Am J Transl Res 2025;17(11):8525-8535
www.ajtr.org /ISSN:1943-8141/AJTR0166990

Original Article

Oral paroxetine improves symptoms and quality of life in refractory irritable bowel syndrome: a retrospective study

Zhiyong Wang*, Huixian Xu*, Zhenfeng Liu

*Department of Gastroenterology, Chongming Hospital Affiliated to Shanghai University of Medicine and Health Sciences, Chongming District, Shanghai 202150, China. *Equal contributors and co-first authors.*

Received June 22, 2025; Accepted September 17, 2025; Epub November 15, 2025; Published November 30, 2025

Abstract: Objective: To evaluate the efficacy and safety of oral paroxetine in improving symptoms and quality of life in patients with refractory irritable bowel syndrome (IBS). Methods: Clinical data of 80 refractory IBS patients treated at Chongming Hospital Affiliated to Shanghai University of Medicine and Health Sciences from January to December 2023 were retrospectively analyzed. The control group (n = 40) received prokinetic agents/pinaverium bromide plus lifestyle and dietary modifications, supplemented with antispasmodics and intestinal flora regulation. The paroxetine group (n = 40) received additional paroxetine hydrochloride (20 mg, once daily). Outcomes were assessed using the Irritable Bowel Syndrome Symptom Severity Scale (IBS-SSS), Bristol Stool Form Scale (BSFS), Self-Rating Anxiety Scale (SAS), Self-Rating Depression Scale (SDS), and IBS Quality of Life (IBS-QoL) before and after intervention. Adverse effects were recorded. Pearson correlation was used to examine associations between IBS-SSS and baseline variables, and logistic regression was applied to identify predictors of post-intervention quality of life. Results: Both groups improved across IBS-SSS, BSFS, SAS, SDS, and IBS-QoL after treatment, but improvements were significantly greater in the paroxetine group, particularly at 12 weeks (all $P < 0.05$). Age ($t = 3.794$, $P = 0.002$) and gender ($F = 4.312$, $P = 0.001$) independently influenced quality of life. Correlation analysis showed that IBS-SSS scores at week 12 were associated with age ($R = -0.335$), height ($R = -0.389$), and marital status ($R = 0.134$; all $P < 0.05$). Conclusion: Oral paroxetine provides significant and sustained relief of symptoms and improves quality of life in refractory IBS patients, with good safety for at least 12 weeks.

Keywords: Paroxetine, refractory, irritable bowel syndrome, early, oral, antidepressants

Introduction

Irritable bowel syndrome (IBS) is one of the most common functional gastrointestinal disorders, characterized by abdominal pain, bloating, altered bowel habits, and abnormal stool characteristics, which may occur persistently or intermittently [1]. In the United States, the prevalence of IBS ranges from 7% to 16%, with an annual economic burden exceeding $1 billion [2, 3]. The Rome Foundation Global Study 2021 [3] reported a global prevalence of 10.1% (9.8-10.5%), underscoring the worldwide impact of IBS. With socioeconomic development, increasing occupational stress, and changing dietary habits, the prevalence of IBS continues to rise.

The pathogenesis of IBS remains unclear, but it is generally recognized to involve multiple physiological, psychological, and social factors [4]. Many patients continue to experience persistent symptoms despite repeated medical visits, progressing to refractory IBS, which severely impairs quality of life. Refractory IBS is strongly associated with anxiety and depression, with patients being approximately three times more likely to develop these conditions compared with healthy individuals [5]. Diminished quality of life in refractory IBS is often driven more by comorbid psychological disorders than by gastrointestinal symptoms themselves [6].

Current treatment strategies for refractory IBS include dietary modification, psychotherapy, pharmacotherapy, and microbiota-targeted therapy [7]. Antidiarrheal agents such as loperamide are considered first-line options [8], but many patients fail to respond adequately, as loper-

https://doi.org/10.62347/BQWP2309

amide primarily improves diarrhea without addressing other IBS symptoms [9]. Antidepressants represent one of the most effective therapeutic options, and evidence suggests that early use of low-dose antidepressants can significantly improve constipation, diarrhea, abdominal pain, and psychological symptoms in IBS patients [10]. Selective serotonin (5-hydroxytryptamine, 5-HT) reuptake inhibitors (SSRI) may slow gastrointestinal transit, alter rectal compliance, and reduce visceral hypersensitivity, thereby alleviating symptoms [11, 12]. In addition, studies have demonstrated the benefit of SSRI in refractory IBS after failure of first-line therapy [13].

Paroxetine, a selective 5-HT reuptake inhibitor, is listed for use in functional gastrointestinal disorders in drug references. Compared with traditional antidepressants, paroxetine has demonstrated higher efficacy, fewer side effects, and a favorable safety profile [14, 15]. More recently, it has been shown to influence gut steroidogenesis and microbiota composition [16, 17]. Based on these findings, the present study aimed to evaluate the efficacy of early oral paroxetine in managing refractory IBS, with a focus on symptom relief and quality-of-life improvement.

Patients and methods

Clinical information

This retrospective study analyzed data from 80 patients with refractory IBS treated in the gastroenterology department of a general hospital between January and December 2023. Patients were divided into a control group and a paroxetine group based on treatment regimens. The control group (n = 40) received prokinetic agents (pinaverium bromide) combined with lifestyle and dietary modifications, antispasmodics, and intestinal flora regulation. The paroxetine group (n = 40) additionally received oral paroxetine hydrochloride (20 mg, once daily). Both groups were treated for 12 weeks. The study was approved by the Ethics Committee of Chongming Hospital Affiliated to Shanghai University of Medicine and Health Sciences.

Inclusion criteria: (1) diagnosis of refractory IBS; (2) age 18-65 years; (3) at least three consecutive treatments with negative stool routine, stool culture, and fecal occult blood tests; and (4) continuous use of prokinetic agents/pinaverium bromide, dietary and lifestyle modifications, antispasmodics, and intestinal flora regulation before enrollment.

Exclusion criteria: (1) intestinal infections or other bowel diseases; (2) severe cardiac, hepatic, pulmonary, renal, or other major organ disease; (3) history of laparotomy; (4) history of psychiatric disorders; (5) incomplete 12-week treatment or follow-up; and (6) incomplete case records.

Data collection: Clinical data were retrieved from inpatient electronic records, outpatient reviews, and patient follow-ups. Baseline variables included demographics, lifestyle factors (smoking, alcohol), disease duration, psychological status, and quality of life. Clinical outcomes and stool characteristics were assessed using validated questionnaires. Adverse events were also recorded.

Outcomes

Primary outcomes: Symptom severity (Irritable Bowel Syndrome Symptom Severity Questionnaire, IBS-SSS [18]) and stool characteristics (Bristol Stool Form Scale, BSFS [19]) at baseline and weeks 4, 8, and 12. IBS-SSS consists of five domains (abdominal pain severity, pain frequency, abdominal distension, satisfaction with defecation, and impact on life), with scores ranging 0-500; higher scores indicate greater severity. BSFS classifies stool into seven types (1 = hard, 7 = watery), with higher scores reflecting looser stools and more severe diarrhea.

Secondary outcomes: (1) Defecation satisfaction: assessed by the IBS-SSS subscale [20]. Scores range from 0 to 100, with higher scores reflecting poorer satisfaction. (2) Psychological status: assessed with the Self-Rating Anxiety Scale (SAS) [21] and Self-Rating Depression Scale (SDS) [22], each containing 20 items scored 1-4, with higher scores indicating more severe symptoms. Evaluated at baseline and week 12. (3) Quality of life: assessed with the IBS Quality of Life questionnaire (IBS-QoL [23, 24]), which includes 34 items across eight domains. Scores are standardized to 0-100, with higher scores indicating better quality of life. Measured at baseline and weeks 4, 8, and 12. (4) Adverse events: eczema, body aches,

Table 1. Comparison of general data between paroxetine group and control group [n (%), $\bar{x} \pm sd$]

Characteristic	Control group (n = 40)	Paroxetine group (n = 40)	χ^2/t	P
Age (years)	49.67±10.64	50.5±9.04	0.021	0.823
Gender			0.083	0.945
Male	15 (37.50)	16 (40.00)		
Female	25 (62.50)	24 (60.00)		
Marital status				
Spouse	19 (47.50)	18 (45.00)	0.012	0.953
Without spouse	21 (52.50)	22 (55.00)		
Smoking history			0.366	0.198
Yes	18 (45.00)	16 (40.00)		
No	22 (55.00)	24 (60.00)		
Drinking history			0.254	0.257
Yes	7 (17.5)	5 (12.50)		
No	33 (82.50)	35 (87.50)		
Height (cm)	170.0±14.3	169.5±12.5	0.575	0.104
Weight (kg)	70.8±16.0	69.0 ±19.5	0.789	0.099
Duration of illness (years)	2.62±4.77	2.18±4.79	0.392	0.176

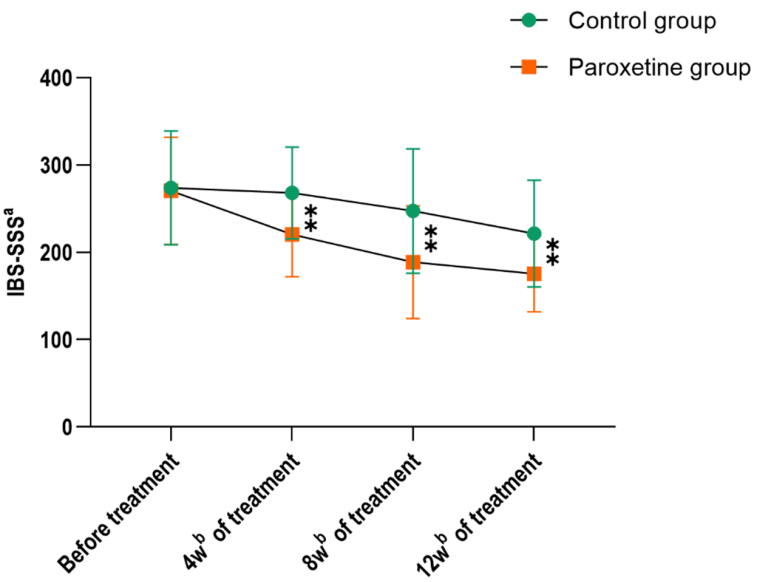

Figure 1. Comparison of total score of irritable bowel syndrome symptom severity questionnaire between paroxetine group and control group. [a]IBS-SSS: Irritable Bowel Syndrome Symptom Severity Questionnaire; [b]W: weeks. Note: Compared with the control group, **P < 0.01.

epigastric burning sensation, cold, cough, diarrhea, diastolic blood pressure below the normal range, fever, burning pain in the hands, headache, hoarseness, knee pain, muscle aches, nausea and vomiting sensation, rash, rhinitis, and vomiting after 12 weeks of treatment.

Statistical analysis: Analyses were performed using SPSS 26.0 and Prism 9. Continuous variables were expressed as mean ± SD and compared with independent t-tests; repeated-measures ANOVA with LSD post-hoc tests was used for longitudinal comparisons. Categorical variables were expressed as n (%) and compared with chi-square tests. Non-normally distributed data were analyzed with the rank-sum test. Pearson correlation assessed associations between IBS-SSS and continuous baseline factors; dichotomous variables (e.g., sex, marital status, smoking, alcohol use) were compared using t-tests. Logistic regression (univariate and multivariate) was applied to identify predictors of post-treatment quality of life. Statistical significance was set at P < 0.05.

Results

Comparison of clinical data

No statistically significant differences were observed between the two groups in age, gender, marital status, smoking and drinking history, height, weight, or disease duration (all P > 0.05; **Table 1**).

Comparison of IBS-SSS scores

ANOVA revealed significant differences in IBS-SSS scores between the groups (P < 0.05), but not within the control group over time (P > 0.05). Post hoc analysis showed significant between-group differences at weeks 4, 8, and 12 (all P < 0.05), with the lowest scores at week 12. At week 12, IBS-SSS scores in the paroxetine group were significantly lower than those in the control group (P < 0.05; **Figure 1**).

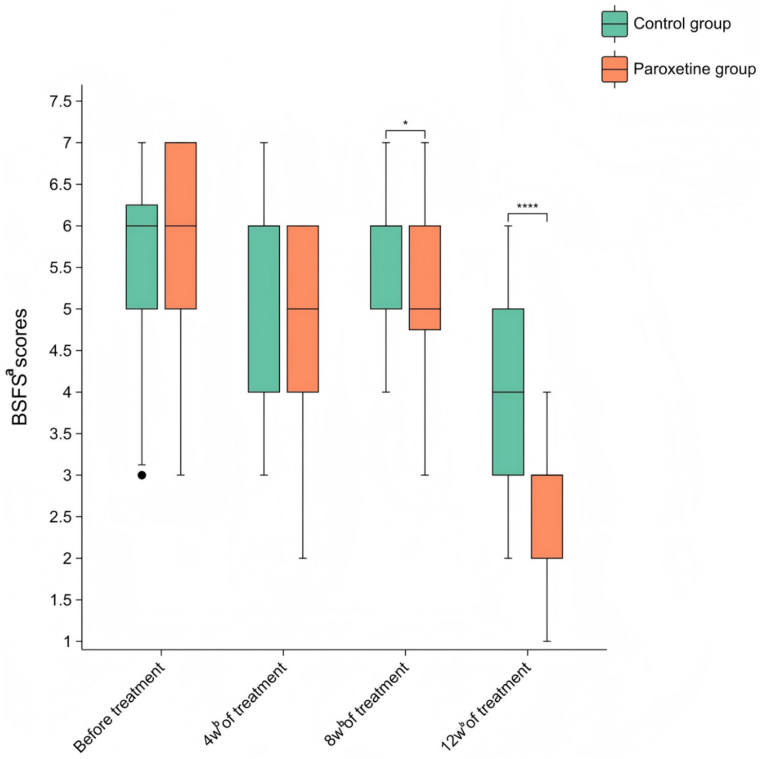

Figure 2. Comparison of bristol stool fecal profile scale between paroxetine group and control group. [a]BSFS: Bristol Stool Fecal Profile Scale; [b]W: weeks. Note: *P < 0.05, ****P < 0.001.

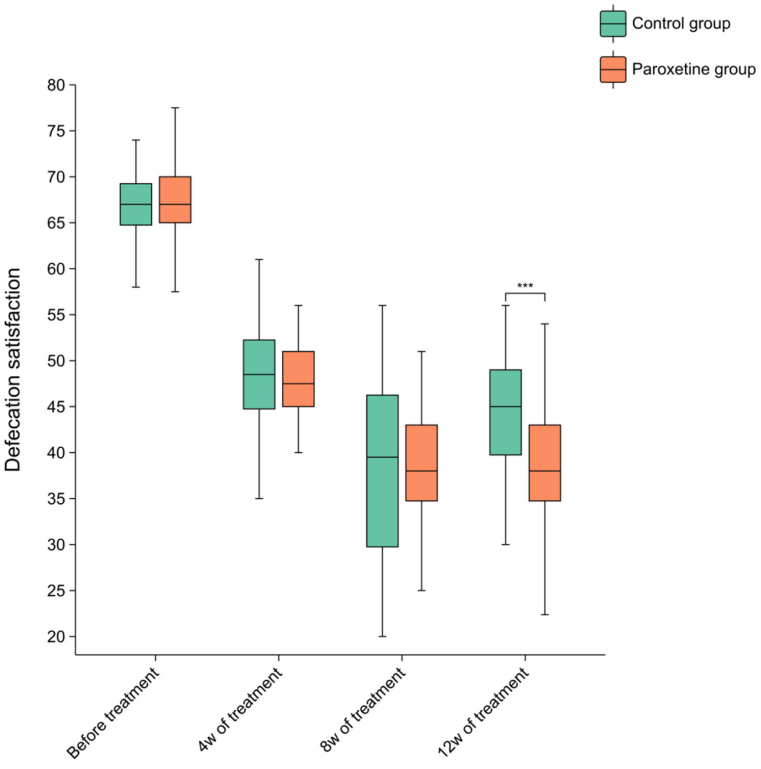

Figure 3. Comparison of defecation satisfaction between paroxetine group and control group. Note: ***P < 0.001. W: weeks.

Comparison of BSFS score

Intragroup analysis showed significant reductions in BSFS scores in both groups ($P < 0.05$). Post hoc analysis revealed significant between-group differences at weeks 4, 8, and 12 (all $P < 0.05$), with the lowest scores at week 12. At weeks 8 and 12, BSFS scores in the paroxetine group were significantly lower than those in the control group (both $P < 0.05$; **Figure 2**).

Comparison of defecation satisfaction

Bowel satisfaction scores in both groups at baseline and weeks 4, 8, and 12 are shown in **Figure 3**. Significant between-group differences were found ($P < 0.05$). Post hoc analysis indicated significant differences at weeks 4, 8, and 12 (all $P < 0.05$), with the lowest scores at weeks 8 and 12. At these time points, the paroxetine group had significantly lower scores than the control group (all $P < 0.05$; **Figure 3**).

Comparison of SAS and SDS scores

SAS and SDS scores were assessed at baseline and week 12 (**Figure 4**). At week 12, both scores were significantly lower in the paroxetine group than those in the control group (both $P < 0.05$).

Comparison of IBS-QoL scores

Mean IBS-QoL scores showed significant improvements in both groups, with between-group differences favoring paroxetine ($P < 0.01$). Post hoc analysis confirmed significant differences at weeks 4, 8, and 12 (all $P < 0.05$), with the high-

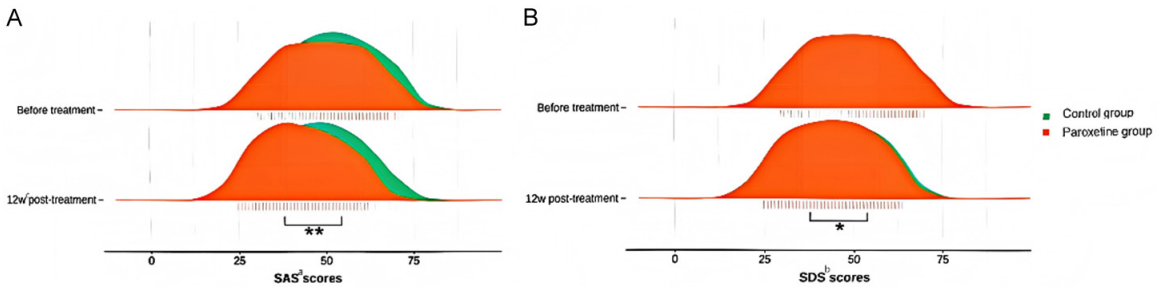

Figure 4. Comparison of SAS and SDS scores between paroxetine group and control group. A: Comparison of SAS scores between paroxetine group and control group. B: Comparison of SDS scores between paroxetine group and control group. [a]SAS: Self-rrating Anxiety Scale scores; [b]SDS: Self-rating Depression Scale; [c]W: weeks. W: weeks.

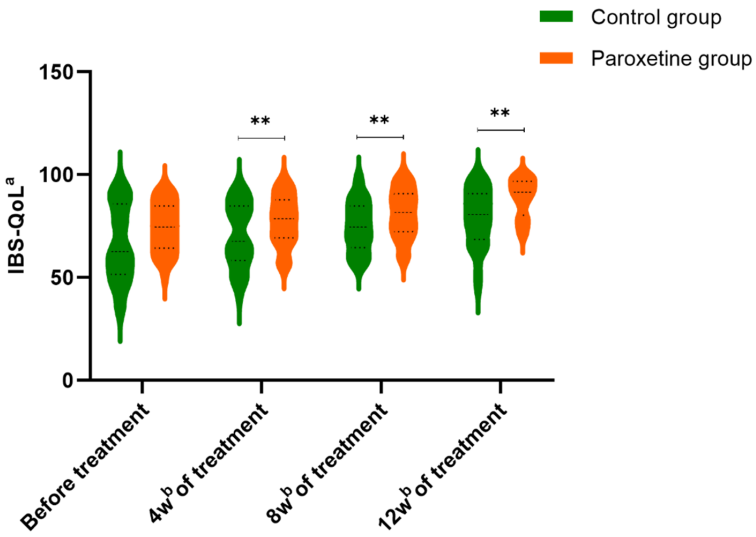

Figure 5. Comparison of total score of irritable bowel syndrome quality of life between paroxetine group and control group. [a]IBS-QoL: Irritable Bowel Syndrome Quality of Life; [b]W: weeks. Note:**P < 0.01. Over time, the IBS-QOL and Paroxetine groups also showed significant improvement compared to the control group.

Comparison of adverse events

All adverse events were mild, and no serious adverse events occurred (**Table 3**). A total of 12 patients reported adverse events, including 8 in the control group and 4 in the paroxetine group.

Correlation between IBS-SSS and baseline variables

Correlation analysis showed that at week 12, IBS-SSS scores were significantly associated with age (R = -0.335, P < 0.05), height (R = -0.389, P < 0.05), and marital status ((R = 0.134; all P < 0.05); **Figure 6**).

Discussion

est scores at week 12. At weeks 8 and 12, IBS-QoL scores were significantly higher in the paroxetine group than those in the control group (P < 0.01; **Figure 5**).

Factors influencing IBS-QoL

Univariate analysis indicated that age (t = 3.794, P = 0.002) and gender (F = 4.312, P = 0.001) independently affected IBS-QoL at week 12 (**Table 2**). Multivariate analysis confirmed both factors as independent predictors (P < 0.05): IBS-QoL decreased by 0.28 points for every 10-year increase in age, and women scored 10.04 points lower than men.

Gastrointestinal motility abnormalities and visceral hypersensitivity are recognized as central features of IBS pathophysiology. Recent advances in neurogastroenterology highlight the role of brain-gut interactions [25]. Although the precise mechanism of early oral paroxetine therapy in refractory IBS remains unclear, antidepressants are known to stabilize the hypothalamic-pituitary-adrenal axis, reduce stress reactivity, and directly influence gastrointestinal sensory neurons [26]. Several classes of antidepressants are available, including tricyclic antidepressants and newer serotonergic agents. In routine gastroenterology practice, low-dose tricyclics are often recommended for

Table 2. Univariate analysis of quality of life scores in irritable bowel syndrome patients

Characteristic	IBS-QoLa	t/F	P
Age (years)	88.95±9.28	3.794	0.002
Gender		4.312	0.001
Male	94.32±8.62		
Female	86.57±9.94		
Marital status			
Spouse	91.93±7.13	0.856	0.153
Without spouse	93.39±7.04		
Smoking history		0.366	0.598
Yes	84.75±3.26		
No	95.53±6.19		
Drinking history		0.254	0.657
Yes	87.72±8.91		
No	93.32±7.11		
Height (cm)	88.95±9.28	0.310	0.627
Weight (kg)	88.95±9.28	0.913	0.099
Duration of illness (years)	88.95±9.28	0.745	0.381

Note: aIBS-QoL: Irritable Bowel Syndrome Quality of Life.

Table 3. Summary of adverse events [n (%)]

Adverse events	Control group (n = 40)	Paroxetine group (n = 40)	X^2/t	P
Total	8 (20.00)	4 (10.00)	6.375	0.001
Acidity	1 (2.50)	0 (0)		
Body ache	1 (2.50)	0 (0)		
Epigastric burning sensation	0 (0)	0 (0)		
Cold	0 (0)	1 (2.50)		
Cough	0 (0)	1 (2.50)		
Diarrhea	1 (2.50)	0 (0)		
Diastolic blood pressure below the normal range	0 (0)	1 (2.50)		
Fever	1 (5.00)	0 (0)		
Hand Burn	0 (0)	0 (0)		
Headache	1 (2.50)	0 (0)		
Hoarseness	0 (0)	0 (0)		
Knee pain	0 (0)	0 (0)		
Muscular pain	0 (0)	1 (2.50)		
Nausea and vomiting sensation	1 (2.50)	0 (0)		
Skin rash	0 (0)	0 (0)		
Rhinitis	0 (0)	0 (0)		
Vomiting	1 (2.50)	0 (0)		

refractory IBS, with established symptom-relieving effects [27, 28]. Tabas et al. [29] demonstrated that paroxetine, as a SSRI, produced significant clinical benefits in IBS.

In the present study, early oral paroxetine significantly improved IBS symptoms, stool characteristics, defecation satisfaction, emotional state, and quality of life. The mechanism may involve direct modulation of the intestinal submucosal plexus, thereby regulating motility and alleviating abdominal discomfort [30]. Our findings are consistent with prior trials showing that antidepressants relieve abdominal pain in

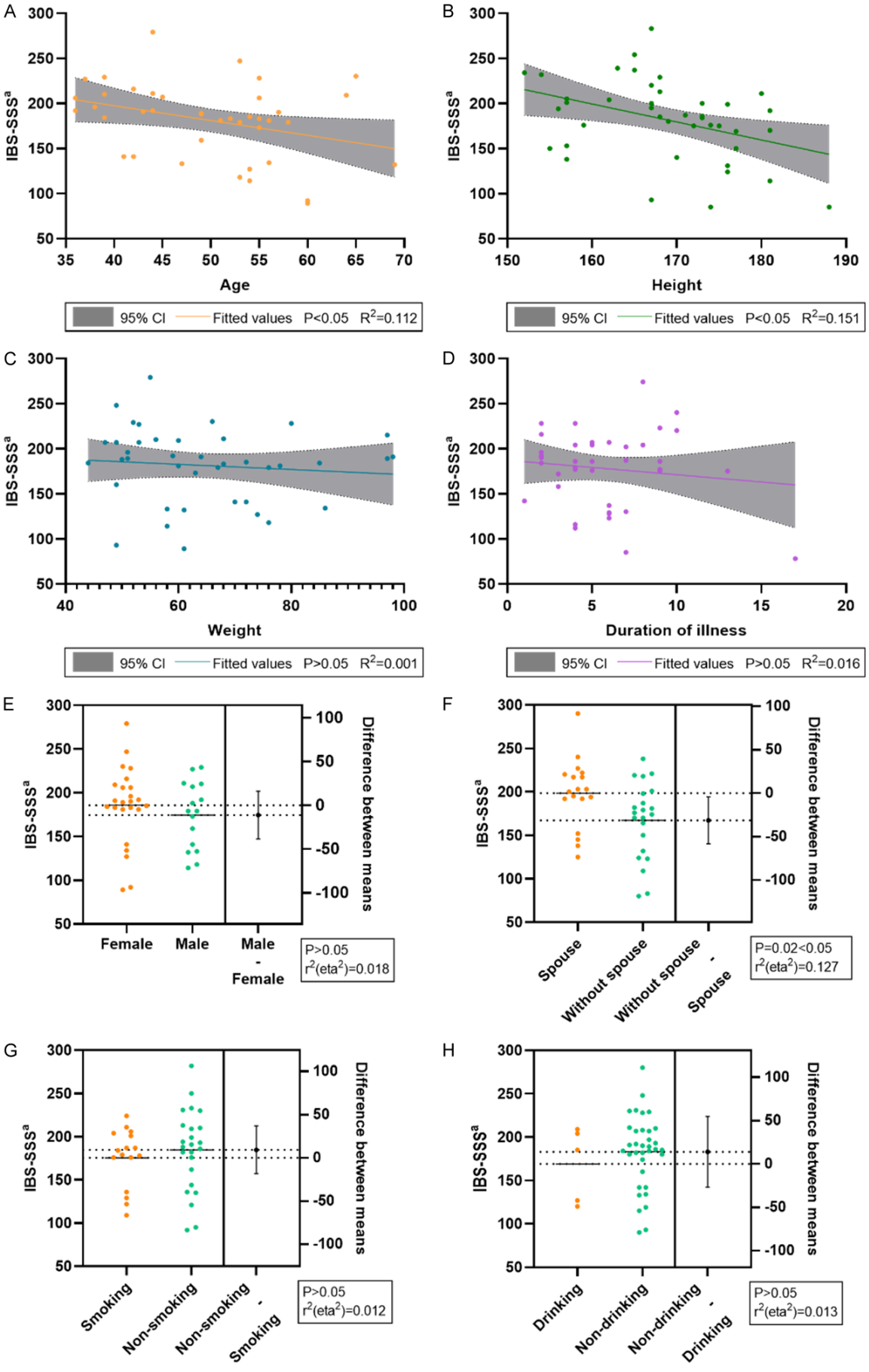
A
IBS-SSS^a
Age
95% CI Fitted values P<0.05 R²=0.112
B
IBS-SSS^a
Height
95% CI Fitted values P<0.05 R²=0.151
C
IBS-SSS^a
Weight
95% CI Fitted values P>0.05 R²=0.001
D
IBS-SSS^a
Duration of illness
95% CI Fitted values P>0.05 R²=0.016
E
IBS-SSS^a
Difference between means
Female
Male
Male - Female
P>0.05
r²(eta²)=0.018
F
IBS-SSS^a
Difference between means
Spouse
Without spouse
Without spouse - Spouse
P=0.02<0.05
r²(eta²)=0.127
G
IBS-SSS^a
Difference between means
Smoking
Non-smoking
Non-smoking - Smoking
P>0.05
r²(eta²)=0.012
H
IBS-SSS^a
Difference between means
Drinking
Non-drinking
Non-drinking - Drinking
P>0.05
r²(eta²)=0.013

Figure 6. Correlation analysis between irritable bowel syndrome symptom severity questionnaire (IBS-SSS) and general data after intervention in paroxetine group. [a]IBS-SSS: Irritable Bowel Syndrome Symptom Severity Questionnaire. Note: *P < 0.05. (A) Correlation analysis between IBS-SSS and age after intervention in paroxetine group; (B) Correlation analysis between IBS-SSS and height after intervention in paroxetine group; (C) Correlation analysis between IBS-SSS and weight after intervention in paroxetine group; (D) Correlation analysis between IBS-SSS and duration of illness after intervention in paroxetine group; (E) Correlation analysis between IBS-SSS and gender after intervention in paroxetine group; (F) Correlation analysis between IBS-SSS and marital status after intervention in paroxetine group; (G) Correlation analysis between IBS-SSS and smoking history after intervention in paroxetine group; (H) Correlation analysis between IBS-SSS and drinking history after intervention in paroxetine group. Age, height, weight and duration of illness (A-D) were evaluated by Pearson correlation test, while gender, marital status, smoking history, and drinking history (E-H) were tested by independent sample t tests.

IBS. Camilleri [8] observed marked improvements in abdominal pain in IBS patients with psychosomatic comorbidities following antidepressant therapy. Singh et al. [31] reported that low-dose amitriptyline reduced abdominal pain and bloating, likely through decreased rectal sensitivity to distension. Kamp et al. [32] further confirmed the efficacy of antidepressants in alleviating abdominal discomfort. Collectively, these results support the effectiveness of early oral paroxetine in reducing IBS symptom severity.

Our study also showed that paroxetine improved stool form. This may reflect serotonergic modulation within the enteric nervous system, enhancing synaptic activity and stool passage. Antidepressants exert differential effects on bowel motility: tricyclics prolong oral-cecal transit via muscarinic inhibition, alleviating diarrhea-predominant IBS (D-IBS), whereas SSRIs such as paroxetine shorten transit time by increasing intestinal serotonin, relieving constipation-predominant IBS (C-IBS) [33, 34]. Prior cohort studies also reported improved stool frequency in both C-IBS and D-IBS patients treated with amitriptyline [35]. Thus, paroxetine may benefit both subtypes.

Psychological assessment likewise demonstrated significant improvement in anxiety and depression symptoms. Depression and anxiety are known to exacerbate gastrointestinal complaints in IBS, and desipramine has been shown to relieve bowel symptoms in IBS patients with psychiatric comorbidities [36]. Alkhowaiter et al. [37] reported that citalopram improved bowel symptoms more effectively in IBS patients with mood disorders than in those without. Lunghi et al. [38] found that antidepressants can also benefit IBS patients without psychiatric conditions, underscoring the bidirectional relationship between somatic and psychosomatic symptoms. The lower doses of tricyclics typically prescribed in IBS compared with psychiatric use suggest that symptom improvement may not be fully attributable to antidepressant effects. By contrast, SSRIs are prescribed at comparable doses in both IBS and depression, raising uncertainty about whether improvements arise from mood modulation or direct gastrointestinal effects [39].

Paroxetine also significantly enhanced quality of life, with age and gender identified as independent influencing factors. Consistent with previous studies, women generally reported lower quality of life in domains such as anxiety and mindfulness, potentially reflecting greater stress vulnerability or emotional dysregulation [40, 41]. Psychological factors are major determinants of well-being in IBS, and age-related psychosocial changes may further affect outcomes.

Adverse events were infrequent and mild, and no serious adverse events occurred. The incidence of adverse events was lower in the paroxetine group compared with controls, and no significant laboratory or vital sign abnormalities were noted, indicating that paroxetine was well tolerated.

Correlation analysis revealed that age and height were negatively associated with IBS-SSS scores, whereas marital status showed a positive association. Although IBS prevalence is lower in older adults, aging-related physiological decline and comorbidities may aggravate symptoms, particularly constipation and defecatory dysfunction. The relationship between height and symptom severity is poorly understood and may be confounded by other factors. Marital status likely reflects psychosocial support, which may buffer symptom severity [42, 43].

This study is the first to evaluate early oral paroxetine for refractory IBS. Limitations include the retrospective design, small sample size, and lack of long-term follow-up. Future large-scale, multicenter randomized controlled trials are needed to validate these findings and clarify underlying mechanisms.

Conclusion

Early oral paroxetine provides significant and sustained relief of IBS symptoms, improves stool characteristics, bowel satisfaction, psychological status, and quality of life, and is safe and well tolerated. It represents a promising therapeutic option for patients with refractory IBS.

Disclosure of conflict of interest

None.

Address correspondence to: Zhenfeng Liu, Department of Gastroenterology, Chongming Hospital Affiliated to Shanghai University of Medicine and Health Sciences, No. 25, Nanmen Road, Chongming District, Shanghai 202150, China. E-mail: 13524087681@163.com

References

[1] Nybacka S, Törnblom H, Josefsson A, Hreinsson JP, Böhn L, Frändemark Å, Weznaver C, Störsrud S and Simrén M. A low FODMAP diet plus traditional dietary advice versus a low-carbohydrate diet versus pharmacological treatment in irritable bowel syndrome (CAR-IBS): a single-centre, single-blind, randomised controlled trial. Lancet Gastroenterol Hepatol 2024; 9: 507-520.

[2] Peery AF, Crockett SD, Murphy CC, Lund JL, Dellon ES, Williams JL, Jensen ET, Shaheen NJ, Barritt AS, Lieber SR, Kochar B, Barnes EL, Fan YC, Pate V, Galanko J, Baron TH and Sandler RS. Burden and cost of gastrointestinal, liver, and pancreatic diseases in the United States: Update 2018. Gastroenterology 2019; 156: 254-272, e211.

[3] Sperber AD, Bangdiwala SI, Drossman DA, Ghoshal UC, Simren M, Tack J, Whitehead WE, Dumitrascu DL, Fang X, Fukudo S, Kellow J, Okeke E, Quigley EMM, Schmulson M, Whorwell P, Archampong T, Adibi P, Andresen V, Benninga MA, Bonaz B, Bor S, Fernandez LB, Choi SC, Corazziari ES, Francisconi C, Hani A, Lazebnik L, Lee YY, Mulak A, Rahman MM, Santos J, Setshedi M, Syam AF, Vanner S, Wong RK, Lopez-Colombo A, Costa V, Dickman R, Kanazawa M, Keshteli AH, Khatun R, Maleki I, Poitras P, Pratap N, Stefanyuk O, Thomson S, Zeevenhooven J and Palsson OS. Worldwide prevalence and burden of functional gastrointestinal disorders, results of rome foundation global study. Gastroenterology 2021; 160: 99-114, e113.

[4] Camilleri M and Boeckxstaens G. Irritable bowel syndrome: treatment based on pathophysiology and biomarkers. Gut 2023; 72: 590-599.

[5] Zamani M, Alizadeh-Tabari S and Zamani V. Systematic review with meta-analysis: the prevalence of anxiety and depression in patients with irritable bowel syndrome. Aliment Pharmacol Ther 2019; 50: 132-143.

[6] Snijkers JTW, Winkens B, Weerts ZZRM, Vork L, Mujagic Z, Hesselink MAM, Leue C, Kruimel JW, Muris JWM, Jonkers DMAE, Masclee AAM and Keszthelyi D. Satisfaction with life in IBS is associated with psychological burden rather than gastrointestinal symptom severity. Am J Gastroenterol 2024; 119: 512-520.

[7] Vasant DH, Paine PA, Black CJ, Houghton LA, Everitt HA, Corsetti M, Agrawal A, Aziz I, Farmer AD, Eugenicos MP, Moss-Morris R, Yiannakou Y and Ford AC. British society of gastroenterology guidelines on the management of irritable bowel syndrome. Gut 2021; 70: 1214-1240.

[8] Camilleri M. Diagnosis and treatment of irritable bowel syndrome: a review. JAMA 2021; 325: 865-877.

[9] Piovezani Ramos G and Camilleri M. Current and future therapeutic options for irritable bowel syndrome with diarrhea and functional diarrhea. Dig Dis Sci 2023; 68: 1677-1690.

[10] Rokkas T, Ekmektzoglou K and Niv Y. Comparative effectiveness of 5-hydroxytryptamine 3 receptor antagonists in irritable bowel syndrome: a network meta-analysis of randomized controlled studies. Ann Gastroenterol 2021; 34: 535-546.

[11] Zhan TT, Dong ZY, Yi LS, Zhang Y, Sun HH, Zhang HQ, Wang JW, Chen Y, Huang Y and Xu SC. Tandospirone prevents stress-induced anxiety-like behavior and visceral hypersensitivity by suppressing theta oscillation enhancement via 5-HT(1A) receptors in the anterior cingulate cortex in rats. Front Cell Neurosci 2022; 16: 922750.

[12] Sun J, Zhang M, Liu W, Liu Y, Zhang D, Fan X, Zhang J, Li T and Lu M. Evaluation of the effectiveness and mechanism of action of the Chang-Kang-Fang formula combined with bifid triple viable capsules on diarrhea-predominant irritable bowel syndrome. Front Microbiol 2023; 14: 1160783.

[13] Lembo AJ, Lacy BE, Zuckerman MJ, Schey R, Dove LS, Andrae DA, Davenport JM, McIntyre G, Lopez R, Turner L and Covington PS. Eluxadoline for irritable bowel syndrome with diarrhea. N Engl J Med 2016; 374: 242-253.
[14] Marasine NR, Sankhi S, Lamichhane R, Marasini NR and Dangi NB. Use of antidepressants among patients diagnosed with depression: a scoping review. Biomed Res Int 2021; 2021: 6699028.
[15] Li YH, Hang LW, Muo CH, Chen SJ and Chen PC. Dose of selective serotonin reuptake inhibitors and risk of upper gastrointestinal bleeding in older adults. J Psychopharmacol 2024; 38: 137-144.
[16] Diviccaro S, Giatti S, Cioffi L, Falvo E, Piazza R, Caruso D and Melcangi RC. Paroxetine effects in adult male rat colon: Focus on gut steroidogenesis and microbiota. Psychoneuroendocrinology 2022; 143: 105828.
[17] Liu X, Li M, Jian C and Qin X. Characterization of "microbiome-metabolome-immunity" in depressed rats with divergent responses to Paroxetine. J Affect Disord 2024; 352: 201-213.
[18] Francis CY, Morris J and Whorwell PJ. The irritable bowel severity scoring system: a simple method of monitoring irritable bowel syndrome and its progress. Aliment Pharmacol Ther 1997; 11: 395-402.
[19] Cellier C, Bouma G, van Gils T, Khater S, Malamut G, Crespo L, Collin P, Green PHR, Crowe SE, Tsuji W, Butz E, Cerf-Bensussan N, Macintyre E, Parnes JR, Leon F, Hermine O and Mulder CJ; RCD-II Study Group Investigators. Safety and efficacy of AMG 714 in patients with type 2 refractory coeliac disease: a phase 2a, randomised, double-blind, placebo-controlled, parallel-group study. Lancet Gastroenterol Hepatol 2019; 4: 960-970.
[20] Longstreth GF, Thompson WG, Chey WD, Houghton LA, Mearin F and Spiller RC. Functional bowel disorders. Gastroenterology 2006; 130: 1480-1491.
[21] Shao R, He P, Ling B, Tan L, Xu L, Hou Y, Kong L and Yang Y. Prevalence of depression and anxiety and correlations between depression, anxiety, family functioning, social support and coping styles among Chinese medical students. BMC Psychol 2020; 8: 38.
[22] Jiang X, Wang X, Zhang M, Yu L, He J, Wu S, Yan J, Zheng Y, Zhou Y and Chen Y. Associations between specific dietary patterns, gut microbiome composition, and incident subthreshold depression in Chinese young adults. J Adv Res 2024; 65: 183-195.
[23] Patrick DL, Drossman DA, Frederick IO, DiCesare J and Puder KL. Quality of life in persons with irritable bowel syndrome: development and validation of a new measure. Dig Dis Sci 1998; 43: 400-411.
[24] Drossman DA, Patrick DL, Whitehead WE, Toner BB, Diamant NE, Hu Y, Jia H and Bangdiwala SI. Further validation of the IBS-QOL: a disease-specific quality-of-life questionnaire. Am J Gastroenterol 2000; 95: 999-1007.
[25] Shin SY, Cha BK, Kim WS, Park JY, Kim JW and Choi CH. The effect of phloroglucinol in patients with diarrhea-predominant irritable bowel syndrome: a randomized, double-blind, placebo-controlled trial. J Neurogastroenterol Motil 2020; 26: 117-127.
[26] Philippe TJ, Bao L, Koblanski ME and Viau V. Sex differences in serotonin 5-HT 1A receptor responses to repeated restraint stress in adult male and female rats. Int J Neuropsychopharmacol 2022; 25: 863-876.
[27] Black CJ, Yuan Y, Selinger CP, Camilleri M, Quigley EMM, Moayyedi P and Ford AC. Efficacy of soluble fibre, antispasmodic drugs, and gut-brain neuromodulators in irritable bowel syndrome: a systematic review and network meta-analysis. Lancet Gastroenterol Hepatol 2020; 5: 117-131.
[28] Ford AC, Wright-Hughes A, Alderson SL, Ow PL, Ridd MJ, Foy R, Bianco G, Bishop FL, Chaddock M, Cook H, Cooper D, Fernandez C, Guthrie EA, Hartley S, Herbert A, Howdon D, Muir DP, Nath T, Newman S, Smith T, Taylor CA, Teasdale EJ, Thornton R, Farrin AJ and Everitt HA; ATLANTIS trialists. Amitriptyline at low-dose and titrated for irritable bowel syndrome as second-line treatment in primary care (ATLANTIS): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet 2023; 402: 1773-1785.
[29] Tabas G, Beaves M, Wang J, Friday P, Mardini H and Arnold G. Paroxetine to treat irritable bowel syndrome not responding to high-fiber diet: a double-blind, placebo-controlled trial. Am J Gastroenterol 2004; 99: 914-920.
[30] Pietrzak A, Skrzydło-Radomańska B, Mulak A, Lipiński M, Małecka-Panas E, Reguła J and Rydzewska G. Guidelines on the management of irritable bowel syndrome. Prz Gastroenterol 2018; 13: 259-288.
[31] Singh R, Zogg H, Ghoshal UC and Ro S. Current treatment options and therapeutic insights for gastrointestinal dysmotility and functional gastrointestinal disorders. Front Pharmacol 2022; 13: 808195.
[32] Kamp K, Yang PL, Friedman E, Lopez A, Iribarren S, Barney P, Munson S, Heitkemper M and Levy R. Formative evaluation of a comprehensive self-management intervention for irritable bowel syndrome, comorbid anxiety, and depression: mixed methods study. JMIR Form Res 2024; 8: e43286.

[33] Juza R, Vlcek P, Mezeiova E, Musilek K, Soukup O and Korabecny J. Recent advances with 5-HT(3) modulators for neuropsychiatric and gastrointestinal disorders. Med Res Rev 2020; 40: 1593-1678.
[34] Hanna-Jairala I and Drossman DA. Central neuromodulators in irritable bowel syndrome: why, how, and when. Am J Gastroenterol 2024; 119: 1272-1284.
[35] Lin WT, Liao YJ, Peng YC, Chang CH, Lin CH, Yeh HZ and Chang CS. Relationship between use of selective serotonin reuptake inhibitors and irritable bowel syndrome: a population-based cohort study. World J Gastroenterol 2017; 23: 3513-3521.
[36] Savarino E, Zingone F, Barberio B, Marasco G, Akyuz F, Akpinar H, Barboi O, Bodini G, Bor S, Chiarioni G, Cristian G, Corsetti M, Di Sabatino A, Dimitriu AM, Drug V, Dumitrascu DL, Ford AC, Hauser G, Nakov R, Patel N, Pohl D, Sfarti C, Serra J, Simrén M, Suciu A, Tack J, Toruner M, Walters J, Cremon C and Barbara G. Functional bowel disorders with diarrhoea: clinical guidelines of the United European gastroenterology and European society for neurogastroenterology and motility. United European Gastroenterol J 2022; 10: 556-584.
[37] Alkhowaiter SS, Alshahrani AH, Almarzouqi HF, Alonazi GK, Alhawassi TM and AlRasheed MM. Feasibility, and barriers to use escitalopram in functional gastrointestinal disorders. Front Pharmacol 2023; 14: 1131354.
[38] Lunghi C, Dugas M, Leclerc J, Poluzzi E, Martineau C, Carnovale V, Stéfan T, Blouin P, Lépine J, Jalbert L, Espinoza Suarez NR, Svyntozelska O, Dery MP, Ekanmian G, Nogueira DM, Akinola PS, Turcotte S, Skidmore B and LeBlanc A. Global prevalence of antidepressant drug utilization in the community: protocol for a systematic review. BMJ Open 2022; 12: e062197.
[39] Colomier E, Algera J and Melchior C. Pharmacological therapies and their clinical targets in irritable bowel syndrome with diarrhea. Front Pharmacol 2020; 11: 629026.
[40] de Bruijn CMA, Rexwinkel R, Gordon M, Benninga M and Tabbers MM. Antidepressants for functional abdominal pain disorders in children and adolescents. Cochrane Database Syst Rev 2021; 2: CD008013.
[41] Saroj A, Tripathi A, Rungta S and Kar SK. Psychiatric co-morbidities and profile of patients with irritable bowel syndrome in Northern India. Brain Sci 2024; 14: 393.
[42] Yao C, Li Y, Luo L, Xie F, Xiong Q, Li T, Yang C and Feng PM. Significant differences in gut microbiota between irritable bowel syndrome with diarrhea and healthy controls in southwest China. Dig Dis Sci 2023; 68: 106-127.
[43] Aziz I, Palsson OS, Törnblom H, Sperber AD, Whitehead WE and Simrén M. Epidemiology, clinical characteristics, and associations for symptom-based Rome IV functional dyspepsia in adults in the USA, Canada, and the UK: a cross-sectional population-based study. Lancet Gastroenterol Hepatol 2018; 3: 252-262.