Research Article

The clinical importance of Magnetic Resonance Imaging with Diffusion weighted images in diagnosis and treatment planning of endometriosis.

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Abstract

Introduction: Endometriosis is a benign gynecologic disease affecting women of reproductive age. It is defined as the presence of endometrial tissue, glands, and stroma located outside the uterine cavity and associated with fibrosis and inflammatory reaction. It is a polymorphic disease that can manifest as superficial implants on the peritoneal surface; ovarian cysts called endometriomas; or deep lesions that infiltrate the peritoneal surface more than 5 mm, a condition known as deeply infiltrative endometriosis. **Patients and Methods:** This prospective study was conducted at the radiology department, Minia university hospital. Our study included twenty three female patients suspected clinically endometriosis with age ranged from (18 to 40) years old and was referred from gynecology and obstetrics department in the period between June 2019 to June 2020 after fulfilling the inclusion criteria. A written consent is taken from all patients after approval of the Medical Ethical Committee of our institution (university). **Discussion:** Endometriosis is a chronic gynecological pathology that affects females of reproductive age. It is identified as presence of functional endometrial glands outside the uterus. Hormonal changes affect these ectopic tissue and consequently the disease's clinical characteristics. The exact underlying pathogenesis remains unclear, but there are three major theories that could explain the presence of endometrial tissue in ectopic locations; these include retrograde menstruation, celomic metaplasia and lymphatic or vascular metastases with the aid of endocrine and immune factors for the development of the clinical manifestations of the disease. The clinical features of endometriosis are variable; however the most common are chronic pelvic pain and infertility. There are three types of endometriosis: ovarian (endometrioma), superficial, and deep infiltrating. Diagnosis of endometriosis depends mainly on the laparoscopy, with histologic confirmation, however it is an invasive procedure, has a risk of complications and false-negative results, also the complexities regarding to the surgical evaluation of the pelvis, so an increasing literature supporting the value of imaging is increasing, particularly ultrasound and MRI in the diagnosis of ovarian and deep infiltrating endometriosis. This prospective study was conducted at the radiology department, Minia university hospital from June 2019 to June 2020. The study included twenty three female patients suspected clinically for endometriosis with age ranged from 22 to 44 years old and referred from gynecology and obstetrics department.

Keywords: Magnetic Resonance, Endometriosis, chronic gynecological pathology

Introduction

Endometriosis is a benign gynecologic disease affecting women of reproductive age. It is defined as the presence of endometrial tissue, glands, and stroma located outside the uterine cavity and associated with fibrosis and inflamematory reaction[(1)]. It is a polymorphic disease that can manifest as superficial implants on the peritoneal surface; ovarian cysts called endometriomas; or deep lesions that infiltrate the peritoneal surface more than 5 mm, a condition known as deeply infiltrative endometriosis[(2)].

The ectopic endometrial tissue responds to hormones and drugs in a similar manner to eutopic endometrium[(3)]. Continued growth of endometriotic tissue, as with that of the endometrium is dependent upon estrogen. Thus, endometriosis is prevalent in the reproductive years with a peak incidence between 30 and 45 years of age[(3, 4)].

Initially hypothesized that retrograde menstruation was the cause of endometriosis. However, the pathogenesis of endometriosis is complex and still debated. Retrograde menstruation is neither sufficient nor necessary for the development of endometriosis. Two other theories postulate that endometriosis develops from the metaplasia of pelvic peritoneal tissue and from the transformation of circulating stem cells[5].

Pain is probably the cardinal symptom of endometriosis. Various types of pain are associated with the disease; dysmenorrhoea, deep dyspareunia and pelvic pain unrelated to intercourse or menstruation, such as pain during defecation or urinating. Infertility is another commonly associated complaint[6].

The diagnosis of endometriosis still presents several problems resulting from similarities in clinical symptoms to other benign or malignant gynecological diseases[6].

Although the definitive diagnosis is based on laparoscopy or surgery with histological verification of endometrial glands and/or stroma, imaging is necessary for treatment planning. Among imaging modalities, magnetic resonance imaging (MRI) is often used as a problem-solving additional examination in complex cases[7].

Currently, MRI is considered the best imaging technique for mapping endometriosis, since it provides a more reliable map of deep infiltrating endometriosis than physical examination and trans-vaginal ultrasound (TV U/S)[8].

MRI has several advantages, it is noninvasive as the imaging components include a large magnetic field and an electromagnetic field produced by radiofrequency (RF) waves. The second feature that makes MRI particularly attractive is its capability for multiplanar imaging without repositioning the patient, axial, sagittal, coronal, and nonorthogonal views may be obtained in a short time. Also MRI has excellent tissue-differentiating capabilities. It has intrinsic sensitivity to flowing blood[9].

However, MRI also has certain limitations. These include a relatively long scanning time and the contraindication to scan patients with cardiac pacemakers, intracranial vascular clips, and large metallic devices[10].

Diffusion weighted imaging (DWI) increases the value of MRI in the evaluation of different gynecological diseases especially in malignancy and endometriotic lesions which show restricted diffusion that is probably due to the intra-cystic blood clots[11].

Its principle is based on measuring the random motion of water molecules; Brownian motion; within a voxel of tissue. Highly cellular tissues or those with cellular swelling exhibit lower diffusion coefficients[11].

Aim of the work

The aim of this work is to emphasize the importance of pelvic MRI examination with diffusion weighted images in diagnosis and treatment planning of endometriosis.

Patients and Methods

This prospective study was conducted at the radiology department, Minia university hospital. Our study included twenty three female patients suspected clinically endometriosis with age ranged from (18 to 40) years old and was referred from gynecology and obstetrics department in the period between June 2019 to June 2020 after fulfilling the inclusion criteria. A written consent is taken from all patients after approval of the Medical Ethical Committee of our institution (university).

Inclusion criteria:

(1) Patients in child bearing period.
(2) Clinical symptoms suggestive of endometriosis, including chronic pelvic pain, dysmenorrhea, dyspareunia and infertility.
(3) Detection of endometriotic lesions at the vaginal fornix or rectum during gynecological examination.
(4) US evidence of endometriotic cysts or peritoneal implants.

Exclusion criteria:

(1) Peri and post-menopausal patients.
(2) Patients with known endometrial carcinoma (or ovarian carcinoma).
(3) Patients with general contraindication to MRI examination as presence of paramagnetic substances as pacemaker and metallic clips as well as claustrophobic patients as our device is closed.

For each patient the following was done:

(1) Full history taking:

- Personal history including age, parity and menstrual history.
- Past history of any gynecological troubles or operations.
- Family history of endometriosis reported in the family.

(2) Pelvic ultrasonography(trans-abdominal and/or trans-vaginal).

(3) MRI examination with Diffusion Weighted Images (DWI).

(4) Post-operative or post laparoscopic histopathological examination.

Methods:

Ultrasound examination:

Sonographic examination was done using an Aplio 500 ultrasound machine (Toshiba Medical Systems Co. Ltd, Tamara, Japan) equipped with a 3.5 to 5 MHz convex transducer as well as a 8.8-13.6 MHz Endocavity/ Endovaginal Transducer. The patients were examined in supine position.

Most ultrasound exams require no preparation. However to better visualize the pelvic organs; it may require a full bladder&fasting.

MRI examination:

MRI study was performed using 1.5 Tesla MR Scanner (Ingenia, Philips Healthcare, Netherlands). All patients were examined in supine position using pelvic phased array coil.

Patient preparation for MRI examination:

To acquire an optimal MRI examination, adequate patient preparation was important for optimization of the technique and to achieve perfect image quality.

Firstly, psychological preparation of the patient about the scanner environment and informing the patient about each step to make the patient felt comfortable and safe; this step was crucial for patient compliance and relaxed patient position which was critical and essential to avoid patient movement that inevitably degrades image quality to a great extent.

All metallic or paramagnetic substances were removed prior to examination.

Antispasmodic agents ashyoscin-N-butylbromide (Buscopan) were used to reduce motion artifacts due to bowel and uterine peristalsis. It can be administered either by intravenous or intra-muscular injection.

Fasting of the patients for at least 3 hours before the time of examination was required to reduce bowel peristalsis. The patient also asked not void 1 hour prior to the examination, this ensured that the bladder was moderately filled as an empty or overfilled bladder may compromise the assessment of the endome-triotic implants in the adjacent structures. Moreover, an overfilled bladder may be the cause of additional motion artifacts due to detrusor activity.

Regarding time of MRI for endometriosis assessment, it can be performed any time regardless of the cycle as mentioned by many studies as most patients with DIE have irregular menstrual cycles make it difficult to predict cycles, and so it is impossible to plan accordingly.

MRI scan protocol:

MRI examination was performed on female pelvis including conventional MRI sequences; Axial, sagittal and coronal T2WIs as well as axial T1WI and axial T1 Fat saturation.

DWI was acquired in the axial plane by using a single shot echo-planar imaging sequence with b values (0, 500, 800, 1000), TR/TE (2871/78), Slice thickness (5 mm), Gap (1.5 mm), FOV (RL 37cm, AP 31cm, FH 16cm) & reconstruction matrix (124x105).

Interpretation of images:

The images were transformed to (Philips 881030 Intelli-Space IX/LX Workstation).

(A) Analysis of conventional sequences:

Conventional MRI sequences with evaluated morphologic features of the lesions including the lesions site, size and complexity + other association findings (fluid collection).

Results

Table 1 : Mean age of 23 females clinically suspected endometriosis.

		Descriptive statistics (n=23)
Age	**Range**	(22-44)
	Mean ± SD	32.1±5.8

- The mean age of females suspected endometriosis was 32.1 years old.

Table 2: The clinical presentations of 23 patients suspected endometriosis.

		Descriptive statistics (n=23)
Pelvic pain	**Yes**	22(95.7%)
	No	1(4.3%)
Vaginal bleeding	**Yes**	13(56.5%)
	No	10(43.5%)
Infertility	**No**	16(69.5%)
	Yes	7(30.5%)
Dysmenorrhea	**No**	18(78.3%)
	Yes	5(21.7%)
Pain with full bladder	**No**	21(91.3%)
	Yes	2(8.7%)

-Pelvic pain was the most common clinical presentation in 23 patients suspected endometriosis.

Table 3: Final diagnosis of total 29 patients suspected endometriosis.

		Descriptive statistics (N=29)
Laparoscopy	**Endometriosis**	18(62.1%)
	Adenomyosis	3(10.3%)
	Endometroid carcinoma	1(3.4%)
	Hemorrhagic cyst	5(17.2%)
	Dermoid cyst	2(6.9%)

- 21 out of 29 patients-suspected endometriosis by MRI- were confirmed as endometriosis by the laparoscopy and histopathology, while other few cases vary between endometroid carcinoma, hemorrhagic cysts and dermoid cysts.

Table 4: Different sites of endometriotic lesions detected by pelvic MRI examination.

		Descriptive statistics (n=29)
Site	**Ovary**	12(41.4%)
	Both ovary	6(20.7%)
	Tube	2(6.9%)
	Ovary & Tube	1(3.4%)
	Anterior abdominal wall	1(3.4%)
	Between anterior abdominal wall & uterus	1(3.4%)
	Myometrium	3(10.3%)
	Urinary bladder	2(6.9%)
	Posterior to the uterus	1(3.4%)

- Unilateral ovarian involvement was the most common site of endometriosis.

Table 5: Different MRI sequences performed in diagnosis of the patients suspected endometriosis.

MRI sequences	Signal intensity	Descriptive statistics (n=29)
T1	**Hyper**	19(65.5%)
	Iso	4(13.8%)
	Mixed	4(13.8%)
	Hypo	2(6.9%)
T2	**Hypo**	14(48.3%)
	Iso	5(17.2%)
	Hyper	6(20.7%)
	Mixed	4(13.8%)
DWI	**Restricted**	17(58.6%)
	Facilitated	12(41.4%)
ADC	**Range**	(0.6-2.1)
	Mean ± SD	1.29±0.61
	Median / (IQR)	0.9/(0.7-2)

- Most of the cases attained high signal intensity in T1WI and low signal intensity in T2WI with 17 out of 29 cases attained variable degrees of diffusion restriction with average ADC value 1.2.

Table 6: P value of MRI sequences in the cases suspected endometriosis.

		Endometriosis		P value
		No	**Yes**	
		N=8	**N=21**	
T1	Hypo	0(0%)	0(0%)	0.009*
	Iso	3(37.5%)	3(14.3%)	
	Hyper	2(25%)	17(81%)	
	Mixed	3(37.5%)	1(4.8%)	
T2	Hypo	1(12.5%)	13(61.9%)	0.029*
	Iso	2(25%)	3(14.3%)	
	Hyper	2(25%)	4(19%)	
	Mixed	3(37.5%)	1(4.8%)	
DWI	Facilitated	5(62.5%)	7(33.3%)	0.218
	Restricted	3(37.5%)	14(66.7%)	
ADC	Range	(0.6-2)	(0.6-2.1)	0.162
	Mean ± SD	1.61±0.56	1.16±0.59	
	Median / (IQR)	1.9/(1.08-2)	0.9/(0.7-2)	

- **Fisher exact test for qualitative data between the two group**
- ***: Significant level at P value < 0.05**

Our study revealed: T1 high signal intensity and T2 low signal intensity were significant in the diagnosis of endometriosis, while DWI and ADC have no significant value in the detection of endometriosis.

Discussion

Endometriosis is a chronic gynecological pathology that affects females of reproductive age. It is identified as presence of functional endometrial glands outside the uterus. Hormonal changes affect these ectopic tissue and consequently the disease's clinical characteristics[12].

The exact underlying pathogenesis remains unclear, but there are three major theories that could explain the presence of endometrial tissue in ectopic locations; these include retrograde menstruation, celomic metaplasia and lymphatic or vascular metastases with the aid of endocrine and immune factors for the development of the clinical manifestations of the disease[13].

The clinical features of endometriosis are variable; however the most common are chronic pelvic pain and infertility. There are three types of endometriosis: ovarian (endometrioma), superficial, and deep infiltrating [13].

Diagnosis of endometriosis depends mainly on the laparoscopy, with histologic confirmation, however it is an invasive procedure, has a risk of complications and false-negative results, also the complexities regarding to the surgical evaluation of the pelvis, so an increasing literature supporting the value of imaging is increasing, particularly ultrasound and MRI in the diagnosis of ovarian and deep infiltrating endometriosis[14].

Transvaginal ultrasound is considered the first line imaging modality for endometriosis because of its availability and low cost. However, MRI has superiority to US in diagnosis and characterization of endometriotic lesions due to better soft tissue resolution, less operator dependence, and ability to image a large volume of the pelvis and consequently inform surgical planning[15]. Thus this study aimed to emphasize the use of MRI with diffusion weighted images in diagnosis and planning for endometriosis treatment.

This prospective study was conducted at the radiology department, Minia university hospital from June 2019 to June 2020. The study included twenty three female patients suspected clinically for endometriosis with age ranged from 22 to 44 years old and referred from gynecology and obstetrics department.

All cases were examined clinically, ultrasonographically and by MRI after fulfilling the inclusion criteria and obtaining informed consent and approval from the Medical Ethical Committee of our institution, then post laparoscopic histopathological examination was done.

The results of our study revealed that the range of age of the examined patients was 22-44 years old with mean 32.1±5.8 which agrees with Abo-Gamra et al.,[16] study. But another study of Jramillo‑Cardoso et al.,[14] included older patients up to 69 years. Endometriosis mainly affects females in child bearing period.

Pelvic pain was the most common presentation of patients included in our study suspected with endometriosis (95.7%) which coincides with Abo-Gamra et al.,[16] and Jramillo‑Cardoso et al.,[14], but on the other hand Ibrahim and Elsaeed [17] reported that most cases presented by abnormal uterine bleeding.
The variability in clinical presentation is attributed to difference in location of endometriotic lesions between different studies.

Regarding appearance of the lesions in MRI sequences, most of the endometriotic lesions appeared hyper intense (65.5%) in T1WI and hypo intense (48.3%) in T2WI with significant difference value in diagnosis of endometriosis (P value < 0.05), these data coincides with both Imaoka et al.,[18] and Abo-Gamra et al.,[16] who concluded that the diagnostic MRI findings of endometriotic lesions had a hyperintense signal in T1W1 probably due to subacute hemorrhage and intermediate or hypo signal intensity in T2 W1.
Endometrioma should be differentiated from dermoid cysts which had high signal on T1 and is differentiated by signal nulling on fat suppression images, compared to endometrioma that does not[19].

Another differential diagnosis is hemorrhagic cyst which usually lacks of T2 dark spot sign that is characteristic to endometrioma; small and multiple foci of low signal intensity on T2 images within the cyst due to long standing hemorrhage as reported by Bourgioti and moulopoulos[20]. Also hemorrhagic cyst may be hypointense on T1 weighted images as revealed by Kanso et al.,[21] this may be explained by early age of hemorrhage and consequently absence or decrease in the methemoglobin.

Conclusion and Recommendation

On the basis of this study we conclude that MRI has a great role in diagnosis of endometriosis and complete assessment of different pelvic compartments at the same time especially in the ultrasonograpically-indeterminate suspected

lesions as those of the uterus and bladder, it could diagnose 20 out of 23 cases through its most diagnostic finding as follow; high signal intensity on T1WI while low signal intensity in T2WI (T2 shading) which occurs due to repeated hemorrhages with consequent differential settling of blood depending on its stage of evolution.

However, this classical finding is usually seen in endometriomas whereas deep pelvic endometriosis may have variable signal intensity and are usually hypointense on both T1 and T2 due to intense desmoplastic reaction with fibromuscular proliferation.

Addition of DWI to routine MRI showed insignificant difference between females who diagnosed as endometriosis and not by MRI and this may be due to small sample size in this study. However ADC value less than 1 is highly suggestive of endometriotic lesions.
We recommend that large sample size should be evaluated.

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