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Prevalence of Irritable Bowel Syndrome in Ankylosing Spondylitis and Its Association with Clinical and Demographic Findings and Gut Pathology

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Abstract: Irritable bowel syndrome (IBS) is common in ankylosing spondylitis (AS) and may be associated with the disease. We aimed to determine the prevalence of IBS in AS patients and its association with clinical and demographic patient characteristics and with macroscopic and microscopic gut lesions. Sixty consecutive AS patients were included in this study. Disease activity was assessed with the BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) and functional status with the BASFI (Bath Ankylosing Spondylitis Functional Index). The ROME III criteria were used to diagnose IBS. Macroscopic lesions were graded during colonoscopies. Biopsy specimens were taken from the terminal ileum, colon (ascending, transverse and descending) and rectum. Histological samples were scored with Cuvelier grading. The prevalence of IBS was 23.3% (14/60). The mean age of 14 IBS subjects (10 male) was 32 ± 8.50., with a higher BASDAI (p = 0.046). Macroscopic lesions were more frequent in IBS cases in the terminal ileum (46.2% vs. 34.9%), ascending colon (21.4% vs. 2.2%) and rectum (21.4% vs. 17.4%), with Grade 2 significantly more prevalent in the ascending colon (p = 0.03). Microscopic lesions did not differ among the IBS-present and -absent groups. In conclusion, the prevalence of IBS was high in AS patients and associated with higher disease activity. Grade 2 macroscopic lesions were more frequent in the ascending colon.

Keywords: ankylosing spondylitis; irritable bowel syndrome; gut lesions; macroscopic and microscopic pathology

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1. Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory disease, previously known as von Bechterew's disease or Marie–Strümpell disease [1]. Sacroiliac and peripheral joint arthritis with enthesopathy, the absence of rheumatoid factors, a high correlation with HLA-B27 and familial aggregation are the hallmarks of spondyloarthropathies (SpA), of which AS is the prototype [2].

Even though the precise origin of AS is still uncertain, immunological systems are believed to play a significant role [3]. There are suggestions that the pathophysiology of AS may involve immune responses targeting gut microorganisms [4]. A strong correlation between HLA-B27-related arthritis and either clinical or subclinical inflammation of the intestinal mucosa had already been reported in 1984–1985 [5]; around 60% of SpA patients had inflammatory gut lesions [6], and some of these may progress to inflammatory bowel disease (IBD) [7]. Macroscopic and microscopic evaluations can establish features specific to

IBD [8]. In Bangladesh, 14% of patients with AS who had short colonoscopies (up to 60 cm) compared to healthy individuals had macroscopic inflammatory lesions [9]. In a Korean study, complete colonoscopies were performed and 37% were found to have macroscopic lesions [10]. In 96 subjects with AS, reactive arthritis and other spondyloarthropathies, Simenon et al. conducted a retrospective study and discovered that 64.9% had macroscopic gut lesions [11]. More abnormalities can be found with multiple biopsies than with a colonoscopy alone, showing that microscopic gut lesions are more common than macroscopic lesions [9]. Microscopic lesions varied in frequency, from 56 to 66.7%, in the majority of studies involving AS patients, and they were primarily mild. In one study conducted in Bangladesh, 73.3% of participants had microscopic gut lesions in the sigmoid, 83.3% in the rectum and 85% in the ascending colon [12]. In the terminal ileum in the AS group there were significantly more macroscopic (38.5 vs. 5%, $p < 0.01$) and microscopic (76.8 vs. 45%, $p = 0.009$) lesions than in controls. The status of HLA-B27 was not associated with a microscopic or macroscopic grading of the colon, and these did also not correlate with the BASDAI and VAS pain scores [12].

Conversely, irritable bowel syndrome, or IBS, is a functional bowel disorder marked by altered bowel habits and pain in the abdomen that resolves after defecation [13]. In addition to having a stronger correlation with psychosomatic conditions like anxiety, depression, fibromyalgia and chronic fatigue syndrome, IBS cannot be explained by an organic pathology [14].

Some studies have reported that IBS has an increased association with chronic inflammatory pathologies such as rheumatoid arthritis (RA), ankylosing spondylitis (AS) and systemic lupus erythematosus (SLE) [15]. Abdominal pain and/or diarrhea were found to be prevalent in AS patients [16].

A recent study in France showed that 25% of AS patients reported IBS symptoms meeting Rome III criteria [17]. They reviewed ten other studies: there were 558 IBS patients among 8395 SpA patients; the prevalence in these studies of IBS in AS varied from 8.8% to 23.3%, (mean 15.4%) [17]. This prevalence differed also when the diagnosis was made using the International Classification of Diseases (ICD) (n = 3) or the Rome III or IV (n = 6) classification questionnaire [17].

A considerable overlap can be found between IBS and IBD. In a meta-analysis of 13 studies, a prevalence of IBS symptoms was reported in up to 40% of IBD patients, even when the disease was inactive or in remission [18].

The findings in the literature regarding the prevalence of IBS in AS differ considerably. As we were able to include both clinical and pathology data of a series of AS patients without IBD in a developing country, we decided to assess the prevalence of IBS meeting the Rome III criteria [19] in patients with AS and the frequency of macroscopic and microscopic gut lesions among the IBS patients.

2. Methods

This observational study was carried out in the Departments of Rheumatology, Gastroenterology and Pathology of BSMMU and the Modern One Stop Arthritis Care and Research Center® in Dhaka from 1 July 2011 to 30 June 2012.

Consecutive AS patients fulfilling the revised New York criterion (1984) [20] were invited to participate, with no history of diarrhea and dysentery within 1 month before enrolment. They had stopped taking DMARDs for more than 3 weeks and had no contraindication for colonoscopy. A total of 60 AS patients were included following this purposive sampling method after we received their written informed consent.

2.1. Patient Evaluation

All AS patients were evaluateded for IBS according to the Rome III criteria [19]: (1) At least 3 months of continuous or recurrent symptoms—abdominal pain or discomfort (a) relieved with defecation or (b) associated with a change in consistency of stool and (2) Two or more of the following on at least on one-fourth of occasions or days—(a) altered

stool frequency (for research purposes "altered" may be defined as more than 3 bowel movements each day or less than 3 bowel movements each week), or (b) altered stool form (lumpy/hard or loose/watery stool), or (c) altered stool passage (straining, urgency, or feeling of incomplete evacuation) or (d) bloating or a feeling of abdominal distention.

All patients were assessed for disease activity (Assessment in Ankylosing Spondylitis (ASAS) core set) [21] using the BASDAI for disease activity, BASFI for physical function, pain-VAS in the past week, the Bath Ankylosing Spondylitis Mobility Index (BASMI) for Spinal mobility (cervical rotation, modified Schober, tragus-to-wall distance, lateral lumber flexion and intermalleolar distance), patients' global assessment (VAS-global for the past week), stiffness (duration of morning spine stiffness in the past week), peripheral joints (number of swollen joints [44 total]) and the Maastricht enthesitis score (MASES) in the range of 0–13 [22].

Laboratory: complete blood count (CBC), ESR and C-reactive protein (CRP) in all participants. Human leukocyte antigen B27 (HLA-B27) was performed when possible.

Radiology: X-rays of the lumbosacral spine (antero-posterior and lateral view) and X-rays of the SI joints (oblique view) were performed for the diagnosis of AS and the current status of radiological disease.

Colonoscopy: After assessment, in all study subjects, the colon was prepared by a gastroenterologist with 20% mannitol; no premedication was used. Biopsy specimens were taken from the terminal ileum, ascending colon, transverse colon, descending colon and rectum of all subjects. Two specimens were taken from all subjects irrespective of the presence or absence of macroscopically evident lesions and another two specimens were taken from macroscopically evident lesions, if available. The biopsy sites of each subject were recorded.

Macroscopic lesions were graded as follows: Grade 0—normal, Grade 1—redness and edema of the mucosa, Grade 2—small ulceration of the mucosa, Grade 3—mucosal edema, ulcerations and hemorrhage [9].

Pathology: Histological features were graded from 0 to 3 in the specimens following Cuvelier et al.'s grading [23]. All measurements and observations were performed at $\times$400 magnification ($\times$10 ocular and $\times$40 objectives).

2.2. Data Analysis and Statistics

Data were entered and calculated using Statistical Package for the Social Sciences (SPSS) 17.1 version for Windows. Descriptive statistics was used to calculate means, SDs, percentages and prevalence.

Associations between categorical variables were analyzed by a Chi-square test (v2) test and Fisher's exact test; the Mann–Whitney U test was used to assess associations between qualitative variables. A p value < 0.05 implies statistical significance.

2.3. Ethics

This study was approved by the Ethics Committee of BSMMU, Shahbagh, Dhaka, Bangladesh (6 June 2011). The study was performed following the principles of the Declaration of Helsinki, and informed consent was obtained from all participants before enrolment.

3. Results

A total of 60 AS subjects were included in this study. A colonoscopy examination of the terminal ileum was not performed in 4/60 individuals as the investigator could not pass the probe through the ileocecal junction. Additional details of the AS subjects have been described previously [12].

The prevalence of IBS was 23.3% (14/60).

HLA-B27 was conducted in only 37/60 cases due to fund constraints; of these, 20 (59%) were HLA-B27-positive (14 male, female 6) and 17 were HLA-B27-negative (male 13, female 4).

Among the 14 IBS patients, HLA-B27 was positive in 3 (21.43%), negative in 2 (14.29%) and not performed in 9 (64.28%) patients. As HLA-B27 was not carried out in all the

IBS patients, selection bias cannot be excluded, especially with these small numbers. The patients had to pay from their own pockets. As we included only confirmed cases of AS, due to resource constraints, poor patients were not asked to have an HLA-B27 performed. Thus, the only selection bias was a financial one, not a medical one.

There was no significant difference between IBS-pos and -neg cases regarding demographics, etc., only regarding the duration of back pain, but the standard deviations were very large and clinical significance was low. The demographics and HLA-B27 status of the IBS-present and -absent groups are shown in Table 1.

Table 1. Comparison of demographics and HLA-B27 status between IBS-present and IBS-absent groups (N = 60).

Characteristics		IBS		*p*-Value
		Yes (n = 14)	No (n = 46)	
Age		32.00 ± 8.50	29.96 ± 9.90	0.489
Gender	Male	10 (71.4)	35 (76.1)	0.734 *
	Female	4 (28.6)	11 (23.9)	
Marital Status	Married	12 (85.71)	25 (54.35)	0.058 *
	Unmarried	2 (14.29)	21 (45.65)	
Education	Undergraduate	8 (57.14)	30 (65.22)	0.807
	Postgraduate	5 (35.71)	16 (34.78)	
Occupation	Housewife	5 (35.71)	7 (15.22)	0.087
	Business	0 (0.0)	6 (13.04)	
	Service	5 (35.71)	9 (19.57)	
	Others	4 (28.58)	24 (52.17)	
Family history of lower back pain	Yes	11(78.57)	33 (71.74)	0.740 *
	No	3 (21.43)	13 (28.26)	
Duration of lower back pain (Months)		30.14 ± 18.136	61.64 ± 68.571	0.480 **
HLA-B27 + ve	Yes	3 (21.43)	17 (36.96)	0.072
	No	2 (14.29)	15 (32.61)	
	Not performed	9 (64.28)	14 (30.43)	

* Fisher's Exact Test, ** Mann–Whitney U Test.

The mean score of the AS disease activity parameters (morning stiffness, VAS, BASFI, BASMI, BASDAI, total swollen joint count, total tender joint count and MASES) of the IBS-present and -absent groups are shown in Table 2. Only the BASDAI was found to be statistically significantly higher in the IBS group ($p = 0.046$). For zero-inflated data (the dataset contains an excessive number of zeros) in the BASMI, the total swollen joint count, total tender joint count and MASES were positively skewed, leading to higher SDs.

Table 2. Comparison of clinical data between IBS-present and IBS-absent groups (N = 60).

Characteristics	IBS		*p*-Value	*p*-Value after Bonferroni Correction
	Yes (n = 14)	No (n = 46)		
Morning Stiffness	41.07 (31.020)	31.22 (29.158)	0.206 **	1.000
VAS	47.14 ± 19.78	44.57 ± 16.96	0.756 **	1.000
BASFI	3.47 ± 1.82	3.16 ± 1.60	0.847 **	1.000

Table 2. *Cont.*

Characteristics	IBS		*p*-Value	*p*-Value after Bonferroni Correction
	Yes (n = 14)	No (n = 46)		
BASMI	1.00 ± 0.88	1.41 ± 1.68	0.805 **	1.000
BASDAI	4.64 ± 1.82	3.54 ± 1.75	0.046	0.368
Total swollen joints	0.43 ± 0.85	0.89 ± 2.28	0.765 **	1.000
Total tender joints	1.86 ± 3.09	2.83 ± 5.30	0.956 **	1.000
Maastricht Enthesitis score	1.64 ± 2.41	1.87 ± 2.97	0.557	1.000

** Mann–Whitney U Test.

Colonoscopic Findings in the IBS-Present and -Absent Groups

In none of the patients was IBD (colitis or Crohn's disease) was found.

The frequency of macroscopic and microscopic lesions in the terminal ileum between the IBS-present and -absent groups are shown in Table 3.

Table 3. Comparison of macroscopic and microscopic lesions in the terminal ileum between IBS-present and -absent groups (N = 56).

	IBS Present (n = 13)	IBS Absent (n = 43)	*p*-Value
	Number (%)	Number (%)	
Macroscopic Grade			
G-0	7 (53.8)	28 (65.1)	0.52
G-1	1 (7.7)	4 (9.3)	1 *
G-2	5 (38.5)	11 (25.6)	0.48
G-3	0 (0)	0 (0)	-
Microscopic Grade			
G-0	3 (23.1)	10 (23.3)	1
G-1	8 (61.5)	25 (58.1)	1
G-2	1 (7.7)	5 (11.6)	1
G-3	1 (7.7)	3 (7)	1 *

* Fisher's exact test; Chi-square test.

In the ascending colon, sigmoid colon and rectum, among the IBS-present and -absent groups, macroscopic lesions were mostly seen in the ascending colon (three, 21.4% vs. one, 2.2%). Only Grade 2 lesions were found statistically significantly ($p = 0.03$) more often in the IBS-present group.

Microscopic lesions between the IBS-present and -absent groups were not found statistically significantly, or the figures were too small (Table 4).

Table 4. Comparison of macroscopic and microscopic lesions in colon between IBS-present and -absent groups (N = 60).

	IBS Present (n = 14)	IBS Absent (n = 46)	*p*-Value
	Number (%)	Number (%)	
Ascending Colon			
Macroscopic Grade			
G-0	11 (78.6)	45 (97.8)	0.03
G-1	0 (0)	0 (0)	-
G-2	3 (21.4)	1 (2.2)	0.03 *
G-3	0 (0)	0 (0)	-

Table 4. *Cont.*

	IBS Present (n = 14)	IBS Absent (n = 46)	*p*-Value
	Number (%)	Number (%)	
Microscopic Grade			
G-0	3 (21.4)	6 (13)	0.42
G-1	8 (57.1)	32 (69.6)	0.51
G-2	1 (7.1)	8 (17.4)	0.67
G-3	2 (14.3)	0 (0)	0.05 *
Sigmoid Colon			
Macroscopic Grade			
G-0	13 (92.9)	45 (97.8)	0.41
G-1	1 (7.1)	0 (0)	0.23 *
G-2	0 (0)	1 (2.2)	1
G-3	0 (0)	0 (0)	-
Microscopic Grade			
G-0	5 (35.7)	10 (21.7)	0.30
G-1	8 (57.1)	30 (65.2)	0.75
G-2	1 (7.1)	5 (10.9)	1 *
G-3	0 (0)	1 (2.2)	1 *
Rectum			
Macroscopic Grade			
G-0	11 (78.6)	38 (82.6)	0.70
G-1	3 (21.4)	7 (15.2)	0.68
G-2	0 (0)	1 (2.2)	1 *
G-3	0 (0)	0 (0)	-
Microscopic Grade			
G-0	3 (21.4)	7 (15.2)	0.68
G-1	9 (64.3)	31 (67.4)	1
G-2	2 (14.3)	7 (15.2)	1
G-3	0 (0)	1 (2.2)	1 *

* Fisher's exact test; Chi-square test.

4. Discussion

This observational study was carried out to determine the prevalence of IBS in patients with AS and to evaluate the macroscopic and microscopic gut lesions among them. To the best of our knowledge, such a study had not yet been conducted in South Asia.

In most industrialized countries, the overall prevalence rates of IBS are similar (10–20%) [24]. A study in Bangladesh in people older than 15 years showed that the overall prevalence of IBS (Rome II criteria) was 7.7% (n = 116), with a male-to-female ratio of 1:1.36 (49 vs. 67) [25]. In the current study, the prevalence of IBS was 23.3%, which is comparable to other studies [17].

A Chinese study looked for symptoms meeting the Rome IV functional bowel disorder (FBD) in 153 AS patients and in 56 controls. FBD symptoms were found in 60 patients (39.2%) and in 23.2% of controls. IBS was found in 18 AS patients (11.8%) and chronic diarrhea in 43. Each of the FBD symptoms and chronic diarrhea were associated with AS disease characteristics, but IBS was not [16]. Fecal calprotectin (FCP) appears to be a biomarker for gut inflammation in SpA [26], but, in the study by Wang et al., FCP levels did not differ between AS patients with/without FBD symptoms, IBS symptoms or chronic diarrhea [16].

In a 14-year retrospective study among 3519 newly diagnosed AS patients, Feng et al. found that the risk of IBS (ICD-9-CM = 564.1) in the AS group was significantly higher than in the comparison group, at an HR (hazard ratio) of 2.41 (95% C.I. = 1.84–3.16) [27].

In our study, the BASDAI was found to be statistically significantly higher in the IBS-present than IBS-absent group (p = 0.04), meaning that higher disease activity may be related to the development of IBS complaints. This is in agreement with the studies of Bernard [17] and of Wallman et al. [28]. Among patients who met the Rome criteria, the prevalence of IBD ranges from 0.4% to 1.9% [29].

Distinguishing IBD from IBS, especially with mild disease activity, can be difficult [30]. Furthermore, IBS-like symptoms are frequently reported before a diagnosis of IBD [30–33]. Current illustrations of immune activation and subtle mucosal inflammation in IBS have raised the probability of a more fundamental association between IBS and IBD [18].

The differentiation between IBS and underlying undiagnosed subclinical IBD is challenging [34]. A study reported that less than 1% of IBS patients were diagnosed with IBD [35]. Contrarily, there is a 2–3 times increased prevalence of IBS-type symptoms in IBD patients than in healthy controls [36]. Additionally, according to a recent meta-analysis, approximately one in three ulcerative colitis patients had symptoms that were similar to those of IBS [37].

In the current study, the frequency of macroscopic lesions in IBS was greater than in IBS-absent group and Grade 2 lesions in the ascending colon were found statistically significantly more often (p = 0.03). This may imply that there is a significant problem in distinguishing between IBD and true IBS with subclinical gut inflammations secondary to occult disease activity. Thus, we cannot exclude that in a follow-up study some of these patients may develop IBD.

In none of our patients was IBD (colitis or Crohn's disease) found, which may be explained by the fact that, in our series, all AS patients with a recent history of diarrhea had been excluded. During the study, special attention was given to looking for IBD both by the gastroenterologist and pathologist. There are no reports from Bangladesh on the prevalence of IBD [38].

In IBS, the precise reason behind the inflammation of the gut mucosa is not known [37]; however, it has been postulated that a persistent, low-grade mucosal inflammation contributes to the disease process of IBS and its symptomology [18]. The enteric immune system may become activated by being exposed to different types of microorganisms and/or food products, with a consequent increase in the number of mucosal immune cells and upregulation of the pro-inflammatory cytokines, resulting in on-going inflammation [18]. One other important sequel to many gut infections is the disruption of normal gut flora, while the altered microbiome and its metabolites are thought to play a role in promoting inflammation and impairing normal lymphocyte function [18]. Studies have reported the increased density and activation of enteric mucosal T-cells and mast cells in colonic biopsies taken from IBS patients and that >10% of patients with infective gastroenteritis may develop postinfectious IBS [18]. In this study, microscopic inflammation in the gut mucosa was found in relatively high frequencies both in the IBS-present and IBS-absent groups of AS patients, without any statistically significant differences (Tables 3 and 4).

The etiopathogenesis of AS involves complex interactions between genetic and environmental factors [4], and it is also known to be triggered by enteric microbial infections [4], which may explain the frequent presence of mucosal inflammation in both the IBS-present and IBS-absent groups in this study. However, the IBS-present and IBS-absent groups may have differed in the relative frequency of activated immune cells in their gut mucosa, as well as in the composition of their altered gut microbiome, due to their metabolites, which are thought to play crucial roles in the pathogenesis of IBS. In addition, increased levels of pro-inflammatory cell infiltrates in the intestinal mucosa and circulating pro-inflammatory cytokines may be involved in producing unremitting mucosal inflammation [39]. In the current study, we did not have the opportunity to compare the inflammatory and immune cell types in patients with and without IBS due to financial restrictions.

For the clinician, our study makes it clear that IBS is quite common in AS and patients with this kind of bowel problem need to be treated accordingly. The fact that diarrhea is very common in Bangladesh means that other causes should always be kept in mind [40].

4.1. Limitations

This study was conducted in a tertiary health care center in the country, which does not reflect a true picture of community. Fecal calprotectin was not carried out, but earlier studies proved that it has no additional value. We had no formal control group but could compare our findings with recent Bangladesh studies.

4.2. Strengths

This is the first study of large series of AS patients with IBS in Bangladesh and a full colonoscopy was performed to evaluate associated gut lesions in the IBS patients.

5. Conclusions

AS patients have a higher prevalence of IBS; higher disease activity is associated with IBS. Macroscopic lesions were more frequent in IBS than in non-IBS patients.

Author Contributions: All the authors contributed to the conception and design of the work the analysis and interpretation of the data, as well as drafting and critically revising the data, and all approve of the final version. The selection of patients and clinical aspects were carried out by N.F. and M.N.I., the colonoscopies and histopathology supervision were by S.A., M.N.I. and J.J.R., M.K. methods and statistics. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: This study was approved by the Ethics Committee of BSMMU, Shahbagh, Dhaka, Bangladesh (6 June 2011). The study was performed following the principles of the Declaration of Helsinki.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: Reseach data can be obtained form Nira Ferdous and Md. Kamruzzaman.

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Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Khan, M.A.; van der Linden, S. Axial Spondyloarthritis: A Better Name for an Old Disease: A Step Toward Uniform Reporting. *ACR Open Rheumatol.* **2019**, *1*, 336–339. [CrossRef] [PubMed]
2. Kavadichanda, C.G.; Geng, J.; Bulusu, S.N.; Negi, V.S.; Raghavan, M. Spondyloarthritis and the Human Leukocyte Antigen (HLA)-B*27 Connection. *Front. Immunol.* **2021**, *12*, 601518. [CrossRef] [PubMed] [PubMed Central]
3. Sieper, J.; Braun, J.; Rudwaleit, M.; Boonen, A.; Zink, A. Ankylosing spondylitis: An overview. *Ann. Rheum. Dis.* **2002**, *61* (Suppl. S3), iii8–iii18. [CrossRef] [PubMed]
4. Zhu, W.; He, X.; Cheng, K.; Zhang, L.; Chen, D.; Wang, X.; Qiu, G.; Cao, X.; Weng, X. Ankylosing spondylitis: Etiology, pathogenesis, and treatments. *Bone Res.* **2019**, *7*, 22. [CrossRef] [PubMed]
5. Mielants, H.; Veys, E.M.; Cuvelier, C.; De Vos, M.; Botelberghe, L. HLA-B27 related arthritis and bowel inflammation. Part 2. Ileocolonoscopy and bowel histology in patients with HLA-B27 related arthritis. *J. Rheumatol.* **1985**, *12*, 294–298. [PubMed]
6. Mielants, H.; De Keyser, F.; Baeten, D.; Van den Bosch, F. Gut inflammation in the spondyloarthropathies. *Curr. Rheumatol. Rep.* **2005**, *7*, 188–194. [CrossRef] [PubMed]
7. Orlando, A.; Renna, S.; Perricone, G.; Cottone, M. Gastrointestinal lesions associated with spondyloarthropathies. *World J. Gastroenterol.* **2009**, *15*, 2443–2448. [CrossRef] [PubMed] [PubMed Central]
8. Derkacz, A.; Olczyk, P.; Komosinska-Vassev, K. Diagnostic Markers for Nonspecific Inflammatory Bowel Diseases. *Dis. Markers* **2018**, *2018*, 7451946. [CrossRef] [PubMed]
9. Islam, M.N.; Chowdhury, M.M.; Haq, S.A.; Kamal, M.; Kabir, A.; Hasan, M.; Rasker, J.J. The colon in patients with ankylosing spondylitis and in normal controls in Bangladesh: A macroscopic and microscopic study. *Clin. Rheumatol.* **2010**, *29*, 13–18. [CrossRef] [PubMed]
10. Ahn, S.M.; Kim, Y.G.; Bae, S.H.; Lim, D.H.; Hong, S.; Park, S.H.; Lee, C.K.; Yoo, B. Ileocolonoscopic findings in patients with ankylosing spondylitis: A single center retrospective study. *Korean J. Intern. Med.* **2017**, *32*, 916–922. [CrossRef] [PubMed] [PubMed Central]

11. Simenon, G.; van Gossum, A.; Adler, M.; Rickaert, F.; Appleboom, T. macroscopic and microscopic gut lesions in seronegative spondyloarthopathies. *J. Rheumatol.* **1990**, *17*, 1491–1494.
12. Ferdous, N.; Islam, M.N.; Ishaque, S.M.; Akhter, S.; Kamal, M.; Rasker, J.J. The colon and terminal ileum in patients with ankylosing spondylitis and controls in Bangladesh: A macroscopic and microscopic study. *Rheumatol. Adv. Pract.* **2018**, *2*, rky016. [CrossRef]
13. Saha, L. Irritable bowel syndrome: Pathogenesis, diagnosis, treatment, and evidence-based medicine. *World J. Gastroenterol.* **2014**, *20*, 6759–6773. [CrossRef] [PubMed] [PubMed Central]
14. Staudacher, H.M.; Black, C.J.; Teasdale, S.B.; Mikocka-Walus, A.; Keefer, L. Irritable bowel syndrome and mental health comorbidity—Approach to multidisciplinary management. *Nat. Rev. Gastroenterol. Hepatol.* **2023**, *20*, 582–596. [CrossRef] [PubMed]
15. Solmaz, D.; Avci, O.; Yildirim, O.; Mete, R. FRI0206 Prevalence of Irritable Bowel Syndrome in Patients with Ankylosing Spondylitis. *Ann. Rheum. Dis.* **2015**, *74*, 499. [CrossRef]
16. Wang, L.; Song, C.; Wang, Y.; Hu, L.; Liu, X.; Zhang, J.; Ji, X.; Man, S.; Zhang, N.; Li, G.; et al. Symptoms compatible with Rome IV functional bowel disorder in patients with ankylosing spondylitis. *Mod. Rheumatol.* **2023**, *33*, 823–829. [CrossRef]
17. Bernard, J.; Barnetche, T.; Amory, C.; Despres, J.; Vandersmissen, M.; Landrin, J.; Gaujoux-Viala, C.; Lukas, C.; Ruyssen-Witrand, A.; Truchetet, M.E.; et al. Frequency of irritable bowel syndrome in spondyloarthritis: A multicentric cross-sectional study and meta-analysis. *RMD Open* **2024**, *10*, e003836. [CrossRef] [PubMed]
18. Ng, Q.X.; Soh, A.Y.S.; Loke, W.; Lim, D.Y.; Yeo, W.S. The role of inflammation in irritable bowel syndrome (IBS). *J. Inflamm. Res.* **2018**, *11*, 345–349. [CrossRef] [PubMed] [PubMed Central]
19. Drossman, D.A.; Whitehead, W.E.; Camilleri, M. Irritable bowel syndrome: A technical review for practice guideline development. *Gastroenterology* **1997**, *112*, 2120–2137. [CrossRef]
20. van der Linden, S.M.; Valkenburg, H.A. Cats A Evaluation of diagnostic criteria for ankylosing spondylitis: A proposal for modification of the New York criteria. *Arthritis Rheum.* **1985**, *27*, 361–368. [CrossRef]
21. van der Heijde, D.; Calin, A.; Dougados, M.; Khan, M.A.; van der Linden, S.; Bellamy, N. Selection of instrument in the core set for DC-ART, SMARD, physical therapy, and clinical record keeping in Ankylosing spondylitis. Progress report of the ASAS Working Group. Assessment in Ankylosing spondylitis. *J. Rheumatol.* **1999**, *26*, 951–954. [PubMed]
22. Heuft-Dorenbosch, L.; Spoorenberg, A.; van Tubergen, A.; Landewé, R.; van der Tempel, H.; Mielants, H.; Dougados, M.; van der Heijde, D. Assessment of enthesitis in ankylosing spondylitis. *Ann. Rheum. Dis.* **2003**, *62*, 127–132. [CrossRef] [PubMed]
23. Cuvelier, C.; Barbaties, C.; Mielants, H.; De Vos, M.; Roels, H.; Veys, E. Histopathology of intestinal inflammation related to reactive arthritis. *Gut* **1987**, *28*, 394–401. [CrossRef] [PubMed]
24. Perveen, I.; Rahman, M.M.; Saha, M.; Rahman, M.M.; Hasan, M.Q. Prevalence of irritable bowel syndrome and functional dyspepsia, overlapping symptoms, and associated factors in a general population of Bangladesh. *Indian J. Gastroenterol.* **2014**, *33*, 265–273. [CrossRef] [PubMed]
25. Perveen, I.; Hasan, M.; Masud, M.A.; Bhuiyan, M.M.; Rahman, M.M. Irritable bowel syndrome in a Bangladeshi urban community: Prevalence and health care seeking pattern. *Saudi J. Gastroenterol.* **2009**, *15*, 239–243. [CrossRef] [PubMed] [PubMed Central]
26. Emad, Y.; Ragab, Y.; Hammam, N.; El-Shaarawy, N.; Fawzi, M.; Amer, A.; El-Makhzangy, H.; Ismail, A.; Ibrahim, O.; Hassan, Y.; et al. The clinical utility of the biomarker Fecal Calprotectin in patients with Undifferentiated Spondyloarthritis. *Reumatol. Clin.* **2020**, *18*, 69–76. [CrossRef] [PubMed]
27. Feng, H.Y.; Chan, C.H.; Chu, Y.C.; Qu, X.M.; Wang, Y.H.; Wei, J.C.C. Patients with ankylosing spondylitis have high risk of irritable bowel syndrome. A long-term nationwide population-based cohort study. *Postgrad. Med.* **2022**, *134*, 290–296. [CrossRef]
28. Wallman, J.K.; Mogard, E.; Marsal, J.; Andréasson, K.; Jöud, A.; Geijer, M.; Olofsson, T. Irritable bowel syndrome symptoms in axial spondyloarthritis more common than among healthy controls: Is it an overlooked Comorbidity. *Ann. Rheum. Dis.* **2020**, *79*, 159–161. [CrossRef] [PubMed]
29. El-Salhy, M. Irritable bowel syndrome: Diagnosis and pathogenesis. *World J. Gastroenterol.* **2012**, *18*, 5151–5163. [CrossRef] [PubMed] [PubMed Central]
30. Schoepfer, A.M.; Trummler, M.; Seeholzer, P.; Seibold-Schmid, B.; Seibold, F. Discriminating IBD from IBS: Comparison of the test performance of fecal markers, blood leukocytes, CRP, and IBD antibodies. *Inflamm. Bowel Dis.* **2008**, *14*, 32–39. [CrossRef]
31. Bercik, P.; Verdu, E.F.; Collins, S.M. Is irritable bowel syndrome a low-grade inflammatory bowel disease? *Gastroenterol. Clin. North. Am.* **2005**, *34*, 235–245. [CrossRef]
32. Burgmann, T.; Clara, I.; Graff, L.; Walker, J.; Lix, L.; Rawsthorne, P.; McPhail, C.; Rogala, L.; Miller, N.; Bernstein, C.N. The Manitoba Inflammatory Bowel Disease Cohort Study: Prolonged symptoms before diagnosis–how much is irritable bowel syndrome? *Clin. Gastroenterol. Hepatol.* **2006**, *4*, 614–620. [CrossRef]
33. Drossman, D.A.; Camilleri, M.; Mayer, E.A.; Whitehead, W.E. AGA technical review on irritable bowel syndrome. *Gastroenterology* **2002**, *123*, 2108–2131. [CrossRef] [PubMed]
34. Quigley, E.M. Overlapping irritable bowel syndrome and inflammatory bowel disease: Less to this than meets the eye? *Ther. Adv. Gastroenterol.* **2016**, *9*, 199–212. [CrossRef] [PubMed] [PubMed Central]
35. Card, T.R.; Siffledeen, J.; Fleming, K.M. Are IBD patients more likely to have a prior diagnosis of irritable bowel syndrome? Report of a case-control study in the General Practice Research Database. *United Eur. Gastroenterol. J.* **2014**, *2*, 505–512. [CrossRef] [PubMed] [PubMed Central]

36. Ozer, M.; Bengi, G.; Colak, R.; Cengiz, O.; Akpinar, H. Prevalence of irritable bowel syndrome-like symptoms using Rome IV criteria in patients with inactive inflammatory bowel disease and relation with quality of life. *Medicine* **2020**, *99*, e20067. [CrossRef] [PubMed]
37. Ejtehadi, F.; Anbardar, M.H.; Imanieh, M.H.; Niknam, R.; Sivandzadeh, G.R. Organic colonic lesions in patients with irritable bowel syndrome: A comparative study. *Rev. Gastroenterol. Mex. Engl. Ed.* **2023**, *88*, 208–213. [CrossRef] [PubMed]
38. Ghosh, C.K.; Islam, S.; Tabassum, N.; Mohiuddin, S.A.; Hossain, M.M.; Sarkar, A.; Bari, A. Quality of Life of Patients With Inflammatory Bowel Disease in Bangladesh. *Cureus* **2023**, *15*, e39929. [CrossRef] [PubMed]
39. Gracie, D.J.; Ford, A.C. IBS-like symptoms in patients with ulcerative colitis. *Clin. Exp. Gastroenterol.* **2015**, *8*, 101–109. [CrossRef] [PubMed] [PubMed Central]
40. Halim, F.B.; Haider, M.Z. Prevalence and economic costs of diarrheal illness among adult slum dwellers in Khulna City, Bangladesh. *J. Health Soc. Sci.* **2017**, *2*, 83–98.

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