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Impact of gastrointestinal and psychological symptoms on disease activity and functional impairment in patients with spondyloarthritis: a cross-sectional study

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Abstract

Introduction Spondyloarthritis (SpA) exhibits predominantly musculoskeletal symptoms but also significant gastrointestinal (GI) and psychological manifestations. Subclinical gut inflammation is common in SpA, with frequent symptoms such as abdominal pain and diarrhea. Psychological issues like depression and anxiety are also prevalent, with a negative impact on quality of life. This study aimed to evaluate the presence of GI and psychiatric symptoms in SpA patients without inflammatory bowel disease (IBD) and their association with disease characteristics.

Methods Cross-sectional study, which included SpA patients from two rheumatology outpatient clinics. Patients were assessed for GI, and depressive symptoms (PHQ-9), perceived stress (PSS-10), disease activity (ASDAS, BASDAI) and functionality (BASFI). Laboratory tests included C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fecal calprotectin, and Secretory IgA. Statistical analysis involved Spearman correlation, linear regression, and multiple correspondence discriminant analysis (MCDA).

Results Among 98 SpA patients, 79.6% had axial SpA. High disease activity and functional impairment were common. 65.3% reported ≥ 2 GI symptoms, predominantly abdominal pain and diarrhea. Depression (PHQ-9 ≥ 10) was observed in 46.7% of patients, being moderate to severe in 25.0%. Depression, perceived helplessness, and lack of self-efficacy were associated with high disease activity and GI symptoms. MCDA identified strong correlations between depression, GI symptoms, and disease activity.

Conclusion This study highlights the association between GI and psychological symptoms with disease activity and functionality in SpA patients. Depression and perceived helplessness are prevalent and closely associated with high disease activity and GI symptoms, suggesting the need for interdisciplinary management from early stages to improve patient outcomes.

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Key points

1. 65.3% of SpA patients had ≥ 2 gastrointestinal (GI) symptoms, and 46.7% showed depression, highlighting significant psychological and GI involvement.
2. Depression correlated strongly with disease activity (BASDAI and BASFI), impacting SpA severity.
3. Patients with ≥ 2 GI symptoms had a higher risk of depression, indicating a strong GI-psychological link.
4. Findings support the need for interdisciplinary management to address both GI and psychological symptoms in SpA.

Keywords Spondyloarthritis, Depression, Mental health, Gastrointestinal symptoms

Introduction

Spondyloarthritis (SpA) is a group of diseases that have common pathophysiological and clinical features despite being phenotypically different [1]. In general, the prevalence varies between 0.1–2.5% [2]. In Latin America, it has been reported between 0.3–0.9% [3]. Subclinical gut inflammation has been reported in 50% of patients with axial spondyloarthritis (axSpA) [4], and a variable degree of patients report gastrointestinal (GI) symptoms such as abdominal distension, abdominal pain, diarrhea, presence of blood in stool, and weight loss in the absence of inflammatory bowel disease (IBD) [5]. With a prevalence as high as 15%, factors such as female sex, unemployment, higher disease activity, and mood symptoms are associated with the presentation of GI symptoms. This correlates with the higher risk of SpA patients having GI symptoms (OR = 1.59; 95% CI [1.05 to 2.40]) [6].

The relationship between the joint and mental health can be explained by the gradual reduction of mobility, stiffness, and fatigue in SpA, which can lead to psychological consequences, including depression and anxiety, which negatively affect quality of life (QoL) [7]. Approximately 30% of patients with axSpA [8] and 17% of patients with psoriatic arthritis (PsA) had depressive symptoms, and about 30% had anxiety symptoms [9]. The incidence of affective and anxiety symptoms increases both in the year before and the year after the diagnosis of inflammatory arthritis [10].

The relationship between the immune system and the GI and mental systems is evidenced by how different stressors affect its functioning [11]. On the other hand, the activation of immune cells and proinflammatory cytokines production has been associated with mood disorders changes, depression, anxiety, fatigue, psychomotor slowing, anorexia, cognitive dysfunction, and sleep disturbances [12]; being possible biomarkers for depression [13].

A link between GI and mood symptoms in relation to the microbiome-gut-brain axis has been observed through the effect of disease activity on QoL in patients with SpA. In this context, psychosocial impairment independent of age, sex, body mass index (BMI), and smoking was reported in a cohort of rheumatoid arthritis (RA) and SpA patients. These patients exhibited abdominal pain, diarrhea, bloating, and reflux, along with anxiety and depression symptoms, fatigue, and sleep disturbances. Conversely, GI symptoms were less frequent in patients whose routine lives were less impacted [14]. Thus, there is a need for comprehensive assessment of SpA patients that extends beyond disease activity to include interventions aimed at improving overall functioning. This could involve nutritional interventions, given the role of microbiota in GI and mood symptoms.

Few studies have evaluated psychological symptoms and GI symptoms simultaneously in SpA patients without IBD. Thus, the present study aimed to evaluate the presence of GI and psychological symptoms in patients with SpA and their association with disease characteristics.

Methods

Patients

The study was designed as a cross-sectional study, conducted in adult patients from two rheumatology outpatient clinics between 2019–2022. The patient must have a clinical SpA diagnosis and fulfill the International Spondyloarthritis Assessment Society (ASAS) classification criteria [15]. The medical record was retrieved to find information about GI symptoms. Those with two or more GI symptoms in the last six months were referred to the gastroenterology clinic. Individuals with concomitant IBD, pregnancy, comorbidities such as malignancies, autoinflammatory or autoimmune diseases, immunodeficiency, acute or chronic pancreatitis, liver disease, or treatment with antibiotics or antiparasitics in the last 3 months were excluded. The study was approved by the Hospital Militar Central Research Ethics Committee (HMC-2017-023, Memo No. 9, May 5, 2017, and Memo No. 19, November 1, 2019). Additionally, the patients provided written informed consent.

Assessment of clinical and laboratory characteristics

A rheumatology specialist collected data related to disease activity, extra-articular manifestations, and treatment at the time of inclusion. Disease activity was assessed using the Axial Spondyloarthritis Disease Activity Score (ASDAS), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), and functionality with the Bath

Ankylosing Spondylitis Functional Index (BASFI) [15, 16].

High-sensitivity C-reactive protein (CRP) was measured using the LKCRP1 chemiluminescence kit (Immulite 1000, Siemens®) according to the manufacturer's instructions, and the reference values were 0–3 mg/dL. The erythrocyte sedimentation rate (ESR) was determined using the Wintrobe quantitative method (mm/hour), according to the manufacturer's instructions. Values above 20 mm/hour were considered high. HLA*B27 allele measurement was performed using DNA Next-Generation Sequencing (NGS): Illumina/PacBio Sequencing with analysis of the second and third exons. The names of the repository/repositories and accession number(s) can be found below:

https://www.ncbi.nlm.nih.gov/, PRJNA843059.

Fecal calprotectin was quantified using the Enzyme-Linked Immunosorbent Assay (ELISA) kit, following the manufacturer's guidelines: DiaSource-Quantitative Fecal Calprotectin KAPEPKT849®, with a suggested cut-off point for levels considered high at > 120 ng/mL, manufactured in Louvain La Neuve, Belgium.

Total serum secretory immunoglobulin A (SIgA) antibody quantitation was performed in an ELISA *in-house* sandwich assay described in previous studies [17], and total serum IgA levels were determined with system kinetic nephelometry IMMAGE Immunochemistry (Kit IMMAGE® IgA Ref. 446460) according to manufacturer's specifications. SIgA values greater than 45 mg/mL and 82 to 453 mg/dL reference values for adults were considered positive respectively for total IgA.

Assessment of gastrointestinal symptoms

A survey was conducted to identify the presence of GI symptoms and diagnosis of SpA, and information was confirmed from medical records: diarrhea (defined as watery and loose stools three or more times in one day), stools with mucus, hematochezia, number of stools per day, abdominal pain, abdominal swelling, food intolerance, and weight loss. Patients with two or more GI symptoms were referred to the gastroenterology clinic. Under gastroenterologist criteria colonoscopy with digital chromoendoscopy with histological analysis was performed to rule-out IBD [18–21].

Assessment of depressive symptoms

The Patient Health Questionnaire-9 (PHQ-9) is a self-administered tool used for screening, diagnosing, monitoring, and measuring the severity of depression [22]. The score is assigned according to the frequency with which symptoms occur, and their severity can be organized into four categories according to this score: 0–4 (none), 5–9 (mild), 10–14 (moderate), 15–19 (moderately-severe), 20–27 (severe). The PHQ-9 has been validated in Colombia in patients using primary care services and in a group of healthy subjects [23].

Assessment of perceived helplessness and lack of self-efficacy

The Perceived Stress Scale (PSS-10) is a self-administered diagnostic tool used to evaluate the perception of stress. It measures how individuals perceive their life as stressful, focusing on the degree to which situations in their life are perceived as unpredictable, uncontrollable, and overwhelming [24] was applied. Questions 1,2,3,6,9,10 refer to perceived helplessness (measuring an individual's feelings of a lack of control over their circumstances or their own emotions or reactions), and questions 4,5,7,8 to lack of self-efficacy (measuring an individual's perceived inability to handle problems). The questions were answered on a Likert frequency scale with scores from 0 to 4, where the higher the score, the higher the perceived helplessness and the lower the lack of self-efficacy. In this study, the subscales of the PSS-10 were reported according to the results of the validation conducted in Colombia [25]. The results were grouped into categories if the participants responded with the following options: never, almost never, and occasionally.

Statistical analysis

Descriptive analyses were performed according to the variable characteristics and distributions. Spearman correlation analysis was performed to assess the strength and direction of associations between continuous variables. Then, linear regression models and multiple correspondence discriminant analysis (MCDA) were used to explore the relationship between GI and psychological symptoms with overall disease activity. Finally, from the MCDA, the significant variables that showed a significant correlation with PQH9 were included in a multinomial logistic regression analysis. Statistical significance was set at p-value < 0.05. The analyses were performed using IBM SPSS version 26 statistical program. Selection bias was addressed by evaluating patients based on ASAS criteria and excluding those with IBD through clinical and paraclinical assessments. Measurements were taken using standardized tools and validated measures. Statistical analyses were conducted to identify associations between relevant variables.

Results

A total of 98 patients with SpA without concurrent IBD were included, with 58.2% male gender and a mean age of 42.3 ± 10.4. The most frequently identified clinical subtype was axSpA (79.6%), followed by PsA, ReA, and undifferentiated SpA. Axial involvement was identified in 77.6% of patients. The HLA*B27 allele was present in 32.7% of the patients. The clinimetric results showed high

disease activity above 50% according to the BASDAI and ASDAS scores, with a similar result in terms of impaired functionality according to the BASFI.

GI symptoms and 65.3% of the patients reported ≥ 2 GI symptoms in the previous month. Other clinical and demographic characteristics are presented in Table 1. The most frequently reported symptoms were abdominal pain and bloating, food intolerance, and diarrhea, lasting for more than four weeks, in addition, fatigue was present at 59.2% and weight loss in 20.4% (Supplementary

Table 1 Patient characteristics according to presence of gastrointestinal symptoms

	SpA patients		Total	*p*-value
	≥2 GI symptoms	<2 GI symptoms		
n (%)	64 (65.3)	34 (34.6)	98 (100.0)	
Age (years)***	43 ± 11	41 ± 10	42 ± 10	0.455
Gender male	35 (54.7)	22 (64.7)	57 (58.2)	0.394
Male				
Educational level (University)				
University	35 (54.7)	11 (32.4)	46 (46.9)	0.163
Marital status (single)				
Single	14 (21.9)	7 (20.6)	23 (23.5)	0.963
BMI > 25 kg/m^2	40 (62.5)	20 (58.8)	60 (61.2)	0.828
SpA subtype				
axSpA	51 (79.7)	27 (79.4)	78 (79.6)	0.205
PsA	5 (7.8)	6 (17.6)	11 (11.2)	
ReA	5 (7.8)	0 (0)	5 (5.1)	
Undifferentiated SpA	3 (4.7)	1 (2.9)	4 (4.1)	
Axial involvement	49 (76.6)	27 (79.4)	76 (77.6)	0.805
Peripheral involvement	15 (23.4)	7 (20.6)	22 (22.4)	0.974
BASFI**	5.3 (3.1–7.4)	1.4 (0.2–5.3)	4.1 (1.6–6.7)	<0.001*
BASFI > 4	40 (62.5)	13 (38.2)	53 (54.1)	0.033*
BASDAI**	5.6 (3.4–7.2)	2.4 (0.8–5.7)	4.9 (2.8–6.8)	<0.001*
BASDAI > 4	43 (67.2)	14 (41.4)	57 (58.2)	0.018*
ASDAS CRP**	2.8 (2.2–3.3)	1.7 (1.1–2.7)	2.5 (1.7–3.1)	<0.001*
ASDAS CRP > 2.1	51 (79.7)	14 (41.2)	65 (66.3)	<0.001*
ASDAS CRP > 3.5	11 (17.2)	3 (8.8)	14 (14.3)	0.367
HLA*B27 (+)	21 (32.8)	11 (32.4)	32 (32.7)	0.963
CRP mg/dL**	0.7 (0.2–2.3)	0.8 (0.2–2.6)	0.8 (0.2–2.6)	0.988
CRP > 3 mg/dL	9 (14.1)	7 (20.6)	16 (16.3)	0.567
ESR mm/h**	10 (5–20)	10 (5–27)	10 (5–21.5)	0.973
ESR > 20 mm/h	15 (23.4)	11 (32.4)	26 (26.5)	0.471
Serum SIgA mg/mL**	52 (46–66)	52.1 (36–63)	52.1 (42–65)	0.183
Serum SIgA > 45 mg/mL	52 (81.3)	18 (52.9)	70 (71.4)	0.005*
Calprotectin ng/mL**	64 (43–153)	49.3 (41–77)	54.8 (43–130)	0.129
Calprotectin > 120 ng/mL	19 (29.7)	5 (16.1)	24 (25.3)	0.21
Treatment				
NSAID intake	3 (4.7)	3 (8.8)	6 (6.1)	
csDMARDs	23 (35.9)	10 (29.4)	33 (33.7)	
bDMARDs	38 (59.4)	21 (61.8)	60 (60.2)	
Mental health scales				
PHQ-9 depression (n = 92)**	10.5 (6–15.3)	4 (2–12)	8 (4–14)	0.003*
PSS-10 helplessness**	11 (8–15)	9 (3.5–14)	10.5 (7–14)	0.093
PSS-10 self-efficacy**	5 (3–7.5)	4 (1.8–8)	5 (3–8)	0.107

axSpA: axial spondyloarthritis; ReA: reactive arthritis; PsA: psoriatic arthritis; SpA: Spondyloarthritis; BMI: Body mass index; BASFI: Bath Ankylosing Spondylitis Functional Index; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; ASDAS: Ankylosing Spondylitis disease activity score; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; HLA: human leukocyte antigen; SIgA: Secretory immunoglobulin A; NSAID: Non-steroidal anti-inflammatory drugs; csDMARD: Conventional synthetic disease-modifying anti-rheumatic drugs; bDMARD: biological disease-modifying anti-rheumatic drug; PHQ-9: 9-question Patient Health Questionnaire; PSS-10: Perceived Stress Scale 10; GI: gastrointestinal

*$p < 0.05$

**Median (IQR)

***Mean ± SD

Table 1). The macroscopic and histological analyses revealed notable GI abnormalities, varying by anatomical region. Macroscopically, rectal involvement was characterized by mucosal alterations and vascular pattern loss, each observed in 21.2% of cases, along with inflammation in 18.2% of patients. In the sigmoid colon, mucosal abnormalities were present in 18.2% of cases, with vascular pattern loss identified in 12.1%. The ileum exhibited the highest prevalence of abnormalities, including mucosal alterations in 51.5% of cases, intestinal villi atrophy in 42.4%, and vascular pattern loss in 33.3%.

Histologically, 72.7% of patients demonstrated abnormalities, predominantly in the ileum, where inflammatory patterns (36.4%), architectural alterations (39.4%), and chronic inflammation (33.3%) were prominent. Cryptitis or atrophy was identified in 30.3% of ileal samples. In contrast, inflammatory patterns were noted in 24.2% of colonic samples and 27.3% of rectal samples.

Furthermore, patients with ≥ 2 GI symptoms exhibited a higher frequency of disease activity (BASDAI, BASDAI > 4, ASDAS-CRP, ASDAS-CRP > 2.1; $p < 0.05$) and greater functional impairment (BASFI and BASFI > 4; $p < 0.05$). These findings underscore significant region-specific GI involvement in SpA, highlighting the need for further investigation into its pathological mechanisms and clinical implications.

The PHQ-9 was administered to 91 patients. 46.7% had depression (≥10), and depression severity was moderate to severe in 25% of patients. The PSS-10 was administered to 90 patients, the perceived helplessness was present more than often for question 1 in 56.7%, question 2 in 71.1%, question 3 in 70.0%, question 6 in 54.4%, question 9 in 62.2%, and question 10 52.2%. Meanwhile, lack of self-efficacy was present more frequently than sometimes for question 4 (65.6 %), question 5 (68.9 %), question 7 (72.2 %), and question 8 (85.6 %).

A higher frequency of depressive symptoms was found in male 34.7%; ($p = 0.015$), patients with BMI ≥ 25 ($p = 0.028$), and those with ASDAS-CRP ≥ 3.5 ($p = 0.013$). Regarding GI symptoms there was a tendence to higher frequency of depressive symptoms compared with absence of GI symptoms (53.2% vs 33.3% respectively, $p = 0.073$), additionally, a higher frequency of depressive symptoms was found in those with blood in stool ($p = 0.028$) and weight loss ($p = 0.001$).

A higher frequency of lack of self-efficacy was found in SpA patients with ASDAS-CRP ≥ 3.5 ($p = 0.001$) and non-high educational level ($p = 0.032$). Regarding GI symptoms, a higher frequency of a lack of self-efficacy was found with food intolerance ($p = 0.031$). There were no significant differences between individual GI symptoms perceived helplessness. Other disease specific variables including HLA or SpA subtype were not significant.

Disease activity and functional indexes and emotional scales

There was a strong positive correlation between the PHQ-9 score (depression severity) and the BASDAI (r = 0.74) and BASFI (r = 0.70) scores, and a moderate positive correlation for ASDAS-CRP (r = 0.59). PSS-10 scores had a moderate positive correlation between helplessness and BASDAI (r = 0.31) and BASFI (r = 0.32). However, there was a weak positive correlation with ASDAS-CRP. For lack of self-efficacy, there was a weak positive correlation, although it was significant with BASDAI and BASFI.

Additionally, patients with high moderate or severe depression more frequently had high disease activity (BASDAI ≥ 4, ASDAS-CRP ≥ 2.1 or ≥ 3.5, $p = 0.001$) and functional impairment (BASFI ≥ 4, $p = 0.001$). Helplessness was more frequently associated with high disease activity (BASDAI ≥ 4, ASDAS-CRP ≥ 2.1 or ≥ 3.5, $p = 0.047$, 0.003, and 0.013, respectively), as well as functional impairment (BASFI ≥ 4, $p = 0.004$). Lack of self-efficacy was also associated with high disease activity (ASDAS-CRP score ≥ 2.1, $p = 0.042$) and functional impairment (BASFI score ≥ 4, $p = 0.028$).

Regression model and multiple correspondence discriminant analysis

As a result of the logistic regression analysis, after controlling for demographic and clinical SpA variables the severity of depression measured by PQH-9 showed associations for mild depression with male gender with an OR 3.9 (95%CI 1.1–15.1). Additionally, there was a positive association for ≥ 2 GI symptoms and depression severity, increasing from mild depression OR 3.7 (95%CI 1.0–15.1) to severe depression OR 23.3 (95%CI, 3.4–160.3) (Table 2).

The PHQ-9 multiple correspondence discriminant model demonstrated good internal consistency

Table 2 Logistic regression model for factors associated with depression by PHQ-9 clinical and demographic variables in patients with SpA

PHQ– 9	Beta (SE)	OR	95%CI
Mild depression	–1.39 (0.50)*		
≥2 GI symptoms	1.32 (0.71)	3.7*	1.0–15.1
Male gender	1.36 (0.69)	3.9*	1.0–15.1
Moderate depression	–0.85 (0.42)*		
≥2 GI symptoms	1.76 (0.73)	5.8*	1.4–24.2
Male gender	–0.20 (0.71)	0.8	0.2–3.3
Moderate-severe depression	–1.86 (0.63)**		
≥2 GI symptoms	2.89 (0.90)	17.9**	3.1–104.1
Male gender	–0.86 (0.86)	0.4	0.1–2.4
Severe depression	–2.32 (0.75)**		
≥2 GI symptoms	3.14 (0.99)	23.2**	3.4–160.3
Male gender	–0.41 (0.86)	0.7	0.1–3.6

$R^2 = 0.293$. LR $x^2 = 30.24$, *$p < 0.05$; **$p < 0.01$. PHQ-9: 9-question Patient Health Questionnaire; GI: Gastrointestinal; SE: Standard error; OR: Odds ratio; CI: Confidence interval

(α = 0.803), generating two dimensions. Dimension 1 included the presence of ≥ 2 GI symptoms [correlation coefficient (CC) = 0.700)], abdominal pain (CC = 0.703), and fatigue (CC = 0.621). Dimension 2 consisted of depression assessed by the PHQ-9 (CC = 0.723), and high disease activity assessed by the BASDAI > 4 (CC = 0.381) (Fig. 1).

A MCDA was conducted to explore multinomial correlations and identify significant variables associated with PQH9. The model demonstrated strong internal consistency, with a Cronbach's alpha of 0.803. Two distinct dimensions were identified: Dimension 1, which grouped > 2 GI symptoms (CC = 0.700), abdominal pain (CC = 0.703), and fatigue (CC = 0.621); and Dimension 2, which included PQH9 (CC = 0.723) and BASDAI > 4 (CC = 0.381) (Fig. 1).

Figure 1 presents a graphical representation of the interconnections among the variables in the model, depicted on a vector map within a Cartesian coordinate system. In this representation, the angle between each pair of variables conveys the strength of their correlation: smaller angles indicate a strong positive correlation, angles nearing 90° suggest no correlation, and angles approaching 180° reflect a strong negative or inverse correlation.

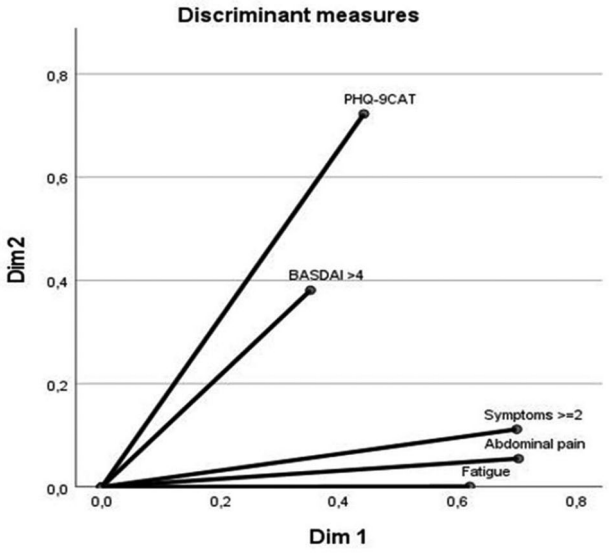

Fig. 1 Multiple correspondence discriminant analysis. Discriminant analysis of multiple correspondence between depression (PHQ9) and disease activity (BASDAI), gastrointestinal symptoms, abdominal pain, and fatigue

Discussion

The present study investigated non-inflammatory GI and psychological symptoms in SpA patients without concurrent IBD, identifying depression in half of the population. The findings revealed significant correlations between depression, helplessness, and lack of self-efficacy with SpA outcomes, such as disease activity and functional impairment. Specifically, mild depression was predominantly observed in male patients with ≥ 2 GI symptoms. Additionally, there was a statistically significant association between moderate depression and SpA patients with ≥ 2 GI symptoms, regardless of gender. These results suggest a relationship between GI and mental health symptoms in individuals with SpA.

Rheumatologic diseases are associated with a higher risk of psychological disorders. The standardized incidence ratios for rheumatoid arthritis (RA), systemic lupus erythematosus, and axSpA were 1.5, 2.4, and 1.7, respectively [26]. Depression is the second most frequent comorbidity in axSpA [27], with a meta-analysis indicating a prevalence of about 15% [28]. In a multinational cohort from Europe, Asia, and South America the prevalence is 32.3% [29], while in Colombia, 22% [30]. Interestingly, most studies used the Hospital Anxiety and Depression Scale (HADS) or the Zung Self-Rating Depression Scale (SDS) for depression diagnosis. Focusing on the PHQ-9 depression prevalence had been reported as high as 36% in India [31], similar to findings from Turkey [32] and China [33]. Meanwhile our results are higher than those reported, suggesting variability across regions.

The coexistence of SpA and IBD is not rare, leading to the development of screening tools for gastroenterology referrals [19]. In our center, diarrhea and abdominal pain were the most prevalent major and minor screening criteria associated with higher disease activity scores [21]. Consistent with previous reports, a higher frequency of GI symptoms, particularly abdominal pain, bloating, and diarrhea, was observed in active disease [34].

A recent study evaluated in RA and SpA European population the association between depression and GI symptoms such as abdominal pain, diarrhea, distension, and reflux. Additionally, there was an association between anxiety and abdominal pain, diarrhea, swallowing disorders, flatulence, and reflux [14]. When other GI diseases are evaluated, such as irritable bowel syndrome (IBS) patients exhibit elevated frequency of psychological symptoms [35, 36]. Meanwhile in IBD patients, the new onset GI symptoms were associated with anxiety [36]. Differentiating GI symptoms and the presence of IBS is challenging due to symptom overlap [37], which could be also challenging in other conditions such as SpA. Interestingly, in axSpA, those patients with depression, anxiety and fibromyalgia associated with IBS reported worse quality of life, global health, fatigue, disease activity, pain, and functional impairment [27]. This aligns with our findings highlighting the significance of the "gut-brain axis", with the interplay between GI symptoms and mental illnesses. Up to 70% of SpA patients exhibit subclinical gut inflammation, and 5–10% of those with more severe

intestinal inflammation progress to clinically defined IBD, which is the most common extra-articular manifestation of AS. This association leads to local inflammation through mechanisms such as molecular mimicry, increased intestinal permeability, IgA immune response, and the overexpression of inflammatory factors. These physiological processes underlying SpA also contribute to the development of depressive symptoms. This is primarily due to the activation of the immune system, resulting in the production and release of cytokines such as interferon-alpha (IFN-α), interleukin (IL)-1, IL-6, and tumor necrosis factor-alpha (TNF-α) [38].

Our study results demonstrate a correlation between high disease activity (BASDAI and ASDAS), functional limitation (BASFI), and psychological symptoms. Durmus et al. also found high disease activity associated with depression, anxiety, and other psychological symptoms, which were also related to functional capacity and fatigue [39]. Additionally, in SpA patients with high BASDAI scores, had increased SIgA levels [40], although the initial results showed evidence of differences in SIgA levels with GI symptoms, no further significant differences were evident in the subsequent analysis.

The male gender was the most affected by moderate depression, consistent with other studies showing higher incidence rates of psychological disorders in males with rheumatic diseases [41]. However, other publications observed an association between females and psychological symptoms with disease activity, sleep disturbances, fatigue, and quality of life [31]. A multinational study an association with female gender and psychological disorders was present, but in further analysis was not significant [42].

Helplessness, resulting from pain catastrophizing, significantly impacts quality of life [43], and it correlates with depression, anxiety, and disease activity in RA and axSpA [44–46]. This factor is rarely explored in conjunction with GI symptoms but are shown in our study to significantly correlate with SpA outcomes, such as disease activity and functional impairment. Penhoat et al. [47], reported persistent catastrophizing scores in patients under bDMARD, similar to our study, where no impact of therapy was evident in these scores. Additionally, lack of self-efficacy was associated with a low educational level. In agreement with another study that identified low education in SpA patients associated with depression and anxiety [32].

In a population-based survey, the presence of anxiety and depression was shown to be associated with non-inflammatory GI symptoms [48]. Similarly, a primary care study demonstrated that the number of GI symptoms increased the risk for anxiety [49]. This relationship appears to be bidirectional, as GI problems have been shown to increase the probability of developing depression by 7% and anxiety by 8.8% [50]. Although the design of our study does not establish causality, our findings contribute important insights into this relationship, specifically within the SpA population these findings suggest that GI symptoms may exacerbate depression in SpA patients [51]. However, it is also possible that baseline depression rates are inherently higher in those with GI symptoms [14, 52], as supported by existing evidence of the gut-brain axis influencing mental health [4]. We observed that GI symptoms were significantly associated with higher rates of depression, including moderate depression. These results suggest that GI symptoms may act as a factor that exacerbates depression in SpA patients, potentially amplifying disease activity and impairing overall quality of life.

Our study has several limitations. First, cross-sectional design restricts our ability to infer causality; while we identified associations between psychological symptoms and disease activity, we cannot determine the directionality of these relationships. Second, the generalizability of our findings is hindered by the relatively small sample size, which may not adequately represent the broader SpA population. Third, variations in reported levels of depression, perceived helplessness, and self-efficacy may arise from the specific cutoff values used for each scale and questionnaire. Despite this, our findings align with those reported in other populations, suggesting some degree of consistency.

Fourth is the exclusive use of self-report measures. While these tools provide valuable insights, they lack the diagnostic rigor of structured clinical interviews, and future studies employing such methods are necessary to validate our findings. Furthermore, we conducted a thorough evaluation of GI symptoms to exclude other underlying conditions that could confound our results. This distinction allows us to explore the relationship between GI symptoms and depression within a subset of patients where inflammation is not the primary driver of GI complaints. However, reliance on self-reporting may introduce bias, as patients' perceptions of their symptoms could be influenced by various factors, including their psychological state.

In summary, the significance of our findings lies in their implications for the clinical management of SpA patients. Addressing GI symptoms as part of a comprehensive treatment approach may not only improve GI health but also reduce the psychological burden of depression and its negative impact on disease outcomes. Further longitudinal studies are essential to better understand the directionality of this relationship and to develop targeted interventions that address both GI and psychological symptoms in SpA patients.

Hence, underscore the importance of interdisciplinary management from early stages, addressing both GI and

psychological symptoms as plausible targets for improving both psychological well-being and disease outcomes, which has important implications for the comprehensive care of SpA patients.

Abbreviations

ASDAS	Ankylosing Spondylitis Disease Activity Score
axSpA	Axial Spondyloarthritis
BASDAI	Bath Ankylosing Spondylitis Disease Activity Index
BASFI	Bath Ankylosing Spondylitis Functional Index
bDMARDs	Biologic Disease-Modifying Antirheumatic Drugs
BMI	Body Mass Index
CRP	C-Reactive Protein
csDMARDs	Conventional Synthetic Disease-Modifying Antirheumatic Drugs
ESR	Erythrocyte Sedimentation Rate
GI	Gastrointestinal
HLA-B27	Human Leukocyte Antigen B27
IBD	Inflammatory Bowel Disease
IFN-α	Interferon-alpha
IL-1, IL-6	Interleukin-1, Interleukin-6
MCDA	Multiple Correspondence Discriminant Analysis
NSAID	Non-Steroidal Anti-Inflammatory Drugs
PHQ-9	Patient Health Questionnaire-9
PsA	Psoriatic Arthritis
PSS-10	Perceived Stress Scale-10
QoL	Quality of Life
RA	Rheumatoid Arthritis
ReA	Reactive Arthritis
SIgA	Secretory Immunoglobulin A
SpA	Spondyloarthritis
TNF-α	Tumor Necrosis Factor-alpha

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s41927-025-00478-y.

Supplementary Material 1

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Author contributions

The authors certify that they have participated sufficiently in the work to take public responsibility for the appropriateness of the design and method of review, as well as the reviewing of the manuscript and approve it for publication: Conceptualization: Ángelo Arzuaga-Hernández, Omar-Javier Calixto, Oscar Gómez, Julián Andrés Sucerquia-Quintero, Wilson Bautista-Molano, Consuelo Romero-Sánchez. Methodology: Ángelo Arzuaga-Hernández, Julián Andrés Sucerquia-Quintero, Consuelo Romero-Sánchez. Formal analysis and investigation: Ángelo Arzuaga-Hernández, Omar-Javier Calixto, Oscar Gómez, Juliette De Ávila, Consuelo Romero-Sánchez. Writing - original draft preparation: Ángelo Arzuaga-Hernández, Omar-Javier Calixto, Oscar Gómez, Wilson Bautista-Molano, Consuelo Romero-Sánchez. Writing - review and editing: Ángelo Arzuaga-Hernández, Omar-Javier Calixto, Oscar Gómez, Juliette De Ávila, Julián Andrés Sucerquia-Quintero, Juan Manuel Bello-Gualtero, Cristian Flórez-Sarmiento, Wilson Bautista-Molano, Consuelo Romero-Sánchez. Funding acquisition: Consuelo Romero-Sánchez. Resources: Consuelo Romero-Sánchez. Supervision: Ángelo Arzuaga-Hernández, Omar-Javier Calixto, Oscar Gómez, Juliette De Ávila, Julián Andrés Sucerquia-Quintero, Juan Manuel Bello-Gualtero, Cristian Flórez-Sarmiento, Wilson Bautista-Molano, Consuelo Romero-Sánchez

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Data availability

The HLA datasets presented in this study can be found in online repositories. The names of the repository/repositories and accession number(s) can be found below: https://www.ncbi.nlm.nih.gov/, PRJNA843059.

Declarations

Ethics approval and consent to participate

The study was designed in compliance with the Helsinki Declaration, and approved by Hospital Militar Central Institutional Ethics Committee (HMC-2017-023). The patients provided written informed consent form.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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