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Role Of Diffusion-Weighted Mri With Apparent Diffusion Coefficient (Adc) Calculation In Chronic Liver Diseases And Fatty Liver

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ABSTRACT

Aim: The aim of the present study was to evaluate the role of Diffusion-weighted MRI with Apparent diffusion coefficient (ADC) calculation in fatty liver and chronic liver diseases.

Methods: The study was conducted at Dr. D. Y. Patil Medical College and Hospital and Research Centre in Pimpri, Pune from September 2020 to July 2022. There were 25 cases and 25 controls in the study.

Results:. The mean liver ADC value among cases vs controls was found to 901.48±79x10-6mm^2/sec vs. 1238±107x10-6mm^2/sec respectively concluding that when compared to the Control group, the mean ADC among Case group was significantly lower. The mean ADC liver among F0 was 1238.72±107.611, F1 was 990.00±24.259, F2 was 926.71±37.326, F3 was 898.20±75.80 and F4 was 826.13±61.98 using MRI elastography-based staging and grading. Mean ADC value decreased with increase in staging of fibrosis maximum sensitivity and specificity were reported for the Non-fibrotic (F0) vs Cirrhosis (F4) with 95.8% and 82.5% respectively with a cut-off value of 1043.50. ADC values showed best performance for discriminating non-fibrotic (F0) from cirrhotic(F4) stage. Lower performance was observed for discriminating differentiate low-stage fibrosis (F1 and F2) from high-stage fibrosis (F3 and F4). The comparison of mean ADC liver between Case group and Control group using the unpaired t-

test showed mean ADC liver was significantly reduced among Case group compared to Control group.

Conclusion: The findings of our research demonstrate that hepatic ADC values demonstrated good diagnostic performance to discriminate non fibrotic from cirrhotic liver. This crucial in the determining early stages of the illness while there is still a chance that it can be aborted and reversed. Detection of advanced stages played pivotal role, for screening for hepatocellular carcinoma or other forms of malignancy in cirrhotic patients.

Keywords: apparent diffusion coefficient, liver disease, diffusion-weighted imaging, fatty liver

INTRODUCTION

Several chronic hepatic diseases may develop cirrhosis in the liver parenchyma. Hepatic steatosis, iron overload, autoimmune hepatitis, chronic viral hepatitis, sclerosing biliary cholangitis, alcohol, and drugs represent the most frequent causes of liver cirrhosis. All these chronic diseases, after an early phase of inflammation, lead to parenchymal fibrosis, which plays an important role in the development of cirrhosis.[1] Fibrogenesis has been defined as a "wound-healing response that engages a range of cell types and mediators to encapsulate injury".[2] It consists of a progressive deposition of extracellular matrix proteins, which reduces widening of interstitial spaces and creates distortion of normal hepatic architecture.[3]

Liver fibrosis is a consequence of sustained prolonged injury from a variety of causes, including alcohol- and drug-induced, viral, autoimmune, cholestatic, and metabolic diseases. Fibrosis indicates liver damage and is an important cause of portal hypertension. Progression of early fibrosis can be reversed by treatment with specific antifibrotic therapy or by removal of the cause, such as viral hepatitis or alcohol-induced disease.[4-6]

Cirrhosis in the liver parenchyma can develop as a result of a number of chronic hepatic disorders.[7] The most common etiology resulting in liver cirrhosis include Hepatic steatosis, iron overload, autoimmune hepatitis, chronic viral hepatitis, sclerosing biliary cholangitis, alcohol, and drugs. Following an initial period of inflammation, all of these chronic illnesses cause parenchymal fibrosis, which further progresses cirrhosis.[8]

Biopsy is the gold-standard modality for assessing the degree of fibrosis and for evaluating necrosis or inflammation. However, it is affected bymany complications, including bleeding, pneumothorax, and procedure-related death, and could be limited by interobserver variability and sampling errors.[9,10] In addition, liver biopsy is not used in the management of disease, especially when we have to repeat the examination after a short interval of time, as reported by Kim et al.[9] For this reason, in the past years many noninvasive tests and diagnostic examinations have been introduced into clinical routine in order to detect liver fibrosis early.

So, currently there is an accelerated focus in hepatology for search of technique that delivers non-invasive diagnosis and quantification of liver fibrosis. With regard to image-based diagnosis, abdominal ultrasound (ultrasound elastography) helps in the assessment of liver fibrosis, but as it is an examiner-dependent method, its reproducibility is limited.

The diffusion-weighted imaging (DWI) technique is a speedy and non-invasive imaging procedure that may be simply incorporated into regular MRI exams utilizing newly developed

devices. The tiny, random movement of molecules (of water) that is induced by the internal thermal energy is referred to as diffusion. Diffusion-weighted magnetic resonance imaging, often known as DWI, is a method that uses changes in the water proton mobility in tissues to quantify cell membrane density, cellularity, and tortuosity of the extracellular and extravascular space.[11] Despite being relatively new, the application of DWI in conjunction with conventional sequences appears quite promising, as it does not require consideration for patients with contrast media allergy[12] and can be performed on patients who are at high risk of developing nephrogenic systemic fibrosis as a result of severe renal insufficiency.

The aim of the present study was to evaluate the role of Diffusion-weighted MRI with Apparent diffusion coefficient (ADC) calculation in fatty liver and chronic liver diseases.

MATERIALS AND METHODS

The study was conducted at Dr. D. Y. Patil Medical College and Hospital and Research Centre in Pimpri, Pune from September 2020 to July 2022. There were 25 cases and 25 controls in the study.

Method of diagnosis: Siemens Magnetom Vida Magnetic Resonance Imaging (3 Tesla). Before beginning, the investigation, approval from the IEC was successfully acquired. Patients were asked for their informed consent as well as their written permission.

INCLUSION CRITERIA

CASE GROUP

1) 18 years of age and older
2) Patient with clinical history of Chronic liver disease (including -viral hepatitis, alcoholic hepatitis, non-alcoholic, steatohepatitis, primary biliary cirrhosis, primary sclerosing cholangitis, etc.)
3) Abnormal Liver function test.

CONTROL GROUP

1) 18 years of age and older
2) Patients without a history of liver disease/healthy volunteers
3) Patients undergo MRI abdomen investigation for other reasons with normal LFT

EXCLUSION CRITERIA

1. Patients with Focal liver lesion, liver neoplasm and liver metastasis
2. Contraindications to MRI-Electrical implants such as cardiac pacemakers or perfusion pumps, Ferromagnetic implants such as aneurysm clips, surgical clips, prostheses, artificial hearts, valves with steel parts, metal fragments, shrapnel, tattoos near the eye, or steel implants
3. Pregnant females
4. Pre-existing medical conditions including a likelihood of developing seizures or claustrophobic reaction

MRI SCAN TECHNIQUE

Patient positioning:

- Placing patients in a supine position with their head pointing toward the magnet.

- Positioning the patient over the spine coil and placing the body coil over the upper abdomen
- Securely tighten the body coil with straps to prevent respiratory artifacts;
- Increasing the degree of comfort may be accomplished by putting cushions under the legs.
- The xiphoid process of the sternum should serve as the focal point for the laser beam localizer when it is positioned.

- **Sequences Used:** -
- Imaging using a T2 weighting in the axial plane.
- In axial plane diffusion-weighted sequence (DWI).
- T1 2D or 3D gradient echo sequences (eg. VIBE) if necessary
- We used b value of 50,400,800 s/ mm^2. Time to repeat (TR) of 5900 msec and Time to Echo of 54 msec were used.
- Additional sequence - 2D gradient-echo sequences with cyclic motion-encoding gradients (MEG) for MR Elastography
- Every single ADC was computed on a workstation using the industry-standard software (Diffusion Calculation) The signal intensities needed for ADC computation were measured using operator-defined regions of interest (ROI). On the ADC maps, two circular regions of interest (ROI) measuring 1-2 centimetres each were put in separate areas. These ROIs were kept at a safe distance from any apparent vasculature, biliary structures, motion or pulsatile artefacts, and the left lobe was avoided.
- The mean ADC value (in x 10^{-6}mm/sec) was calculated after taking an average of the values and used for analysis
- ADC values of the healthy control group were compared with the cases group.
- As a point of comparison, MRI elastography-based staging and grading.
- **Data collection method and statistical analysis:** On a Performa that had been pretested, data was obtained from the participants and included as Appendix-A.
- The information was put into an Excel sheet, and then it was examined. The MEAN and SD were used to provide a summary of the quantitative data.
- Suitable test of significance such as T test will be carried out. In order to be declared statistically significant, the p-value has to be lower than 0.05.
- In order to evaluate the overall usefulness of the ADC in predicting fibrosis and differentiating between the stages of fibrosis, receiver operating characteristic (ROC) curves of sensitivity vs. 1-specificity were developed, and the area under the ROC curve was computed. Both of these methods were used to evaluate the overall usefulness of the ADC (AUC).
- It was determined via the use of a ROC curve what the minimum value of the ADC should be in order to discriminate between people with chronic liver disorders and healthy controls.

RESULTS

Table 1: Description of the study groups as per Gender and as per Hepatomegaly

Gender	**Groups**		**Total**
	Case group	**Control group**	
Male	15	16	31
	60.0%	64.0%	62.0%
Female	10	9	19
	40.0%	36.0%	38.0%
Total	25	25	50
	100.0%	100.0%	100.0%
χ^2 value = 0.085, p-value = 0.771			

When comparing the number of men and females in the Case and Control population using the chi-square test, it was found that there was no statistical difference in the distribution of males and females between the two groups.

Table 2: Description of the study groups as per Hepatomegaly

Hepatomegaly	**Groups**		**Total**
	Case group	**Control group**	
Absent	17	23	40
	68.0%	92.0%	80.0%
Present	8	2	10
	32.0%	8.0%	20.0%
Total	25	25	50
	100.0%	100.0%	100.0%
χ^2 value = 15.789, p-value = 0.001*			

The comparison of the distribution of Hepatomegaly between Case and Control population using the chi-square test demonstrated that Hepatomegaly was statistically significantly more among Case group compared to Control group.

Table 3: Description of the study groups as per LFT

LFT	**Groups**		**Total**
	Case group	**Control group**	
Abnormal	23	0	23
	92.0%	0.0%	46.0%
Borderline	2	0	2
	8.0%	0.0%	4.0%
Normal	0	25	25
	0.0%	100.0%	50.0%
	25	25	50

	100.0%	100.0%	100.0%
χ^2 value = 50.000, p-value = 0.001*			

When the distributions of LFT were examined between the Case and Control population using the chi-square test, it was found that LFT was statistically significantly higher among the Case group than it was among the Control group.

Table 4: Description of the study groups as per

USG appearance of Liver	**Groups**		**Total**
	Case group	**Control group**	
Coarse echotexture	19	0	19
	76.0%	0.0%	38.0%
Increased echogenicity/FATTY	6	2	8
	8.0%	8.0%	16.0%
Normal	0	23	23
	0.0%	92.0%	46.0%
Total	25	25	50
	100.0%	100.0%	100.0%
χ^2 value = 50.000, p-value = 0.001*			

The comparison of the distribution of USG appearance of liver between Case and Control population using the chi-square test abnormal USG findings were statistically more significantly among Case group compared to Control group.

Table 5: Description of the study groups as per

Groups	**ADC liver**		
	Mean	**Std. Deviation**	**p-value**
Case group	901.48	78.98	0.001*
Control group	1238.72	107.61	

The comparison of mean ADC liver between Case group and Control group using the unpaired t-test showed mean ADC liver was significantly reduced among Case group compared to Control group.

Table 6: ROC Curve

	Area under the curve	**ADC value**	**Sensitivity**	**Specificity**
Nonfibrotic (F0) vs Cirrhosis (F4)	0.903 (0.778-0.976)	1043.50	95.8 (84.9-99.2)	82.5 (70.2-96.8)
F0 and F1 vs F2, F3 and F4	0.702 (0.559-0.796)	972.50	75.2 (54.2-89.4)	62.1 (59.9-76.3)
F1 and F2 vs F3 and F4	0.684 (0.501-0.813)	924.50	55.4 (44.1-79.6)	72.3 (60.2-86.1)

With a cut-off value of 1043.50, the Nonfibrotic (F0) group was shown to have the highest sensitivity and specificity in comparison to the Cirrhosis (F4) group, with 95.8 percent and 82.5 percent, respectively. With a threshold value of 972.50, the sensitivity and specificity for F0 and F1 in comparison to F2, F3, and F4 were 75.2 and 62.1 percent, respectively. With a cut-off value of 924.50, the sensitivity and specificity were found to be 55.4 percent and 72.3 percent, respectively, for F1 and F2 in comparison to F3 and F4, respectively.

IMAGE 1

Diffusion-weighted image with (b 400 s/mm^2) image and ADC map of liver for a case of F0 stage (mean ADC value 1268 x 10^{-6}mm/sec)

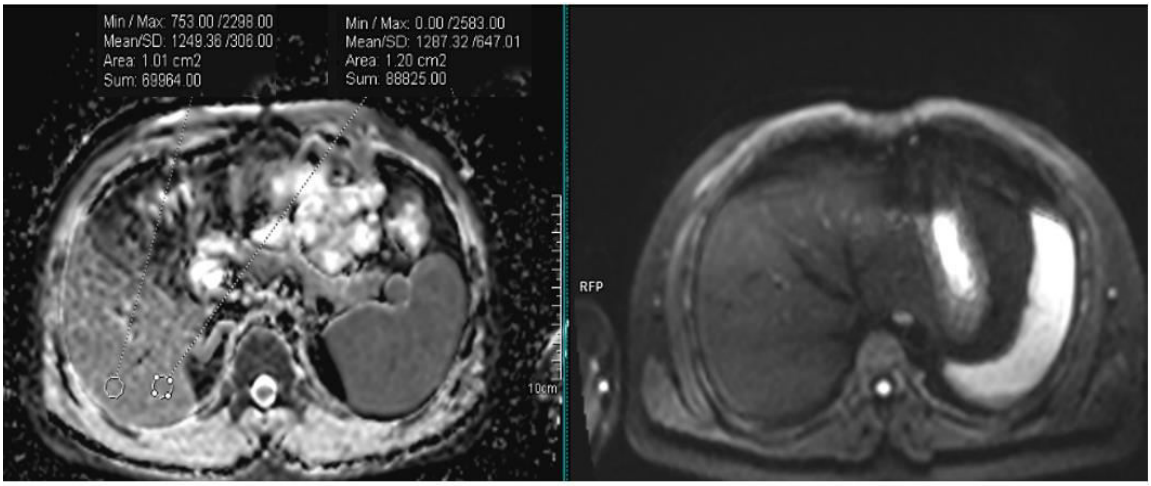


IMAGE 2

Diffusion-weighted image with (b 400 s/mm^2) image and ADC map of liver for a case of F1 stage (mean ADC value 1060 x10^{-6}mm/sec)

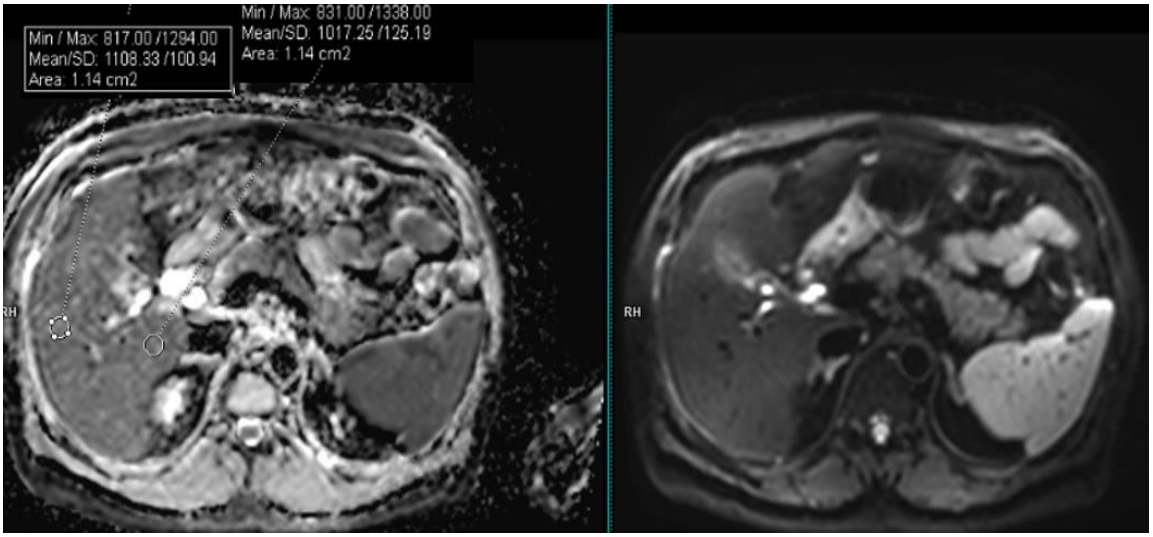


IMAGE 3

Diffusion-weighted image with (b 400 s/mm^2) image and ADC map of liver for a case of F2 stage (mean ADC value 975 x 10^{-66}mm/sec)

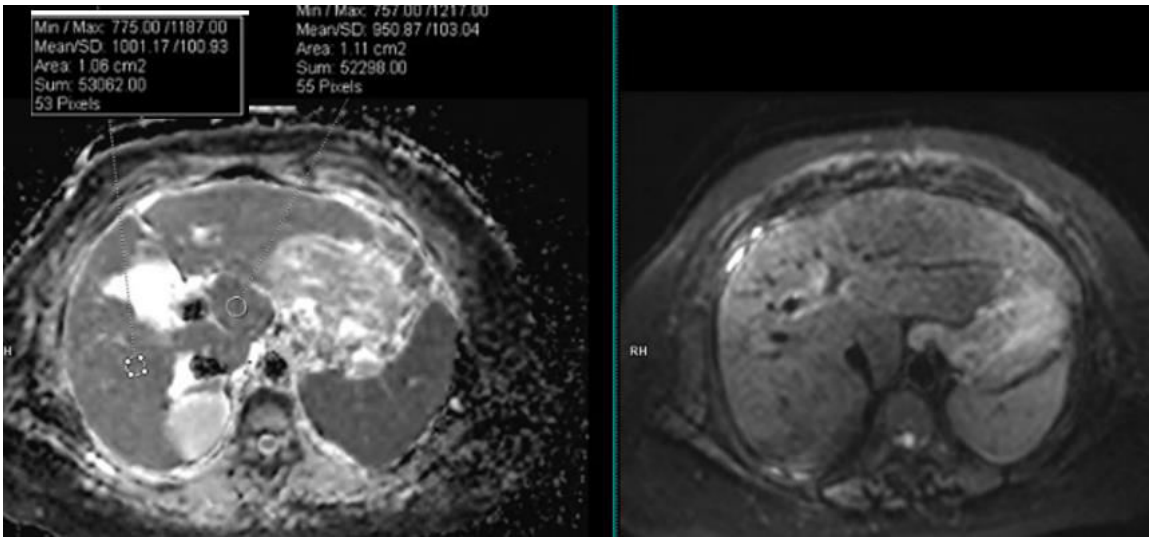


IMAGE 4

Diffusion-weighted image with (b 400 s/mm^2) image and ADC map of liver for a case of F3 stage (mean ADC value 864x 10^{-66}mm/sec)

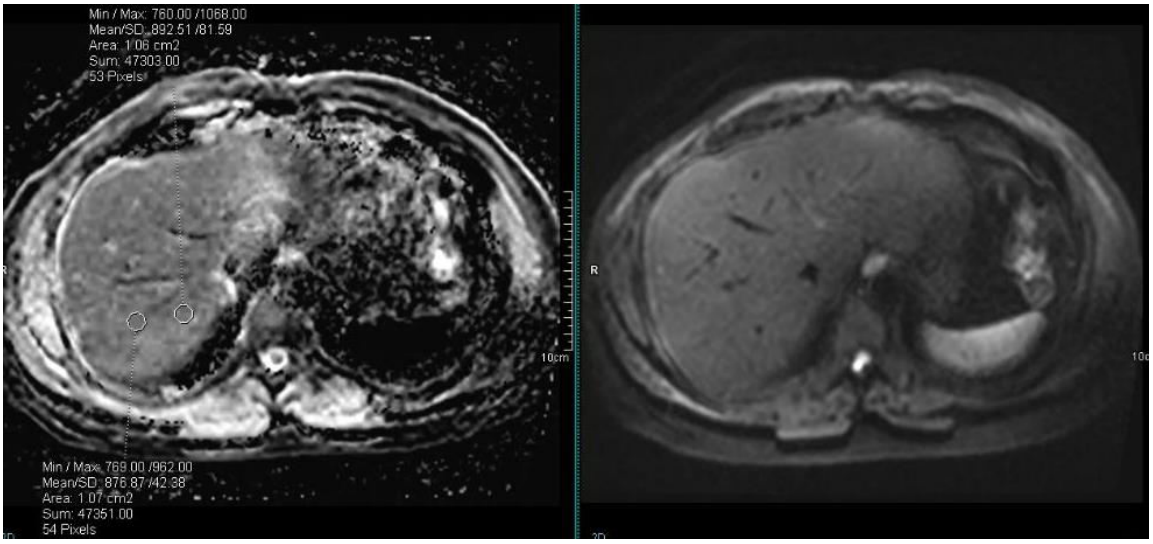
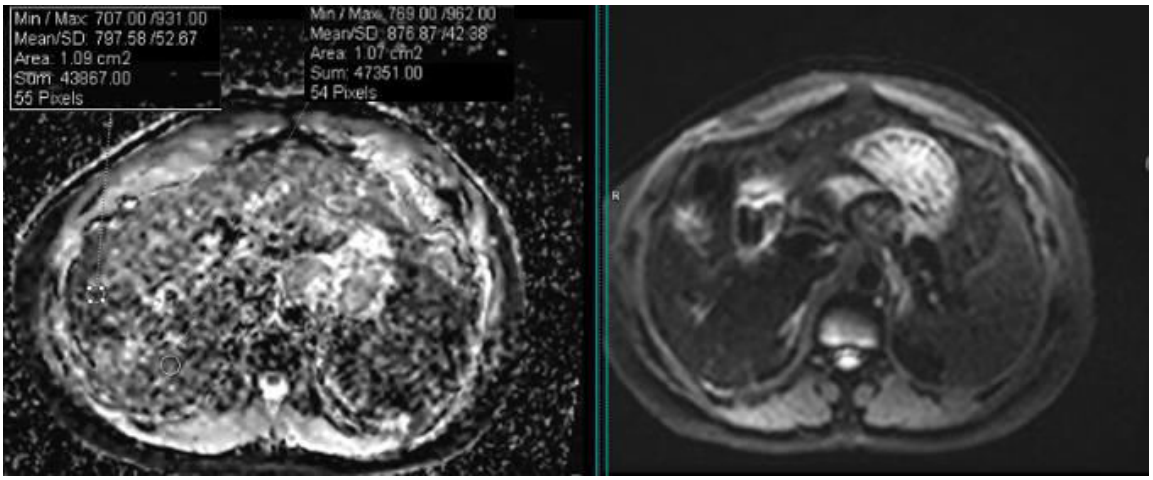


IMAGE 5

Diffusion-weighted image with (b 400 s/mm^2) image and ADC map of liver for a case of F4 stage (mean ADC value 840x 10^{-66}mm/sec)



DISCUSSION

Liver fibrosis results in extracellular accumulation of collagen, glycosaminoglycans, and proteoglycans that may restrict the molecular diffusion of water, thus suggesting that diffusion-weighted imaging (DWI) may be useful for assessing fibrosis. However, DWI of the liver is beset with several problems. These problems include susceptibility to motion artifact and eddy currents and poor signal-to-noise ratio, particularly when strong diffusion-sensitizing gradients (i.e., high b values) are used in the scan sequence. Most studies of DWI have found that the apparent diffusion coefficient (ADC) of cirrhotic livers is significantly lower than that of normal livers.[10,13-16]

In our study, when compared to the Control group, the Case group had a considerably higher mean age than Control group. The present analysis did not find a statistically significant variation in the distribution of males and females between the Case population and the Control group. Our result is similar to the studies conducted by Sandrasegaran et al.[17] and Makhija et al.[18]

In our present study the mean liver ADC value among cases vs controls was found to 901.48 ± 79 x 106 mm2/sec vs. 1238 ± 107 x 106 mm2/sec respectively concluding that when compared to the Control group, the mean ADC among Case group was significantly lower. Research conducted by R. Girometti [19] came to the same conclusion as ours, noting that the mean ADC was much lesser among cirrhotic subjects than compared to the control group. This finding was in keeping with the findings of our investigation (1110 ±160 vs. 1540±120 x 10-6 mm2/s). One of the important goals of our study was to find non-invasive alternatives for the early detection of fibrosis. MRE showed relatively high sensitivity and specificity for predicting the stage of fibrosis[20], so we used MRE as a reference for fibrosis staging.

In the present study, there were 20.0% cases of F1 stage, 28.0% cases of F2 stage, 20.0% cases of F3 stage and 32.0% cases of F4 stage. The mean liver ADC value among F0 was

1238.72±107.611 x 10^{-6}, F1 was 990.00±24.259 x 10^{-6}, F2 was 926.71±37.326 x 10^{-6}, F3 was 898.20±75.80 x 10^{-6} and F4 was 826.13±61.98 x 10^{-6}. We reported that as fibrosis stages advanced from 0 to 4, ADC values decreased. Studies using a standard histological (METAVIR) scoring system as reference concluded similar results. Researchers Sandrasegaran et al.[17] and Taouli et al.[10] discovered that there was a correlation between the levels of hepatic ADC and the advancement of fibrosis stages.

In the present study, we were able to establish that there is a statistically significant difference between the hepatic ADC values of patients who were non-fibrotic (F0) and those who were cirrhotic. This difference was seen in both groups of patients (F4). Nevertheless, there is a crossover between the ADC values of F2 and F4. There is no minimal value for the ADC that could reasonably differentiate between low-stage fibrosis (F1 and F2) and high-stage fibrosis (F3 and F4). This was in agreement with the study done by Sandrasegaran et al.'s study[17], showing that only between stages 0 and 4 did ADC values alter statistically substantially, whereas ADC values were not useful in differentiating between other stages (histological METAVIR scoring system). On the other hand, Taouli et al.[10] discovered that the ADC values of patients at all stages of fibrosis differed from one another in a manner that was statistically significant (Batts-Ludwig classification).

LIMITATIONS

Our research contains several important limitations. To begin, the main limitation was the lack of pathological validation. Biopsy correlation was not available. For obtaining a valid statistically relevant link between hepatic ADC value and degrees of fibrosis, a large-scale multicentre investigation needs to be carried out that needs to include a similar number of patients in every stage of fibrosis.

CONCLUSION

The findings of our research demonstrate that hepatic ADC values demonstrated good diagnostic performance to discriminate non fibrotic from cirrhotic liver. This crucial in the determining early stages of the illness while there is still a chance that it can be aborted and reversed. Detection of advanced stages played pivotal role, for screening for hepatocellular carcinoma or other forms of malignancy in cirrhotic patients. Further progression and treatment response can also be monitored. DWI as an adjunct to routine MRI protocol is capable of providing anatomical and structural information in cirrhotic patients. It is important to standardize ADC measurements before utilising in clinical settings. The protocol should include DWI, chemical shift-based fat-water separation, dynamic contrast-enhanced MRI, and MR elastography to reliably stratify the various phases of fibrosis Furthermore, a future meta-analysis of these studies might be able to establish clear, evidence-based cut-offs to assess capability of DWI MRI in quantifying degrees of hepatic fibrosis and its use as an alternative to liver biopsy.

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