

Evaluation of Gastro-Duodenal (GD) Mucosa of Non-IBS / Non-EGD Disorders in Calculous Cholecystitis and Dyslipidemia

Mohamed Darwish Ahmed Abd Alla*, Ahmed Mohamed Khairy, Ahmed Mansour Yosuf Kandil, Ahmed Fathallah Khattab Khattab

1*Department of Hepatology, Gastroenterology, and Infectious diseases, Faculty of Medicine, Al- Azhar University, Cairo, Egypt.
2Department of pathology, Faculty of Medicine, Al- Azhar University, Cairo, Egypt

Corresponding Author: Mohamed Darwish Ahmed Abd Alla, Gouhar Al-Kaed Street, El-Husseini University Hospital, Al-Azhar University, Al-Darasah, Cairo 11675, Egypt. Tel: +2 01007477212, Fax: +2 25123091, E-mail: darwish0716@azhar.edu.eg

ABSTRACT

Background: Irritable bowel syndrome (IBS) is a disorder of gut-brain interaction in which low-grade mucosal immune activation may contribute to symptoms. Chronic calculous cholecystitis (CCC) and dyslipidemia may also be associated with microscopic gastro-duodenal inflammation.

Aim of the work: To assess gastro-duodenal mucosal histopathological changes in IBS versus non-IBS patients in relation to CCC and dyslipidemia.

Methods: This cross-sectional study included 153 symptomatic adults undergoing upper gastrointestinal endoscopy and mucosal biopsy. Patients were classified as IBS (n=63) or non-IBS (n=90). Overlapping exposure strata were CCC (n=45), dyslipidemia (n=32), and no CCC/no dyslipidemia (n=95).

Results: Among IBS patients, moderate gastric lymphocytic infiltration was more frequent with dyslipidemia (78.6%) and CCC (65.5%) than with neither exposure (25.8%), with significant comparisons for dyslipidemia versus unexposed patients ($P=0.001$) and CCC versus unexposed patients ($P=0.004$). Average gastric infiltration was more frequent in unexposed IBS patients than in the CCC or dyslipidemia strata (both $P<0.001$). No significant gastric pairwise differences were detected among non-IBS patients. Duodenal differences were less robust; average infiltration was higher in unexposed than dyslipidemic IBS patients (48.4% vs 14.3%, $P=0.046$).

Conclusion: CCC and dyslipidemia were associated with selected microscopic gastro-duodenal inflammatory changes, most clearly gastric lymphocytic infiltration in IBS patients. These exploratory findings require prospective validation.

Keywords: Irritable bowel syndrome; Non-IBS; Chronic calculous cholecystitis; Dyslipidemia; Gastro-duodenal mucosa; Lymphocytic infiltration; Upper gastrointestinal endoscopy.

INTRODUCTION

Irritable bowel syndrome (IBS) is a prevalent disorder of gut-brain interaction characterized by recurrent abdominal pain associated with changes in stool form and/or frequency. It is diagnosed using symptom-based criteria after exclusion of alarm features and clinically relevant organic disease [1,2]. Population-based data show that IBS carries a substantial clinical burden, and its reported frequency varies according to diagnostic criteria and methodology [3].

Although IBS has traditionally been considered a functional disorder, modern concepts increasingly recognize that low-grade mucosal immune activation, altered epithelial barrier function, microbial interactions, bile acid disturbance, and visceral hypersensitivity may contribute to symptoms in a subset of patients [4,5]. Therefore, microscopic mucosal changes may be clinically relevant even when routine endoscopic inspection is not remarkable.

Patients with IBS and non-IBS functional gastrointestinal presentations frequently report upper gastrointestinal manifestations such as dyspepsia, epigastric pain, nausea, and reflux-like complaints. These symptoms may overlap with chronic calculous cholecystitis (CCC) and dyslipidemia. Gallstone disease is linked to metabolic risk factors, and adverse lipid profiles have been associated with gallstone disease risk in different populations [6,7].

Bile acids are not only digestive molecules but also signaling mediators that influence lipid metabolism, gut microbiota composition, epithelial integrity, and immune-cell recruitment [8]. Disturbance of bile-acid composition or enterohepatic cycling may expose the gastric and duodenal mucosa to irritant bile-acid and lipid-related signals, potentially inducing microscopic lymphocytic infiltration even when the gross mucosal appearance is normal.

The present study evaluates gastro-duodenal mucosal histopathological changes in IBS patients compared with non-IBS patients. The study focuses on demographic characteristics, symptoms, serum laboratory variables, and mucosal lymphocytic infiltration in relation to CCC and dyslipidemia.

AIM OF THE WORK

To assess and compare histopathological changes of the gastro-duodenal mucosa in IBS versus non-IBS patients, with evaluation of chronic calculous cholecystitis and dyslipidemia as comorbidities of interest.

PATIENTS AND METHODS

Study design and population

This prospective cross-sectional case-control study was conducted at the Hepatology and Gastroenterology Department, Sheikh Zayed Specialized Hospital, Egypt. A total of 153 out of 462 adult patients were included in the final analysis. All patients were symptomatic adults undergoing upper gastrointestinal endoscopy for gastro-duodenal manifestations.

Symptom-Based Patient Stratification

Enrolled subjects (n = 153) were segregated based on their symptoms against the Rome IV criteria into two primary cohorts: **IBS** (n = 63) and **non-IBS** (n = 90). The IBS Cohort fulfilled the definition of Rome IV criteria. Non-IBS Cohort Included patients with "IBS-like" symptoms (partially fulfilling Rome IV criteria, characterized by recurrent abdominal pain with alternating bowel habits for less than the required threshold) and "IBS-free" subjects presenting with vague gastro-colonic manifestations (e.g., postprandial dyspnea, isolated abdominal distension, persistent flatulence, borborygmi, etc.). CCC and dyslipidemia exposure categories were analyzed as overlapping categories: CCC (n=45), dyslipidemia (n=32), and no CCC/no dyslipidemia (n=95). Because some patients had both CCC and dyslipidemia, subgroup totals do not equal the total study population.

Inclusion criteria

- Age > 18 years.
- Symptomatic patients presenting with gastro-duodenal manifestations.
- Patients undergoing upper gastrointestinal endoscopy, either for the first time or after previous screening without apparent macroscopic gastro-duodenal lesions.
- Patients with documented CCC, dyslipidemia, both conditions, or neither condition as a comparison exposure group.

Exclusion criteria

- Age <18 years.
- Follow-up of previously diagnosed structural gastro-duodenal disease.
- Documented infectious gastrointestinal disease or active untreated chronic hepatitis C.
- Hepatocellular carcinoma or extrahepatic malignancy unless disease-free according to the protocol.
- Uncompensated liver disease or severe coagulopathy, including bilirubin >3 mg/dL, albumin <2.8 g/dL, INR >1.7, or platelet count <50,000/mm³.
- Severe debilitating systemic disease or non-compliance.

Clinical and laboratory assessment

Clinical assessment focused on upper gastrointestinal symptoms, biliary manifestations, metabolic risk factors, smoking status, and Rome IV criteria. Laboratory assessment included complete blood count, liver and kidney function tests, lipid profile, HDL, uric acid, TSH, and other tests when clinically indicated. Abdominal ultrasonography was used to assess gallbladder status and calculous disease.

Endoscopy and mucosal biopsy

Upper gastrointestinal endoscopy was performed using standard preparation and screening protocols. Mucosal biopsies were obtained from gastric mucosa and duodenal mucosa. The current manuscript reports the summarized tables for gastric and duodenal lymphocytic infiltration according to the available final dataset.

Histopathological examination

Biopsy specimens were fixed in 10% neutral buffered formalin, processed, embedded in paraffin, sectioned at 3-5 µm, and stained with hematoxylin and eosin. Microscopic examination was performed by an experienced gastrointestinal pathologist blinded to clinical data. Lymphocytic infiltration was quantified per high-power field (HPF) and categorized as average (<10 cells/HPF), mild (11-30 cells/HPF), or moderate (>31 cells/HPF).

Statistical analysis

Continuous variables were expressed as mean $\pm$ standard deviation. Categorical variables were expressed as frequencies and percentages. Welch's t-test was used for continuous variables. Fisher's exact test was used for categorical pairwise comparisons. P values less than 0.05 were considered statistically significant.

RESULTS

Demographic data

The final analyzed population included 153 patients, classified as IBS (n=63) and non-IBS (n=90). Age was significantly higher in dyslipidemic patients compared with the other exposure groups, particularly among non-IBS patients (A vs B and B vs C, $P<0.001$) and among IBS patients when dyslipidemia was compared with no CCC/no dyslipidemia (B vs C, $P=0.030$). Gender and smoking distribution were comparable across exposure groups (Table 1).

Gastrointestinal symptoms

Gastro-esophageal symptoms showed no statistically significant difference across exposure groups, although non-IBS patients with CCC showed borderline higher frequency than those without CCC/dyslipidemia. Epigastric symptoms were frequent in IBS patients with CCC and dyslipidemia. Colonic symptoms were significantly higher among non-IBS patients with CCC compared with non-IBS patients without CCC/dyslipidemia (25.0% vs 6.2%, $P=0.047$) (Table 2).

Routine laboratory results

Cholesterol was significantly higher in the dyslipidemia subgroup compared with CCC and no CCC/no dyslipidemia subgroups in both IBS and non-IBS patients. Triglycerides showed selected significant differences, mainly when dyslipidemia was compared with no CCC/no dyslipidemia. HDL levels showed no statistically significant differences. Uric acid and TSH were interpreted cautiously because of missing values (Table 3).

Gastric mucosal lymphocytic infiltration

Moderate gastric lymphocytic infiltration was more frequent among IBS patients with dyslipidemia (78.6%) and CCC (65.5%) than among IBS patients without CCC/dyslipidemia (25.8%). The difference was statistically significant for dyslipidemia versus no CCC/no dyslipidemia ($P=0.001$) and for CCC versus no CCC/no dyslipidemia ($P=0.004$). Average gastric lymphocytic infiltration was significantly more frequent in IBS patients without CCC/dyslipidemia compared with both CCC and dyslipidemia subgroups (both $P<0.001$). No statistically significant pairwise differences were detected among non-IBS patients across the exposure categories (Table 4).

Duodenal mucosal lymphocytic infiltration

Duodenal moderate lymphocytic infiltration tended to be more frequent in IBS patients with dyslipidemia (50.0%) and CCC (44.8%) than in IBS patients without CCC/dyslipidemia (22.6%); however, these differences did not reach statistical significance. Average duodenal lymphocytic infiltration was significantly more frequent in IBS patients without CCC/dyslipidemia than in dyslipidemic IBS patients (48.4% vs 14.3%, $P=0.046$). Mild duodenal lymphocytic infiltration showed no statistically significant differences between exposure groups in either IBS or non-IBS patients (Table 5).

Table 1. Demographic data in IBS versus non-IBS in all study populations (n=153)

Study groups	Mean $\pm$ Standard Deviation or percent positive					
	Age		Gender		Smoking	
	IBS	Non-IBS	IBS -Male -female	Non-IBS -Male -female	IBS -Smoker -None	Non-IBS -Smoker -None
A. CCC (n=45)	n=29 38.79 $\pm$ 13.13	n=16 36.56 $\pm$ 13.49	12/29 (41.4%) 17/29 (58.6%)	8/16 (50.0%) 8/16 (50.0%)	7/29 (24.1%) 22/29 (75.9%)	0/16 (0.0%) 16/16 (100.0%)
B. Dyslipidemia (n=32)	n=14 46.57 $\pm$ 14.53	n=18 56.33 $\pm$ 13.63	7/14 (50.0%) 7/14 (50.0%)	11/18 (61.1%) 7/18 (38.9%)	6/14 (42.9%) 8/14 (57.1%)	4/18 (22.2%) 14/18 (77.8%)

C. No CCC / No dyslipidemia (n=95)	n=31 36.52 + 10.16	n=64 37.06 + 12.32	14/31 (45.2%) 17/31 (54.8%)	26/64 (40.6%) 38/64 (59.4%)	7/31 (22.6%) 24/31 (77.4%)	8/64 (12.5%) 56/64 (87.5%)
P value						
A vs B	0.103	<0.001**	0.745	0.730	0.292	0.105
A vs C	0.458	0.894	0.800	0.577	1.000	0.347
B vs C	0.030*	<0.001**	1.000	0.180	0.286	0.449

Age was significantly higher in dyslipidemic patients compared with the other groups, particularly among non-IBS patients (A vs B $P<0.001$; B vs C $P<0.001$) and among IBS patients when dyslipidemia was compared with no CCC/no dyslipidemia (B vs C $P=0.030$).

No significant differences were observed regarding gender or smoking distribution across the study groups ($P>0.05$).

Statistical tests: Welch's t-test for age; Fisher's exact test for gender and smoking. CCC and dyslipidemia are overlapping exposure categories.

Table 2. Gastrointestinal symptoms in IBS versus non-IBS in all study populations (n=153)

Study groups	Gastro-esophageal symptoms		Epigastric symptoms		Colonic symptoms	
	IBS	Non-IBS	IBS	Non-IBS	IBS	Non-IBS
A. CCC (n=45)	3/29 (10.3%)	3/16 (18.8%)	24/29 (82.8%)	8/16 (50.0%)	0/29 (0.0%)	4/16 (25.0%)
B. Dyslipidemia (n=32)	1/14 (7.1%)	1/18 (5.6%)	13/14 (92.9%)	11/18 (61.1%)	0/14 (0.0%)	2/18 (11.1%)
C. No CCC / No dyslipidemia (n=95)	4/31 (12.9%)	2/64 (3.1%)	20/31 (64.5%)	48/64 (75.0%)	2/31 (6.5%)	4/64 (6.2%)
P values						
A vs B	1.000 (NS)	0.323 (NS)	0.645 (NS)	0.730 (NS)	1.000 (NS)	0.387 (NS)
A vs C	1.000 (NS)	0.052 (NS)	0.148 (NS)	0.069 (NS)	0.492 (NS)	0.047*
B vs C	1.000 (NS)	0.530 (NS)	0.070 (NS)	0.252 (NS)	1.000 (NS)	0.608 (NS)

Gastro-esophageal symptoms showed no statistically significant difference across exposure groups, although non-IBS patients with CCC showed a borderline higher frequency than the no CCC/no dyslipidemia subgroup (18.8% vs 3.1%; $P=0.052$).

Epigastric symptoms were frequent in IBS patients with CCC (82.8%) and dyslipidemia (92.9%), but pairwise comparisons did not reach statistical significance.

Colonic symptoms were significantly higher among non-IBS patients with CCC compared with non-IBS patients without CCC/dyslipidemia (25.0% vs 6.2%; $P=0.047$).

Table 3. Routine serum laboratory results in IBS versus non-IBS in all study populations (n=153)

Study groups	Harmful lipids		Beneficiary lipid (HDL)		Uric acid		TSH	
	IBS	Non-IBS	IBS	Non-IBS	IBS	Non-IBS	IBS	Non-IBS
A. CCC (n=45)	n=29 Chol: 195.79 ± 33.24 TG: 116.97 ± 31.32	n=16 Chol: 199.50 ± 23.55 TG: 130.19 ± 34.21	n=29 50.86 ± 6.25	n=16 51.69 ± 7.53	n=1 5.90 ± 0.00	n=2 4.90 ± 1.41	n=3 1.35 ± 0.66	n=1 3.10 ± 0.00
B. Dyslipidemia (n=32)	n=14 Chol: 226.29 ± 27.05 TG: 134.79 ± 45.29	n=18 Chol: 227.33 ± 11.16 TG: 145.11 ± 44.92	n=14 49.64 ± 6.33	n=18 49.22 ± 7.61	n=1 5.90 ± 0.00	n=3 5.30 ± 1.04	n=0 —	n=2 1.52 ± 0.48

C. No CCC / No dyslipidemia (n=95)	n=31 Chol: 172.74 ± 13.18 TG: 107.26 ± 20.69	n=64 Chol: 175.00 ± 14.83 TG: 104.83 ± 25.10	n=31 50.06 ± 6.38	n=64 50.95 ± 6.77	n=5 5.26 ± 1.02	n=11 5.53 ± 0.65	n=3 1.79 ± 0.34	n=12 1.81 ± 1.05
P values								
A vs B	Chol: 0.003* TG: 0.200	Chol: <0.001** TG: 0.281	0.558	0.350	—	0.769	—	—
A vs C	Chol: 0.001* TG: 0.166	Chol: <0.001** TG: 0.012*	0.627	0.726	—	0.643	0.377	—
B vs C	Chol: <0.001** TG: 0.046*	Chol: <0.001** TG: 0.002*	0.838	0.391	—	0.747	—	0.568

Harmful lipids: cholesterol was significantly higher in the dyslipidemia subgroup compared with CCC and no CCC/no dyslipidemia subgroups in both IBS and non-IBS patients ($P < 0.01$).

HDL showed no statistically significant differences between the studied subgroups in either IBS or non-IBS patients ($P > 0.05$). Uric acid and TSH results should be interpreted cautiously because of missing values; p-values were not calculated when either comparison arm had fewer than two available observations.

Table 4. Gastric mucosal lymphocytic infiltration (G. M. LCI) in IBS versus non-IBS in all study populations (n=153)

Study groups	Average (<10 cells/HPF)		Mild (11 to 30 cells/HPF)		Moderate (>31 cells/HPF)	
	IBS	Non-IBS	IBS	Non-IBS	IBS	Non-IBS
A. CCC (n=45)	4/29 (13.8%)	8/16 (50.0%)	6/29 (20.7%)	1/16 (6.2%)	19/29 (65.5%)	7/16 (43.8%)
B. Dyslipidemia (n=32)	1/14 (7.1%)	9/18 (50.0%)	2/14 (14.3%)	3/18 (16.7%)	11/14 (78.6%)	6/18 (33.3%)
C. No CCC / No dyslipidemia (n=95)	21/31 (67.7%)	20/64 (31.2%)	2/31 (6.5%)	12/64 (18.8%)	8/31 (25.8%)	32/64 (50.0%)
P values						
A vs B	1.000	1.000	1.000	0.604	0.491	0.725
A vs C	<0.001**	0.240	0.140	0.448	0.004**	0.782
B vs C	<0.001**	0.169	0.578	1.000	0.001**	0.287

Moderate G. M. LCI was more frequent among IBS patients with dyslipidemia (78.6%) and CCC (65.5%) than IBS patients without CCC/dyslipidemia (25.8%).

Average G. M. LCI was significantly more frequent in IBS patients without CCC/dyslipidemia compared with CCC and dyslipidemia groups (A vs C $P < 0.001$; B vs C $P < 0.001$).

No statistically significant pairwise differences were detected among non-IBS patients across CCC, dyslipidemia, and no CCC/no dyslipidemia categories.

Statistical test: two-sided Fisher's exact test. Moderate category includes LCI grades 2, 3 and 4. CCC and dyslipidemia are overlapping exposure categories.

Table 5. Duodenal mucosal lymphocytic infiltration (DU. LCI) in IBS versus non-IBS in all study populations (n=153)

Study groups	Average (<10 cells/HPF)		Mild (11 to 30 cells/HPF)		Moderate (>31 cells/HPF)	
	IBS	Non-IBS	IBS	Non-IBS	IBS	Non-IBS
A. CCC (n=45)	7/29 (24.1%)	7/16 (43.8%)	9/29 (31.0%)	2/16 (12.5%)	13/29 (44.8%)	7/16 (43.8%)
B. Dyslipidemia (n=32)	2/14 (14.3%)	6/18 (33.3%)	5/14 (35.7%)	5/18 (27.8%)	7/14 (50.0%)	7/18 (38.9%)
C. No CCC / No dyslipidemia (n=95)	15/31 (48.4%)	32/64 (50.0%)	9/31 (29.0%)	16/64 (25.0%)	7/31 (22.6%)	16/64 (25.0%)

P values						
A vs B	0.693	0.725	1.000	0.405	1.000	1.000
A vs C	0.064	0.782	1.000	0.503	0.100	0.215
B vs C	0.046*	0.287	0.734	0.770	0.088	0.252

Moderate DU. LCI tended to be more frequent in IBS patients with dyslipidemia (50.0%) and CCC (44.8%) than IBS patients without CCC/dyslipidemia (22.6%), but the differences did not reach statistical significance.

Average DU. LCI was significantly more frequent in IBS patients without CCC/dyslipidemia than in dyslipidemic IBS patients (48.4% vs 14.3%; B vs C P = 0.046).

Mild DU. LCI showed no statistically significant differences between exposure groups in either IBS or non-IBS patients.

Statistical test: two-sided Fisher's exact test. Moderate category includes LCI grades 2, 3 and 4. CCC and dyslipidemia are overlapping exposure categories.

DISCUSSION

In the current cohort of symptomatic adults undergoing upper gastrointestinal endoscopy, patients with chronic calculous cholecystitis and dyslipidemia showed microscopic gastro-duodenal mucosal alterations despite non-specific or apparently normal macroscopic endoscopic screening. The dominant abnormality was lymphocytic infiltration rather than severe structural destruction of the duodenal mucosa. Collectively, these findings suggest that CCC and dyslipidemia may be associated with microscopic gastro-duodenal mucosal injury in both IBS and non-IBS patients.

IBS is usually framed as a disorder of gut-brain interaction rather than a purely structural disease, according to Rome-based definitions and contemporary guidelines [1,2]. However, biologically defined IBS subgroups may show low-grade mucosal immune activation and microinflammation [4,5]. In the current dataset, IBS status alone did not fully explain the histopathologic changes observed when CCC and dyslipidemia were present. This suggests that CCC and dyslipidemia may contribute to the observed mucosal changes.

A clinically important observation is that dyslipidemic patients were older, especially in the non-IBS group, while gender and smoking were not significantly different. Epigastric symptoms were frequent among IBS patients with CCC and dyslipidemia, supporting the presence of a wider gastro-duodenal symptom phenotype when functional bowel symptoms coexist with CCC and dyslipidemia. This agrees with the concept that IBS frequently overlaps with other upper gastrointestinal symptom clusters and that immune activation may be magnified by systemic comorbidities.

The laboratory profile confirmed that cholesterol was significantly higher in the dyslipidemia subgroup in both IBS and non-IBS patients. Gallbladder disease has established epidemiologic relationships with metabolic risk factors [6], and pooled evidence links adverse lipid profiles to gallstone disease risk [7]. From a clinical perspective, this supports the interpretation that the gastro-duodenal mucosa may respond to a systemic lipid and biliary disordered environment, not simply to functional bowel symptom status.

Gastric mucosal lymphocytic infiltration was particularly informative. Moderate Gastric LCI was significantly higher in IBS patients with dyslipidemia (78.6%) and CCC (65.5%) compared with IBS patients without CCC or dyslipidemia (25.8%; B vs C P=0.001 and A vs C P=0.004). Conversely, average Gastric LCI was significantly more frequent in unexposed IBS patients (67.7%) than in CCC (13.8%) and dyslipidemia (7.1%) subgroups (both P<0.001). The absence of statistically significant differences among non-IBS patients indicates that this effect was strongest within the IBS phenotype and should be interpreted as an exposure-related inflammatory pattern rather than an IBS-specific diagnostic marker.

Duodenal lymphocytic infiltration provided a more modest supportive pattern. Moderate DU.LCI tended to be more frequent in IBS patients with dyslipidemia (50.0%) and CCC (44.8%) than in IBS patients without CCC/dyslipidemia (22.6%), although the pairwise comparisons did not reach statistical significance. The significant duodenal result was the higher frequency of average DU.LCI in IBS patients without CCC/dyslipidemia compared with dyslipidemic IBS patients (48.4% vs 14.3%, P=0.046), suggesting a shift from average toward higher infiltration categories in the dyslipidemia subgroup. Non-IBS comparisons did not reach statistical significance, so the duodenal findings should be interpreted as a trend consistent with a mucosal response associated with CCC and dyslipidemia rather than as a definitive independent duodenal marker.

These findings support further evaluation of the potential diagnostic value of gastro-duodenal biopsy in selected symptomatic patients with CCC and/or dyslipidemia despite non-specific or apparently normal endoscopic findings. Many histopathological changes were not restricted to IBS patients. Therefore, biopsy findings should be interpreted as evidence of a possible mucosal response associated with CCC and/or dyslipidemia rather than as diagnostic proof of IBS.

Several limitations should be acknowledged. This was a single-center study, and the final analyzed sample size was smaller than the originally planned protocol sample. CCC and dyslipidemia were overlapping exposure categories, and bile acid biomarkers, detailed medication exposures, dietary variables, and standardized symptom severity scores were not fully

incorporated. Future longitudinal studies should evaluate bile acid profiles, lipid control, cholecystectomy status, medication exposure, and standardized histologic thresholds in relation to symptom outcomes.

CONCLUSION

Chronic calculous cholecystitis and dyslipidemia are associated with microscopic gastro-duodenal mucosal inflammatory changes among symptomatic patients despite non-specific or apparently normal endoscopic screening. The association was most evident for gastric lymphocytic infiltration in IBS patients, while duodenal lymphocytic infiltration showed a directional but less robust pattern. Overall, these findings suggest a possible association of chronic calculous cholecystitis and dyslipidemia with gastro-duodenal mucosal inflammation particularly in IBS patients.

Conflict of interest: Author has nothing to disclose.

Author contributions: MDAA contributed to study design, data analysis, and writing the manuscript. AFKK recruited patients, obtained informed consent, and was involved in data collection. AMK and AFKK performed the endoscopic examination. AMYK was involved in the histopathological examination of biopsies. All were involved in critical revision, reviewing the manuscript and approved the final version of the manuscript including the authorship list.

Financial support: This study did not receive any specific funding.

Consent to participate: Informed written consent was obtained from all study participants.

Ethics approval: The study was approved by the ethical committee at the department of Hepatology, Gastroenterology, and Infectious diseases and by the ethical committee at Al-Azhar school of medicine. Certificate Registration Number: Trop.Med._1Med.Research_Inf.GIT.Liv.Dis._1405. The study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments.

Availability of data and materials: Data generated or analyzed during this study are included in this manuscript.

REFERENCES

1. Mearin F, Lacy BE, Chang L, Chey WD, Lembo AJ, Simren M, et al. Bowel Disorders. *Gastroenterology*. 2016;150(6):1393-1407.e5.
2. Lacy BE, Pimentel M, Brenner DM, Chey WD, Keefer LA, Long MD, et al. ACG Clinical Guideline: Management of Irritable Bowel Syndrome. *Am J Gastroenterol*. 2021;116(1):17-44.
3. Oka P, Parr H, Barberio B, Black CJ, Savarino EV, Ford AC. Global prevalence of irritable bowel syndrome according to Rome III or IV criteria: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol*. 2020;5(10):908-917.
4. Sinagra E, Pompei G, Tomasello G, Cappello F, Morreale GC, Amvrosiadis G, et al. Inflammation in irritable bowel syndrome: Myth or new treatment target? *World J Gastroenterol*. 2016;22(7):2242-2255.
5. Aguilera-Lizarraga J, Hussein H, Boeckxstaens GE. Immune activation in irritable bowel syndrome: what is the evidence? *Nat Rev Immunol*. 2022;22:674-686.
6. Stinton LM, Shaffer EA. Epidemiology of gallbladder disease: Cholelithiasis and cancer. *Gut Liver*. 2012;6(2):172-187.
7. Zhang M, Mao M, Zhang C, Hu F, Cui P, Li G, et al. Blood lipid metabolism and the risk of gallstone disease: a multi-center study and meta-analysis. *Lipids Health Dis*. 2022;21:26.
8. Jia W, Xie G, Jia W. Bile acid-microbiota crosstalk in gastrointestinal inflammation and carcinogenesis. *Nat Rev Gastroenterol Hepatol*. 2018;15(2):111-128.