Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 2, 2021, Pages. 1142 - 1156
Received 20 January 2021; Accepted 08 February 2021.

Role of Diffusion Weighted Imagining in Evaluating Uterine Mass Lesions

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ABSTRACT

To assess role of Diffusion Weighed Imaging in diagnosinguterine lesions.The aim of the study is to evaluate the importance of DWI sequence and ADC values in differentiating benign and malignant lesion.To evaluate Diffusion Weighed Imaging characteristics ofvarious uterinelesions.The study targets the role of DWI in detecting adenomyosis and leiomyoma (fibroids) based on ADCvalues.The study also targets the role of DWI in detectingcarcinoma endometrium and carcinoma cervix based on ADCvalues.

Keywords:

1. Introduction

Uterine tumours are a frequently visualised in in postmenopausal women as well as reproductive age group. These are either benign or malignant masses of the uterus. The uterine leiomyoma, Adenomyosis and endometrial polyps are common benign lesions of the uterus, whereas, malignant lesions of the uterus are cervical carcinoma and endometrial carcinoma.[1] Among benign tumours of the myometrium, uterine leiomyoma is most common. It is frequently termed as “fibroids”. They are the commonest benign uterine lesions. Nearly 70% women were found to have uterine fibroids before menopause. These lesions has a great consequence on their health are commonly seen in women of reproductive age, however they remain asymptomatic. The most frequent symptoms include pain in abdomen, dysmenorrhea and excessive menstrual bleeding. The principal line imaging modality preferred in the analysis of uterine fibroids is ultrasound. One of the sensitive methods for evaluation of uterine fibroids is Tran abdominal sonography (TAS) or Transvaginal ultrasound sonography (TVS).[2,3] However, ultrasound has poor sensitivity for small lesions (<5mm).2 Another mode of diagnosing uterine fibroids are Computed tomography (CT). However it has disadvantage over than pelvis ultrasonography (USG), in that there is radiation exposure in CT. Magnetic resonance imaging (MRI) is a betterelineator of soft tissue and it is more sensitive for uterine leiomyoma imaging.[3]

The most common benign lesions seen in cases of reproductive age group are adenomyosis. They present with dysmenorrhea, menorrhagia and lower abdominal pain. Both uterine fibroids and adenomyosis have same clinical presentation and may overlap making the diagnosis challenging.[4]

In developed countries the commonest gynaecological malignancy is Endometrial carcinoma and it stands as the second commonest gynaecological cancer in developing countries, next to cervical cancer.9 Worldwide incidence of endometrial carcinoma is found to be 26/ 100000 women.10 The incidence is found to be 5.9 /100,000 women in developing countries and is 4.3 /100,000 women in India. [5,6] The carcinoma is more prevalent in postmenopausal women, as the incidence is approximately 60- 70% in postmenopausal women, 20-25% in perimenopausal and only ~5% in premenopausal women. High oestrogen levels or unopposed oestrogen, nulliparity/ low parity, early menarche, late menopause, polycystic ovarian syndrome (PCOS), functional ovarian tumours tamoxifen therapy, obesity.[7]

It is mandatory to discriminate between benign and malignant conditions as treatment changes accordingly. Lesions of benign origin usually are treated conservatively or set for follow-up,

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rarely surgical intervention is done, whereas for lesions of malignant origin require surgery with or without adjuvant therapy and this remains as protocol in treating these patients.[8] Despite of availability of different imaging techniques like pelvis sonography, CT and MRI of pelvis, still it cannot be completely relied to differentiate between the benign and malignant uterine lesions. Hence, the newer techniques have to be adopted which are non-invasive and easy to discriminate between benign conditions and malignant conditions of uterus12. One such sequence is a newer MRI technique called Diffusion-weightedimaging equence.[9] It works on the base of water molecules diffusion (Brownian motion) in the extra-cellular space. It was designed to detect lesions in brain, but now it is being increasingly used to evaluate extra-cranial regions including the female pelvis. There are many such studies done which emphasis the role of ADC value in in normal layers of uterus and the various masses. Few literature studies about the role of ADC in assessment of uterus and uterine lesions using the diffusion-weighted MR imaging has been done.[10,11]

2. Materials And Methods

This was a descriptive study done in the Department of Radio diagnosis Sri Lakshmi Narayan Medical college (SLIMS). The patients who came with chief complaints of uterine symptoms or referred from gynaecology department for further evaluation or on any imaging modality who fulfilled the inclusion criteria or were referred for MRI-pelvis were involved in the study group with consent. The study was performed between December 2018 and July 2020.

Inclusion criteria:

- All patients with clinical and ultrasound or Computed Tomography diagnosis of uterine lesion will be included.
- All patients who were referred for MRI Pelvis with clinical and ultrasound suspicion of uterinelesions.
- Age more than 18years

Exclusion criteria:

☐ Patients who have contraindication for Magnetic Resonance Imaging like those with pacemakers, cochlearimplants.

☐ Claustrophobicpatients

Sampling:

- Sampling population: All women who attended the department of Obstetrics and Gynaecology/ referred for MRI/ diagnosed to have uterine lesion based on clinical presentation and imagingmodalities like Ultrasonography and biopsy between December 2018 and July 2020.
- Sampling technique: Convenience sampling of eligible candidatesas per inclusioncriteria.

STUDY PERIOD: 18 months

Study procedure:

Equipment details:

Machine name: SIEMENS, 1.5 T MAGNETOM ESSENZA MRI scanner(Image-8).

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Field strength: 1.5 TESLA Bore size: 60cm
Magnet length: 131 cm

Mri protocol:
MRI protocol consisted of the following A phased array body coil was used.

Sequences:
MR imaging was done for all the 47 patients in department of Radio-diagnosis using Siemens 1.5 T MAGNETOM ESSENZA MRI scanner. Weobtained the following MRI sequences as Axial turbo spin echo T1 weightedsequence, sagittal turbo spin echo T2 weighted sequence, DWI sequences.
Apparent diffusion co-efficient maps will be automatically generated by using software supplied with the Magnetic Resonance unit. Apparent diffusion co-efficient maps will be reconstructed from theseimages

Parameters:
The parameters for various sequences (table 3) are provided in a table below. Gap 35%, ; no of slices-30Averages 5 Acquisition time- 3 min, parallel acquisition technique factor,; free breathing ; b values of 50, 400 and 800s/mm2

TABLE 3: PARAMETERS USED IN MRI

	TR (MS)	**TE (MS)**	**SLICE THICKNESS (MM)**	**INTERSLICE GAP %**	**FOV (MM)**
T1WI	580	21	4	10	220
T2WI	4000	79	4	10	220
DWI	3500	76	4	10	200

The T1-weighted gradient echo sequence was obtained in axial plane with above mentioned factors. The T2-weighted gradient echo sequence was obtained in sagittal plane. The T1 and T2 weighted images was used to assess the signal intensity of the lesion (isointense, hypointense and hyper intense).
The DWI sequence was obtained in axial plane. This DWI had three b values of 50,400 and 800 sec/mm2 with diffusion encoding gradient. The time consumed to image DWI was 3-4 minutes. The imaging soft-ware automatically generated a pixel based ADC map in console.

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ADC values of the mass lesion were calculated by placing region of interest (ROI) in the solid area of lesion. It was made sure that vessels, cystic areas are excluded with the help of T2 images for localization of lesions and were mirrored to ADC maps. Care was taken to place the ROI in pathological tissue and avoid non-pathological area. It was further categorized as benign or neoplastic based on the apparent diffusion co- efficient values and diffusion characteristics. ADC values of pathological endometrium, myometrium and cervix were taken in patients with benign and malignant conditions of the uterus by placing the ROI and ADC values were calculated. ADC values were correlated with clinical features and histopathological reports.

Parameters studied in mri images:

1. Location of the lesion- whether the lesions are focal ordiffuse.
2. Lesion conspicuity- Well defined or illdefined.
3. Signal intensity of the lesion T1 and T2 WI – we compared the intensity of the lesion to the back ground myometriumas

a. Hypointense ,hypointensity means the lesion is showing low signal when compared to muscle surroundingit.
b. Isointense, the signal intensity is similar to that of muscles aroundit.
c. Hyperintense, the signal intensity is higher than that of muscles aroundit.

4. Diffusion weightedimages:

a. Restriction, when the signal is bright on the imaging when compared to surroundingstructures.
b. No restriction, when the signal is dark on the imaging when compared to surrounding structures.

5. ADC value calculation from ADC maps is doneautomatically.

3. Results

In our study out of the 47 patients included in study with uterine lesions, a clinical diagnosis of benign was made in 19 patients that included 5 cases of adenomyosis and 14 cases of fibroids. A cytopathological diagnosis of malignancy was made in 28 patients that included 19 cases of carcinoma of cervix and 9 cases of carcinoma endometrium. The findings are shown in graph (figure1) and table-4.

FIGURE-1: TOTAL CASES OF BENIGN AND MALIGNANT LESIONS OF THEUTERUS.

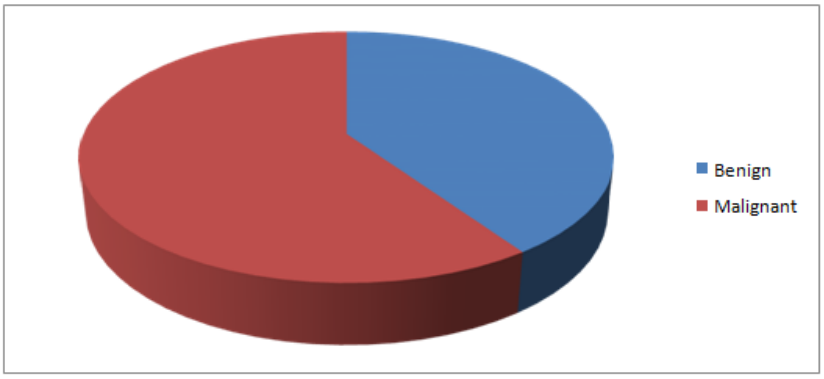

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TABLE -4: TOTAL CASES OF BENIGN AND MALIGNANT LESIONS OF THEUTERUS.

FINAL DIAGNOSIS	NUMBER OF CASES
Benign	19 (40.42%)
Malignant	28 (59.57%)

Case-1

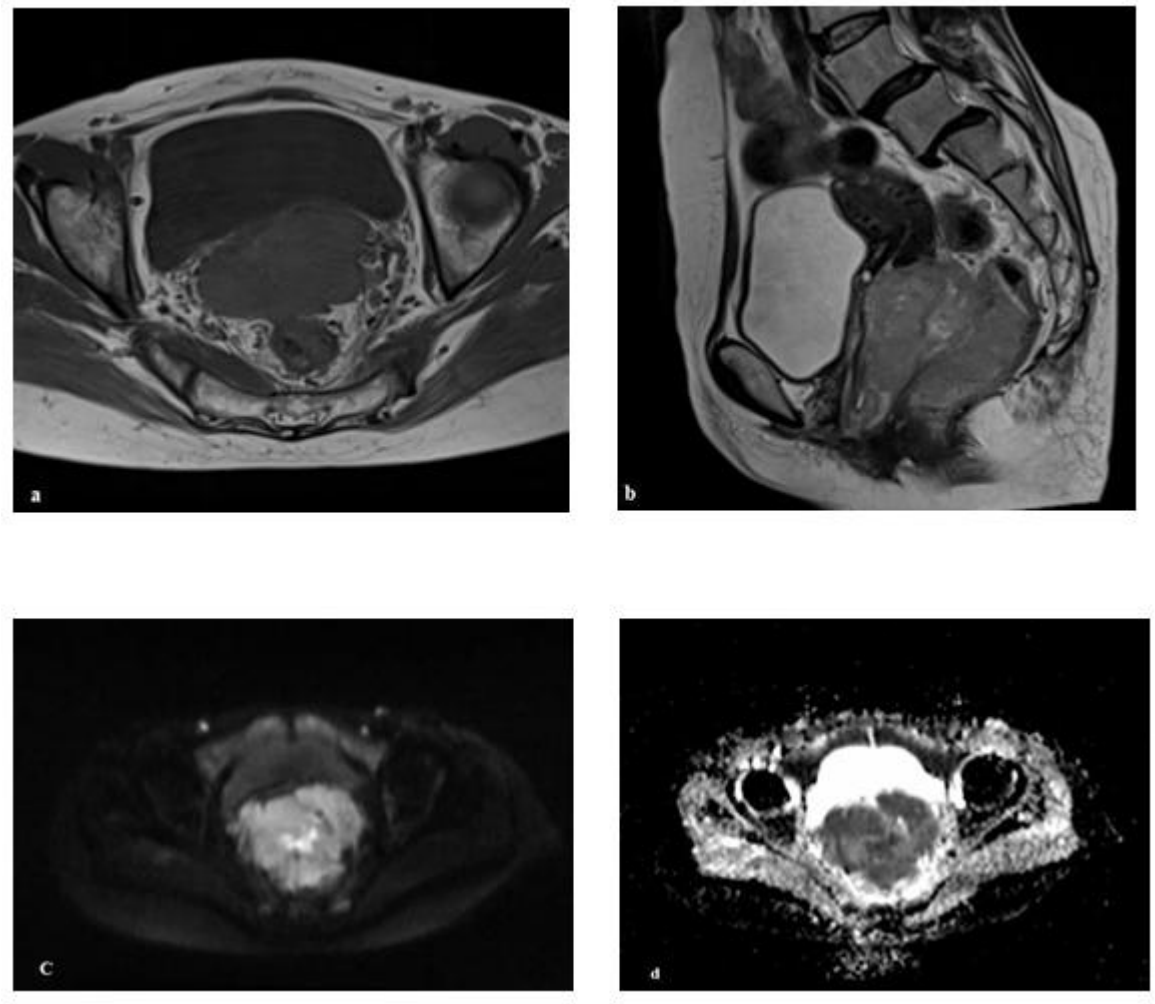

IMAGE-9: (a)T1W axial sequence shows that there is a distinct isointense lesion noted comprising the posterior wall of the cervix, with extension into the posterior and right lateral wall of cervix.(b) T2W sagittal sequence shows that there is a distinct hyperintense lesion noted comprising the posterior wall of the cervix, with extension into the posterior and right lateral wall of cervix, invading the rectum. (c)DWI axial sequence shows areas of hyperintensity in the mass

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lesion. (d) ADC axial sequence shows there is corresponding low ADC values (0.698x10-3 mm2/sec) suggestive of restricted diffusion.

In our study out of the 47 patients included in study with uterine lesions, a cytopathological diagnosis of benign was made in 19 patients that included 5 cases of adenomyosis and 14 cases of fibroids. A cytopathological diagnosis of malignancy was made in 28 patients that included 19 cases of carcinoma of cervix and 9 cases of carcinoma endometrium. The findings are shown in graph (figure2) and table-5.

FIGURE-2: COMPONENTS OF BAR DIAGRAM SHOWING DISTRIBUTION OF BENIGN AND MALIGNANT UTERINE LESIONS

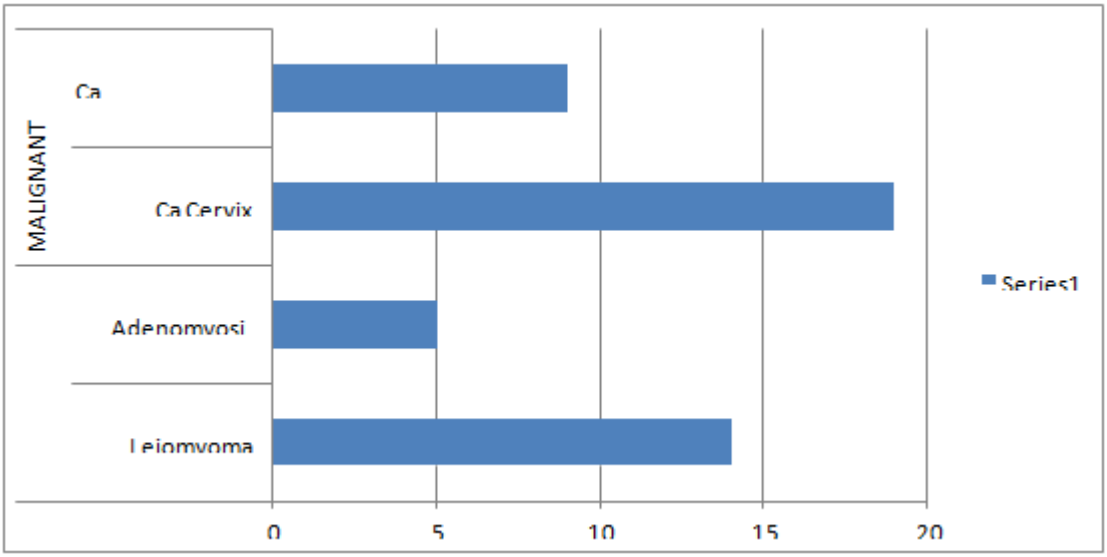

TABLE-6: FREQUENCY DISTRIBUTION OF AGE IN BENIGN AND MALIGNANT UTERINE LESIONS

Age (years)	Benign (percentage)	Malignant (percentage)
21-40	6 (31.58%)	0
41-60	13 (68.42%)	21 (75%)
61-80	0	7(25%)

Of the 19 benign cases included in study with uterine lesions, Majority of the leiomyoma were multiparous, i.e 11 (78.57%) and 2 cases (14.29%) were nulliparous and one case (7.14%) was

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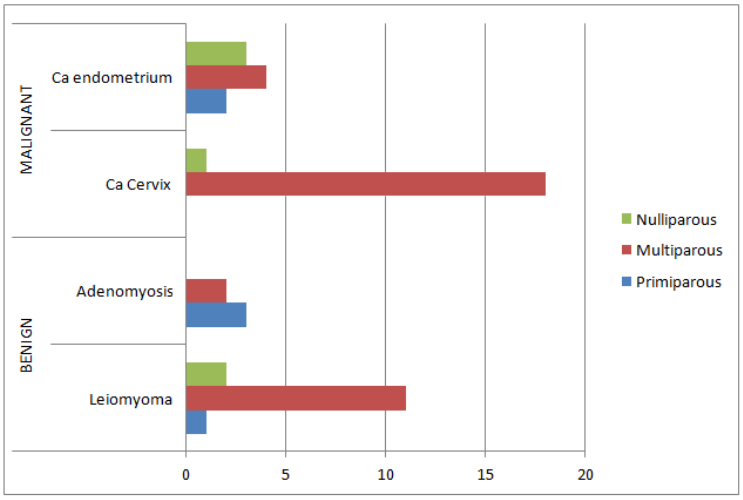
primiparous. Whereas in Adenomyosis 3 cases were primiparous and 2 cases were multiparous. Of the 28 malignant cases included in study with uterine lesions, majority of the carcinoma cervix (94.74%) and carcinoma endometrium (44.44%) cases were multiparous. A few cases of carcinoma endometrium 3 (33.33%) were nulliparous. The findings are shown in graph (figure-4) and table-7.

FIGURE-4: COMPONENETS OF BAR DIAGRAMSHOWING CHARACTERISTICS OF PARITY WITH MALIGNANT AND BENIGN UTERINELESIONS.



Case-3:

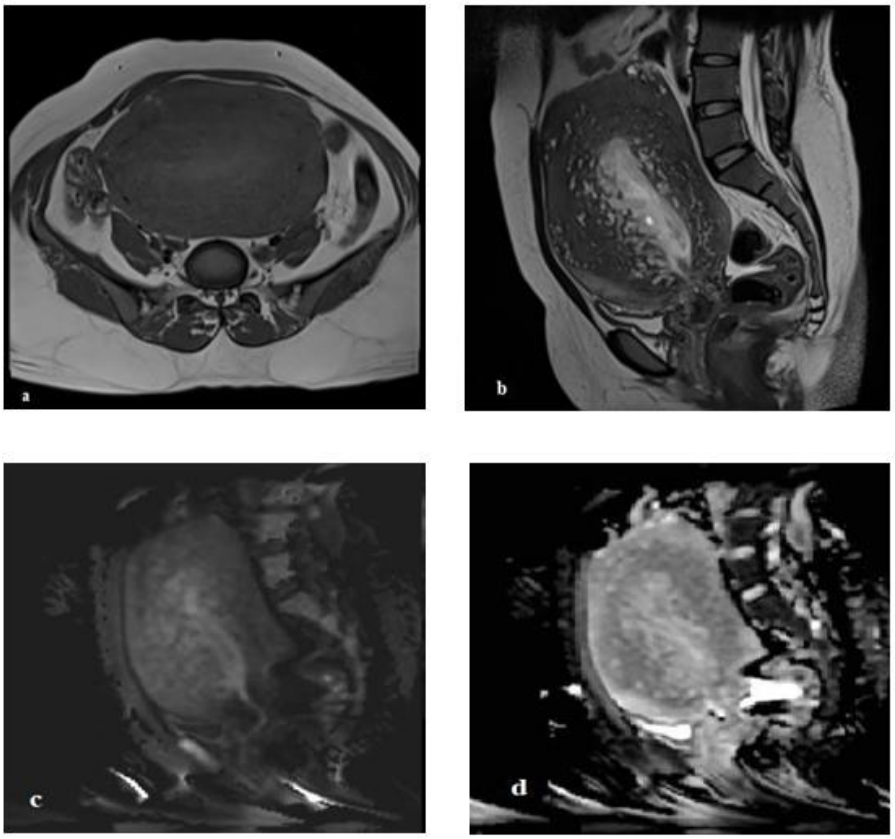


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IMAGE -11: (a)T1W axial sequence shows enlarged uterus with asymmetric thickening of junctional zone which shows homogenously isointense signal.(b) T2W sagittal sequence shows that there is ill-defined hypointensemyometrial lesion with multiple tiny hyperintense foci embedded within myometrium. (c)DWI sagittal sequence shows areas of low signal in the solid areas of mass lesion. (d) ADC sagittal sequence shows there are corresponding high ADC values (1.231X10-3mm2/sec.)

TABLE-7: FREQUENCY DISTRIBUTION SHOWINGCHARACTERISTICS OF PARITY WITH MALIGNANT AND BENIGN UTERINE LESIONS.

	BENIGN		MALIGNANT	
	Leiomyoma (percentage)	Adenomyosis(percentage)	Carcinoma Cervix (percentage)	Carcinoma Endometrium (percentage)
Primiparous	1(7.14%)	3(60%)	0(0%)	2(22.22%)
Multiparous	11(78.57%)	2(40%)	18(94.74%)	4(44.44%)
Nulliparous	2(14.29%)	0(0%)	1(5.26%)	3(33.33%)
Total	14	5	19	9

Characterization of lesions on t1 wi:
The lesions were interpreted as hypointense (benign group-14 lesion, malignant group-6 lesions), isointense (benign group- 5, malignant group-22) on T1 WI images with their distribution given in figure-7 and table-10.

FIGURE-7 COMPONENTS OF BAR DIAGRAM SHOWING T1 –WI CHARACTERIZATION OF LESION IN MALIGNANT AND BENIGN GROUP

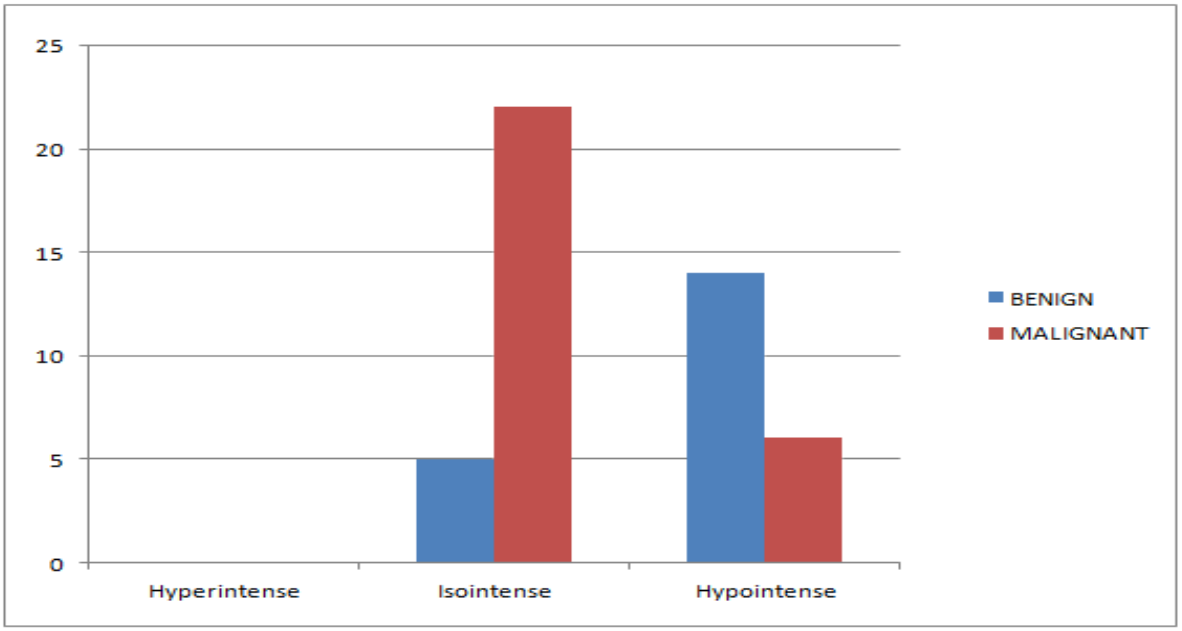

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TABLE-10: DISTRIBUTION OF T1 CHARACTERIZATION OF UTERINE LESIONS IN MALIGNANT AND BENIGN GROUPS.

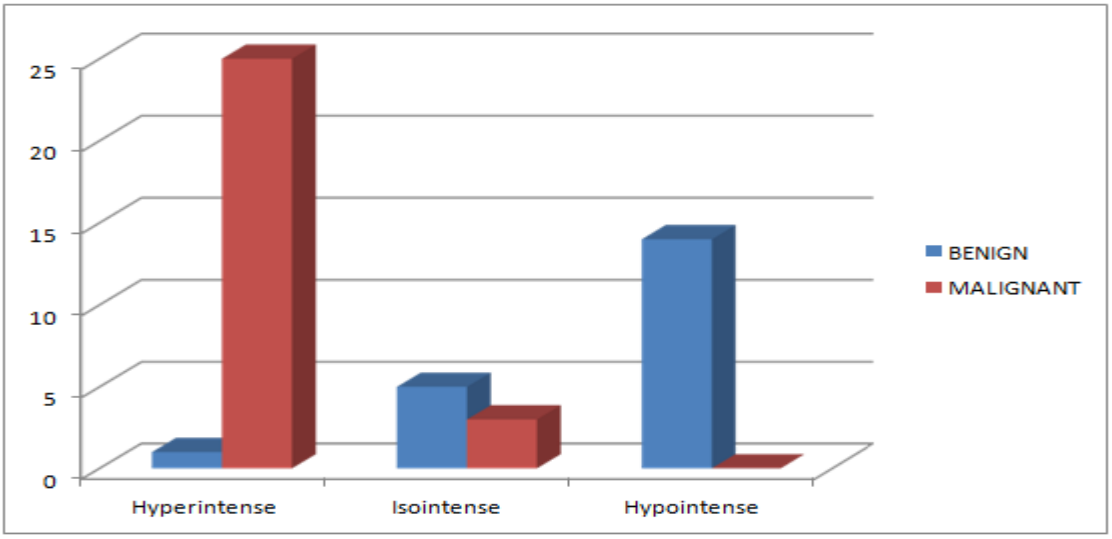
	Hyperintense	Isointense	Hypointense	Total	p-value
Benign	0	5(26.31%)	14(73.69%)	19	<0.01
Malignant	0	22(78.57%)	6(21.42%)	28	
Total	0	27	20	47	

*Fishers Exact test. The distribution of T1 depiction of the lesion was statistically significant among the benign, malignant groups (p- value 0.0004)

Characterization of lesions on t2 wi:

The lesions were interpreted as hyperintense (Benign group-1, malignant group-25) hypointense (benign group-14 lesion), isointense (benign group- 5, malignant group-3) on T2 WI images with their distribution given in figure-8 andtable-11.

FIGURE 8: COMPONENTS OF BAR DIAGRAM SHOWING T2 –WI CHARACTERIZATION OF LESION IN MALIGNANT AND BENIGN GROUP



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Case-5:

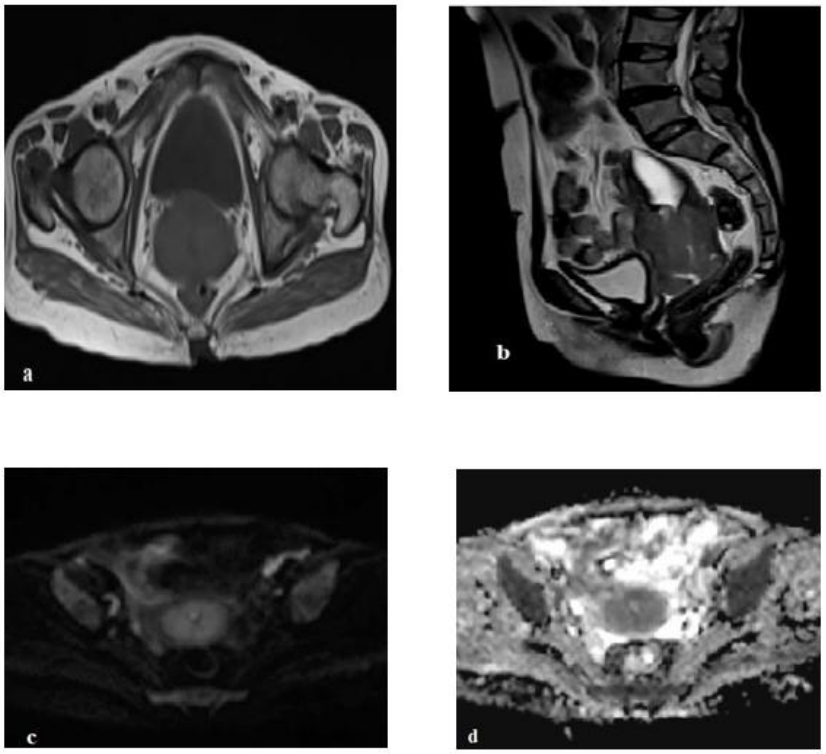

IMAGE -13: (a)T1W axial sequence shows that there is a distinct isointense lesion noted circumferentially in the wall of the cervix, with anterior and posterior extension.(b) T2W sagittal sequence shows that there is a distinct hyperintense lesion noted circumferentially in the wall of the cervix, with extension posteriorly and anteriorly into bladder mucosa (c)DWI axial sequence shows areas of hyperintensity in the mass lesion. (d) ADC axial sequence shows there are corresponding low ADC values (0.892x10-3 mm2/sec) suggestive of restricted diffusion.

Mean a

TABLE-13: MEAN ADC VALUES OF UTERINE LESIONS IN MALIGNANT AND BENIGN GROUP.

Group	N	Mean(x 10^{-3})	Std. Deviation	p-value
Malignant	19	**0 .827**	0.152	<0.01
Benign	28	**1.373**	0.126	

*Used Unpaired t-test,

The depiction of the lesion in terms of ADC values was statistically significant between benign and malignant groups (p-value=0.0001)

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TABLE-14: MEAN ADC VALUES OF VARIOUS UTERINE LESION

Diagnosis	N	Mean	Std. Deviation
Carcinoma Cervix	19	0.826	0.152
Carcinoma Endometrium	9	0.835	0.047
Leiomyoma	14	1.356	0.133
Adenomyosis	5	1.415	0.209

A total 47 patients were included in study, benign lesions were 19 and malignant cases were 28 in number. Out of 19 benign cases, 5 cases were adenomyosis and 14 cases were of fibroids/ leiomyoma. Out of 28 malignant cases 9 were carcinoma endometrium and 19 were carcinoma cervix. The results showed that between 41-60 years of age group benign and malignant conditions were more common, however 6 out of 19 benign cases was between 20-40 years of age group. It was found that majority of the leiomyoma were multiparous women, i.e 11 (78.57%), whereas in Adenomyosis 3 cases were primiparous. Of the 28 malignant cases, majority of the carcinoma cervix (94.74%) and carcinoma endometrium (44.44%) cases were multiparous. A few cases of carcinoma endometrium 3 (33.33%) were nulliparous. Around 78.23% benign cases presented with dysmenorrhea and 21.05% cases presented with symptoms of abnormal uterine bleeding.

4. Discussions

In our study using 1.5 T MRI ,we estimated the ADC values of uterine benign and malignant lesions .Of the 47 patients with uterine lesions malignant group comprises 59.57 % and benign group comprises 40.43% we included malignant lesion like Carcinoma Cervix and Carcinoma Endometrium. Benign lesions include Leiomyoma and Adenomyosis.[12]

In our study the patients with benign and malignant lesion mean age range was 40-60 years. However, >60 years age group malignant lesions were noted, whereas in the age group <40years benign lesions were present in this study. A statistically significant difference was observed between the age of patients with malignant and benign groups.The majority of cases in our study were carcinoma cervix, and it was associated with factors which included active sexual life, multiparity and increased usage of OCP's which a significant outcome.[13]

Since malignant lesions have the capacity to replicate, they have more number of cells which is why they show diffusion restriction on DWI sequence. In the Malignant group lesions out of 28 patients, 27 patients showed restriction of diffusion on DWI and in 1 patient showed no restriction of diffusion. In the benign group out of 19 patients all lesions did not show diffusion restriction.[14] To detect ADC values, the region of interest chosen was solid areas. The solid areas were chosen on T2W sequence and the ROI cursor was placed at the desired area in ADC sequence. Thereby, the ADC values were calculated.There are few studies done which compared mean ADC values of benign and malignant lesions ,Fujii et alwas one among them. The mean and standard deviation of ADC values (×10−3 mm2 /s) for sarcoma, (0.97±0.02) Endometrial

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carcinoma, (0.98±0.21); Endometrial polyp;(0.58±0.45); sub mucosal Leiomyoma;(1.37±0.28) .The ADC values differed significantly between malignant (0.98±0.19) and benign lesions (1.44±0.34) (P<0.01). They determined malignant lesions with ADC value of less than 1.15×10−3mm2/sec for acquiring the highest accuracy.[15-17] Sensitivity, specificity, and accuracy are 84.6%, 100%, and 92%, respectively. ADC measurement can give useful information in differentiating malignant from benign uterine lesions.

In our study we measured difference between ADC values of benign and malignant lesions using Student's t-test. The ADC values in a study could distinguish between malignant (0.796±0.138) and benign lesions (1.278±0.273) found to be statistically significant (p-value <0.01).[18] Our findings Correlated with results of study done by Fujii et al. According to Kilickesmez et al43 the ADC values could distinguish between malignant (0.88±0.11) and benign lesions (1.55±0.33) p-value <0.01. The malignant lesions cut off value was 1.05×10−3 mm2/s, yielded a sensitivity, specificity, and accuracy of 95.83%, 94.55%, and 94.94%, respectively.[19]

In our study 59.57 % patients belongs to malignant group which comprised of 19 patients with carcinoma cervix, and 9 patients with

carcinoma endometrium.[20,21] The study done by us showed that mean ADC of malignant lesions was (0 .827 x 10−3 mm2/sec) lower than benign lesions. In our study we took cut-off ADC value for malignant lesion of 1.01×10−3 mm2/s yielded sensitivity, specificity, of 95.00% and 100.00% respectively. The findings that we obtained tallies with the study done by Kilickesmez et al. Tamai et al, which describes that DWI is useful to differentiate sarcomas of uterus from benign fibroids.

The ADC values of myometrial zone, junctional zone is influenced by changes in the hormones, however the normal myometrial and leiomyoma's, degenerated were found to be higher than that of uterine sarcomas. On histopathology, the large fibroids when microscopically seen were found to have fibrosis with central necrosis.56The malignant conditions of uterus or highly cellular tumours of uterus (cellular leiomyoma) showed a hyperintense signal on DWI sequence whereas uncomplicated leiomyoma's and most degenerated leiomyoma displayed hypointense signal. The mean ADC value (10−3 mm2/s) of malignant conditions of uterus was 0.826 ± 0.15 for carcinoma cervix and 0.835± 0.05 for carcinoma endometrium. which was found to be less than that of myometrium in healthy individuals (1.62 ± 0.11) and degenerated leiomyoma's (1.70 ± 0.11). [22] In our study, out of the 14 leiomyoma cases one case was of degenerated leiomyoma. The degenerated leiomyoma has characteristic lesion which showed a well-defined lesion with areas of cystic within whichappeared

hypointense on T1W sequence and hyperintense on T2W sequence. This lesion displayed hypointense signal on DWI sequence with high ADC value. In a study done by Yang et al69 the mean ADC value of adenomyosis was found to be remarkably higher than mean ADC values of uterine leiomyoma, the study was conducted using 3.0-Tesla MRI and they proposed that uterine has high ADC values that leiomyomas, however in our study we did not find much difference. In another study conducted by Tian et at, showed that mean ADC values of fibroid and focal Adenomyosis of uterus showed that there was no statistically significant difference. Even ADC value (10−3 mm2/seconds) of Endometrial cancer was (0.88±0.16) and the mean ADC value of normal endometrium (1.53±0.10), thus the carcinoma of endometrium showed significantly lower ADC values (P<0.01).[23]

In a study done by, Tomohiro Namimoto54, the DW imaging sequences plays a vital role in demonstrating status of carcinoma endometrium and benign conditions of uterus and thus DWI sequence can help distinguish between benign and malignant condition.[24,25]Carcinoma endometrium (0.835±0.15) was remarkably lower than normal endometrium (p-value<0.001). A

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study done by Patrick Z. McVeigh et al showed that the assessment of cervical cancer with respect to measurement of ADC values in MRI. The study included 47 patients with cervical carcinoma who underwent chemotherapy and 26 normal controls. The study revealed that the normal cervix ADC values were high (2.09±0.46) and the median ADC (mADC) of cervical carcinomas was relatively lesser (1.09±0.20) (p- value <0.001) and hence carcinoma cervix had significantly lower ADC values in our study. [26] The study that we conducted showed that the mean ADC value of carcinoma cervix (0.826±0.15) was remarkably lower than normal cervix and other study done by Naganawa et al(p-value <0.001).
The staging of the tumour was not analysed. The histopathological degree of differentiation of the malignant tumours did not correlate with the obtained ADC values. There was no difference between the low grade or high grade malignancy when they were compared with ADC values.

5. Conclusions

We conclude that diffusion weighted magnetic resonance imaging (DWI) is a valuable tool to differentiate benign uterine mass lesions from malignant uterine masslesions.Benign uterine lesions show high ADC values whereas malignant uterine lesions show low ADC values on DWI. The ADC values of benign lesions were found to be more than 1.01×10−3mm2/s and that of benign were less than 1.01×10−3mm2/s.Significant correlation was noted between DWI characteristicsand histopathological diagnosis (Benign/ Malignant). There was no significant association between DWI and clinicalpresentations.Hence, DWI has the potential to reliably characterize neoplastic potential of uterine lesions based on apparent diffusion co-efficient (ADC)values.
Funding: No funding sources
Ethical approval: The study was approved by the Institutional Ethics Committee

Conflict of interest
The authors declare no conflict of interest.

Acknowledgments
The encouragement and support from Bharath University, Chennai is gratefully acknowledged. For provided the laboratory facilities to carry out the research work.

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