Diagnostic Value of Upper and Lower Endoscopy in Assessment of Patients with Microcytic Hypochromic Anaemia without Site-specific Gastrointestinal Manifestations

Mohammed Tag-Adeen Said Hussien[a], Huda Abdelhamied Mohammed Dardeer[a], Mahmoud Aboelsoad Gehlan Ali[a*], Asmaa Abd elhakim Nafady[b]

[a]Department of Internal Medicine, Faculty of Medicine, South Valley University, Qena, Egypt
[b]Department of Clinical Pathology, Faculty of Medicine, South Valley University, Qena, Egypt

Abstract

Background: Iron deficiency anemia (IDA), is often caused by digestive disorder and should always be assessed, as its causes could be severe illness such as cancer.

Objectives: To study the diagnostic value of both upper and lower endoscopic examinations among patients with microcytic hypochromic anaemia without site -specific gastrointestinal (GIT) manifestations.

Patients and methods: A total of 50 Egyptian patients with IDA were included. Patients were clinically evaluated and investigated for: Complete blood picture, serum ferritin, serum iron and total iron binding capacity (TIBC). Patients were screened with Esophagogastroduodenoscopy (EGD) and colonoscopy.

Results: The mean ±SD age of the patients was 36.4 ± 16.7, 19 males (38%) and 31 females (62%). The most common finding of EGD was Gastritis, it was present in 20 patients (40%) followed by Peptic ulcer in 9 patients (18%). There were 2 patients (4%) with celiac disease, 1 patient (2%) with crohn's disease, 2 patients (4%) with Gastric cancer, and 1 patient (2%) with angiodysplasia while there were 14 patients (28%) with normal EGD. Both procedures showed negative findings in 10 patients (20%), both procedures showed positive findings in 8 patients (16%) while 1 procedure only showed positive finding in 32 patients (64%).

Conclusion: Bidirectional endoscopies are valuable to detect the cause of IDA in patients without site –specific (GIT) manifestations. The most common GIT lesions were gastritis followed by peptic ulcer.

Keywords: IDA; Endoscopy; Gastritis.
DOI: 10. 21608/svuijm.2023.199049.1550
***Correspondence** mahmoudaboelsoad107777@gmail.com
Received: 11 Februray,2023.
Revised: 14 March, 2023.
Accepted: 1 April, 2023.
Published: 8 April, 2023

Cite this article as: Mohammed Tag-Adeen Said Hussien, Huda Abdelhamied Mohammed Dardeer, Mahmoud Aboelsoad Gehlan Ali, Asmaa Abd elhakim Nafady. (2023). Diagnostic Value of Upper and Lower Endoscopy in Assessment of Patients with Microcytic Hypochromic Anaemia without Site-specific Gastrointestinal Manifestations. *SVU-International Journal of Medical Sciences*. Vol.6, Issue 2, pp: 140-151.

Introduction

Due to its role as a constituent of heme, iron sulphur proteins, and other enzymes, iron supports chemical reactions that are necessary for life. Pathological conditions are linked to both iron excess and iron shortage **(Silva et al., 2015).** Inflammation, dietary iron loss, liver illness, improper iron absorption, frequent blood transfusions and abnormal erythropoiesis, overwhelm physiological systems that maintain iron homeostasis **(Wang et al., 2019)**.

According to the World Health Organization (WHO), iron insufficiency is the most prevalent micronutrient deficiency globally and one of the most significant public health issues, impacting over 25% of the global population **(Nambiema et al., 2019).** When iron deficit is severe enough to affect erythropoiesis, iron deficiency anaemia (IDA) develops. The most common form of chronic anaemia is this one. Either excessive loss of iron or, less frequently, reduced absorption can lead to an iron deficit **(Johnson-Wimbley, 2011).**

IDA frequently results from occult GIT bleeding. According to recent research, the majority of IDA patients have a significant GI tract pathological abnormality **(Reddy et al., 2021).** The GI tract should be examined in patients with unexplained IDA who don't have any visible bleeding. The American Gastroenterological Association advise both EGD and Colonoscopy bidirectional endoscopy **(Ko et al., 2020).** The ideal diagnostic test for individuals whose signs or symptoms suggest upper gastrointestinal disease, such as dyspepsia, dysphagia, and non-cardiac chest discomfort, is EGD **(Lai et al., 2016)**. Successful optical colonoscopy allows inspection from rectum to caecum and permits diagnostic biopsy and management with immediate elimination of any polyps in a pre-cancerous stage (**Burton et al.,2020).** The aim of our research is to study the diagnostic value of both upper and lower endoscopic examinations in individuals with microcytic hypochromic anaemia without site–specific GIT manifestations

Patients and methods

50 Egyptians patients with unexplained IDA were enrolled in the current study.

The inclusion criteria were: Patients aged 18 years or more who were proved as having unexplained IDA.

Exclusion criteria were Patients suffering from chronic liver and kidney diseases, complaining haemorrhagic diseases, and other types of anemia other than IDA.

All participants provided written informed consent before their inclusion in the study. The study is approved by the institutional ethical committee of the Faculty of Medicine, Qena, with an approval number (SVU-MED-MED018-1-22-2-337).

All subjects were assessed to the following

I. History and Clinical Examination

1- History taking, which include personal history, history of present illness and history of comorbidities such as HTN, cardiac disease, DM and Medication history.
2- Full Clinical Examination was assessed with focus on anemia and GIT manifestations.
3- Anthropometric measurements: Weight, height and body mass index (BMI).

II. Laboratory Investigations: All the following investigations were done with evaluation of indices:

1. Complete blood count by Erma Automated Blood Count instrument (Tokyo, Japan): red blood cells (RBCs), hemoglobin concentration (Hb %), platelet count, white blood cells (WBCs).
2. Serum ferritin was evaluated by the Architect 2000 system (Abbott Diagnostics, Dallas, USA).
3. Serum iron and total iron binding capacity (TIBC) were estimated by the Cobas-C311 (Roch Diagnostics, Mannheim, Germany).
4. Liver profile: (ALT) Alanine aminotransferase. (AST) aspartate aminotransferase, prothrombin time (PT) and INR, which were normal.
5. Renal function test: serum urea and serum creatinine, which were normal.
6. ESR and CRP, which were normal.
7. HBs Ag (Hepatitis B surface antigen) and HCV Ab (Hepatitis C antibodies), which were normal.

III. Oesophagogastroduodenoscopy (EGD) and colonoscopy: This was done as known by the center policy at Qena University Hospitals from February 2022 to February 2023 using sterile upper and lower GIT video scope after good patients' preparation. An endoscopic examination was done following an overnight fast for 6 hours with or without sedation according to the patient. All endoscopies were carried out using Pentax machine (I series model, Pentax Corporation, Tokyo, Japan) under local xylocain spray of the throat. The gastric inspection findings were recorded.

Statistical analysis

The data was analyzed using the Statistical Software for Social Sciences (SPSS) version 26.0. Continuous data was presented as mean ± standard deviation (M ± SD), whereas qualitative variables were described as frequency and percentage (%) and were compared using Student's t-test.

Results

The mean age of all studied patients was 36.4 ± 16.7 years old, there were 19 males (38%) and 31 females (62%) with predominance of females, and most females were housewives (**Table 1**). There were 10 smokers (20%), 7 hypertensive patients (14%), 7 diabetic patients (14%) and 12 patients (24%) took NSAIDs.

Table 1. Demographic description of the patients.

Variables		**Patients (N = 50)**	
Age (years)	**Mean ±SD**	36.4 ± 16.7	
	Min – Max	13 – 80	
Sex	**Male**	19	38%
	Female	31	62%
Residence	**Rural**	31	62%
	Urban	19	38%

As regard laboratory data, the mean of Hb, MCV, RBCs, HCT, and MCH were 9.5 ± 2.1, 69.6 ± 6.8, 4.4 ± 0.7, 29.6 ± 5.5, and 21.9 ± 4.1, respectively (**Table 2**). The mean serum iron, transferrin, ferritin, and TIBC were 27.6, 12.2, 11.4 and 497.1, respectively (**Table 3**).

Table 2. Description of CBC in the studied patients

(n = 50)	Mean±SD (Minimum - Maximum)	Normal reference range
Hb (g/dl)	9.5±2.1 (4.3-12.8)	11.5 : 15.2
MCV (Fl/cell)	69.6±6.8 (49.3-77)	77 : 97
RBCs (x10³/ul)	4.4±0.7 (2.2-5.2)	3.8 : 5.2
HCT (%)	29.6±5.5 (15.9-39.3)	35 : 46
MCH (pg/cell)	21.9±4.1 (12.5-29.8)	26 : 34
MCHC (g/dl)	29.7±2.4 (22.7-34.1)	32 : 35
RDW (%)	19.4±4.8 (11.5-31.8)	37 : 49
PLTs (x10³/ul)	317.8±74.9 (172-520)	150 : 400
WBCs (x10³/ul)	6.6±1.8 (3.98-10.5)	3.5 : 10
Neutrophil (x10³/ul)	3.8±1.3 (2-6.8)	1.6 : 7
Lymphocytes (x10³/ul)	2.1±0.7 (1.3-3.4)	1 : 3
Monocytes (x10³/ul)	0.5±0.4 (0.1-1.3)	0.2 : 0.8
Eosinophil (x10³/ul)	0.12±0.07 (0-0.4)	0.0 : 0.5
Basophil (x10³/ul)	0.02±0.03 (0-0.1)	0.0 : 2

Table 3. Iron panel findings among the included patients

(n = 50)	Mean±SD (Minimum- Maximum)	Normal reference range
Iron (ug/dl)	27.6±5.6 (9.5-34)	33 : 193
Transferrin (ug/dl)	12.2±2.3 (1-15)	15 : 50
Ferritin (ug/dl)	11.4±2.7 (3-15)	15 : 200
TIBC (ug/dl)	497.1±59.3 (450-764)	250 : 450

Pelvi-abdominal U/S was normal in 46 patients (92%) and abnormal in 4 patients (8%), 3 patients had mild splenomegaly and 1 patient had mild hepatomegaly. The most common finding upper GIT endoscope was gastritis (**Fig.1A,B,C,D,& E**), it was present in 20 of patients (40%) followed by peptic ulcer (**Fig.2A,B,C,D,& E; Fig.3A &B; Fig.4A,B &C**) in 9 patients (18%).

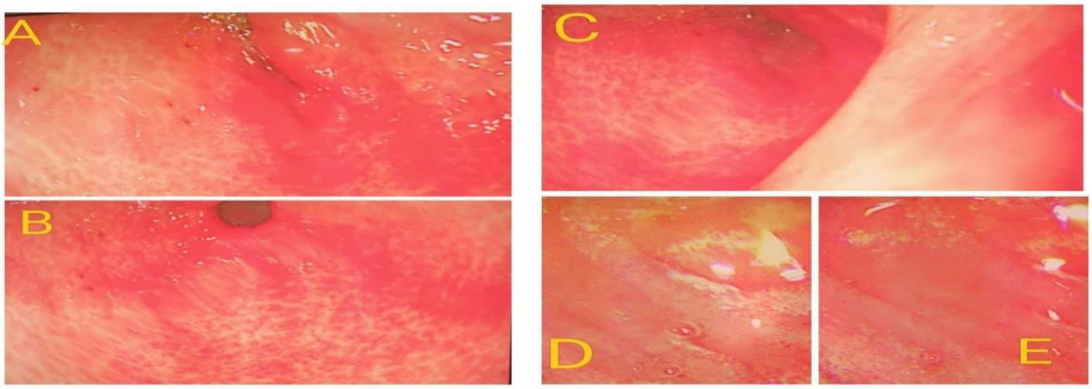

Fig. 1 :(A,B,C,D,E): Gastric hyperemic mucosa with multiple erosions and mosaic appearance suggesting HPI.

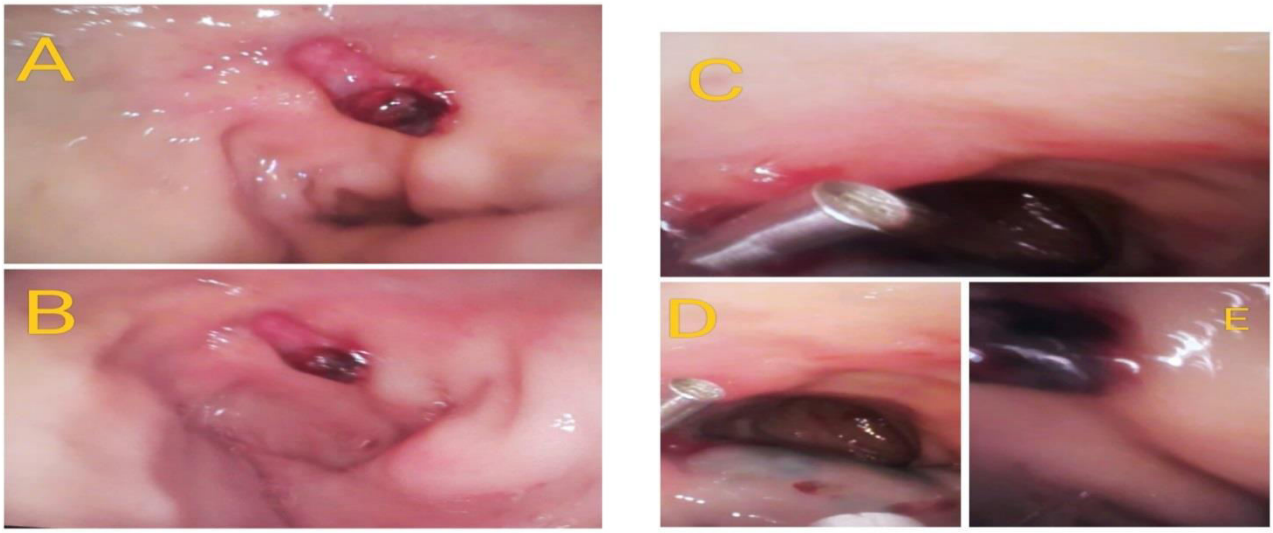

Fig.2. (A ,B): Duodenal bulb ulcer with clot on it , forrest class IIa: (C,D,E): After removing clot from the ulcer and stopping bleeding with haemoclips

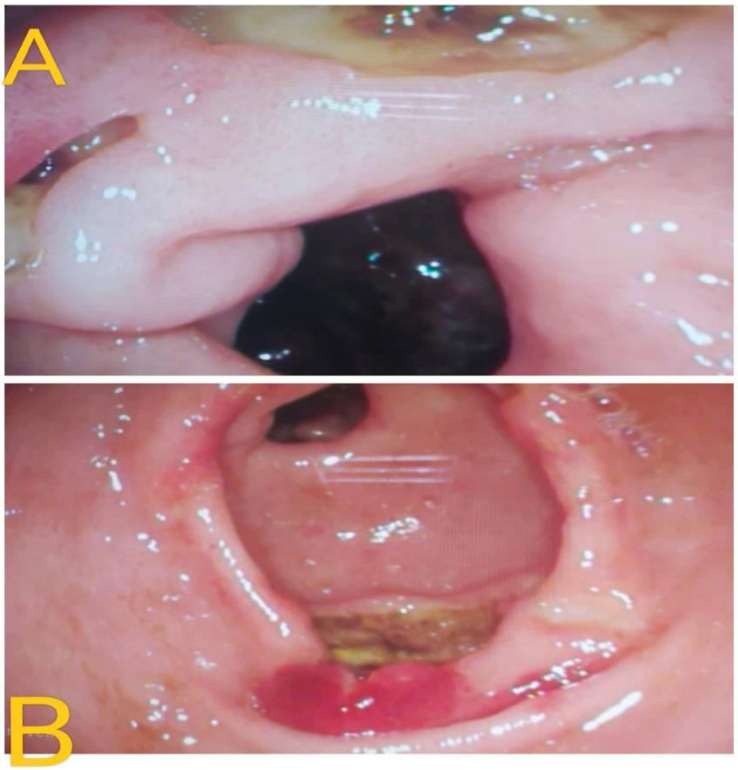

Fig.3. (A,B): Large antral ulcer with dirty base and raised edges oozing blood, forrest class IIc .

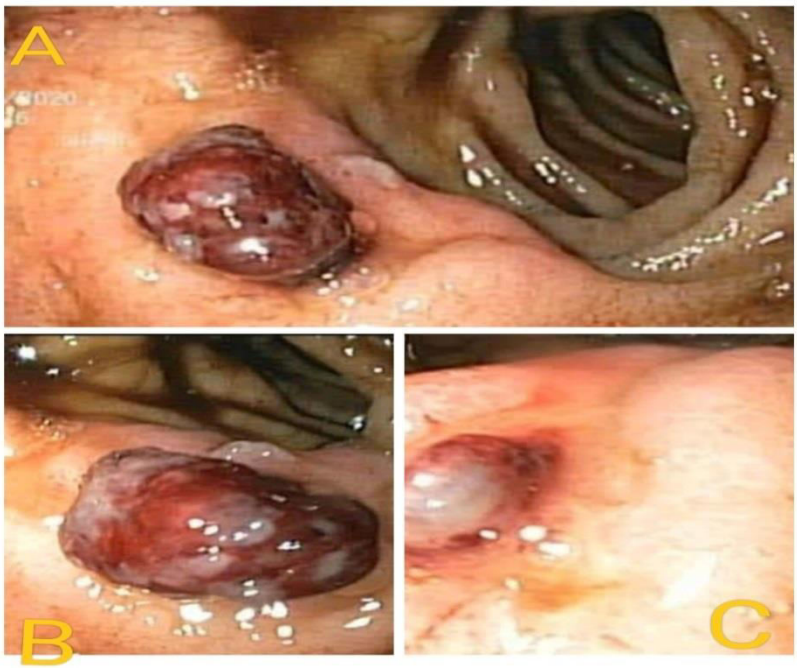

Fig.4. (A.B.C) : Duodenal bulb ulcer with clot on it , forrest class IIa .

There were 2 patients (4%) with Celiac disease (**Fig.5A,B &C**) (1 with upper oeophageal web removed with Atrophic duodenal mucosa and the other only with atrophic duodenl mucosa), 1 patient (2%) with Crohn's disease(with severe inflammatory mucosa which suggest diagnosis after doing the lower endoscope which showed ulcers with skip lesions in ileum and ascending colon), 2 patient (4%) with Gastric cancer (**Fig.6A &B**), and 1 patient (2%) with Angiodysplasia (in the second part of duodenum) ,while there were 14 patients (28%) with normal upper GIT endoscope (**Table 4**).

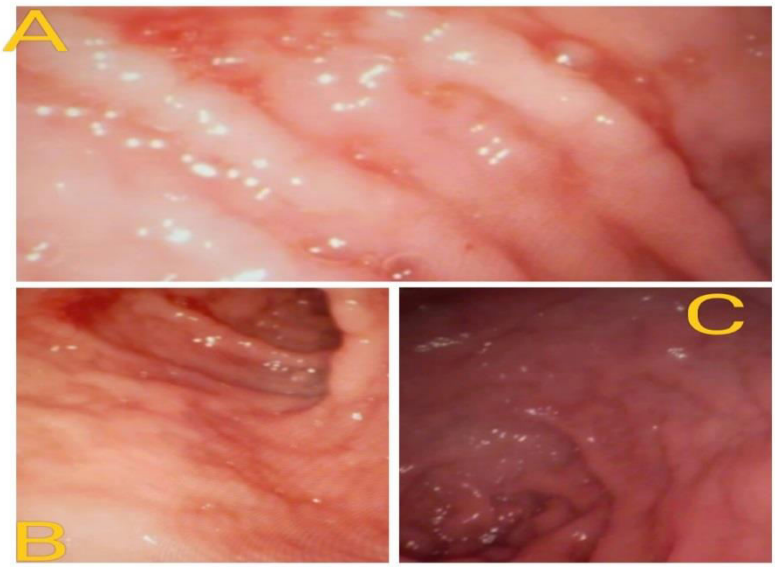

Fig.5 (A,B,C) : Duodenal mucosa showed Villous atrophy pattern with fissuring and Scalloping of Celiac disease.

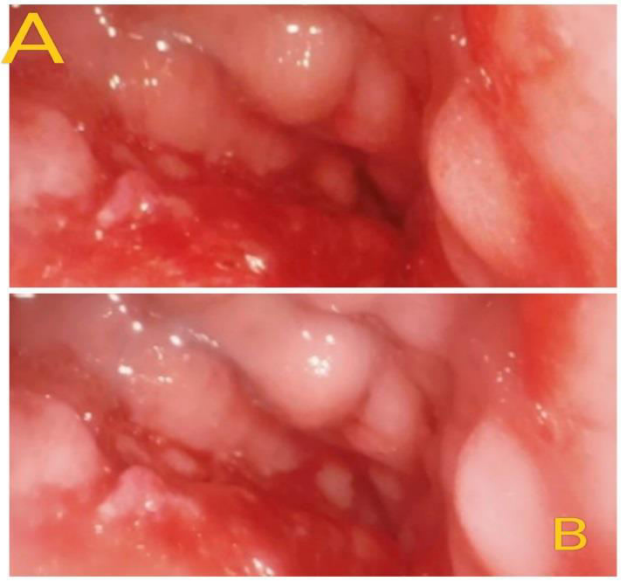

Fig. 6 (A,B): Hypertrophied gastric mucosal folds with oozing(Gastric cancer)

Table 4. Description of upper GIT endoscope results among patients.

Variables		Patients (N = 50)	
Upper GIT endoscope results	**Normal**	14	28%
	Esophageal web	1	2%
	Gastritis	20	40%
	Peptic ulcer	9	18%
	Celiac disease	2	4%
	Crohn's disease	1	2%
	Gastric cancer	2	4%
	Angiodysplasia	1	2%

The most common finding of lower GIT endoscope was angiodysplasia in 3 patients (1 in recto-sigmoid, 1 along the whole colon and the last in the descending colon) (6%) and colon polyp (**Fig.7 A,B &C**) in 3 patients (6%) followed by crohn's disease (**Fig.8 A,B ,C & D**) (ulcers with skip lesions in ileum and ascending colon with signs of severe inflammation in upper GI in one of the 2 patients), in 2 patients (4%) and 1 patients (2%) with each of the following Celiac disease(superficial ileal ulcer) , terminal ileitis, Ulcerative colitis(multiple erosions with pseudopolyp along the colon) and Bilharziasis while there were 35 patients (70%) with normal lower GIT endoscope (**Table 5**).

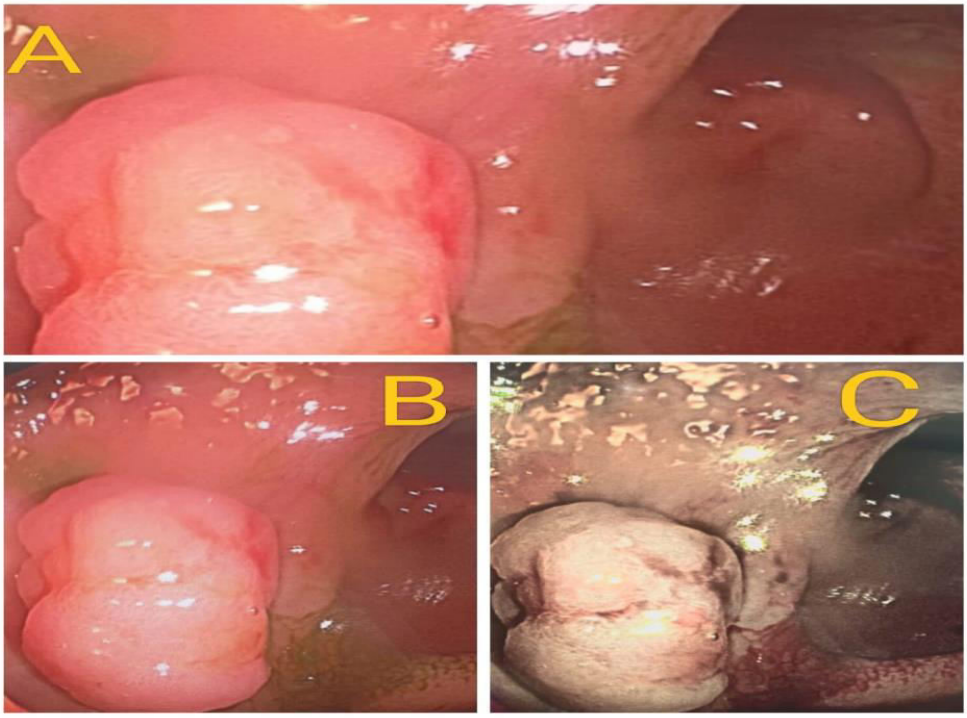

Fig.7 : (A,B): Colon polyp about 3 cm in diameter ,paris class0-1p .
(C) : Enace image with iScan Kudo II

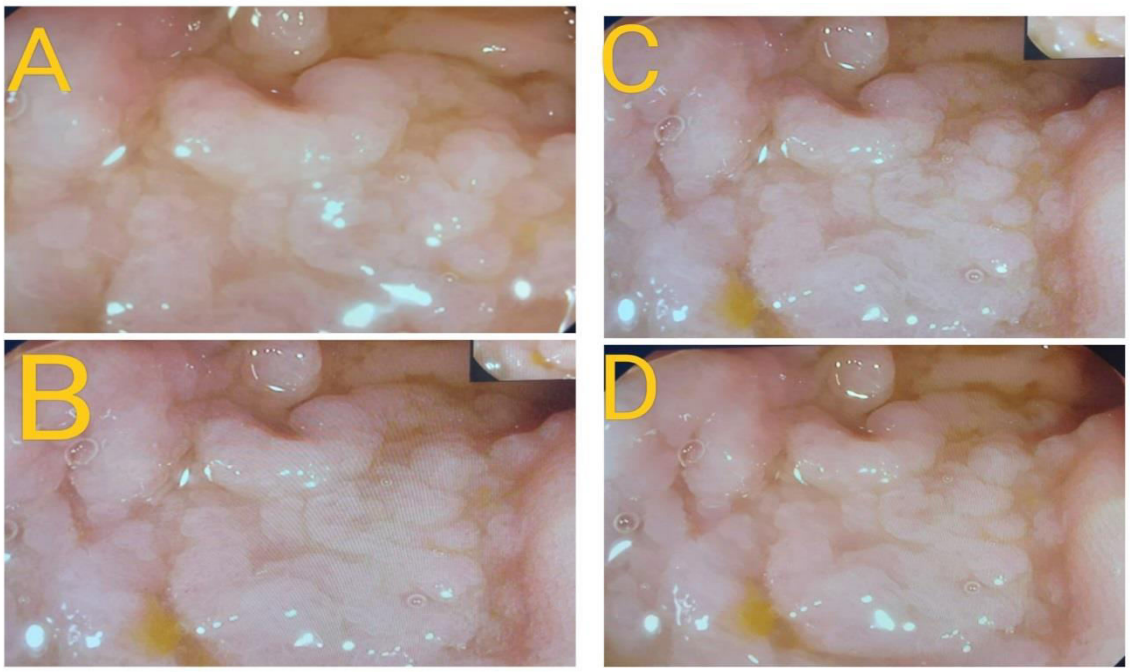

Fig.8 (A,B,C,D): Ileal mucosa showed granular surface with loss of villous pattern and submucosal vascular pattern. (Cobble stone of crohn's disease).

Table 5. Colonoscopy findings among the patients.

Variables		Patients (N = 50)	
Colonoscopy results	Normal	35	70%
	Colon polyp	3	6%
	Crohn's disease	2	4%
	Celiac disease	1	2%
	Angiodysplasia	3	6%
	Terminal ileitis	1	2%
	Ulcerative colitis	1	2%
	Bilhariziasis	1	2%
	Cancelled *	3	6%

*Cancelled because patient had significant pathology in EGD as gastric cancer.

Regarding the description of overall outcome in all studied patients. Both endoscopies showed negative findings in 10 patients (20%), both endoscopies showed positive findings in 8 patients (16%) while 1 endoscope only showed positive finding in 32 patients (64%) (**Table 6**).

.

Table 6. Description of overall outcome in the patients

Variables		Patients (N = 50)	
Overall outcome	Both endoscopies negative	10	20%
	1 endoscopy positive	32	64%
	Both endoscopies positive	8	16%

Discussion

Our results showed that Bidirectional endoscopies detected the cause of IDA patients without site-specific GIT manifestations in 80% of cases. mean age of all studied patients was 36.4 ± 16.7 years old. in these 50 patients 16% (8 patients) had lesions in both upper and lower endoscopy while 64% (32 patents) had lesion only in upper or lower endoscopy. The most common findings of upper GIT endoscope were gastritis, it was present in 20 patients (40%) followed by peptic ulcer in 9 patients (18%). There were 2 patients (4%) with Celiac disease, 1 patient (2%) with Crohn's disease, 2 patients (4%) with Gastric cancer, and 1 patient (2%) with Angiodysplasia (in the second part of duodenum). the most common findings of lower GIT endoscope were angiodysplasia in 3 patients (1 in recto-sigmoid,1 in along the whole colon and the last in the descending colon) (6%) and colon polyp in 3 patients (6%) followed by crohn's disease (ulcers with skip lesions in ileum and ascending colon), in 2 patients (4%) and 1 patients (2%) with each of the following Celiac disease , terminal ileitis, Ulcerative colitis (multiple erosions with pseudo polyp along the colon) and Bilharziasis.

Our study concluded that upper and lower endoscopy are an efficient maneuvers to detect the aetiology of IDA patients without GIT manifestations and their use should be promoted.

In agreement with our findings, (**Abd El-Hafez et al., 2022**) carried out a cross-sectional study with 50 patients who had IDA but with no evident symptoms. Of the 50 anaemic individuals that were investigated, 38 (or 76%) had GIT lesions found during an EGD, a Colonoscopy, or both. 12 individuals (24%) were recommended for additional testing because they had no lesions found on an EGD or Colonoscopy. 33 patients had lesions found by EGD, and 4 of those patients also had lesions found by CS. 29 patients had EGD lesions as their only condition. 9 patients had lesions found during colonoscopies, and of those nine, 4 had lesions found during an EGD.

Our findings were in line with (**Annibale et al., *2013)*** who demonstrated a probable cause of IDA was found in 85% and was undetected among 15%.

Rockey found lesions of the upper GIT among 41% of patients with IDA and remarkable lower GIT lesions were detected among 22% of IDA patients (**Rockey,1999).**

(**Sanchez et al.,2000**) studied 66 patients with IDA and mean age of 73 years. At least one lesion responsible for anemia was found in 46 patients (70%), 31 patients (46.9%) presented a lesion in the upper GIT and 13 patients (19.6%) presented with lesions in the lower GIT. Cancer colon was diagnosed in 8 patients (12.1%) and GIT cancer in one patient (1.5%). In two remaining patients, peptic ulcer and colorectal cancer were found simultaneously. A diagnosis of minor lesions was found in 15 patients (23%).

Masoud et al.(2005) evaluated 60 IDA patients, 36 males (60%) and 24 females (40%) aged 15-65 years. Out of sixty patients, a total of 24 patients (40%) had positive upper endoscopic lesions, 18 patients (30%) had positive lower endoscopic lesions and 10 patients (16.7%) had positive findings on both upper and lower endoscopy. The most common upper GIT lesions were hiatus hernia with esophagitis in 11 patients (18.3%), erosive gastritis in 9 patients (15%), gastric ulcerations in 6 patients (10%), gastric tumors in 5 patients (8.3%) and duodenitis in 7 patients (11.7%), while the most common lower GIT lesions were proctocolitis in 10 patients (16.7%), piles in 7 patients (11.7%), colonic polyps in 5 patients (8.3%) and cancer colon in 6 patients (10%). Eleven patients (18.3%) had GIT malignancy, 5 in stomach (8.3%) and 6 in the colon (10%). They concluded that upper and lower GIT endoscopy are efficient tools for investigating IDA patients and their use should be promoted**.**

There were 75 individuals with unexplained IDA underwent EGD and Colonoscopy with biopsies participated in a cross-sectional observational study. The study included 81 participants, with 31 men and 44 women, ranging in age from 20 to 81 years. Patients in Group A (n=44) had a mean age of 58.57 11.68 years, while those in Group B (n=31) had a mean age of 49.68 14.45 years. The presence of GIT endoscopic lesions that are the cause of IDA was statistically significantly linked with advanced age, a history of weight loss, and faecal occult blood (p-value 0.05) on multivariate analysis. Most IDA-causing lesions were discovered in the stomach (48%), but erosive and inflammatory lesions were more prevalent in the upper GIT. In 12% of instances, peptic ulcers were discovered. In 14.66% of the individuals, GIT cancers were discovered. Upper GIT cancer was less

than colorectal cancers, 6.66% and 8%, respectively **(Reddy et al., 2021).**

Bidirectional endoscopies and CT scans of the abdomen were used in a research by Niv et al. (2008) that found the cause of IDA in 71% of cases. Patients' anaemia was caused by lesions in the upper GIT in 29% of cases, the lower GIT in 33% of cases, and the combined upper and lower GIT in 6% of cases (**Niv et al., 2008).**

In a related study, **Majid et al. (2008)** enrolled 95 individuals in a row who had a laboratory-based diagnosis of IDA but no GIT symptoms. 71% of patients had a possible anaemia aetiology identified, and 53% had lesions associated with bleeding. In 41% of individuals with lesions due to bleeding, upper GIT lesions were discovered. They noted bidirectional endoscopy showed the reason of unexplained IDA among 51/95 patients.

Conclusion

Bidirectional endoscopies are valuable to detect the cause of IDA patients without site–specific GIT manifestations. The most common GIT lesions were gastritis followed by peptic ulcer.

Study's Limitations

The present study has some limitations, the study included small sample size, further researches with larger sample size is required in this field. secondly, random biopsies from healthy apparent mucosa were not done in this study.

List of Abbreviation

IDA: Iron deficiency anemia.
GIT: gastrointestinal.
TIBC: total iron binding capacity.
EGD: Esophagogastroduodenoscopy.
BMI: body mass index.
RBCS: red blood cells.
HG %: hemoglobin concentration.
WBCS: white blood cells.
M ± SD: mean ± standard deviation.

References

- **Abd El-Hafez MR, Shalaby HA, El-Gendy AA , Al-Boraie MAA .(2022).** Detection of Gastrointestinal Lesions causing iron deficiency anemia using Gastrointestinal Endoscopy. Al-Azhar Med. J, 51 (1): 485-494
- **Annibale B, Capurso G , Chistolini A. (2013).** Gastrointestinal causes of refractory iron deficiency anemia in patients without gastrointestinal symptoms. Am J Med., 24: 111-439.
- **Burton JK, Yates LC, Whyte L, Fitzsimmons E , Stott JD. (2020).** New horizons in iron deficiency anaemia in older adults. Age and Ageing, 49(3): 309-318.
- **Johnson-Wimbley TD. (2011).** Diagnosis and management of iron deficiency anemia in the 21st century. Therap Adv Gastroenterol. , 4(3): 177–184.
- **Ko C, Siddique S, Patel A, Harris A, Sultan S, Altayar O, Falck-Ytter Y. (2020).** AGA clinical practice guidelines on the gastrointestinal evaluation of iron deficiency anemia. Gastroenterology, 159(3):1085-94.
- **Lai KC, Lam SK , Chu KM. (2016).** Lansoprazole for the prevention of recurrences of ulcer complications from long term lowdose aspirin use. N Engl J Med, 346(26): 2033-8.
- **Majid S, Salih M, Wasaya R, Jafri W (2008).** Predictors of gastrointestinal lesions on

endoscopy in iron deficiency anemia without gastrointestinal symptoms. BMC Gastroenterol, 8(1):52.

- **Masoud AM, Amer MM, Mostafa NF, Ismail SA, El-Nadry MH, Badawy YK (2005).** Evaluation of gastrointestinal tract in Egyptian patients with IDA without symptoms or signs by using upper and lower endoscopy. AAMJ,.3(2).
- **Nambiema A, Robert A , Yaya I (2019).** Prevalence and risk factors of anemia in children aged from 6 to 59 months in Togo: Analysis from Togo demographic and health survey data, 2013-2014. BMC Public Health, 19:1-9.
- **Niv E, Elis A, Zissin R, Naftali T, Novis B, Lishner M. (2005).** Iron deficiency anemia in patients without gastrointestinal symptoms—A prospective study. Fam Pract. 22(1):58-61.
- **Reddy S, Vaishnav B, Sharma P, Tonde T, Bamanikar A, Barla DR, Basha F (2021).** Upper and Lower Gastrointestinal Endoscopic Lesions in Patients with Unexplained Iron Deficiency Anaemia- A Cross-sectional Study. Journal of Clinical and Diagnostic Research, 15(8): OC49-OC53.
- **Rockey DC. (1999).** Gastrointestinal tract evaluation in patients with iron deficiency anemia. Semin Gastrointest Dis ,10:53–64.
- **Sanchez Martinez F, Vila Santasuana A, Cid Panella R, Gomez Vaquero C. (2000).** Iron deficiency anemia in hospitalized males and postmenopausal females. Diagnostic approach] Gastroenterol Hepatol, 23(5):219-23.
- **Silva B, Faustino P. (2015).** An overview of molecular basis of iron metabolism regulation and the associated pathologies. Biochim Biophys Acta, 1852; 1347–59.
- **Wang C–Y, Babitt JL (2019).** Liver iron sensing and body iron homeostasis. Blood, 133:18–29.