**ORIGINAL RESEARCH** 

# Comparative role of diffusion weighted imaging and contrast enhanced MR enterography in evaluation of inflammatory bowel disease

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Received: 03 March, 2025

Accepted: 27 March, 2025

Published: 07 April, 2025

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# **INTRODUCTION**

Crohn's disease and ulcerative colitis are two systemic diseases of unknown chronic inflammation predominantly involving bowel and usually affecting the young patients that requires lifelong medical and often surgical therapy. These diseases are characterized by repeated acute exacerbations and periods relative lack of of symptoms. Immunosuppressive medications are mainstay of therapy. Correct administration of immunosuppressive therapies in these diseases rely on accurate detection of acute inflammation - so called "active disease", who are likely to respond well to the treatment. There is no straightforward single reliable method to identify such patients. Medical history, various physical examinations (such as Crohn's disease activity index, Harvey Bradshaw Index) and laboratory data (CRP, ESR etc.) are used to assess disease activity and complications. But these are subjective and prone to significant inter observer variability<sup>1</sup>. Colonoscopy is gold standard for evaluation of mucosal changes seen in patients of IBD<sup>2</sup>. But it cannot assess extra mucosal and extra mural changes and also it is an invasive procedure. Capsule endoscopy can improve our visualization of the small bowel<sup>3</sup> mucosa but it also shows some limitations, particularly disease with luminal stenosis and stricture. Hence radiological imaging is usually required. Former radiological

methods (small bowel follow through, enteroclysis etc) examination are no more used because of limited utility and associated complications. CT enterography is a very good investigation for evaluation of mucosa, transmural and extra-intestinal pathology. However, due to the risk of ionizing radiation it is less ideal investigation for inflammatory bowel disease as compared to MR enterography, since the patients are relatively younger and usually require repeated investigations and thus result into large cumulative dose of radiation. Since the development of rapid sequences in MRI imaging techniques, possible to perform in one breath-hold, small bowel imaging by MRI has become much popular in recent times. With MR enterography and enteroclysis, not only can luminal pathologies be better visualized, but it also has the capability to look at extra-luminal pathologies, which is not possible with endoscopic techniques. MR imaging provides better soft tissue contrast and visualization of fluid and edema<sup>4,5</sup> without ionizing radiation. Minimal inflammatory change can be easily detected by use of gadolinium enhanced MRI imaging. Steady state free precession (SSFP) sequences can be used to assess bowel motility. It is helpful in distinguishing between permanent and transient segmental bowel narrowing. A recent sophisticated advancement has been added in MRE, that is diffusion weighted imaging (DWI) and ADC

(apparent diffusion coefficient) value calculation. It obtains its high tissue contrast from the differences in motion of water molecules in various tissues<sup>6</sup>, thus avoiding gadolinium induced nephrotoxicity and systemic fibrosis<sup>7</sup>. Diffusion weighted MR imaging is integrated with most of the standard MR imaging protocols and neither additional hardware nor extra software equipment is necessary and may be added to any routine MR imaging protocol. Thus, there is possibility that DWI-ADC might be an ideal alternative method of gadolinium enhanced imaging for long time follow up of in IBD.

### **OBJECTIVE**

- To evaluate extent of disease by magnetic resonance enterography.
- Identification of active stage or acute inflammation in patients of inflammatory bowel disease.
- Correlate DWI findings and ADC values with biochemical and clinical parameters.
- Calculate cut-off ADC value to detect actively inflamed bowel loops.
- Comparing DWI-ADC sequence with gadolinium enhanced MRE in assessment of disease activity in Crohn's disease.

#### METHODOLOGY

After getting the ethical committee clearance, we conducted one prospective, observational and analytical study over a time span of approximately 18 months in the department of Radiology and gastroenterology of I.P.G.M.E & R. Since, it was observational study, we did not have to calculate formal sample size for this. We used Harvey-Bradshaw Index (HBI)score, value of C-reactive protein and ADC value as study variables. Statistical

analysis was done after completion of study using standard and appropriate statistical methods.

Inclusion criteria: 1) Proven cases of Crohn's disease for restaging of disease or to check extent of disease and to see response to therapy. 2) Highly suspected cases of IBD as per clinical and laboratory findings (biochemistry, radiology, colonoscopy and biopsy). 3) Proper consent given by patients.

Exclusion criteria: 1) Contraindications to MRI (cochlear implant, pacemaker, neurostimulators, severe claustrophobia, metallic implants). 2) History of active ischaemic heart disease, renal impairment, BPH, acute glaucoma, severely ill patients who could not hold breath, patient could not drink adequate amount of water for examination and 3) Who did not provide proper consent.

#### **RESULTS AND ANALYSIS**

Majority of patients in our study were between 21 to 50 years of age, corresponding to 76% of total study population. Most of the patients in our study were male, corresponding to 69%. Jejunum, ileum, terminal ileum and/or ileo-caecal junction, caecum - ascending colon, transverse colon, descending colon and sigmoid colonrectum were involved in 5, 24, 50, 18, 3, 16 and 23 patients (6.3%, 30%, 62.5 %, 22.5 %, 3.8%, 20% and 28.8% respectively). Only small bowel (Image 1) was involved in 35 patients (43.75%) and only large bowel was involved in 14 patients. Both small bowel and large bowel were involved in 31 patients comprising of 38.75% of total cases. Marked post-contrast enhancement (Image 1) of bowel wall was present in 78 patients and true diffusion restriction (Image 2)of bowel wall was present in 73 patients. Other indicators of active inflammation were (table relatively less 1). Extra-intestinal complications were present in 18 patients (table 2)

TABLE1: DISTRIBUTION OF INDICATOPRS OF ACTIVE INFLAM	AMATION IN IBD
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INDICATORS OF ACTIVE INFLAMMATION	NO. OF PATIENTS
TRUE DIFFUSION RESTRICTION	73 (91.25%)
MESENTERIC INFLAMMATION	13 (16.3%)
COMB'SSIGN	5 (6.3%)
REACTIVE ADENOPATHY	9 (11.3%)
MARKED POST CONTRAST ENHANCEMENT	78(97.5%)

#### **TABLE-2: EXTRA- INTESTINAL COMPLICATIONS**

<b>EXTRAINTESTINAL COMPLICATIONS</b>	<b>NO. OF PATIENTS</b>	PERCENTAGE
ENTEROENTERIC FISTULA	6	33.33
ENTEROCUTANEOUS FISTULA	4	22.22
FISTULAINANO	1	5.55
INFLAMMATORY PHLEGMON	2	11.11
ABSCESS	3	16.66
SACROILIITIS	2	11.11
TOTAL	18	100

Imaging markers of chronic disease like mesenteric fibrofatty proliferation (8 patients corresponding to 10%) and luminal stenosis (8 patients corresponding

to 10%) were evaluated in our study. Features of active disease in chronic patients and only active disease were also evaluated separately which

comprised 20% (16 out of 80 patients) and 80% (64 out of 80 patients) of total cases respectively. Comparative evaluation of inflammation with DWI -

ADC and gadolinium enhancement MRE were evaluated with reference to total number of bowel segments involved in 80 patients (table 3)

# TABLE 3: COMPARATIVE EVALUATION OF INFLAMMATION BY DWI-ADC AND CONTRAST ENHANCED MRE (CE MRE)

TOTAL INVOLVED BOWEL SEGMENTS n =189

Investigation		CE MRE		Total
		Positive Findings	Negative Findings	
DWI	Positive Findings	154	5	159
	Negative Findings	18	12	30
Total		172	17	189

- Sensitivity of DWI in comparison to gadolinium enhanced MRE = 89.53%
- Specificity of DWI in comparison to gadolinium enhanced MRE = 70.58%
- Accuracy of DWI = 87.83%
- Positive predictive value of DWI = 96.85%
- Negative predictive value of DWI = 40%

Comparative evaluation of DWI-ADC and contrast enhanced MRI was done for evaluation of various complications of bowel wall penetration. Total 16 bowel segments showed penetrating complications at CE MRE: 6 segments with entero-enteric fistula, 4 segments with entero-cutaneous fistula, 1 with fistulain-ano, 3 with abscess, 2 with inflammatory phlegmon. Penetrating complications are found in 13 out of 16 patients with the help of DWI MR enterography. There was failure to detect 2 enteroenteric and 1 entero-cutaneous fistula by DWI-ADC but no penetration were reported as unseen at CEMRE. DWI and CE MRE findings mismatch were found in 2 of 13 segments: two peri enteric abscess as seen at CE MRE were interpreted as phlegmon and entero-enteric fistula (Image 3) by DWI MRE.

D'Agostino-Pearson test for Normal distribution of ADC (of affected gut loops) and CRP values were evaluated (with reject normality of P<0.0001) and both these parameters were correlated [(Spearman's coefficient of rank correlation (rho)]. The value of rho was found to be -0.473. Similarly, correlation [(Spearman's coefficient of rank correlation (rho)] between ADC value and HBI value was calculated and value of rho was -0.735. ROC analysis was done to see if a cut-off can be deduced to predict inflammation status from ADC value. Associated criterion was deducted to be  $\leq 2.17$ . Thus, ADC value  $\square$  2 .17 suggests that below this cut-off the chance of having inflammation is high. The cut-off is providing sensitivity of 96.25% (95% confidence interval 89.4 -99.2%) and specificity of 96.25% (95% confidence interval 89.4 - 99.2%). Software used: Med Calc version15.8 [Mariakerke, Belgium: MedCalc Software 2015]

#### DISCUSSION

We studied about 155 patients attending gastroenterology OPD with clinical suspicion of inflammatory bowel disease or already diagnosed case

of IBD. MR enterography was done in department of Radiodiagnosis, IPGME&R and SSKM hospital, their recent blood CRP values(within1week) were documented and HBI scoring were done. Out of 155patients, 80 patients who were positive for one or more indicators of active IBD in MRE, were selected for final evaluation. So, our sample size was 80.

Based on specific MRE findings, we classified the IBD patients into IBD with active inflammation, chronic IBD and active inflammation on chronic IBD. Patients having true diffusion restriction of bowel lesion<sup>8,9</sup>, high post- contrast enhancement of bowel lesions<sup>10,11,12,13</sup>, comb sign (engorged vasa recta)<sup>14,15,16</sup>, mesenteric inflammation or reactive adenopathy (lymph nodal oedema seen in fat suppressed HASTE and homogeneous enhancement in gadolinium enhanced imaging)17,18 singly or in combination were categorized as having active inflammation. Patients having low post-contrast lesions<sup>10</sup>, enhancement of bowel fibro-fatty proliferation14 mesenteric and fibro-stenosis [Mazziotti, MRE] in isolation or combination, were marked as chronic IBD. Patients who had both types of features (that is active inflammation and chronic disease), were marked as active inflammation in chronic IBD. Those who were categorized as having active inflammation and active inflammation in chronic IBD were chosen for our study.

As per wall thickening of segments of bowels with abnormal contrast enhancement (high or low enhancement)<sup>10,11,12,13</sup>, we evaluated segmental distribution of disease in bowel loops. We also identified complications and extra- intestinal manifestations like fistulae, intra-abdominal inflammatory phlegmon, segmental luminal stenosis with proximal dilatation and abscess formation and sacroiliitis.

In 80 patients with IBD, 189 bowel segments showed wide range of findings in contrast study were selected for analysis. DWI sequences were examined to find out those segments showing true restriction or not and thus the sensitivity, specificity, accuracy, positive predictive value and negative predictive value of DWI in comparison to contrast enhanced MRE were calculated.

For calculating ADC value of affected gut loop, one (when unique) or the more severely (when multiple)

affected gut loop were identified in each patient. A normal gut loop was used as internal control for comparison. ADC values of the affected and normal gut loops were measured (Image 4) by drawing a circular region of interest between 20-40 mm<sup>2</sup> and using an advantage workstation with FUNCTOOL software (GE Healthcare)

Lastly, we compared ADC values of affected gut loops, with biochemical marker CRP and clinical marker HBI in each patient.

Previous studies show, majority of IBD patients belong to 15-30 years of age<sup>19</sup> but it can affect people of all ages. Up to 20% of IBD cases are diagnosed during childhood<sup>20</sup>.

In our study, majority of patients were in the age group of 21-40 years. Hence, there is no major gender predominance in  $IBD^{19}$ .

In our study, 68.8% of affected patients were male and rest 31.3% of patients were female.

Martin DR et.al<sup>21</sup> showed that, in about 70–80 % of patients with IBD (CD), small bowel involvement was there, and in about 20–30%, the it is only limited to the small bowel. The colon can be affected either with small intestine (50 % of cases) or without (15–20 %) small intestine.

In our study, in about 82.5% of patients with IBD there was small bowel involvement and large bowel involvement was seen in 56.25% of patients. Only small bowel and only large bowel was affected in 43.75% and 17.50% of patients respectively.

Due to multiplanar capability and high soft-tissue contrast resolution of MRI, extra-intestinal lesions and complications can be well assessed by MRE. Fistula formation is not uncommon in CD, affecting between 17% and 50% of patients<sup>22</sup>.

In our study, we found 11 fistulae in 8 patients, out of them, 1 was ano-rectal fistula, 6 were entero-enteric fistulae and 4 were entero-cutaneous fistulae. Among all extra intestinal complication, other than stenosis, 33.33% was entero-enteric fistula, 22.22% was entero-cutaneous fistula,5.55% was ano-rectal fistula. The exact location of fistula was clearly seen on MRI. We observed that a dedicated high-resolution perianal MR protocol study is much more superior in detection of the thin and small fistulous tracts.

Abscess is a relatively common complication in Crohn's disease, occurring in 10- 30% of patients over the normal course of the disease<sup>23</sup>. There is significant clinical challenge in this aspect. First, immunosuppressant drugs often mask clinical and laboratory signs of abscess. Second, abscess is a contraindication to the use of biologic agents (including anti-TNFs) and corticosteroids<sup>23</sup>.

We have seen intra-abdominal inflammatory phlegmon in 2 patients and abscess in 3 patients, i.e. 11.11 and 16.66% of total extra intestinal complications respectively.

Sacroiliitis is one of the most frequent extraintestinal manifestation in IBD. There is 3-fold higher prevalence of sacroiliitis in IBD compared to normal individual.

We found 2 patients with sacroiliitis out of 80, that is, 11.11% of total extraintestinal complications.

The differentiation between acute and chronic changes is important for guiding clinical management, particularly in patients with signs and symptoms of acute exacerbation. Findings that are consistent with acute inflammation may be managed by medications, whereas findings related to fibrosis or chronic stricture usually need surgical intervention<sup>24</sup>.

In our study, 20% patients showed acute exacerbation on top of chronic disease.

Diffusion weighted imaging is a very promising MRI sequence in evaluating bowel inflammation and may improve diagnostic performance of MR enterography in patients suffering from IBD. E Gangemi et al<sup>25</sup> in 2014 compared DWI-ADC values in normal and affected bowel loops and found that a ADC cut-off value of 2.416mm<sup>2</sup>/scan be used to discriminate normal from affected bowel loops.

In our study we found cut-off ADC value of  $\Box$  2.170. This suggests that below this cut-off there is high chance of active inflammation. The cut-off is providing sensitivity of 96.25% (95% CI 89.4 - 99.2%) and specificity of 96.25% (95% CI 89.4 - 99.2%).

In routine practice intravenous contrast is used in MR enterography. However, patients with risk for contrast material allergy or other adverse reactions, those with impaired renal function, or pregnancy, cannot be evaluated by intravenous contrast material–enhanced (CE) MR. These risks are important to patients with IBD as the occurrence of renal insufficiency is not very rare (18% in a recent study<sup>26</sup>), and many patients with CD are in child bearing age group.

Additionally, there is risk of serious side effect of gadolinium-based contrast material known as nephrogenic systemic fibrosis. Young patients may be at a higher risk because of long-term gadolinium retention from repeated examinations<sup>27, 28</sup>. Therefore, performing MR enterography without using intravenous contrast material in patients with CD would allow for increased flexibility in clinical practice, not to mention cost savings. Diffusion-weighted imaging (DWI) is widely accepted as a new imaging technique for the assessment of bowel inflammation in CD.

Many studies have found strong correlations between diffusion restriction in bowel wall or a composite index derived from DWI-ADC sequence and the degree of gut wall inflammation assessed by gadolinium enhanced MR enterography in patients with CD. Hence, it was proposed that DWI-ADC may potentially validate non-enhanced MR enterography (with DWI-ADC) for assessment of CD.

We found 89.53% sensitivity, 70.58% specificity and 87.83% accuracy of DWI in comparison to CE MRE. These findings suggest that MR Enterography performed with DWI-ADC without use of intravenous contrast material is a viable substitute for the International Journal of Life Sciences, Biotechnology and Pharma Research Vol. 14, No. 4, April 2025

Online ISSN: 2250-3137 Print ISSN: 2977-0122

DOI: 10.69605/ijlbpr\_14.4.2025.57

evaluation of IBD patients with well distended small bowel. Many discordant findings between DWI and CE MRE in this study were, negative bowel inflammation at DWI and positive at CE MRE. That can be due to our study was done in well prepared and/or distended small bowels. Positive DWI MR enterography findings and negative CE MRE findings may occur more frequently in less well prepared and less distended bowel segments. Some observer variability existed in the interpretation of DWI findings. Thus, discrepancy between DWI and CE MRE may be more or less in practice. However, avoiding use of gadolinium enhanced MRI examinations in IBD as a routine standard practice, is not suggested.

Considering penetrating bowel wall complications in our study, there is greater discrepancy between DWI and CE MR enterography. This is because DWI-ADC sequence greatly lacks anatomic details (poor spatial resolution). In this regard, CE MR enterography is well known and reliable method for the diagnosis of penetrating complications in  $CD^{29}$ . There is a less data in the literature for evaluation of role DWI in penetrating complications. The results of our study also didn't show clear effectiveness of DWI over contrast MRI in this regard. In our study also discordance was considerable (although the sample size was small). This is an important limitation. This aspect may be further studied with large sample.

So, it is a proposal from this study that, in a tertiary care center like ours, where there is a huge patient burden and majority of patients present in young age<sup>30</sup>, after first traditional protocol, in follow up of the patients, we may use DWI-ADC as a screening sequence to assess the disease activity and effectiveness of treatment. We can go for CE MRE and T2W sequences after that, if required, as a staged MRI protocol. It will not only reduce the time and cost but also patient co-operation and comfort will be satisfactory. We can also use ADC value in follow up study to assess and compare disease activity in the course of treatment.

Laboratory markers have been investigated in IBD for various purposes— diagnosis, differential diagnosis, monitoring of disease activity, response to therapy, and prediction of relapse. Although various laboratory markers have been investigated in IBD, none has been shown to be ideal or superior to our current diagnostic tools. Nevertheless, CRP is a useful marker and should be preferred in CD as it correlates well with disease activity. CRP has a short half-life (19 hours). It therefore rise early after the onset of inflammation and also rapidly disappear from blood after resolution of the inflammation.

Till now no study was done in literature to evaluate whether there is any correlation between ADC value of affected gut loop and blood CRP level. We found Spearman's coefficient of rank correlation (rho) -

0.473, which suggest there is mild negative (inverse) correlation in between them. Probable explanation is CRP level can be normal in up to one third of active IBD patients and opposite is also true, for other inflammatory processes in the body, CRP level may rise & give false positive value. Hence imaging biomarker is more important than the biochemical marker.

Various clinical trials of Crohn's disease usually employ the Crohn's Disease Activity Index to assess disease activity. However, these are complex, timetaking, and sometimes impracticable. The Harvey– Bradshaw Index, was equally effective in assessing disease severity which consists of only clinical parameters and the patient has to recall the details for the previous day only.

We calculate whether there is any correlation between ADC value of affected gut and HBI and found Spearman's coefficient of rank correlation(rho) - 0.735, which suggests there is good negative(inverse) correlation in between them.

# CONCLUSION

The present study revealed that Inflammatory bowel disease is more common in young adults and male are slightly more commonly affected than female. Primary CE MRE findings in IBD are segmental bowel wall thickening, abnormal enhancement and terminal ileum is the most common bowel segment affected.

Gadolinium based contrast MR enterography is better than DWI-ADC to identify complications/extraintestinal manifestations of IBD-like stricture formation, fistulae, inflammatory phlegmon, abscess and sacro-iliitis.

Based on various imaging characteristics, MR enterography is capable of categorising patients into IBD with active inflammation, chronic IBD and active inflammation in chronic IBD.

MR Enterography performed in IBD patients with DWI-ADC without intravenous contrast material can be considered as an acceptable option with good diagnostic yield, particularly in patients who are at risk for use of contrast material for various reasons. But there is considerable discordance in the diagnosis of penetrating complications.

ADC value  $\Box$  2.17 suggests that below this cut-off the chance of having inflammation is high. The cut-off is providing sensitivity of 96.25% (95% CI 89.4 - 99.2%) and specificity of 96.25% (95% CI 89.4 - 99.2%). There is mild negative (inverse) correlation between ADC value of affected gut and biochemical activity marker CRP levels.

There is good negative correlation (i.e inverse relationship) between ADC value of affected gut loops and clinical disease activity marker Harvey-Bradshaw Index.

Online ISSN: 2250-3137 Print ISSN: 2977-0122

DOI: 10.69605/ijlbpr\_14.4.2025.57



Image 1: Wall thickening and enhancement at terminal ileum and I-C region



Image 2: True diffusion restriction of segmental bowel lesions



Image 3: Stellate sign (entero-enteric fistula) in DWI and contrast study

Online ISSN: 2250-3137 Print ISSN: 2977-0122

DOI: 10.69605/ijlbpr\_14.4.2025.57



Image 4: DWI b=1000 axial image and corresponding ADC map. ADC value of a pathological gut wall is measured by keeping ROI above it and the value was (1.05±0.232)×10<sup>-3</sup> mm<sup>2</sup>/sec.

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