to 66.71%)
Diaphragm lesions	20.00% (0.51% to 71.64%)	98.83% (97.29% to 99.62%)	16.67% (2.75% to 58.62%)	99.06% (98.56% to 99.39%)	97.92% (96.09% to 99.05%)
Ascites	66.67% (9.43% to 99.16%)	98.83% (97.30% to 99.62%)	28.57% (10.92% to 56.63%)	99.76% (98.84% to 99.95%)	98.61% (97.00% to 99.49%)
Wall endometriosis	6.67% (0.17% to 31.95%)	96.64% (94.43% to 98.15%)	6.67% (0.99% to 33.70%)	96.64% (96.17% to 97.06%)	93.52% (90.77% to 95.65%)
Iliac vascular involvement	11.11% (0.28% to 48.25%)	99.53% (98.31% to 99.94%)	33.33% (4.74% to 83.41%)	98.14% (97.67% to 98.52%)	97.69 (95.79% to 98.89%)

*The vales in () show the 95% confidence interval for the estimated measures.

Table3. Diagnostic value of MRI in comparison with clinical examination.

	sensitivity	specificity	Positive Predictive Value	Negative Predictive Value	Accuracy
Vaginal involvement	0 (0.00% to 84.19%)	97.22% (95.19% to 98.55%)	0.00	99.52% (99.52% to 99.53%)	96.77% (94.63% to 98.22%)
Cervical motility	42.86% (29.71% to 56.78%)	53.05% (47.87% to 58.18%)	11.94% (8.96% to 15.75%)	86.21% (83.01% to 88.88%)	51.73% (46.91% to 56.53%)
cul-de-sac involvement	77.27% (4.63% to 92.18%)	31.14% (26.69% to 35.87%)	5.67% (4.53% to 7.07%)	96.24% (92.12% to 98.25%)	33.49% (29.05% to 38.15%)
Right uterosacral	67.24% (53.66% to 78.99%)	40.53% (35.52% to 45.69%)	14.89% (12.55% to 17.57%)	88.89% (84.43% to 92.19%)	44.11% (3 9.37% to 48.93%)
Left uterosacral	73.53% (61.43% to 83.50%)	37.53% (32.55% to 42.72%)	17.99% (15.70% to 20.52%)	88.39% (83.37% to 92.04%)	43.19% (38.47% to 48.00%)
Right adnexal adhesion	57.14% (44.75% to 68.91%)	49.04% (43.78% to 54.31%)	17.78% (14.70% to 21.33%)	85.58% (81.61% to 88.80%)	50.35% (45.53% to 55.15%)
Left adnexal adhesion	56.98% (45.85% to 67.61%)	42.94% (37.67% to 48.33%)	19.84% (16.78% to 23.30%)	80.11% (75.42% to 84.09%)	45.73% (40.96% to 50.55%)
Right adnexal mass	36.40% (30.15% to 43.01%)	70.73% (63.99% to 76.86%)	58.04 (51.28% to 64.52%)	50.0% (46.71% to 53.29%)	52.66% (47.83% to 57.44%)
Left adnexal mass	40.23% (34.28% to 46.39%)	70.06% (62.50% to 76.89%)	68.15% (61.93% to 73.79%)	42.39% (39.02% to 45.84%)	51.73% (46.91% to 56.53%)
Rectovaginal septum	45.0% (29.26% to 61.51%)	70.74% (65.97% to 75.19%)	13.53% (9.71% to 18.56%)	92.67% (90.46% to 94.40%)	68.36% (63.75% to 72.72%)

*The vales in () show the 95% confidence interval for the estimated measures.

Discussion

In this cross-sectional study, 433 patients with endometriosis who were candidates for laparoscopic surgery were selected to evaluate diagnostic experiences (such as MRI, clinical examination, and pathologic). The average estimated duration of disease symptoms (months) was 40.58±42.33. With MRI technique, the most prevalent observations were cysts, followed by solid cystic tumors. The predictive value of clinical symptoms is weak compared to MRI. However, the probability that the disease is not present when the clinical signs be negative is acceptable in most of the endometriosis sites. MRI considerably shows the true negative rate, but its sensitivity is only relatively acceptable for the diagnosis of ascites (67.66%).

According to the results of the study of G.Hudelist et al., the average time interval from the onset of the first symptoms to the diagnosis of the disease is 10.4±7.9 years, while the time interval from the onset of the first symptoms to seeking a physician is 2.3 years **(21)**. These results clearly show that the rapid diagnosis of this disease is a challenging problem all over the world. MRI can be used as the method of choice in the diagnosis of suspected deep infiltrating endometriosis **(22)**. Also, it should be noted that the results of some articles show that the use of MRI is useful for the diagnosis of deep endometriosis **(23-27)**. The results of this study show that cysts are the most common observation by MRI and the results of the study of Koninckx et al. **(27)**, confirm it. According to a study by Koninckx et al., MRI is accurate for detecting ovarian cysts, but it cannot detect small, delicate, and abnormal lesions **(28)**. Nowadays, clinical diagnosis is performed without standardization and a unified approach **(3, 16)**. Agarwal et al. have presented a unified approach and an algorithm for the clinical diagnosis of endometriosis. This algorithm is easily applicable to most physicians and the most important benefit of this algorithm is faster diagnosis of the disease and initiation of treatment without delay and invasive methods. In general, persistent pain and worsening of recurrent or persistent pelvic pain, along with other symptoms associated with endometriosis, evaluation of the patient's history and clinical examination findings may indicate endometriosis. If clinical findings are unclear, other options such as MRI may be helpful for diagnosis **(29)**.

Unfortunately, despite extensive research, there are no suitable and accurate non-invasive methods for diagnosing endometriosis. The evaluations of this study show that MRI and clinical examination alone are not useful for definitive diagnosis and it is better to examine artificial intelligence and biomarkers for non-invasive and accurate diagnosis of this disease. For example, the results of a cohort study show that CA-125, which is a glycoprotein with a high molecular

weight and is produced in the epithelium, can be a suitable marker for the diagnosis and follow-up of endometriosis **(30)**. The results of some studies also show that artificial intelligence can be used as a screening method by physicians in the future and replace diagnostic laparoscopy **(12, 31)**. Also, increasing public awareness about the symptoms of endometriosis, such as pain during menstruation, intercourse, and infertility, can lead to an early visit to the doctor and a faster diagnosis of the disease. In addition to raising public awareness, training courses to improve the diagnostic skills of general practitioners and obstetricians can help diagnose the disease more quickly.

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Authors' Contribution

BN: project administration, study design, data collection, editing, and review; MA: contributed in the study conduct, drafting the paper; MN: contributed in drafting, editing the paper, and data collection.

Conflict of Interest

The authors declare that they have no conflict of interest.

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