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Original Research Article

Role of Diffusion Weighted Imaging (DWI) of MRI Study in Differentiation Between Adenomyosis and Fibroids of the Uterus in Al-Hilla Teaching Hospital

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Abstract
The uterine fibroid is most common solid uterine tumour , it is single or multiple benign neoplasm and present in 20-40% of women in productive age. There are several factors that are attributed to underlie the incidence and development of these common tumors, but this further corroborates their relatively unknown etiology. The most likely presentation of fibroids is by their effect on pelvic pressure symptoms or the woman's menstrual cycle .Adenomyosis of the uterus is benign uterine pathology. It is thought by many to be on the spectrum of endometriosis, with ectopic endometrial glandular tissue in the myometrium. Adenomyosis may present with dysmenorrhea and menorrhagia. Ultrasound and MRI are imaging modalities that may show characteristic findings. Diffusion weighted image in MRI has been applied to evaluate the intracranial lesion ,but technical advancement make it possible to use in extra cranial sites. The aim of this study was to assess the differences, if any, in the apparent diffusion coefficient (ADC) values of adenomyosis and fibroids. Methods and Material Total patient of sample study 56 ,Patients (*n*= 25) diagnosed by ultrasound as uterine fibroids and (n=31) as adenomyosis, who underwent pelvic MR imaging with DWI, were included in this cross section study. DWI was achieved with using a 1.5 T scanner , different *b* factors of (0, 400, and 600 s/mm) and ADC region of interest(ROI) size were located over an area of Adenomyosis, a fibroid and unaffected normal myometrium all results are correlate with histopathological result which was considered as gold standard diagnostic methods. Results using Student's *t* test to compare the ADC values of adenomyosis and fibroids. The standard deviation and the mean of the ADC values were as follows: adenomyosis 0.75 ± 0.30, fibroid 0.63 ± 0.29 and myometrium 1.39 ± 0.36. Statically, there was significant difference between the ADC values of normal myometrium and adenomyosis ($p < 0.0001$), normal myometrium and fibroids ($p < 0.0001$), and fibroids and adenomyosis ($p < 0.001$). Conclusion The present study display that ADC values have the possible to quantitatively and significantly differentiate between Adenomyosis and fibroids.

Key Words: Adenomyosis, fibroid, ADC value, leiomyoma, myoma, MRI.

دور التصوير بالانتشار المرجح للرنين المغناطيسي في التفريق بين غدي الرحم والورم الليفي للرحم

الخلاصة

الورم الليفي في الرحم هو الأكثر شيوعاً الأورام الحميدة في الرحم وموجودة في ٢٠-٤٠% نساء في سن الإنتاج. وهناك العديد من العوامل التي تعزى إلى وتكمن وراء الإصابة والتنمية هذه الأورام الشائعة، ولكن هذه المسببات غير معروف نسبيا. الاعراض الأكثر احتمالاً للأورام الليفية بأثرها على الضغط على الحوض أو الدورة الشهرية للمرأة. أدينوميوسيس (غدي الرحم) الرحم أمراض الرحم حميدة. ويعتقد الكثيرون أن تكون في نطاق بطانة الرحم المهاجر .الاعراض المصاحبة للمرض تكون غالبا الم مصاحب للدورة الشهري او نزف رحمي .الفحص بالموجات فوق الصوتية والرنين المغناطيسي للحوض يبين مميزات الحالتين المرضيتين. الغرض من الدراسة هو على الرغم من أن التصوير بالرنين المغناطيسي وكثيراً ما قادراً على التمييز بين الأورام الليفية و غدي الرحم ، أحياناً تتداخل الميزات تصوير الأورام الليفية والتنسيق أدينوميوسيس. تصوير بالرنين الانتشاري(DWI) قد يوفر معلومات مفيدة في التفريق بين الأمراض. ولذلك، كان غرض دراستنا لتقييم الاختلافات، إذا وجدت، في قيم معامل الانتشار الواضح (ADC) بين غدي الرحم والأورام الليفية. مجموع المرضى في عينة الدراسة ٥٦، بعد التشخيص بالموجات فوق الصوتية عدد المرضى مع الاورام الليفيه (*ن* = ٢٥) و غدي الرحم (*ن* = ٣١)، الذي خضع لدراسة الرنين المغناطيسي للحوض التصوير بما في ذلك الانتشار وأجرى الانتشار مع ب عوامل ٠ و ٤٠٠ و ٦٠٠ s/مم باستخدام ماسح ضوئي 1.5 T. وضعت القياسات دوروا ADC على مساحة أدينوميوسيس، الليفي وانسجة جدار الرحم العادية وقورنت النتائج مع نتائج الفحص النسيجي للمرض الذي يعتبر كمعيار الذهب للتشخيص. مقارنة قيم معامل النتشار الواضح لغدي الرحم والأورام الليفية استخدام الطالب تي اختبار. المتوسط والانحراف المعياري للقيم ADC(معامل الانتشار الواضح) وكانت كما يلي: ± لغدي الرحم 0.30 0.75 ، الورم الليفي ٠,٦٣ ± ٠,٢٩ و جدار الرحم العادي 0.36 ± 1.39 . وكان هناك فرقا يعتد به إحصائيا بين قيم ADCجدار الرحم العادي و غدي الرحم (ف < ٠,٠٠٠١)، ميوميتريوم العادي والأورام الليفية (ف < ٠,٠٠٠١)، والأورام الليفية و adenomyosis (ف < ٠,٠٠١). الدراسة الحالية تعرض قياسات ADC(معامل الانتشار الواضح) التي يمكن كمياً التفريق بين adenomyosis والأورام الليفية.

الكلمات المفتاحية : أدينوميوسيس(غدي الرحم)، الليفي، ADC القيمة (معامل نشر الظاهر)، ليوميوما، أورام العضلية، التصوير بالرنين المغناطيسي.

Introduction

Uterine fibroids (leiomyoma) are the most common benign solid uterine tumor. These are compose from smooth muscle with variable amount of fibrous tissue, it is present in up to 20% of women. They are specially common and present at a younger age in black women [1]. Fibroid (leiomyomas) represent an overgrowth of uterine smooth muscle. they usually grow gradually during the menstrual years and may decrease in size after menopause

Fibroid are hormone-dependent, increase. Adenomyosis (endometriosis interna) is ectopic endometrial gland within myometrium associated with adjacent myometrial hyperplasia .it is usually diffuse but may be focal mass or adenomyoma [1]. It is a common uterine disorder with an incidence of 20-40% [3]. clinical finding are dysmenorrhea, vaginal bleeding, irregular menstrual cycle with tender bulky uterus [1]. These two diseases often coexist together between 35% [4]. Magnetic resonance imaging (MRI) is an accurate assessment of uterine fibroids and Adenomyosis about site, size and characteristic signal intensity [1]. However focal Adeno-myosis may indistinct and overlapped from fibroid still with MRI [5,6]. As DWI can reveal abnormal signal in pathologic foci based upon measuring the random in water molecules movement (diffusion) in generally highly cellular tissue or cellular swelling has lower diffusion coefficient, we assume that ADC values may be distinct in Adenomyosis as a compared to fibroid, in uncommon case when difficult in differentiate between two entities. ADC maps were measured of the magnitude of diffusion within the tissue (calculate using different b values 0-1000s/mm^2).

The aim of this study was to estimate the apparent diffusion coefficient (ADC) values of fibroid and Adenomyosis, to differentiate between Adenomyosis and fibroid when there is atypical picture in [2]. although frequently asymptomatic, they may present with pain, abnormal bleeding, abdominal distension , recurrent miscarriage or sub fertility the symptoms depending to a certain extent on the site and size of the fibroids their location in the uterus is described as:

1.submucous_ within the cavity .
2.mural _ arising within the myometrium.
3.subserosal _ deep to the serosa.
4. pedunculated on a pedicle usually from the serosal surface.
5.cervical _rare.

convention MRI and when these two pathology coexist together, and to help those patient whom cannot take contrast and change the treatment where there is quite different in management.

Materials and Methods

The study was a cross- sectional study, This type of study characterized by its less cost, studies the relationship between different variables at a point in time. Cross-sectional analysis relates to how variables affect each other at the same time and period. The study was conducted at radiological department in Al-Hilla teaching hospital, which is the major teaching hospital at Babylon governorate, central part of Iraq.

The study was carried out during the period from November, 20th, 2016 to July 1st, 2017. The study involved any female with productive age the mean of age (42.14 years) with standard deviation $\pm$ 7.78 who present to radiological department for pelvic MRI.

56 patients were included in the study underwent radiological department and after full history and diagnosis by ultrasound as fibroid in 25 patients and 31patients as Adenomyosis ,All patient underwent to MRI examination with DWI and ADC map and the results correlate with histopathalogical results which was use as gold standard diagnostic method.

MRI protocol: fast spin echo sequences study of routine conventional pelvic MRI as well as DWI used by 1.5 Tesla of

Philips unit using SENSE (Sensitivity encoding) coil, In each patient, (ROI) was located over each lesion either fibroids or Adenomyosis with various *b* values of 0,400and 600 mm^2 /s (fig. 1.1) and (fig. 1-2). Echo-planar DWI (TR=3500 ms, TE=100 ms), post processing on the workstation and quantitative analysis was done automatically, ADC map were calculated automatically by software and then display as parametric map that reflect the degree of diffusion (the ADC value less than 1.0 to$1.1x10^{-3}mm^2/s$ are consider in adult as restriction in diffusion).

Fig:1-1 ADC mean and value in a case of Adenomyosis.

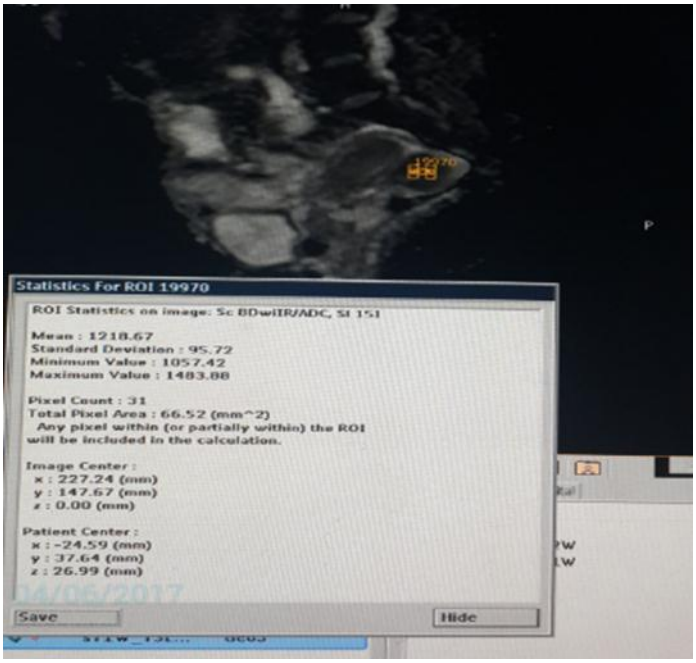

Fig: 1-2 ADC mean and value in a case of fibroid.

Inclusion and exclusion criteria: There are 56 female patient agreed to participate in the study and met the inclusion criteria of the study, and only three patient refused to participate. They were attending the radiological department for follow up and to correlate with histopathological report and exclusion criteria include those women whose to perform MRI examination had phobia, metallic material and allergy to contrast.

Tool of data collection:

A structured questionnaire was used for data collection consisting of two parts; The first part was filled by the patient, and includes questions on the demographic information includes age, social, medical, surgical gynecological & obstetric history of the patient.

The second part filled by the researcher includes the examination results includes MRI finding are Restriction with DWI and different in ADC value mean for fibroid and Adenomyosis.

Statistical Analysis:

Data were translated into a computerized database structure. The database was examined for errors using range and logical data cleaning methods, and inconsistencies were remedied. Statistical analyses were done using SPSS, Version 21 computer software for windows.

Student t-test was used to compare the means of ADC and size of myometrium

Missed data in some variables due to in complete filling of the data collecting form, when they found, were excluded from calculation.

Level of significance (P. value) ≤ 0.05 considered as significant and (P. value $\leq$ 0.01) considered as highly significant. Finally results were presented in tables and graphs.

Ethical issue:

Official approvals were granted from ministry of education. Verbal consent was obtained from the patients Keeping names and all personal information anonymous.

Results

The study sample composed of 56 female patient who presented to the radiology unit at Al-Hilla teaching hospital for diagnostic M.R.I.

The sample characteristic of the study are shown frequency distribution of age in Figure-2

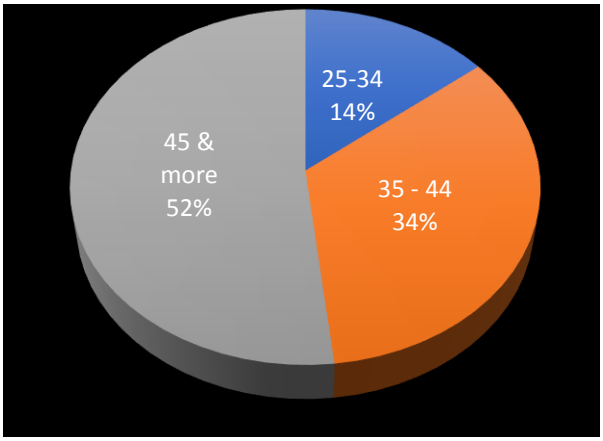

Figure-2: Frequency distribution of the age in study sample.

The sample consisted of 56 female patient who presented to the radiology unit at Al-Hilla teaching hospital. The mean age of study sample was (42.14 years) with standard deviation of (± 7.87), (51.8%) were 45 years and more, (33.9%) were between 35-44 years and (14.3%) were between 25 – 34 years

The social-demographic characteristics of study samples are shown in table -1.

The majority of study sample were married (91.1%) while only (8.9%) of them were unmarried, (60.7%) of the study sample were housewives & (39.3%) were public employee, (51.8%) of the study sample were primary school level, (8.9%) were secondary and preparatory level while (39.3%)were college graduated, (60.7%) were of medium socioeconomic class, (30.4%) were of low socioeconomic class and (8.9%) of high socioeconomic class.

The relation between the medical history and surgical history with study sample are shown in table (2) At this table, 60.7% of study samples had negative medical history while 8.9% has DM and 30.4% has HT.

Table 1: Social history of study samples

		No.	%	Cumulative Percent
Social status	Unmarried	*5*	*8.9*	*8.9*
	Married	*51*	*91.1*	*100.0*
	Total	*56*	*100*	
Occupation	Housewife	*34*	*60.7*	*60.7*
	public employee	*22*	*39.3*	*100.0*
	Total	*56*	*100.0*	
Education level	Primary	*29*	*51.8*	*51.8*
	secondary & preparatory	*5*	*8.9*	*60.7*
	college graduate	*22*	*39.3*	*100.0*
	Total	*56*	*100.0*	
Socio economic status	Low	*17*	*30.4*	*30.4*
	Medium	*34*	*60.7*	*91.1*
	High	*5*	*8.9*	*100.0*
	Total	*56*	*100.0*	

so 69.6% not take any drugs of chronic disease but 21.4% take antihypertensive treatment and 8.9% take hypoglycemic treatment. About the family history of chronic disease 60.7% have no family history, 39.3% have positive family history of HT. The surgical history of study sample 57.1% have negative surgical history, 21.4% have C/S, 12.5% have appendectomy and 8.9% have thyroidectomy.

Table 2: gynecological history of study samples

		No.	%	Cumulative Percent
Menstrual history	Irregular menses	*27*	*48.2*	*48.2*
	Regular menses	*29*	*51.8*	*100.0*
	Total	*56*	*100.0*	
Duration of menses	3-7 days	*32*	*57.1*	*57.1*
	>7 days	*24*	*42.9*	*100.0*
	Total	*56*	*100.0*	
Dysmenorrhea	No	*10*	*17.9*	*17.9*
	Yes	*46*	*82.1*	*100.0*
	Total	*56*	*100.0*	

The relation between the gynecological history and study sample are display in table (2) and shows that 48.2% have irregular menstrual cycle and 51.8% has regular cycle. 57.1% of study sample have normal duration of menses while 42.9% have long duration. 82.1% have dysmenorrhea compare with 17.9% have no dysmenorrhea.

The obstetrical histories of study sample with Adenomyosis and fibroid are shown in table (3). The obstetrical history show that 57.1% have parity history less than 2 child, 33.9% have 3-5 child and 8.9%

have >6 child .69.6% of study sample have no history of abortion, and majority have no contraceptive pills (51.8%) while 39.3% take pills and 8.9% uased IUCD. 51.8% of study sample have no history of infertility, but 30.4% have secondary infertility.

Table 3: Obstetric history of study sample.

		No.	%	Cumulative Percent
Parity	<=2	*32*	*57.1*	*57.1*
	3-5	*19*	*33.9*	*91.1*
	>=6	*5*	*8.9*	*100.0*
	Total	*56*	*100.0*	
Abortion	No	*39*	*69.6*	*69.6*
	Yes	*17*	*30.4*	*100.0*
	Total	*56*	*100.0*	
Hx. of contraception	None	*29*	*51.8*	*51.8*
	Pills	*22*	*39.3*	*91.1*
	IUCD	*5*	*8.9*	*100.0*
	Total	*56*	*100.0*	
Hx. of infertility	None	*29*	*51.8*	*51.8*
	Primary	*10*	*17.9*	*69.6*
	secondary	*17*	*30.4*	*100.0*
	Total	*56*	*100.0*	
Duration of infertility	5 or less	*15*	*26.8*	*55.6*
	5-10	*7*	*12.5*	*81.5*
	more than 10	*5*	*8.9*	*100.0*
	Total	*27*	*48.2*	

The frequency distribution of fibroid and Adenomyosis among the study sample are shown in table (4) the sample study divided in two group by ultrasound study to fibroid (no.25) 44.6% of study sample and Adenomyosis (no.31) 55.4% of study sample. The student T-test of ADC of both Adenomyosis and fibroid are show in table (6).

Table 4: Frequency distribution of fibroid & adenomyosis among study sample.

		No.	%	Cumulative Percent
	Fibroid	25	44.6	44.6
	Adenomyosis	31	55.4	100.0
	Total	56	100.0	

Table 5: Mean, standard deviation & standard error of the mean of ADC of both adenomyosis & fibroid.

	No.	Mean	Std. Deviation	Std. Error Mean
ADC. Of fibroid	25	.6320	.09946	.01989
ADC of Adenomyosis	31	.7529	.10609	.01905

Table 6: Student T- test of ADC of both adenomyosis & fibroid.

	Test Value = 0					
	t	D. f	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
ADC.fib	31.773	24	.000	.63200	.5909	.6731
ADC of adenomyosis	39.514	30	.000	.75290	.7140	.7918

Table 7: Mean, standard deviation & standard error of the mean of myometrium among study samples

	No	Mean	Std. Deviation	Std. Error Mean
normal myometrium	56	1.3018	.05644	.00754
Myometrium of adeno	31	1.3065	.05947	.01068
Myometrium of fibroid	25	1.2960	.05307	.01061

The student T-test of myometrium among study sample are shown in table-8

Table 8: Student T- test of myometrium among study sample

	T	d.f	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
Normal myometrium	172.592	55	.000	1.30179	1.2867	1.3169
Myometrium of adeno	122.309	30	.000	1.30645	1.2846	1.3283
Myometrium of fibroid	122.098	24	.000	1.29600	1.2741	1.3179

Discussion:

The fibroids and Adenomyosis are common gynecological problems between the productive age females. The mean age in our study (42.14 years) with stander deviation ± 7.78 but several studies has reported a mean age over (50 years) for women undergoing hysterectomy for Adeno-myosis [7-9] and the mean age of fibroid (40.4±6.9 years) [10]. One of the causes in these different in mean ages of the patient are due to developing of diagnosis modalities specially the MRI. DWI is a form of MRI based upon measuring the random Brownian motion of water molecules within avoxel of tissue, any restriction in movement of water indicate the abnormal cell member and cellularity of pathological tissue [11]. The ADC of a structure represents the slope of the signal vs. *b* value. The degree of restriction depend on integrity of cell membranes and the cellularity of the tissue [12-13]. Generally, the malignancy associated with restricted diffusion, due to increase cellularity, since water diffusion is restricted in highly cellular tumors [14,15]. Adenomyosis and fibroids, demonstrate region of low-signal intensity on T2-weghted image [11]. Therefore we need additional imaging tool to separate these two entities with very different treatment option. We establish a significant difference in the ADC values of Adenomyosis and fibroid, with the difference of their values with normal myometrium. The mean ADC of adenomyosis ($0.75x10^{-3}mm^2/s$), of fibroid ($0.63x10^{-3}mm^2/s$). A recent study reported similar finding in 12 patient [16]. By compare with other study, about 50 patient with fibroid and 43 patients with adenomyosis, underwent pelvic MRI imaging including ADC value. The mean of ADC value of fibroid higher than our ($0.64x10^{-3}mm^2/s$, in our study $0.63x10^{-3}mm^2/s$) and adenomyosis higher than our study ($0.86x10^{-3}mm^2/s$,in our study $0.75x10^{-3}mm^2/s$) and myometrium (1.39± 0.36). There was significant different statistically between the ADC of normal myometrium and fibroid ($p<0.0001$), normal myometrium with Adenomyosis ($p<0.0001$) and fibroid and Adenomyosis ($p<0.001$). Recently, there have been other reports of DWI for characterization of Adenomyosis, leiomyomas and normal uterine tissue although fewer in number of patient than our study [16,17]. The values reported in this study tend to vary significantly not only for pathology such as fibroids, Adenomyosis but also for myometrium. The values reported for Adenomyosis are higher than we found ($1.76x10^{-3}mm^2/s$), vs. our study ($0.75x10^{-3}mm^2/s$). The values reported for fibroid were also higher than our study ($1.7x10^{-3}mm^2/s$), vs. our study ($0.63x10^{-3}mm^2/s$). Many method-logical factors contribute for these different results. The MRI systems used are from different vendor .Two of the previous studies used a method involving different *b*- values in 1st study used three b values (50,400 and 800), and in 2nd study involving only two *b*–values (0,1000), which could be overestimated ADC values. Our technique used three *b* factors of (0, 400, and 600 s/mm) using a 1.5 T scanner. The three b values method may be accurate because it minimized the effect of perfusion effect. Finally, the different values and different varies in results obtained in the various studies could also arise from different patient samples .variability of reported ADC values has been seen with other condition, including metastasis [18,19]. and Because of differences in imaging sequences and system Therefore, the reader should exercise caution and a need for standardization of protocols to allow for reproducibility among imaging sites and vendors.

Conclusion:

We have established a significant difference in the ADC values of leiomyoma and Adenomyosis These difference of ADC values may be exploited to differentiate between these two entities when the convention imaging features are non –diagnostic.

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