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Evaluation Of Colonic Mucosa Of Non-IBS / Non-Endoscopic Large Bowel Disorders In Diabetes Mellitus And Bronchial Asthma

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Abstract

Background: *Irritable-Bowel-Syndrome (IBS) is a functional gastrointestinal disorder that affects a considerable percentage of population. Diabetes Meletus (DM) and Bronchial Asthma (BA) share similar symptomatology.*

Objective: *our study aimed to assess histopathologic changes of colonic mucosa of IBS compared to non-IBS patients in Diabetics and Asthmatics.*

Subjects and Methods: *All populations (n=250) had free colonoscopic screening. They were classified into diabetics (n=74), asthmatic (n=58) and no. DM/no.BA (n=118). Each group is divided into IBS and non-IBS subgroups. They were submitted to colonoscopy and mucosal biopsy. Mucosal-lymphocytic-infiltration (MLCI) was graded according to number of cells per high-power-field (HPF) into average(<10cells/HPF), mild (10 to 30cells/HPF), and moderate(>30cell/HPF). Mucosal-bacterial-invasion (MBI) was also graded into no microorganism(0/HPF), few microorganisms(<10/HPF), and moderate number of microorganisms(≥10/HPF).*

Results: *The average MLCI showed close frequencies in the IBS subgroups of diabetics (74.3 %), asthmatics (84.4 %), and no. DM/no.BA (91.5 %) groups (P>0.05). The non-IBS population in both DM (13.5%) and BA (8.6 %) showed significantly increased frequency of average MCLI when compared with no. DM/no.BA population (4.23 %) (P<0,05). Absent colonic MBI in IBS showed insignificant variation in DM (74.3 %), BA (82.7 %), and no. DM/no.BA (94.06 %) (P>0.05). The non-IBS population in DM group (20.72%) had significantly increased frequency of invasion with few microorganisms when compared with no. DM/no.BA populations (4.2 %) (P<0,05), but not with asthmatic patients (10.54 %) (P>0.05).*

Conclusion: *Average colonic MLCI is found in non-IBS patients who have Diabetes-Meletus and bronchial asthma. Low levels of Mucosal-Bacterial-Invasion is only seen in the none-IBS asthmatic patients.*

Keywords: *Diabetes-Mellitus, Bronchial-Asthma, colonic-mucosa, Histopathology*

1. INTRODUCTION

Irritable bowel syndrome (IBS) is a prevalent functional gastrointestinal condition that impacts the quality of life for patients. IBS is marked by symptoms including abdominal pain or discomfort, changes in bowel habits, and alleviation of symptoms after defecation. aggravation due to psychological stress, periods without symptoms during sleep, and the lack of physical irregularities found in colorectal assessments. The prevalence is between 10% and 15% among the overall population in major developed regions[1]. ROME IV Characterized IBS as a recurrent abdominal pain over average at least one day per week at the last three months that is related with two criteria or more of the following:

a. relation to defecation.

b. association with a change in frequency of bowel evacuation.

c. changes in stool consistency.

These criteria should be fulfilled for the last three months, with onset of symptoms for six months prior to the diagnosis[2].

The diagnosis relies on a thorough clinical history, which includes current symptoms and a disease duration of at least six months[3]. The diagnostic effectiveness of colonoscopy in patients with IBS is quite

limited. Nevertheless, specific "alarm signs" (such as unexplained weight loss, blood in the stool, anemia, and recent changes in bowel habits) warrant further investigation for other conditions before attributing symptoms solely to IBS[4]. The Rome IV symptom-based diagnostic criteria currently serve as the gold standard for diagnosing IBS. Although they provide a definitive diagnosis, these criteria can be cumbersome and lack high reliability. Moreover, several organic conditions, such as Crohn's disease, ulcerative colitis, and celiac disease, present symptoms similar to those of IBS. Due to these overlapping clinical features, many doctors choose to perform invasive tests to exclude organic diseases prior to establishing a diagnosis of IBS[5].

Microscopic colitis (MC) includes two main subtypes: collagenous colitis and lymphocytic colitis. Collagenous colitis (CC) is characterized by a distinctive subepithelial collagen band next to the basal membrane, while lymphocytic colitis (LC) is marked by a significant infiltration of lymphocytes within the epithelium. This condition is more prevalent in women and often leads to a change in bowel habits toward looser stools, frequently accompanied by abdominal discomfort. Reports indicate that the incidence of MC ranges from 2.6 to 21.0 cases per 100,000 people each year. The three essential components of this condition include a clinical history of persistent watery diarrhea, a colonoscopy displaying normal or nearly normal macroscopic features of the colon, and a specific histologic pattern[6]. There is a significant link between autoimmune disorders and these conditions. As many as 20% to 60% of individuals with LC and 17% to 40% of those with CC also have an autoimmune disease[7]. Retrospective studies of patients with MC have indicated a higher occurrence of autoimmune diseases and the use of anti-inflammatory medications. Therefore, autoimmunity has been proposed as a possible cause[8].

2. SUBJECTS AND METHODS:

Study Design and Population

This cross-sectional case-control place at the Hepatology, Gastroenterology & Infectious Diseases department (HGID) Department of Al-Azhar University Hospitals and Theodor Bilharz Research Institute (TBRI). A sample size of 250 patients was calculated to detect a 50% difference between groups with 80% power ($\alpha = 0.05$). Adult patients (>18 years) were submitted to colonoscopy because of hind gut relate symptoms.

Study Groups: Patients were stratified into:

IBD, Cancer colon, Diverticulosis, Polyposis or no evident pathology – each compared between diabetics/asthmatics and non-diabetics/non-asthmatics. A subgroup analysis focused on patients with no macroscopic lesions, further classified by: Histopathologic/histochemical findings (with/without Rome IV IBS criteria). In addition to Diabetic/asthmatic status.

The 250 cases recruited were classified into the following: group A included patients with Diabetes Meletus (n=74), group B consists of cases with Bronchial Asthma (n=58), and group C contains no. DM/no.BA (n=118). Each group was divided into IBS and non-IBS subgroups.

Inclusion Criteria: Age >18 years, Symptomatized patients with lower GI manifestations, the submitted patients to colonoscopy will be differentiated into naïve (colonoscopy for the first time) or experienced (repeated colonoscopy) with no apparent colonic lesion in previous screening, currently having DM and / or Bronchial asthma.

Exclusion Criteria: Age <18 years old, Follow up of pre-diagnosed gastric diseases, short or long history of documented GIT diseases: a. co-infection with HIV, HBV, COVID-19 virus b. Salmonellosis c. food poisoning e.g. E. coli, Shigellosis, Staph aureus, Bacillus coeruleus d. Pseudo-membranes colitis (CDF) e. Schistosomiasis, Pregnant female, Hepatocellular carcinoma except 6 months after cure or other extrahepatic malignancy except two years after free interval, Total serum bilirubin higher than three mg/dl, Unexplained rise in ALT and / or AST, and decrease in serum albumin to < 2.8 g/dl, INR > 1.7, Platelet count fewer than 50,000/mm, Patients with recently diagnosed active untreated chronic hepatitis C virus (CHCV), Patients with chronic debilitating diseases other than DM or bronchial asthma e. g. uremic patients, cases with congestive heart failure, patients with impaired consciousness and Non-compliant patients

Clinical Assessment was performed with emphasis on GIT symptoms and signs in association with

Diabetes Meletus and Bronchial Asthma. The related risk factors were also evaluated in all study population.

Laboratory Tests: included routine (CBC, liver/kidney function, lipids, HbA1c) and sometimes specific tests for exclusion like H. pylori antigen, fecal calprotectin, tumor markers.

Colonoscopy and biopsies: Patient preparation and screening will be performed according to the invented protocol. Four mucosal biopsies will be taken from each of the following sites: a. terminal ilium b. ascending colon c. transverse colon d. descending colon e. sigmoid colon f. rectum

Histopathology: Preparation of slides begins with fixation of biopsies in 10% neutral buffered formalin. The biopsies are then processed in Leica (TP) tissue processor overnight, through graded alcohols, cleared in xylene, and embedded in paraffin to create tissue blocks. Thin slices (3-5 μm) are prepared using a microtome and placed on glass slides. For H&E staining, the slices are deparaffinized, hydrated, and stained with hematoxylin. counterstained with eosin, dehydrated, and cover slipped. For Masson Trichrome staining, sections are similarly deparaffinized and hydrated, then sequentially stained with Weigert's iron hematoxylin, followed by acid fuchsin, and aniline blue. The slides are dehydrated, cleared, and mounted for microscopic evaluation. Microscopic examination from ileocolonic biopsies will be blindly carried out by an experienced gastrointestinal pathologist without any previous knowledge about case selection or presentation.

Statistics: Data was analyzed using SPSS v25. Normality was assessed via Shapiro-Wilk test; homogeneity of variance via Levene's test including Quantitative data: Mean ± SD (independent T-test), Categorical data: Frequency (%) (chi-square test), Significance threshold: $P \leq 0.05$.

Ethics approval: This research was endorsed by the ethical committee at the department of Hepatology, Gastroenterology, and Infectious diseases and by the ethical committee at Al-Azhar faculty of medicine. Written consent was endorsed by subjects.

Sample size calculation: We were planning a study of subjects in which we regressed the values of patients against control. Prior data indicated that the standard deviation of control was 0.9 and the standard deviation of the regression errors were 1.94. If the true slope obtained by regressing patients against control is 1.4, we needed to study 35 subjects at least for each group, to were able to reject the null hypothesis that this slope equals zero with probability (power) 90%. The Type I error probability associated with this test of this null hypothesis is 0.05. The formula for calculating a z-score is $z = (x-\mu)/\sigma$, where x was the raw score, μ was the population mean, and σ is the population standard deviation.

3. RESULTS:

The demographic data for participants with irritable bowel syndrome (IBS) and non-IBS individuals across three study groups DM, BA, and None (no DM/no BA) were illustrated in table (1). There were no statistically significant differences between groups regarding age, gender and smoking.

Table 1. Demographic Data in IBS versus non-IBS in all study populations (n=250)

Study groups	Age		Gender		Smoking	
	IBS	Non – IBS	IBS Male: female	Non – IBS Male: female	IBS Smoker: Non	Non – IBS Smoker: Non
DM (n=74)	46.63 ±12.87	42.50 ±12.54	30 (40.5%): 26 (35.1%)	8 (10.8%): 10 (13.5%)	24 (32.4%): 35 (47.2%)	7 (9.45%): 8 (10.8%)
BA (n=58)	49.02 ±18.38	44.00 ±15.97	21 (36.2%): 29 (50.0%)	5 (8.6%): 3 (5.2%)	14 (24.1%) 38 (65.5%)	3 (5.17%): 3 (5.17%)
no.DM/no.BA (n=118)	47.32±14.32	42.32±11.53	53 (44.9%)	9 (7.63%) 10	39(33.05%) 55 (46.6%)	8(6.7%) 16(13.5%)

			46 (38%)	(8.47%)		
P values						
DM vs BA	0.26	0.54	0.233	0.395	0.117	0.79
DM vs None	0.67	0.9	0.99	0.99	0.98	0.85
BA vs None	0.42	00.39	0.76	0.34	0.056	0.52

Continuous variables data are expressed as Mean ± standard deviation (SD)

Regarding GIT symptoms in IBS patients, Among the DM group (n=74), 22.9% reported gastro-esophageal symptoms, 25.6% experienced epigastric symptoms, and a significant 47.2% had colonic symptoms. In contrast, the BA group (n=58) showed markedly lower incidences, with only 6.8% reporting gastro-esophageal symptoms, 3.4% for epigastric symptoms, and 10.34% for colonic symptoms. The no. DM/no.BA (n=118) had 16.1% reporting gastro-esophageal symptoms, 6.7% for epigastric symptoms, and an overwhelming 81.35% with colonic symptoms. Statistically significant differences were observed, particularly between DM and BA ($p<0.001$ for colonic symptoms) and DM versus None ($p<0.001$ for colonic symptoms).

Among non-IBS patients, the prevalence of gastro-esophageal symptoms in the DM group was 2.7%, epigastric symptoms were reported by 5.4%, and colonic symptoms were noted in 16.2%. The BA group (n=58) exhibited higher percentages for gastro-esophageal (8.6%) and epigastric symptoms (12.06%), but a lower rate of colonic symptoms (5.27%). The no. DM/no.BA group (n=118) had 6.7% reporting gastro-esophageal symptoms, 10.16% for epigastric symptoms, and 5.9% for colonic symptoms. Statistically significant differences were found between DM and BA for gastro-esophageal ($p=0.014$) and epigastric symptoms ($p=0.003$). The comparison between DM and no. DM/no.BA for epigastric symptoms also showed significance ($p=0.02$) as in table2.

Table 2. GIT symptoms in IBS versus non-IBS in all study populations (n=250)

Study groups	**Gastro-esophageal symptoms**		**Epigastric symptoms**		**Colonic symptoms**	
	IBS	Non – IBS	IBS	Non – IBS	IBS	Non – IBS
DM (n=74)	17 (22.9 %)	2 (2.7%)	19(25.6%)	4 (5.4 %)	35(47.29%)	12(16.2%)
BA (n=58)	4 (6.8 %)	5 (8.6 %)	2 (3.4%)	7 (12.06%)	6 (10.34%)	3 (5.17%)
no.DM/no.BA (n=118)	19 (16.1%)	8(6.77 %)	16(13.5%)	12(10.16%)	96(81.35%)	7 (5.9%)
P values						
DM vs BA	0.003	0.014	<0.001	0.003	<0.001	0.219
DM vs None	0.11	0.062	0.016	0.02	<0.001	0.07
BA vs None	00.07	0.42	0.034	0.248	<0.001	1.00

Categorical variables data are expressed in their absolute and relative frequencies (number and percentage)

Regarding risk factors associated with IBS, in the DM group (n=74), 20.27% had antirheumatic medicine administration, 35.14% exhibited a disturbed lipid profile, and 33.78% had eczema. The BA group (n=58) reported similar figures, with 24.14% having antirheumatic drugs administration, 24.14% showing a disturbed lipid profile, and 32.76% had eczema. In contrast, the no. DM/no.BA group (n=118) had a significantly higher prevalence of indication to use antirheumatic medicine at 51.69%, only 16.9% for a disturbed lipid profile, and 4.24% had eczema. Notably, the p-values indicate a statistically significant difference between DM and no. DM/no.BA for the disturbed lipid profile ($p<0.001$) and between BA and no. DM/no.BA for antirheumatic conditions ($p=0.001$).

Among non-IBS patients, The DM group reported 6.76% with antirheumatic usage, 14.86% with a disturbed lipid profile, and 12.16% with eczema. The BA group had similar findings, with 3.45% having antirheumatic use and 5.17% with a disturbed lipid profile, while 12.07% reported eczema. In contrast, the no. DM/no.BA group had significantly lower rates of these risk factors, with only 0.085% for antirheumatic usage, 1.69% for a disturbed lipid profile and 4.24% for Eczema. Statistically significant

differences were observed between DM and no. DM/no.BA for the disturbed lipid profile (p=0.001) and eczema (p=0.012) as in table 3.

Table 3, Risk factors in IBS versus non-IBS in all study populations (n=250)

Study groups	Antirheumatic		Dist. Lipid Profile		Eczema		Oral Aphthous	
	IBS	Non-IBS	IBS	Non-IBS	IBS	Non-IBS	IBS	Non-IBS
DM (n=74)	15 (20.27%)	5 (6.76%)	26 (35.14 %)	11 (14.86 %)	25 (33.78 %)	9 (12.38%)	21 (28.38%)	7 (9.46%)
BA (n=58)	14 (24.14%)	2 (3.45%)	14 (24.14)	3 (5.17%)	19 (38%)	7 (12.07%)	24 (41.38%)	5 (8.62%)
no.DM/no. BA (n=118)	61 (51.69%)	1 (0.085 %)	20 (16.95 %)	2 (1.69%)	5 (4.24%)	5 (4.24%)	8 (6.77 %)	4 (3.39%)
P values								
DM vs BA	0.67	1.00	0.187	4.0	1.00	0.203	0.162	0.383
DM vs None	0.00	99.0	0.005	0.28	<0.001	0.381	<0.001	0.422
BA vs None	0.001	21.0	0.351	0.001	<0.001	0.012	<0.001	0.099

Categorical variables data are expressed in their absolute and relative frequencies (number and percentage)

In IBS patients, the BA group had lower cholesterol levels averaging 191.94 ± 33.55 mg/dL, while the no. DM/no.BA group showed a mean cholesterol of 186.32 ± 30.32 mg/dL. Statistically significant differences were observed in cholesterol levels between DM and BA (p=0.023) and DM and no. DM/no.BA (p=0.0004), indicating a higher lipid profile in the IBS population. The uric acid levels and TSH also showed significant differences between DM and no. DM/no.BA (p=0.001). Among non-IBS patients, DM group showed harmful lipid levels with a mean cholesterol of 218.17 ± 34.32 mg/dL, while the BA group reported a slightly higher mean of 221.50 ± 43.22 mg/dL. The no. DM/no.BA group had a lower mean cholesterol of 194.67 ± 54 mg/dL. Statistically significant differences were noted between DM and no. DM/no.BA for cholesterol levels (p=0.125) and TSH (p=0.0002). In terms of the disturbed lipid profile, only DM vs. no. DM/no.BA reached statistical significance (p=0.0015) as in table 4.

Table 4, Routine serum laboratory results in IBS versus non-IBS in all study populations (n=250)

Study groups	Harmful lipids		Beneficiary lipid		Uric acid		TSH	
	IBS Chol.TG.	Non-IBS Chol.TG.	IBS	Non-IBS	IBS	Non-IBS	IBS	Non-IBS
DM (n=74)	205.46 ±31.37	218.17 ±34.32	44.21 ±5.07	44.72 ±4.59	6.16 ±2.5	5.36 ±1.55	1.16 ±0.73	2.33 ±0.58
	173.52 ±50.82	198.44 ±51.91						
BA (n=58)	191.94 ±33.55	221.50 ±43.22	45.22 ±6.13	43.25 ±2.57	5.81 ±3.25	4.81 ±1.03	2.03 ±0.79	3.45 ±0.64
	156.28 ±41.47	173.75 ±32.08						
no.DM/no.BA (n=118)	186.32 ±30.32	194.67 ±54	46.28 ±6.76 .	45.26 ±8.1	4.91 ±2.43	4.65 ±3.24	2.26 ±1.09	2.35 ±1.64
	156 ±76.54	134.14 ±61						

P values								
DM vs BA	0,023,0.05	0.83, 0.217	0.6	0.7	0.79	0.243	0.01	0.0002
DM vs None	0.004,	0.12, 0.015	0.22	0.62	0.213	0.43	0.001	0.93
BA vs None	0128	0.22, 0.021	0.627	0.42	0.64	0.22	0.59	0.08
	0.36, 0.99							

Continuous variables data are expressed as Mean ± standard deviation (SD)

Table 5 describes grading of colonic mucosal lymphocytic infiltration (MLCI). The IBS subgroup showed almost the same frequency in DM (74.3 %), BA (84.4 %), and no. DM/no.BA (91.5 %) (P>0.05) regarding average MLCI. 0n the other hands, the non-IBS population in both diabetics (13.5%) and asthmatics (8.6 %) showed significantly increased frequency of average MCLI when compared with no. DM/no.BA population (4.23 %) (P<0,05). There was no difference among the three groups (DM, BA, and no. DM/no.BA) regarding other grades (mild and moderate) of MLCI in both IBS and Non-IBS categories (P>0.05).

Table 5. Colonic mucosal Lymphocytic infiltration (MLCI) in IBS versus non-IBS in all study populations (n=250)

Study groups	**Average (<10 cells/HPF)**		**Mild (11 to 30 cells / HPF)**		**Moderate (> 31 cell/HPF)**	
	IBS	Non - IBS	IBS	Non - IBS	IBS	Non - IBS
DM (n=74)	55 (74.3 %)	10 (13.5%)	1(1.35 %)	6 (8.1 %)	0 (0.0 %)	2 (2.7 %)
BA (n=58)	49 (84.4 %)	5 (8.6 %)	1 (1.7 %)	3 (5.17 %)	0 (0.0 %)	0 (0.0 %)
no.DM/no.BA (n=118)	108(91.5 %)	5 (4.23 %)	0 (0.0 %)	4 (3.3 %)	0 (0.0 %)	1(0.84 %)
P values						
DM vs BA	1.00	1.00	1.00	1.00	1.00	1.00
DM vs None	0.325	0.01	1.00	0.47	1.00	1.00
BA vs None	0.311	0.026	1.00	0.633	1.00	1.00

Categorical variables data are expressed in their absolute and relative frequencies (number and percentage)

Table 6 describes grading of colonic mucosal bacterial invasion (MBI). The IBS subgroup showed close frequency rates in DM (74.3 %), BA (82.7 %), and no. DM/no.BA (94.06 %) (P>0.05) regarding no microorganism's invasion. The non-IBS population in DM group (20.72%) showed significantly increased frequency of invasion with few microorganisms when compared with no. DM/no.BA populations (4.2 %) (P<0,05), but not with asthmatic patients (10.54 %) (P>0.05). There was no significant difference among the three groups (DM, BA, and no. DM/no.BA) regarding mucosal invasion with a moderate number of microorganisms in both IBS and Non-IBS subgroups (P>0.05).

Table 6. Colonic mucosal Bacterial invasion (MBI) in IBS versus non-IBS in all study populations (n=250)

Study groups	**No microorganism (0 / HPF)**		**Few microorganisms (<10 / HPF)**		**Moderate number of microorganisms (≥10 / HPF)**	
	IBS	Non - IBS	IBS	Non - IBS	IBS	Non - IBS
DM (n=74)	55 (74.32 %)	15(20.72%)	1(1.35 %)	3 (4.05 %)	0 (0.0 %)	0 (0.0 %)
BA (n=58)	48 (82.7 %)	6 (10.54 %)	2(3.44 %)	2 (3.44 %)	0 (0.0 %)	0 (0.0 %)
no.DM/no.BA (n=118)	111 (94.06 %)	5 (4.2 %)	1(0.84 %)	1(0.84 %)	0 (0.0 %)	0 (0.0 %)
P values						

DM vs BA	0.615	0.615	1.00	0.99	1.00	1.00
DM vs None	0.663	1.00	1.00	0.134	1.00	1.00
BA vs None	0.372	0.032	1.00	0.267	1.00	1.00

Categorical variables data are expressed in their absolute and relative frequencies (number and percentage)

4. DISCUSSION:

The findings of this study provide valuable insights into the histopathologic changes in the colonic mucosa in patients with Diabetes Mellitus (DM) and Bronchial Asthma (BA), particularly in those without macroscopic lesions on endoscopy. The results highlight significant associations between these chronic conditions and gastrointestinal (GI) manifestations, as well as the role of microscopic inflammation and bacterial invasion in GI symptomatology.

The study revealed no significant differences in age, gender distribution, or smoking status between the non-IBS and IBS groups for both DM and BA. The current research indicated that the average age of patients diagnosed as MC was 50.8 ± 7.3 years. This aligns with that reported by Pardi[9] who revealed that MC was more common in older people. Additionally, this observation was consistent with another study conducted by Miehlke et al.[10] and demonstrated that MC is more common in the elderly. Conversely, our results contrast Rahman et al.[11] study on microscopic colitis, where the average age of patients was (31.13 ±7.54) years, likely due to smaller sized sample of patient compared to our research. There was significant difference (P<0.05) between the three groups with eczema. On comparing each two groups, difference is significant between group A and each other group.

There were significant differences (P<0.05) between the three groups regarding anti-rheumatic drugs. On comparing each two groups, difference is significant between Diabetics and each other group (Asthmatic and no. DM/no.BA). Thisagree with P ervez et al.[12] who revealed that non-steroidal anti-inflammatory drugs (NSAIDs) are considered critical risk factors for both subtypes of MC. This can be explained by the ability of the NSAIDs to affect the permeability of the epithelial membrane and inhibit the anti-inflammatory prostaglandins regardless of the dose.

This agree with Rutkowski et al.[13] who found that The etiological factors for MC include auto immune diseases [such as ankylosing spondylitis (AS), psoriasis, Hashimoto's disease, Graves–Basedow disease, and type 1 diabetes], as well as medications used such as NSAIDs, PPIs (Proton Pump Inhibitors), SSRIs (Selective Serotonin Reuptake Inhibitors), and ICPIs (immune check-point inhibitors).

There were significant differences between the studied groups regarding Colonic mucosa cellular infiltrate and bacterial invasion.

This agrees with Wildt et al.[14] Using data from a national registry, microscopic colitis was linked to various autoimmune diseases, particularly those related to the gastrointestinal system, including diabetes and asthma. The likely cause of the coexistence of autoimmune diseases in individuals with microscopic colitis is chronic inflammation confined to the GI tract, which can trigger immune system dysregulation. This aligns with the findings of Kang et al.[15] who noted that the diagnosis in patients with microscopic colitis was nearly 80% more common compared to the general populace. This strong association appears to be valid and not merely a result of residual confounding among full siblings, but may be connected to the use of medications linked to the onset of microscopic colitis. They found that 352 (3.7%) of the 9,600 cases of microscopic colitis had a diagnosis of type 1 diabetes (T1D), compared to 945 (2.0%) in 47,870 matched controls, leading to an overall odds ratio of 1.79 (95% CI: 1.56-2.05). The association was more pronounced in those with collagenous colitis (OR, 2.15; 95% CI: 1.70-2.71) than in those with lymphocytic colitis (OR, 1.62; 95% CI: 1.37-1.92) and remained statistically significant even when comparing full siblings (OR, 1.46; 95% CI: 1.18-1.81). When accounting for medications, the association diminished to non-significant levels in females (OR: 1.02; 95% CI: 0.82-1.27) but persisted in males (OR: 1.45; 95% CI: 1.11-1.90).

Pre-existing autoimmune and allergic conditions were prevalent among patients with MC. The lack of specific symptoms should not be used to dismiss the diagnosis. The occurrence of autoimmune diseases was similar in both groups (LC: 10 patients 36%, CC: 30 patients, 40%, difference: 4%, p = .7124). Food-related hypersensitivities were more frequently observed in CC (LC: 1 patient, CC: 17 patients). The rates of allergic diseases (asthma, rhinitis, urticaria) were comparable between the groups (LC: 6

patients, 21%; CC: 21 patients, 28%, difference: 7%, p = .4739). Approximately one-third of the patients did not report experiencing chronic diarrhea. These patients primarily exhibited chronic constipation as their main symptom (34 patients, 33%).[16]

IN CONCLUSION, this study demonstrates average colonic MLCI in non-IBS patients who have Diabetes-Meletus and bronchial asthma. Low levels of Mucosal-Bacterial-Invasion is only seen in the non-IBS asthmatic patients. Variable differences in histopathological changes and bacterial invasion in the colonic mucosa of IBS and non-IBS patients in diabetes Meletus and bronchial asthma are reported. The findings underscore the importance of considering microscopic inflammation and bacterial invasion in the evaluation and management of GI symptoms in these populations. Further research is warranted to explore targeted interventions that address these underlying mechanisms.

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