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Original Article

Role of Intestinal Ultrasound in Diagnosis of Patients with Crohn's Disease and Assessing activity and Possible Complications

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Abstract:

Background: Crohn's disease (CD) can cause transmural ulceration of any part of the gut , mostly affecting the terminal ileum and colon .

Aim of the Work: assess the role of Intestinal ultrasound In diagnosis of Chron's Disease , assessing activity and possible complications.

Patients and Methods: A Cross sectional study of 30 Patients with Chron's disease from inpatient and outpatient clinics of Gastroentrology department of Ain Shams University Hospitals , in the period from July to December 2021.

Results: the mean age of patients was 54.3± 7.69 years with range from 38-68 years , (70%) were males while (30%) were females (ratio 2.33: 1). the mean hemoglobin level was 11.66 ± 1.46 mg/dl, and the mean RBC 4.18±0.48. The mean platelets was 267.73±61.94 (K/UL), mean WBCs was 9.94 ± 1.83 (K/UL), neutrophils was 7648.57 ± 1460.02 (/UL), and lymphocytic count was 1356.50 ±469.30 (UL) and neutrophil/ lymphocyte ratio (NLR) was 5.93 ±1.35. the mean serum urea, creatinine and uric acid were 46.43-±10.18, 1.10-±0.25 and 5.30-±0.68 mg/dl respectively. the mean AST was 37.63 ±8.27 U/L, the mean ALT was 26.30 ±8.36 U/L, the mean total bilirubin was 1.01±0.17 mg/dl and the mean direct bilirubin was 0.60 ±0.27 mg/dl. We found that the mean PT was 14.17±2.65 sec. and the mean Serum Albumin was 4.16 ± 0.29 g/dl. the mean CRP was 4.91 ±4.55, the mean ESR at first hour was 21.67 ±4.22 and 2nd hour was 47.43±10.94. Kappa statistics revealed poor agreement between IUS and colonoscopy , CTE and MRE results in assessment of studied Crohn's patient

KEYWORDS: Intestinal Ultrasound; Chron's Disease

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Introduction

Inflammatory bowel disease (IBD) are chronic inflammatory disorders of the genetically susceptible individuals who are exposed to environmental factors that alter their intestinal microbiome. [(1)] more than 200 genes were identified in the development of IBD , involved in the intestinal immune interaction with the microbiome. [(2)] the environmental factors which affected patients earlier in life, increase the developmental of IBD later in their lives. [(3)]

IBD include diseases differentiated by site and depth of involvement inside the bowel wall. Ulcerative colitis (UC) is limited to colonic mucosa , Mostly affects the rectum (proctitis), but it can extend into the sigmoid (proctosigmoiditis), beyond the sigmoid (distal ulcerative colitis), or entire colon into the cecum (pan colitis). Crohn disease (CD) causes transmural inflammation with ulceration of any part of the gut mostly affecting the terminal ileum and adjacent colon. CD also is assessed through phenotype into inflammatory, structuring or penetrating. [(4)]

Mucosal recovery (assessed with colonoscopy) is the conventional target for treatment as it is related to reduced rate of medical relapse. The limitations of colonoscopy, safety, cost and affected person preference, have increased the importance of non invasive imaging for monitoring of intestinal inflammation.

Computed tomography (CT) and magnetic resonance enterography (MRE) are the most recent imaging for the assessment of CD, Although MRE is considered the gold imaging modality for assessing CD in the small bowel with specificity and sensitivity drawing close a 100% as ulceration, strictures, and fistulas. C.T is useful for the detection of extra luminal affection of C.D as perforation and abscess with sensitivity of 80-88 % . however CT causes exposture to ionizing radiation so, not preferred for repeated use, while MRE is costy and not available in each setting. this increase the benefits of intestinal ultrasound done by the gastroenterologist with taking decisions immediately from the clinic. [(4)]

Aim Of The Work

To assess the sensitivity & specificity of Intestinal ultrasound in diagnosis of patients with Chron's Disease , assessing activity and possible complications.

Patients And methods

Type of Study: Cross sectional study. **Study Setting**: inpatient and outpatient clinics of Gastroenterology Department of Ain Shams University Hospitals. **Study Population**: 30 patients with Chron's disease selected from inpatient and outpatient clinics in the period from July to December 2021.

Inclusion Criteria: Patients with Crohn's disease diagnosed with clinical, laboratory, endoscopical and histopathological evaluation , age > 18 years old, both sexes and following up with inpatient and outpatient clinics of gastroenterology department of Ain Shams University Hospitals.

Exclusion Criteria: All patients with other causes of colitis either inflammatory or autoimmune or intestinal malignancy, patients aged < 18 year and patients unwilling to be a part in the study .

Thirty Chron's patients were included in this study , subjected to the following: Informed written consent after explaining the study purpose, method and benefits to the patients,

GIUS was performed by consultant radiologist using an ultrasound machine with convex (1– 5 MHz).The entire abdomen was systematically scanned, starting from the right iliac fossa. The findings of small intestinal ultrasound study were correlated with the findings of CT/MRI enterography, colonoscopy and histopathological findings in diagnosis and assessing the activity, complications of CD.

Study Method: All selected patients signed written consent after explaining the study purpose, method and benefits to the patients and all patients were subjected to the following:

History Taking:

General and demographic history: Age, Sex, Residence and age at diagnosis.

History of the disease: Duration (from date of diagnosis until now), history of the disease , its presenting manifestation, other symptoms, and signs, Presence of medical co-morbidities, past medical history (including past or present drug history) and family history of the same condition .

Clinical examination:

Complete general examination: Including Vital

signs (BP , temperature, respiratory rate, heart rate).

Local examination: cardiac , chest and abdominal examination to exclude other comorbidities.

Lab investigations:

Complete blood count (CBC) with differential: Haemoglobin (Hb), Platelets (PLT), White blood cells (WBCs), neutrophils, monocytes, eosinophils, I/T ratio, band cells and RBC indices [Average RBCs size (MCV), Hemoglobin amount per RBC (MCH) and the amount of hemoglobin relative to the size of the RBC (hemoglobin concentration) (MCHC)].

Venous Blood sample obtained from patients with Crohn's disease, 3 ml were taken in ethylene diamine tetraacetic acid (EDTA) anti-coagulated evacuated tube for complete blood count (CBC), erythrocyte sedimentation rate, C reactive protein and fecal calprotectin.

Kidney function tests: Serum urea, serum Creatinine, Sodium, Potassium, BUN and uric acid.

Liver function tests: Aspartate aminotransf-erase (AST), alanine aminotransferase (ALT), total and Direct Bilirubin and serum Albumin.

Colonoscopy with biopsy for histopathology (Fujifilm, made in Singapore (*EC- 600)*, length: 1.63m , with waterjet , version of 2020)

Study Tools: All selected patients were subjected to sign written consent after explaining the study purpose, method and benefits to the patients.

Gastrointestinal ultrasonography (GIUS) was performed by consultant radiologist using an ultrasound machine with convex (1–5 MHz).

The entire abdomen was systematically scan-ned, starting from the right iliac fossa till whole abdomen. Each examination included gray scale and color Doppler sonography. The sonographic exams were performed after the patient had fasted. The examinations were performed by consultant radiologist using GE Logiq P7 Ultrasound Machine , using Convex Probe:C1-5-RS [1.75-4.95Mhz],Micro Convex Probe:8C-RS [3.6-10.0Mhz], Endo Micro Convex Probe: E8C-RS [3.6-10.0Mhz], Linear Probe:L6-12-RS [5.38-10.0Mhz], Phased Array Sector Probe: 3Sc-RS [1.45-4.2Mhz], Phased Array Sector Probe: 6S-RS [2.2-7.0Mhz], Convex Volume Probe: RAB2-6-RS [1.7- 4.8Mhz], and CW Split Crystal Probe: P8D [8Mhz].

Neither preparation nor intravenous contrast were used. The following parameters were assessed :

Bowel wall thickness (BWT), measured on the anterior wall of the intestine in the longitudinal direction, avoiding haustrations and mucosal folds; measurement was taken from the interface between the mucosa and the lumen to the interface between the serosa and the muscularis propria layer.

Possible complications were assessed as: pre-stenotic dilatation, fistulas or the presence of abscess.

Bowel wall stratification was assessed as present or absent.

Doppler activity of bowel wall was graded semi-quantitatively based on the Limberg scale from 0 to 4.

Mesenteric fatty wrapping was considered abnormal if covering more than half of the bowel circumference or thicker than 10 mm or thicker than the normal BWT.

(If the patient has one or more finding from the above criteria, patient was considered as active Chron's disease)

The findings of intestinal ultrasound were correlated with the findings of CT/MRI enter-ography, colonoscopy and histopathological findings for diagnosis and assessing the sever-ity, complications of Chron's disease.

Statistical analysis: The collected data was tabulated, and statistically analyzed using SPSS program (Statistical Package for Social Sciences) software version 26.0, Microsoft Excel 2016 and MedCalC program software version 19.1 Descriptive statistics were done for numerical parametric data as mean ± SD (standard deviation) and minimum & maxim-um of the range and for numerical non parametric data as median and 1^{st}& 3^{rd} inter-quartile range, while they were done for categorical data as number and percentage. Inferential analyses were done for quantitative variables using independent t-test in cases of two independent groups with parametric data and Mann Whitney U test in cases of two independent groups with non-parametric data. Receiver operating characteristic (ROC curve) analysis was used to find out the

overall productivity of parameter in and to find out the best cut-off value with detection of sensitivity and specificity at this cut-off value. Inferential analyses were done for qualitative data using Chi square test for independent groups. The level of significance was taken at P value <0.05 is significant, otherwise is non- significant. The p-value is a statistical measure for the probability that the results observed in a study could have occurred by chance.

Results

Table (1): Demographic characteristics in the studied patients .

Parameters		Studied patients (n=30)	
		N	%
Age (years)	Mean± SD	54.3± 7.69	
	Median (IQR)	54.0 (49.25- 60.5)	
	Range	38- 68	
Gender	Male	21	70.0%
	Female	9	30.0%

Table (1) : *the mean age of our patients was 54.3 ± 7.69 years (range from 38-68 years) with 21 patients were males (* 70.0%) and 9 patients were females (30.0%) .
SD= standard deviation, IQR: interquartile range .

Table (2): CBC in studied patients .

CBC findings	Studied cases (n=30)				
	Mean	SD	Median	Minimum	Maximum
Hemoglobin (G/DL)	11.66	1.46	12.00	9.20	13.50
Hematocrit (%)	39.85	2.56	39.00	36.00	45.00
R.B.Cs count (M/ UL)	4.18	0.48	4.10	3.50	4.98
MCV (FL)	82.68	5.44	81.00	74.00	91.50
CBC findings	**Studied cases (n=30)**				
	Mean	**SD**	**Median**	**Minimum**	**Maximum**
MCH (PG)	30.84	2.51	30.00	27.50	36.00
MCHC (g/DL)	34.06	2.05	33.10	32.00	37.00
RDW-CV (%)	12.44	0.99	12.40	11.00	13.80
Platelet Count (K/UL)	267.73	61.94	244.00	176.00	392.00
W.B.Cs count (K/UL)	9.94	1.83	9.85	6.51	12.50
neutrophil count (/UL)	7.65	1.46	7.75	4.50	9.50
lymphocytic count(UL)	1.36	4.69	1.20	9.90	2.63
neutrophil/lymphocyte ratio	5.93	1.35	5.90	3.40	7.90

Table (2) : the mean Hemoglobin results was 11.66 gm ± 1.46 (range from 9.2 to 13.5 gm) with mean Hematocrit result was 39.85 ± 2.56 .
The mean platelet count was 267.73 ± 61.94 (range from 176 to 392) .
The mean neutrophil/lymphocytic ratio was 5.93 ± 1.35 (range from 3.4 to 7.9) .
CBC : Complete Blood Count . **RBCs** : Red Cell Corpuscles . **MCV** : Mean Corpuscular volume .
MCH : Mean Corpuscular Hemoglobin . **MCHC** : Mean Corpuscular Hemoglobin Concentration .
RDW-CV : Red Cell Distribution Width - Corpuscular Volume . **WBCs** : White Blood Corpuscles .

Table (3): Renal function tests and electrolyte profile in studied patients :

	Studied cases (n=30)				
	Mean	**SD**	**Median**	**Minimum**	**Maximum**
Serum Urea (mg/dl)	46.43	10.18	50.00	26.00	61.00
Serum Creatinine (mg/dl)	1.10	0.25	1.00	0.80	1.50
Serum Sodium (mEq / L)	140.43	3.50	140.00	135.00	146.00
Serum Potassium (mEq/L)	3.82	0.26	3.90	3.40	4.20
Serum Uric acid (mg/dl)	5.30	0.68	5.10	4.50	6.50

Table (3) : the mean Serum Urea level of patients was 46.43 ± 10.18 mg/dl (range from 26 to 61) .
The mean Serum Creatinine level was 1.1 ± 0.25 mg/dl (range from 0.8 to 1.5) .
The mean Serum Sodium level was 140.43 ± 3.5 mEq / L (range from 135 to 146) .
The mean Serum Potassium level was 3.82 ± 0.26 mEq / L (range from 3.4 to 4.2) .
The mean Serum Uric acid level was 5.3 ± 0.68 mg/dl (range from 4.5 to 6.5) .

Table (4): Liver function tests in the studied patients .

	Studied cases (n=30)				
	Mean	**±SD**	**Median**	**Minimum**	**Maximum**
AST (U/L)	37.63	±8.27	35.00	29.00	51.00
ALT (U/L)	26.30	±8.34	25.00	17.00	45.00
Total bilirubin (mg/dl)	1.01	±0.17	1.00	0.80	1.30
Direct bilirubin (mg/dl)	.60	±0.27	.70	0.10	1.00
Prothrombin time (12-15s)	14.17	±2.65	13.50	11.00	19.00
Serum Albumin (g/dl)	4.16	±0.29	4.00	3.80	4.70

Table (4) : the mean AST level was 37.63 ± 8.27 U/L (range from 29 to 51) .
The mean ALT level was 26.3 ± 8.34 U/L (range from 17 to 45) .
The mean total bilirubin level was 1.01 ± 0.17 mg/dl (range from 0.8 to 1.3)
The mean direct bilirubin level was 0.6 ± 0.27 mg/dl (range from 0.1 to 1) .
The mean prothrombin time was 14.17 ± 2.65 sec (range from 11 to 19 sec) .
The mean albumin level was 4.16 ± 0.29 g/dl (range from 3.8 to 4.7) .
AST: Aspartate aminotransferase, **ALT**: Alanine aminotransferase .

Table (5): Inflammatory markers in the studied patients .

	Studied cases (n=30)				
	Mean	**±SD**	**Median**	**Minimum**	**Maximum**
CRP	4.91	±4.55	5.60	0.00	12.00
ESR 1st hour	21.67	±4.22	20.00	13.00	27.00
ESR 2nd hour	47.43	±10.94	48.00	20.00	61.00

Table (5) : the mean CRP level was 4.91 with SD ± 4.55 (range from 0.0 to 12) .
The men ESR 1 st hour level was 21.67 with SD ± 4.22 (range from 13 to 27) .
The mean ESR 2 nd hour was 47.43 with SD ± 10.94 (range from 20 to 61).
SD : Standard Deviation , CPP : C-Reactive Protein , ESR : Erythrocyte Sedimentation Rate .

Table (6): Distribution of intestinal ultrasonography findings among the studied patients.

Parameters		Studied patients(n=30)	
		n	%
Bowel wall thickness	Mean± SD	4.53± 1.66	
	Median	5.0	
	Range	1.0- 6.50	
Bowel wall Stratification	Absent	9	30.0%
	Present	21	70.0%
Doppler activity	Grade 0	10	33.3%
	Grade 1	17	56.7%
	Grade 2	0	0.0%
	Grade 3	3	10.0%
enteric fat (fattywrapping)	Abnormal	0	0.0%
	Normal	30	100.0%

Table (6) : the mean bowel wall thickness was 4.53 ± 1.66 (range from 1 to 6.5) .
The bowel wall stratification was absent in 9 patients (30 %) while was present in 21 patients (70 %) .
In Doppler activity : grade 0 in 10 patients (33.3%) , grade 1 in 17 patients (56.7%) , grade 2 in 0 patients (0.0 %) , grade 3 in 3 patients (10%) .
Mesentric fat was normal in 30 patients (100%) .
SD : Standard Deviation.

Table (7): Distribution of intestinal ultrasonography findings of complications among the studied patients

Parameters		Studied patients (n=30)	
		n	%
Complications	No	24	80.0%
	Secondary reactive edema	3	10.0%
	Superficial infection, subcutaneous granulation tissue	3	10.0%

Table (7) : Intestinal Ultrasound findings of complications were absent in 24 patients (80%) while secondary reactive edema was present in 3 patients (10%) while superficial infection and subcutaneous granulation tissue was present in 3 patients (10%).

Table (8): Results of assessing the activity based on Intestinal US findings among the studied patients

Parameters	Studied patients(n=30)	
	n	%
Active	23	77.0%
Inactive	7	23.0%

Table (8) : Intestinal Ultrasound showed active disease in 23 patients (77%) and inactive disease in 7 patients (23%) .

Table (9): Distribution of colonoscopy findings among the studied patients

Parameters		Studied patients (n=30)	
		n	%
	Normal	3	10.0%
	Abnormal	27	90.0%
Colonoscopy findings	**diffuse ulceration with mucosal hyperemiamarkedly at rectosigmoid**	7	23.3%
	hyperemic mucosa with skip lesions located at sigmoid colon and ileum	4	13.3%
	non specific	3	10.0%
	terminal ileitis	10	33.3%
	terminal ileum stricture	6	20.0%
	Total	30	100.0%

Table (9) : Colonoscopy findings in patients was normal in 3 patients (10%) with non specific findings and abnormal in 27 patients (90%) which included diffuse ulceration with mucosal hyperemia , markedly at rectosigmoid in 7 patients (23.3 %) , hyperemic mucosa with skip lesions located at sigmoid colon and ileum in 4 patients (13.3%) ,terminal ileitis in 10 patients (33.3%) , and terminal ileum stricture in 6 patients (20%) .

Table (10): Distribution of CTE findings among the studied patients

Parameters		Studied patients (n=30)	
		n	%
	Normal	6	20.0%
	Abnormal	24	80.0%
CT findings	**Distal ileal long segment of circumferential mural thickening and submucosal edema with adjacent mesenteric congestion**	3	10.0%
	Normal	6	20.0%
	Recto sigmoid thickening	7	23.3%
	Terminal ileum thickening	14	46.7%
	Total	30	100.0%

Table (10) : CT findings were norrmal in 6 patients (20 %) and abnormal in 24 patients (80 %) which included Distal ileal long segment of circumferential mural thickening and submucosal edema with adjacent mesenteric congestion in 3 patients (10 %) , recto-sigmoid thickening in 7 patients (23.3%) and terminal ileum thickening in 14 patients (46.7) .
CT : Computerized Tomography.

Table (11): Distribution of intestinal MRE findings among the studied patients

Parameters		Studied patients (n=30)	
		n	%
	normal	2	7.0%
	Abnormal	28	93.0%
	Distal ileum loops and terminal ileum: mural thickening up to 5mm with mild luminal irregularity and deep fissures noted in terminal ileum.	4	13.0%
	Normal	2	7.0%
Parameters		**Studied patients (n=30)**	
		n	%
MRE findings	Terminal ileum circumferential thickening	18	60.0%
	recto sigmoid thickening	6	20.0%
	Total	30	100.0%

Table (11) : Intestinal MRE findings were normal in 2 patients (7%) and abnormal in 28 patients (93%) which included Distal ileum loops and terminal ileum: mural thickening up to 5mm with mild luminal irregularity and deep fissures noted in terminal ileum in 4 patients (13%) , Terminal ileum circumferential thickening in 18 patients (60%) and recto-sigmoid thickening in 6 patients (20%).

Table (12): Inter-rater agreement (relation) between intestinal US with colonoscopy in assessment of studied Crohn's patients

	Intestinal U/S findings	Colonoscopy findings	Test value	P-value	Kappa agreement (95% CI)
	No. = 30	No. = 30			
Normal	7 (23.3%)	3 (10.0%)	1.920	0.166	-0.163 (-0.303 – -0.024)
Abnormal	23 (76.7%)	27 (90.0%)			

P value< 0.05 is significant, P value< 0.01 is highly significant.

Table (12) : Non significant relation between Intestinal Ultrasound findings and Colonoscopy findings in the assessment of studied patients.

Table (13): Inter-rater agreement (relation) between intestinal US with C.T Enterography inassessment of studied Crohn's patients

	Intestinal U/S findings	C.T Entrography findings	Test value	P-value	Kappa agreement (95% CI)
	No. = 30	No. = 30			
Normal	7 (23.3%)	6 (20.0%)	0.098	0.754	-0.275 (-0.421 to -0.128)
Abnormal	23 (76.7%)	24 (80.0%)			

P value< 0.05 is significant, P value< 0.01 is highly significant.

Table (13) : Non significant relation between Intestinal Ultrasound findings and CT Entrography findings in the assessment of studied patients .

Table (14): Inter-rater agreement (relation) between intestinal US with M.R.E results in assessment of studied Crohn's patients

	Intestinal U/S findings	M R. Entrography findings	Test value	P-value	Kappa agreement (95% CI)
	No. = 30	No. = 30			
Normal	7 (23.3%)	2 (6.7%)	3.268	0.071	-0.116 (-0.249 to 0.017)
Abnormal	23 (76.7%)	28 (93.3%)			

P value< 0.05 is significant, P value< 0.01 is highly significant.

Table (14) : Non significant relation between Intestinal Ultrasound findings and MR Entrography findings in the assessment of studied patients .

Table (15): Correlation in validity of intestinal US in comparsion to Colonoscopy in diagnosis of patients with Crohn's Disease

		Colonoscopy findings		Test value	P-value	Sig.
		Normal	Abnormal			
		No. = 3	No. = 27			
Intestinal U/S findings	Normal	0 (0.0%)	7 (25.9%)	1.014	0.314	NS
	Abnormal	3 (100.0%)	20 (74.1%)			

Colonoscopy findings	TP	TN	FP	FN	Sensitivity	Specificity	PPV	NPV	Accuracy
Intestinal U/S findings	20	0	3	7	74.1%	0.0%	87.0%	0.0%	0.667

P value< 0.05 is significant, P value< 0.01 is highly significant.

Table (15) : Non significant correlation in validity of Intestinal US in comparison to Colonoscopy in diagnosis of patients with Crohn's disease with accuracy 0.667 .

Table (16): Correlation in validity of intestinal US in comparsion to C.T Enterography in diagnosis of patients with Crohn's Disease

		C.T Entrography findings		Test value	P-value	Sig.
		Normal	Abnormal			
		No. = 6	No. = 24			
Intestinal U/S findings	Normal	0 (0.0%)	7 (29.2%)	2.283	0.131	NS
	Abnormal	6 (100.0%)	17 (70.8%)			

C.T Entrography findings	TP	TN	FP	FN	Sensitivity	Specificity	PPV	NPV	Accuracy
Intestinal U/S findings	17	0	6	7	70.8%	0.0%	73.9%	0.0%	0.567

Table (16) : Non significant correlation in validity of Intestinal US in comparison to CT Entrography in diagnosis of patients with Crohn's disease with accuracy 0.567 .

Table (17): Correlation in validity of intestinal US in comparsion to M.R. Enterography in diagnosis of patients with Crohn's Disease

		M R. Entrography findings		Test value	P-value	Sig.
		Normal	Abnormal			
		No. = 2	No. = 28			
Intestinal U/S findings	Normal	0 (0.0%)	7 (25.0%)	0.652	0.419	NS
	Abnormal	2 (100.0%)	21 (75.0%)			

M R. Entrography findings	TP	TN	FP	FN	Sensitivity	Specificity	PPV	NPV	Accuracy
Intestinal U/S findings	21	0	2	7	75.0%	0.0%	91.3%	0.0%	0.700

Table (17) : Non significant correlation in validity of Intestinal US in comparison to MR Entrography in diagnosis of patients with Crohn's disease with accuracy 0.700 .

Discussion

IBD include idiopathic intestinal diseases , differ in their site and level of involvement in the bowel wall. Ulcerative colitis (UC) causes inflammation of the colonic mucosa , usually affects the rectum (proctitis), but it may extend proximally to the sigmoid (proctosigmoiditis), beyond the sigmoid (distal ulcerative colitis), or affecting the entire colon into the cecum (pan colitis). [(4)]

Crohn's disease (CD) causes transmural inflammation and ulceration of any part of the gut , with preference of the terminal ileum and colon . Both diseases are classified based on their severity (mild, moderate, or severe) and location. CD is also characterized according to its phenotype into inflammatory, structuring, or penetrating. [(4)]

Mucosal healing, assessed by colonoscopy, is the therapeutic target which is associated with lower rates of clinical relapse and costs.

Because of the disadvantages of colonoscopy as safety, accessibility, expense, and patient preference, cross-sectional imaging had become increasingly important for the routine monitoring of IBD. [(5)]

Current imaging modalities for the assessment of IBD include computed tomography (CT) and magnetic resonance enterography (MRE) , however CT is associated with ionizing radiation exposure so , unsuitable for repeated use, while MRE is expensive and not available in each setting. MRE however, is the gold standard imaging modality for detecting active disease, especially in the small intestine.[(6)]

The advantages of doing an Intestinal Ultrasound performed by a Gastroenterologist who is involved in patient care are numerous , including taking medical decisions in management at the bedside quickly from the clinic. [(7)]

This Cross sectional study was conducted in the inpatient and outpatient clinics of Gastroenterology department in Ain Shams University Hospitals on patients diagnosed with CD , to assess the sensitivity & specificity of Intestinal Ultrasound In diagnosis of patients with CD, assessing activity and possible complications.

The mean age of our patients was 54.3 ± 7.69 years (range from 38-68 years) which is close to ***Ripollés et al.*** [(8)] as the mean age of their patients was 45.6 ± 15.46 years. Also , ***El Megeed et al .*** [(9)] and ***Lenze et al.*** [(10)] had ages ranging between (34 - 65 years) and (22- 63 years) respectively

which agree with our age range.

On the other hand, our study disagreed with ***Neye et al.*** [11] as the mean age in their study was 36.3 years with range between 13-86 years. Also , ***Girlich et al.*** [12] the median age of their patients was 34.9 years, with range from 25 to 48 years. This difference may be related to the different inclusion and exclusion criteria .

In our study , males cases were more than females ones, as (70%) were males while (30%) were females (ratio was 2.33: 1) , which agree with ***Girlich et al*** [12] as 55% of their patients were males and 45% were females and ***Lahat et al.*** [13] who found 53.6% of their cases were males and 46.4% were females.

While ***Ripollés et al.*** [8] and ***El Megeed et al.*** [9] had equal numbers of both sexes (50% males and 50% females). also, our study disagree with ***Neye et al. (11)*** and ***Lenze et al.*** [10] as their female were more than males with females percentages were 53.44%, 56.6% respectively. This can be explained as gender- specific differences had been reported for CD, but not UC, although data are conflicting depending on geographic areas. In Europe and the United States, ***Wagtmans et al.*** [14] found that CD was higher in females than in males, while in Asia as in ***Prideaux et al.*** [15] and ***Leong et al.*** [16] , the opposite has been noted .

Shah et al. [17] revealed more complex relation between sex and CD , as they found that young females aging 10–14 years showed a significantly lower risk (up to 20%) for CD compared to men. Females aged between 25 and 29, and especially older than 35 , are more prone to CD than their male counterparts (up to 40%) . This was due to longer diagnosis delay for females. which was related to an increase in IBD complications and a higher risk of related intestinal surgery.

Our study revealed that the mean hemoglobin level was 11.66 ± 1.46 mg/dl, and the mean RBC, 4.18 ± 0.48 , the mean platelets was 267.73±61.94 (K/UL), WBCs was 9.94 ± 1.83 (K/UL), neutrophils was 7648.57 ± 1460.02 (/UL), and lymphocytic count was 1356.50 ±469.30 (UL) and neutrophil/ lymphocyte ratio (NLR) was 5.93 ±1.35.

This agrees with ***Harewood and Markovic*** [18] whose CBC results as they had the mean hemoglobin level was 11.0 g/dl , the mean WBC was 6 and the mean platelets was 330 and ***Al-Ghamdi et al.*** [19] as their patients mean hemoglobin level was 10.8 ± 1.89, the mean platelets was 429.9 ± 161 and the mean WBC count was 9.06 ± 3.95 and ***Pipili et al.*** [20] where hemoglobin level was was 12 g/dl with HCT at 37.5% and MCV of 90 FL, while they had platelet count at 369 × 103/μL, and WBC at 7.1 × 103/μL with 72.1% neutrophils, 18.7% lymphocytes, 6.8% monocytes, and 0.5% eosinophils.

While ***Feagan et al.*** [21] showed a little difference as the mean Hb levels for their two groups in their study were 13.42 ± 1.57 and 13.14 ± 1.80, WBC were 10.6 ± 3.7 and 11.0 ± 3.1, their mean Platelet count were 352 ± 113 and 363 ± 110. Also , ***El Megeed et al.*** [9] revealed that the mean Hb levels for their two groups were 10.14 ± 0.59 and 9.87 ± 0.63, HCT were 35.9 ± 2.9 and 36.32 ± 2.9, WBC were 12.25 ± 0.9 and 14.3 ± 1.4, and their mean Platelet count were 519.2 ± 54.3 and 498.42±44.3. Moreover, ***Neary et al.*** [22] disagreed with our results as the mean WBC was lower than our results , as their results were 7.9 and 9.5, and their HCT were 37.8 ± 5.2 and 36.0± 5.5 and the mean Platelet counts were 307.3 ± 104.9 and 336.5 ± 126.2.

Feng et al. [23] disagreed with our results as the mean WBC was 5.79, the mean Neutrophil was 3.49, mean Lymphocyte was 1.44 ± 0.74 mean Monocyte was 0.48 with mean Platelet count was 237.00.

The differences in CBC findings can be explained by several factors that affect the CBC in CD patients as it was active or not, patients on medical treatment and its type , symptoms as recurrent diarrhea and blood loss. Many factors can cause anemia in CD patients as cobalamin or folic acid deficits, iron deficiency and anemia of chronic disease. Chronic intestinal bleeding, iron malabsorption, or poor food intake can also lead to iron insufficiency.

Xu et al.[24] and ***Cherfane et al.***[25] revealed that the RDW and the NLR were increased in active UC and CD, However , ***Demir et al.***[26] ***and Goa et al.*** [27] reported that the NLR had no value in assessing the disease activity , so , the role of the NLR in predicting the activity of UC and CD remains controversial.

Regarding the renal function tests and electrolyte

profile , the mean serum urea, creatinine and uric acid were 46.43 ±10.18, 1.10 ±0.25 and 5.30±0.68 mg/dl which agreed with ***Takazono et al .*** [28] who found that the mean urea was 17.0 mg/dl and the mean creatinine was 0.92 mg/dl and ***Neary et al.***[22] who found that the mean blood urea was 11.8 ± 6.5 and 12.1± 6.2 and the mean Serum creatinine was 0.78 [0.20, 6.5].

This disagreed with ***Pipili et al.*** [20] who found higher results of renal functions tests as mean creatinine 2.5 mg/dL (0.6–1.0), blood urea 54 mg/dL (15–40) and uric acid was 8.3 mg/dL (2.6–6.0).

This can explained by ***Izzedine et al.***[29] who revealed that renal manifestations are rare in CD, but renal complications as different types of glomerulonephritis, tubulointerstitial nephritis , AA amyloidosis, tubular defects, and hyperoxaluria could occur. they suggested that mesalamine was responsible for the development of chronic nephropathy. While ***Tovbin et al.*** [30] suggested that IBDs were not included in the pathogenesis of chronic interstitial nephritis either in nephrology textbooks or general reviews.

Our study revealed that the mean levels of Na and K were 140.43-±3.50 and 3.82±0.26 mEq/L respectively which agreed with ***Takazono et al.*** [28] as the mean Na was 135 mEq/l, and the mean K was 3.8 mEq/l and ***Neary et al.*** [22] mean levels of Na was 139.0 ± 2.7 and 138.4 ± 3.0.

Regarding the Liver function tests , We found that the mean AST was 37.63 ±8.27 U/L, the mean ALT was 26.30 ±8.36 U/L, the mean total bilirubin was 1.01±0.17 mg/dl and the mean direct bilirubin was 0.60 ±0.27 mg/dl , the mean Prothrombin time (PT) was 14.17±2.65 sec. and the mean Serum Albumin was 4.16 ± 0.29 g/dl. This agreed with ***Neary et al.*** [22] who revealed that total bilirubin was 0.40, the mean Albumin was 3.7 ± 0.64 and 3.3 ± 0.74, the mean PT was 13.2 and 11.6 sec and ***Pipili et al.*** [20] and ***Takazono et al.*** [28] found that all their liver functions were normal .

On the other hand,the results disagreed with ***Sævik et al.*** [31] who found that their main albumin levels were 45.0 and 30.7 respectively with increased AST and ALT levels 144.9±215.8 U/L and 88.8±112.5 U/L respectively. Their total and direct bilirubin levels were 5.1±7.7 mg/dL and 4.1±7.7 mg/dL, respectively.also, ***Cappello et al.*** [32] reported that abnormal liver chemistry was detected in 20.9% of their patients and in 27.1% of ***El-Shabrawi et al.*** [33] results . Their findings agreed with ***Broomé et al.*** [34] who found that 1.4%-7.5% of their patients developed PSC during the course of disease and usually presented with jaundice.

In this study , the mean CRP was 4.91 ±4.55, the mean ESR at first hour was 21.67 ±4.22 and 2nd hour was 47.43±10.94. This agreed with ***Sævik et al.*** [31] as CRP was 1.5 and ***Al-Ghamdi et al.*** [19] who found that, the mean ESR was 42.8 ± 27.8 and ***Menees et al.*** [35] who found normal CRP and ESR. this can be explained that these serum biomarkers evaluated have no clear role in IBD .

While ***Henriksen et al.***[36] revealed that an elevated CRP was present in patients with Crohn's disease than ulcerative colitis.

Regarding the Intestinal Ultrasonography findings among the studied patients, the mean bowel wall thickness (BWT) was 4.53± 1.66, the mean Bowel wall stratification was found in (70%). Doppler activity: Grade 1 was the commonest between studied cases (56.7%) . the normal mesenteric fat was found in all cases (100%).

As regard the Complications findings , secondary reactive edema was found in 10% of the cases, also, the superficial infection and the subcutaneous granulation tissue were found in 10% of the patients.

Many studies revealed that the most important parameter is BWT, with a threshold > 3.0 mm which agreed with our findings. ***Ramaswamy et al.***[37] stated that the BWT was greater in patients with active disease as compared to those in endoscopic remission (6 mm vs. 2.45 mm).

Bhatnagar et al. [38] revealed that BWT ranged from 3 to 12 mm as the mean BWT was 6.2 mm and the median was 5.5 mm. also, ***Rosenbaum et al.*** [39] demonstrated that surgical group had increased mean BWT 6.1 ± 1.8 mm VS 4.7 ± 1.7 mm for the non surgical group.they compared Intestinal US findings with resection specimens to evaluate different mural and extramural US features as potential imaging predictors of histologic inflammation and confirmed a significant association of BWT and mucosal layer thickness with acute inflammation, while mesenteric fat echogenicity correlated with chronic inflammation. Furthermore, ***Maconi et al.*** [40]

revealed that BWT was best indicator of inflamematory activity in CD.

Also, ***Novak et al.*** [41] revealed that BWT was the most important indicator of disease activity for ultrasound with a very high inter-rater agreement with correlation with disease activity. A BWT of 3 mm had 88% sensitivity and 93% specificity for diagnosing IBD in a study by ***Panés et al.*** [42] **,** they added that When using a cut-off of 4 mm, the specificity increased to 97%. also, ***Ramaswamy et al.*** [37] stated that BWT of > 3 mm had a sensitivity and specificity of 100% and 83%, respectively, for detecting active CD; BWT of > 4 mm had a specificity of 91.6%. also , ***Kucharzik et al.*** [43] revealed that increased bowel vascularity as indicated by increase Doppler signals, correlated with clinical and endoscopic disease activity in CD .

Castiglione et al. [44] demonstrated that transmural healing with normalization of the BWT (e.g., 3 mm) was strongly correlated with mucosa healing(found in up to 25% of patients treated with anti-TNF drugs) . also , ***Castiglione et al.*** [45] discovered good concordance of BWT with both ileocolonoscopy and MRI, indicating the possible role of IUS in monitoring CD patients, even in pediatric age. Moreover, ***Spalinger et al.*** [46] discovered that the persistence of enhanced vascularity following therapy was a sign for an increased risk of relapse.

Also, ***Kucharzik et al.*** [43] found the BWT corresponded with clinical activity markers with the common cutoff values for the small intestine were 2 mm and 3-4 mm for the large intestine. Also , ***Livne et al.*** [47] found an association between IUS findings specifically in terminal ileum thickness and mesenteric fat hypertrophy, and the MaRIA score.

Also , the small bowel US had high sensitivity and specificity for the diagnosis of small bowel CD, as in ***Castiglione et al.*** [44] ***Quaia et al.*** [48] who found that it was ranging from 86% to 97% and 83%, respectively.

Calabrese et al. [49] revealed that IUS had 80% sensitivity and 97% specificity for the CD diagnosis when compared with reference standards as clinical evaluation, endoscopy, histology and/or radiology**.** ***Parente et al.*** [50] found that the accuracy of US depended on the site and severity of CD**.** In comparison with ***Panés et al.*** [42] who found that as compared to endoscopy, cross-sectional imaging were less accurate to detect mild inflammatory intra-luminal lesions**.**

Carter et al. [51] found that in suspected small intestinal CD , IUS and small bowel capsule endoscopy (SBCE) had similar findings. with 72% of sensitivity and 84% of specificity. On the same point, ***Kopylov et al.,*** [52] revealed that this percentages could be increased by using oral contrast agents (e.g., SICUS) specially in the assessment of proximal small intestine .

Furthermore, ***Greenup et al.*** [53] and ***Rimola*** [54] discovered that IUS had an accuracy comparable to CTE and MRE for CD diagnosis, with a sensitivity and specificity ranging between 75% and 100%. also, ***Rimola*** [54] demonstrated that IUS had high specificity for strictures, fistulas, and abscesses .

While ***Calabrese et al.*** [49] found that the role of IUS in assessing disease activity is still debatable , ***Rimola et al.*** [54] discovered that four US-based parameters (wall thickening, Doppler signal, loss of stratification, and reduced peristalsis/ compressibility) showed good correlation with endoscopic reference standard. ***Castiglione et al.*** [55] reported that sensitivity could be enhanced using oral contrast, with a BWT greater than 4 mm had a sensitivity and specificity of 86% and 96% .

Buisson et al. [56] indicated a high efficacy in the identification of mucosal healing, with high specificity (82%). ***Yuksel et al.*** [57] stated that the US had equal accuracy to MRE in detecting endoscopic activity, with the most significant IUS sign was increased BWT (>3 mm) . the US approach was more sensitive in detecting ascites, whereas other mesenteric characteristics were comparable between the two procedures. When contrast enhancement US (CEUS) was usedy by ***Paredes et al.*** [58] , a combination of wall thickness >5 mm, contrast enhancement >70%, or the presence of a fistula had a sensitivity of 94.1% and a specificity of 73.1 % for severe postoperative recurrence.

Also , ***Cicero and Mazziotti*** [59] found that loss of mural stratification in the surgical cases was 86% and in the non-surgical cases was 50% with increased fibro fatty proliferation in the surgical cases more than in the non- surgical cases . When compared to a CT scan, ***Maconi et al.*** [40] revealed that the Mesenteric fatty wrapping had sensitivity and specificity of > 83 %. They also

demonstrated that in patients who responded well to treatment, the mesenteric fat wrapping reduced. Also,

Bryant et al. [60] indicated that diminished peristalsis was noticed in affected bowel segments, however, because it is a subjective dependant, it was not well standardized.

Castiglione et al. [45] found a high correlation in detecting stricturing and penetration.US showed reduced sensitivity for stricture diagnosis, especially pelvic lesions when compared to MRE.

Ramaswamy et al. [37] ***and Panés et al.*** [42] stated that GIUS was beneficial in assessing complications as strictures, fistulae, and abscess with sensitivity 79% and the specificity 92% in detecting stensosis .

Maconi et al. [40] used CEUS that increased the sensitivity for detecting stenosis in CD by up to 89%. In the study of ***Ramaswamy et al.*** GIUS detected stenosis in 75% of the patients. GIUS had a sensitivity of 74% and a specificity of 95% for the detection of fistulae in CD. In the postoperative scenario, in CD, BWT > 3 mm on GIUS done 1 year after surgery had a sensitivity of 77 to 81 % and specificity of 86 to 95 % for detecting recurrence. According to ***Panés et al.,*** [42] GIUS could detect intestinal abscesses with a sensitivity of (83 - 100 %) and a specificity of (84 -94%) .

In this study, 27 of our patients were detected by colonoscopy and 3 were not. The findings were included diffuse ulceration with mucosal hyperemia markedly at recto-sigmoid in 23.3% of the patients, hyperemic mucosa with skip lesions located at sigmoid colon and ileum in 13.3% of the patients, terminal ileitis in 33.3% patients and terminal ileum stricture in 20.0% patients. this is consistent with ***Leighton et al.*** [61]

Allocca et al. [62] discovered that endoscopically active CD was present in all of their subjects .***Huang et al.*** [63] reported that (78%) of their patients detected by colonoscopy by taking into account the clinical presentation, endoscopic and histological results with the experimental treatment. even more double-balloon enteroscopy (DBE) assisted in the diagnosis in 86% of the patients.

Feakins et al. [64] showed a disagreement between clinical and endoscopic remission, but the assessment of mucosal healing during IBD therapy was relevant to clinical practice.In addition, ***Rahman et al.*** [65] found that enteroscopy allowed for macroscopic and histological evaluation as well as therapeutic intervention but had limited role in the care of patients with IBD . Furthermore, ***Leighton et al.*** [61] and **Xie X and *McGregor*** [66] indicated that the vedio capsule endoscopy allowed for direct and less invasive imaging of the small intestinal mucosa with detection of superficial lesions that were missed by endoscopy and standard radiography. It is helpful for the initial diagnosis of CD, detecting recurrences, the degree of the disease, assessing response to medication, and distinguishing betwween unexplained UC and CD.

In this study out of all patients, 80% were detected by CT and 20% were not detected. The findings were distal ileal long segment of circumferential mural thickening and submucosal edema with adjacent mesenteric congestion in 10% of the patients, recto sigmoid thickening in 23.3% and terminal ilium thickening in 46.7%.

Saade et al. [67] revealed that on CT findings , inflammation was found in the terminal ileum in 91% of patients. 9% patients had other identified affected segments including sigmoid colon, jejunum, and the ileo-colic anastomosis in patients with previous bowel resection. The length of the affected segments ranged between 1.2 cm and 40 cm with a mean of 9.2 cm.

Huang et al. [63] discovered that the imaging techniques MRE and CT have great sensitivity and specificity for diagnosing active inflammation in the small bowel, particularly stenosis, penetration, and extra-intestinal symptoms.

According to ***Park and Lim,*** [68] the most important CT finding in CD patients was thickening of the intestinal wall, which was seen by CT in at least 80% of their patients, which is consistent with our findings. Another finding in ***Bruining et al.*** [69] study ,the abnormalities in CT should differ from those in cryptogenic multifocal ulcerous stenosing enteritis, intestinal involvement of connective tissue disease, and chronic ischemic bowel illness.

Spektor et al. [70] demonstrated that the sensitivity of CT in detecting the most relevant acute findings of CD (i.e., abscess, fistula, bowel wall thickening, free fluid, stricture, and bowel obstruction) was significantly similar to MRE.

Furthermore, ***Deepak et al.*** [71] noted that high rates of sensitivity and specificity (up to 90%) have been found for CD identification when compared to clinical, histologic, and endoscopic characteristics,. Moreover ***Fiorino et al.***[72] reported sensitivity ranging from 67 to 95 % and specificity ranging from 70 to 90 %.

Mao et al. [73] discovered 87.5 % sensitivity and 100 % by developing their own CT scoring grade for comparing imaging findings with endoscopic grade.

In our study. Kappa statistics revealed poor agreement between IUS and colonoscopy results in assessment of studied Chron's patients ,(k=-0.163) .this is supported by the study revealed that it couldn't accept that intestinal US can replace colonoscopy, but it could be a valid non-invasive tool that can be combined with inflammatory biomarkers to avoid colonoscopy, ***(Maconi et al).*** [40]

Howerver, a study used ileocolonoscopy as a comparative investigation, showed the normalization of the IUS parameters in 62.8% of the patients, with a significant correlation of the endoscopic modifications. These results also prove the usefulness of IUS when monitoring the evolution and treatment response in patients with Crohn's disease ***(Moreno et al).*** [74]

Also in our study, Kappa statistics revealed poor agreement between Intestinal US and MRE results in assessment of studied Chron's disease patients (k=-0.116). This is supported by a study showed some limitations about the use of intestinal US in CD. The most common is that the accuracy of IUS in evaluating CD depends on the anatomical distribution of the disease, resulting in lower detection of lesions in jejunum and rectum**.** Also, intestinal US is highly operator- dependent ***(Calabrese et al)*** [49]

However, a study explained that the sensitivity, specificity, and accuracy of IUS compared with MRE alone for all considered parameters [localisation, enhancement, active disease, strictures, fistulas, abscesses] was more than 80% (***Mariangela Allocca et al)*** [75]

Also ,Kappa statistics revealed poor agreement between Intestinal US and CTE results in assessment of studied Charon's patients (k=0.275).

CTE Showed limited ability to detect. especially the complications as fibrosis by the study ***(Adler et al).*** [76]

With comparison with IUS , CTE had superior outcomes for the detection of fistulas with taking shorter time than Intestinal US during the procedure ***(Greenup et al)*** [53]

Greenup et al. [53] concluded that CT, MRE, and US had equivalent efficacy for the overall diagnosis of CD, with US being the preferred method for distinguishing fibrosis from inflammation.

In our included studies, imaging, particularly CTE and US, appears to have comparable outcomes to endoscopy for the detection of postoperative recurrence. They proposed that, while stenosis diagnosis may be restricted, detection of transmural problems as abscesses and fistulas is a definite advantage of small bowel imaging over endoscopic screening alone. ***(Borthne et al)*** [77] in this study; they compared MRI and US in pediatric patients with probable IBD, using ileocolonoscopy as the gold standard. The sensitivity of US was higher than that of MRI (93 % vs. 82 %), but the sample size was small and , more critically, only the terminal ileum, the area with the best accuracy for US, was studied.

Maffè et al. [78] in conjunction with our study, our findings, and the papers we searched, we can state that transabdominal bowel US, color and power Doppler, Contrast-enhanced US, and Small intestine contrast US, is quite valuable in the diagnosis and, more importantly, the follow-up of Crohn's disease. although not specific, US is sensitive and can promptly lead further investigations in the initial diagnosis; on the other hand, in the follow-up, it can assess the site and extent of disease and detect complications , including extra intestinal complications .

In a meta-analysis involving 33 patients, ***Horsthuis et al.***[79] investigated the accuracy of MRI, CT, and US in the diagnosis of IBD when compared to colonoscope . mean sensitivity estimates for the diagnosis of IBD (including CD and/or ulcerative colitis) were high and did not differ significantly between the 3 imaging modalities (90 %, 93 %, and 84% for US, MRI and CT respectively). This, together with the need to limit radiation exposure, makes the use of US or MRI preferable.

The current findings, however, emphasize that, while colonoscopy is the gold standard in CD, US, such as CT and MRI, can provide information about the luminal side and serous of the

bowel and the peripheral structure; additionally, US is repeatable, safe, and well-accepted, but unlike CT is radiation-free, and unlike MRI is cheap, virtually hazard-free, and available to all patients without contraindications.

This is an exploratory study, and we propose that US can be used to assess disease activity in CD. US is useful with other imaging modalities such as MRE and CT, as well as endoscopy. US conducted by skilled Gastroenterologists behaves similarly to MRE.

CONCLUSION

Crohn's disease (CD) is a progressive, inflamematory disease that occurs in genetically predisposed individuals which necessitates continuous monitoring and development of various methods for diagnostic and therapeutic treatment options, as well as the discovery of new medications.

While colonoscopy is the gold standard in CD, US, CT and MRI, can provide information not only about the luminal side of the bowel but also about the serous side and the peripheral structure; additionally, US is repeatable, safe, and well-accepted, but unlike CT is radiation-free, and unlike MRI is inexpensive, virtually hazard-free, and available to all patients without contraindications.

US can be used to assess disease activity in CD when combined with other imaging modalities such as MRE and CT, as well as endoscopy.

US performed by expert Gastroenterologists performs similarly to MRE, and it can be a very valuable technique in the absence of high-quality MRE in resource-constrained settings.

The US is accurate in locating active illness in CD and may also be useful in assessing CD sequelae. US could be used to monitor disease activity in the future, reducing the need for biomarkers and costly examinations like MRE.

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