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Gastrointestinal Symptom Burden in Comorbid Anxiety and Depression Compared With Anxiety Alone and Depression Alone: A Cross-Sectional Study from a Tertiary Care Centre in North-West India.

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ABSTRACT

Background: Anxiety and depressive disorders frequently co-occur, and both are individually associated with gastrointestinal (GI) symptoms. Whether their co-occurrence carries a greater GI symptom burden than either alone has rarely been examined directly within a psychiatric outpatient population.

Objectives: To compare GI symptom burden, assessed by the IBS-SSS and GSRS, among patients with comorbid anxiety and depression, anxiety alone, and depression alone, and to examine whether any difference tracked psychiatric symptom severity.

Methods: A cross-sectional study was conducted in the psychiatry department of SMS Hospital, Jaipur, between March and June 2026. Adults aged 18–60 years with a DSM-5 diagnosis of anxiety only, depression only, or comorbid anxiety and depression were enrolled. Severity was graded with the HAM-A and PHQ-9. Groups were compared using Kruskal-Wallis and Fisher exact tests, with effect estimates from Firth penalised logistic regression.

Results: Thirty-two patients were analysed (comorbid, n=11; depression only, n=16; anxiety only, n=5). Clinically relevant IBS symptomatology (IBS-SSS ≥75) was present in 8/11 (72.7%, 95% CI 43.5–91.7) of the comorbid group, 1/16 (6.2%, 0.7–25.7) with depression alone, and 0/5 (0.0%, 0.0–37.9) with anxiety alone ($p<0.001$). Severe GSRS scores (≥40) occurred only in the comorbid group (6/11, 54.5%; p=0.003). Comorbidity remained associated with IBS symptomatology after adjustment for age and sex (OR 27.36, 95% CI 3.09–241.93; p=0.003). HAM-A and PHQ-9 distributions did not differ across groups (p=0.906; p=0.577).

Conclusion: In this small single-centre sample, comorbid anxiety and depression was associated with greater GI symptom burden than either alone, unexplained by psychiatric symptom severity.

Recommendation: Brief GI symptom screening should be considered for psychiatric outpatients with comorbid anxiety and depression, and the association should be confirmed in larger, multicentre, longitudinal studies.

Keywords: *Anxiety Disorders; Depressive Disorder; Irritable Bowel Syndrome; Gastrointestinal Diseases; Comorbidity*
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INTRODUCTION

Anxiety and depressive disorders are the most prevalent psychiatric conditions encountered in Indian clinical practice. The National Mental Health Survey of India (2015–16) estimated a current prevalence of mental disorders of 10.6% among adults, with depressive and anxiety disorders accounting for the largest share, and documented treatment gaps exceeding 80% for these common mental disorders.[1,2] These conditions rarely occur in isolation: a substantial proportion of patients presenting to psychiatric outpatient services meet criteria for both an anxiety and a depressive syndrome, a presentation associated in large treatment cohorts with greater symptom severity, more somatic complaints, and poorer treatment response than either condition alone.[3–5]

Gastrointestinal symptoms are among the somatic complaints most consistently linked to affective illness. Disorders of gut-brain interaction (DGBI) affect approximately 40% of adults worldwide, and psychological distress is one of their strongest correlates.[6,7] In the Rome Foundation Global Epidemiology Study, participants with clinically relevant psychological distress or somatic symptom severity had over four times the odds of meeting criteria for at least one DGBI.[7] Conversely, meta-analytic evidence indicates that a substantial proportion of patients with irritable bowel syndrome (IBS) have clinically

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significant anxiety or depressive symptoms.[8] Bidirectional communication along the gut-brain axis, involving vagal afferent signalling, hypothalamic-pituitary-adrenal (HPA) axis regulation, and immune and microbial pathways, is generally invoked to explain this overlap.[9]

What remains poorly characterised is whether the co-occurrence of anxiety and depression carries a gastrointestinal symptom burden that exceeds that of either disorder alone. Most of the existing literature approaches the question from the gastroenterological side, recruiting patients with an established gastrointestinal diagnosis and then measuring psychological distress as a correlate. Studies that begin from the psychiatric side, stratify patients by diagnostic presentation, and compare gastrointestinal symptom burden across anxiety-only, depression-only, and comorbid groups within the same clinical setting are scarce, and are particularly scarce in Indian populations. As a result, it is not known whether comorbidity is simply a marker of greater overall psychiatric severity, in which case gastrointestinal burden would be expected to scale with anxiety and depression severity scores, or whether the comorbid presentation is associated with a distinct pattern of gut symptom reporting.

This distinction is clinically consequential. If gastrointestinal symptom burden in psychiatric outpatients is concentrated in those with comorbid presentations, and is not simply a function of symptom severity, then diagnostic status alone would identify a subgroup in whom systematic gastrointestinal enquiry is warranted at the point of psychiatric assessment, rather than after gastroenterological referral. Given that psychotropic prescribing in these patients frequently involves agents with gastrointestinal adverse effects, and that unrecognised gastrointestinal symptoms may contribute to non-adherence, the question has practical bearing on routine outpatient care.

Aim of the Study

The aim of this study was therefore to investigate whether patients with comorbid anxiety and depression exhibit greater gastrointestinal symptom burden than patients with anxiety alone or depression alone, and, secondarily, to examine whether any difference observed tracks anxiety and depressive symptom severity.

MATERIALS AND METHODS

Study design

This was a hospital-based, observational, cross-sectional study, reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for cross-sectional studies.[10]

Setting

The study was conducted in the Department of Psychiatry of Sawai Man Singh (SMS) Hospital, Jaipur, Rajasthan, India. SMS Hospital is the principal teaching hospital of SMS Medical College and the largest government-run public hospital complex in Rajasthan, with a bed strength exceeding 6,000. It functions as an apex tertiary care and referral centre for Jaipur and the surrounding districts of north-west India, and provides round-the-clock emergency care, outpatient and inpatient services across the major clinical specialties (including general medicine, general surgery, paediatrics, orthopaedics, and obstetrics and gynaecology), super-specialty services such as cardiology, neurology, nephrology, and gastroenterology, and comprehensive diagnostic, laboratory, and imaging support. Services are provided free of charge or at nominal cost under state government health schemes, so the hospital draws a large and socioeconomically diverse population from both urban and rural areas.

Psychiatric services of SMS Medical College are delivered through its Department of Psychiatry and the attached Psychiatric Centre, Jaipur, which offers daily general psychiatry outpatient clinics, inpatient and emergency psychiatric care, de-addiction services, child and adolescent psychiatry, geriatric psychiatry, clinical psychology services including psychometric assessment and psychotherapy, and psychosocial rehabilitation. Recruitment and data collection were carried out over a four-month period from March 2026 to June 2026, coinciding with outpatient department (OPD) days at the hospital during this period. Data collection was conducted in multiple sittings for all participants, in order to reduce respondent fatigue and to accommodate OPD scheduling.

Participants

The source population comprised adults attending the psychiatry OPD during the study period. Patients were eligible if they were aged between 18 and 60 years and carried a confirmed clinical diagnosis, following structured psychiatric assessment, of depression only, anxiety only, or comorbid anxiety and depression, as per the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria.[11]

Patients were excluded if they had any other psychiatric comorbidity (for example, bipolar disorder or anorexia nervosa); if they had any medical comorbidity, in order to minimise the confounding influence of concurrent illness or medication on gastrointestinal symptom reporting; if they had not undergone a structured psychiatric assessment; or if their questionnaires could not be completed because of non-compliance.

Eligible patients were enrolled consecutively during OPD sessions. Diagnostic grouping was determined from the recorded DSM-5 diagnosis: patients with mixed anxiety and depressive disorder were assigned to the comorbid group; patients with generalised anxiety disorder or another anxiety disorder without a depressive diagnosis were assigned to the

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anxiety-only group; and patients with major depressive disorder or another depressive diagnosis without an anxiety diagnosis were assigned to the depression-only group.

Variables

The primary outcomes were gastrointestinal symptom burden assessed on two dimensions: IBS-specific symptom severity, graded by the Irritable Bowel Syndrome-Symptom Severity Scale (IBS-SSS), and general gastrointestinal symptom severity, graded by the Gastrointestinal Symptom Rating Scale (GSRS). The primary exposure was diagnostic group (comorbid anxiety and depression versus anxiety alone versus depression alone). Anxiety severity, measured with the Hamilton Anxiety Rating Scale (HAM-A), and depressive severity, measured with the Patient Health Questionnaire-9 (PHQ-9), were treated as secondary explanatory variables and as potential mediators of any group difference. Age, sex, locality, marital status, education, employment status, family type, monthly family income, duration of illness, family history of psychiatric illness, and history of substance use were recorded as potential confounders or effect modifiers.

Data sources and measurement

Anxiety severity was assessed using the HAM-A, a clinician-administered instrument, and graded as mild (≤17), mild to moderate (18–24), moderate to severe (25–30), or severe to very severe (31–56).[12] Depressive severity was assessed with the PHQ-9 and graded as minimal (0–4), mild (5–9), moderate (10–14), moderately severe (15–19), or severe (20–27).[13] IBS symptom severity was assessed with the IBS-SSS, a five-item instrument scored from 0 to 500, using the originally validated bands of symptom-free (<75), mild (75–175), moderate (175–300), and severe (300–500).[14] General gastrointestinal symptom burden was assessed with the GSRS, a 15-item instrument covering reflux, abdominal pain, indigestion, diarrhoea, and constipation domains, and graded as mild (0–19), moderate (20–39), or severe (40–105).[15,16] For all four instruments, data were recorded and made available for analysis as ordered severity categories rather than as continuous total scores. Sociodemographic and clinical variables were collected on a structured proforma at the time of interview.

Bias

Several measures were taken to limit bias. Consecutive enrolment during OPD sessions was used in preference to convenience selection, in order to reduce selection bias. Diagnostic assignment was made on the basis of structured psychiatric assessment performed independently of gastrointestinal symptom assessment, limiting diagnostic misclassification driven by somatic presentation. Patients with any medical comorbidity were excluded, reducing the contribution of organic gastrointestinal disease and non-psychotropic medication to symptom reporting. Two instruments assessing overlapping but non-identical gastrointestinal constructs were administered, so that a finding restricted to a single instrument could be identified as such. Residual bias arising from recall, from social desirability in symptom reporting, and from unmeasured psychotropic exposure could not be eliminated.

Study size

No formal a priori sample size calculation was performed. The study enrolled all eligible patients presenting during the fixed four-month recruitment window, and the achieved sample size was therefore determined by patient flow rather than by a target precision. Consequently, precision is reported alongside every effect estimate, the resulting confidence intervals are wide, and this is addressed explicitly in the Limitations.

Quantitative variables

Age, duration of illness, and number of family members were analysed as continuous variables and summarised as mean with standard deviation (SD) and as median with interquartile range (IQR). HAM-A, PHQ-9, IBS-SSS, and GSRS severity grades were analysed as ordinal variables and, for effect estimation, additionally dichotomised at pre-specified clinically meaningful thresholds: IBS-SSS ≥75 (any clinically relevant IBS symptomatology versus symptom-free) and GSRS ≥20 (moderate or severe versus mild). A severe GSRS grade (≥40) was examined separately. Monthly family income was analysed in the seven bands in which it was recorded.

Statistical methods

Analyses were performed in Python 3.11 using pandas 2.x, SciPy 1.17, and statsmodels 0.14. Distributional assumptions for continuous variables were tested with the Shapiro-Wilk test; age ($p=0.010$) and duration of illness ($p<0.001$) departed from normality, and non-parametric methods were therefore used throughout. Continuous and ordinal variables were compared across the three diagnostic groups with the Kruskal-Wallis test, followed where indicated by pairwise Mann-Whitney U tests with Bonferroni adjustment for three comparisons; the rank-biserial correlation was reported as the effect size. Categorical variables were compared using the chi-square test with a Monte Carlo permutation p-value (5,000 to 20,000 resamples), because expected cell counts were small; pairwise comparisons used the Fisher exact test. Proportions are presented with Jeffreys 95% confidence intervals (CIs), which behave appropriately at proportions near 0 and 1. Odds ratios (ORs) for 2×2 comparisons were calculated with the Haldane-Anscombe correction where a zero cell was present.

Because several outcome cells contained no events, conventional maximum-likelihood logistic regression was

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subject to separation. Firth penalised logistic regression was therefore used for adjusted analyses.[17,18] Given the number of events available, adjustment was restricted a priori to age and sex, and no further multivariable modelling was attempted. Associations between ordinal severity grades were quantified with the Spearman rank correlation coefficient, with Fisher z-transformed 95% CIs. Two-sided p-values are reported to three decimal places, with $p<0.001$ used where smaller; the significance threshold was 0.05. No data were missing for any variable used in the primary analysis, and no imputation was performed.

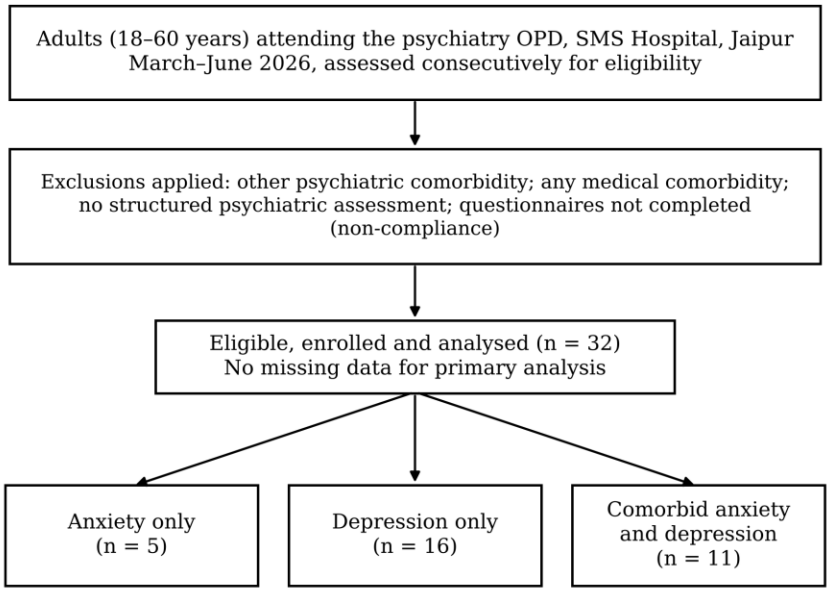
Ethics

The study protocol was reviewed and approved by the Institutional Ethics Committee of SMS Medical College, Jaipur, before the commencement of recruitment. Written informed consent was obtained from every participant before enrolment, after explanation of the study purpose and procedures in a language the participant understood. Participation was voluntary, refusal carried no consequence for clinical care, and data were anonymised at entry. The study was conducted in accordance with the principles of the Declaration of Helsinki.

RESULTS

Participants

Thirty-two patients meeting the eligibility criteria were enrolled and analysed. Of these, 11 (34.4%) had comorbid anxiety and depression, 16 (50.0%) had depression alone, and 5 (15.6%) had anxiety alone (Figure 1). No participant had missing data for any variable used in the primary analysis.



Diagnostic group assigned from the recorded DSM-5 diagnosis

Figure 1: Paripant Flow Chart
tic

Note. OPD = outpatient department; DSM-5 = Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition.

Descriptive data

The mean age of the sample was 37.97 ± 14.43 years (median 39.0, IQR 23.0–49.8, range 17–60). Eighteen participants (56.2%) were male and 14 (43.8%) were female; 18 (56.2%) resided in rural areas; 19 (59.4%) were married; 21 (65.6%) were unemployed; and 13 (40.6%) reported a monthly family income in the second income band. The median duration of illness was 3.0 years (IQR 1.0–6.4, range 0.5–32.0). A family history of psychiatric illness was reported by 11 participants (34.4%) and a history of substance use by 6 (18.8%). Full baseline characteristics by diagnostic group are presented in Table 1.

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Table 1: Baseline Sociodemographic and Clinical Characteristics of Participants, by Diagnostic Group

Characteristic	Total (n = 32)	Anxiety only (n = 5)	Depression only (n = 16)	Comorbid (n = 11)	*p*
Age (years)					.348
Mean ± SD	37.97 ± 14.43	34.80 ± 10.94	41.50 ± 15.37	34.27 ± 14.24	
Median (IQR)	39.0 (23.0–49.8)	31.0 (30.0–46.0)	46.0 (23.8–55.2)	33.0 (22.5–44.0)	
Sex, *n* (%)					.038
Male	18 (56.2)	5 (100.0)	6 (37.5)	7 (63.6)	
Female	14 (43.8)	0 (0.0)	10 (62.5)	4 (36.4)	
Locality, *n* (%)					.127
Urban	14 (43.8)	3 (60.0)	4 (25.0)	7 (63.6)	
Rural	18 (56.2)	2 (40.0)	12 (75.0)	4 (36.4)	
Marital status, *n* (%)					.437
Single	11 (34.4)	1 (20.0)	4 (25.0)	6 (54.5)	
Married	19 (59.4)	4 (80.0)	11 (68.8)	4 (36.4)	
Widowed	2 (6.2)	0 (0.0)	1 (6.2)	1 (9.1)	
Education, *n* (%)					.503
Illiterate	9 (28.1)	0 (0.0)	7 (43.8)	2 (18.2)	
Below primary	5 (15.6)	1 (20.0)	2 (12.5)	2 (18.2)	
Matric	1 (3.1)	0 (0.0)	1 (6.2)	0 (0.0)	
Secondary school	5 (15.6)	2 (40.0)	1 (6.2)	2 (18.2)	
Graduate / postgraduate	12 (37.5)	2 (40.0)	5 (31.2)	5 (45.5)	
Employment status, *n* (%)					.017
Unemployed	21 (65.6)	0 (0.0)	12 (75.0)	9 (81.8)	
Self-employed	8 (25.0)	3 (60.0)	3 (18.8)	2 (18.2)	
Private job	1 (3.1)	1 (20.0)	0 (0.0)	0 (0.0)	
Government job	2 (6.2)	1 (20.0)	1 (6.2)	0 (0.0)	
Religion, *n* (%)					.508
Hindu	28 (87.5)	5 (100.0)	13 (81.2)	10 (90.9)	
Muslim	4 (12.5)	0 (0.0)	3 (18.8)	1 (9.1)	
Type of family, *n* (%)					.499
Nuclear	14 (43.8)	1 (20.0)	7 (43.8)	6 (54.5)	
Joint	18 (56.2)	4 (80.0)	9 (56.2)	5 (45.5)	
Family members, median (IQR)	6 (4.8–7.0)	7 (5.0–8.0)	6 (5.0–8.0)	5 (4.0–6.0)	.250
Monthly family income band, *n* (%)					.812
Band 1 (≤₹7,988)	7 (21.9)	1 (20.0)	5 (31.2)	1 (9.1)	

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Characteristic	Total (n = 32)	Anxiety only (n = 5)	Depression only (n = 16)	Comorbid (n = 11)	*p*
Band 2 (₹7,989–23,869)	13 (40.6)	2 (40.0)	6 (37.5)	5 (45.5)	
Band 3 (₹23,870–39,829)	3 (9.4)	0 (0.0)	1 (6.2)	2 (18.2)	
Band 4 (₹39,830–59,794)	5 (15.6)	2 (40.0)	2 (12.5)	1 (9.1)	
Band 5 (₹59,795–79,755)	1 (3.1)	0 (0.0)	1 (6.2)	0 (0.0)	
Band 6 (₹79,756–1,59,585)	2 (6.2)	0 (0.0)	1 (6.2)	1 (9.1)	
Band 7 (≥₹1,59,586)	1 (3.1)	0 (0.0)	0 (0.0)	1 (9.1)	
Duration of illness (years), median (IQR)	3.0 (1.0–6.4)	2.0 (0.5–5.0)	2.5 (1.0–6.2)	3.0 (2.2–7.2)	.612
Family history of psychiatric illness, *n* (%)	11 (34.4)	3 (60.0)	5 (31.2)	3 (27.3)	.469
History of substance use, *n* (%)	6 (18.8)	3 (60.0)	0 (0.0)	3 (27.3)	.004

Note. $N = 32$. SD = standard deviation; IQR = interquartile range. Continuous variables were compared with the Kruskal-Wallis test; categorical variables were compared with the chi-square test using a Monte Carlo permutation *p* value. Percentages are column percentages within each diagnostic group.

Groups were comparable with respect to age (Kruskal-Wallis H=2.109, p=0.348), duration of illness (H=0.982, p=0.612), family size (H=2.770, p=0.250), marital status (p=0.437), education (p=0.503), locality (p=0.127), religion (p=0.508), family type (p=0.499), income band (p=0.812), and family history of psychiatric illness (p=0.469). Three characteristics differed across groups: sex (permutation p=0.038; all five anxiety-only patients were male), employment status (permutation p=0.017), and history of substance use (permutation p=0.004; reported by 3 of 5 patients in the anxiety-only group, 3 of 11 in the comorbid group, and none in the depression-only group).

Psychiatric symptom severity

HAM-A severity grades did not differ across the three groups (Kruskal-Wallis H=0.197, df=2, p=0.906); the median grade was 2 (mild to moderate) in every group. PHQ-9 severity grades likewise did not differ (H=1.098, df=2, p=0.577), with a median grade of 3 (moderate) in every group. Distributions are shown in Table 2.

Table 2: Anxiety (HAM-A) and Depressive (PHQ-9) Severity Grades by Diagnostic Group

Severity grade	Total (n = 32)	Anxiety only (n = 5)	Depression only (n = 16)	Comorbid (n = 11)	*p*
HAM-A, *n* (%)					.906
Mild (≤17)	5 (15.6)	2 (40.0)	1 (6.2)	2 (18.2)	
Mild to moderate (18–24)	15 (46.9)	1 (20.0)	10 (62.5)	4 (36.4)	
Moderate to severe (25–30)	5 (15.6)	0 (0.0)	3 (18.8)	2 (18.2)	
Severe to very severe (31–56)	7 (21.9)	2 (40.0)	2 (12.5)	3 (27.3)	
Median grade (IQR)	2 (2–3)	2 (1–4)	2 (2–3)	2 (2–3.5)	
PHQ-9, *n* (%)					.577
Mild (5–9)	13 (40.6)	2 (40.0)	7 (43.8)	4 (36.4)	
Moderate (10–14)	13 (40.6)	1 (20.0)	8 (50.0)	4 (36.4)	
Moderately severe (15–19)	6 (18.8)	2 (40.0)	1 (6.2)	3 (27.3)	
Median grade (IQR)	3 (2–3)	3 (2–4)	3 (2–3)	3 (2–3.5)	

Note. HAM-A = Hamilton Anxiety Rating Scale; PHQ-9 = Patient Health Questionnaire-9; IQR = interquartile range. p values are from the Kruskal-Wallis test on ordinal severity grade. No participant scored in the minimal (0–4) or severe (20–27) PHQ-9 bands.

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Gastrointestinal symptom burden: unadjusted findings

IBS-SSS severity grade differed significantly across diagnostic groups (Kruskal-Wallis H=14.079, df=2, p<0.001). Clinically relevant IBS symptomatology (IBS-SSS ≥75) was present in 8 of 11 patients (72.7%, 95% CI 43.5–91.7) with comorbid anxiety and depression, compared with 1 of 16 (6.2%, 95% CI 0.7–25.7) with depression alone and 0 of 5 (0.0%, 95% CI 0.0–37.9) with anxiety alone (chi-square=16.569, Monte Carlo permutation p<0.001). In pairwise comparison, the comorbid group differed from the depression-only group (Fisher exact p<0.001) and from the anxiety-only group (Fisher exact p=0.026), whereas the anxiety-only and depression-only groups did not differ from each other (p=0.655). Bonferroni-adjusted Mann-Whitney comparisons of the ordinal grade gave the same pattern: comorbid versus depression-only, adjusted p=0.004 (rank-biserial r=0.619); comorbid versus anxiety-only, adjusted p=0.049 (r=0.727); anxiety-only versus depression-only, adjusted p>0.999.

GSRS severity grade also differed across groups (Kruskal-Wallis H=6.446, df=2, p=0.040). The difference was concentrated in the severe category: a severe GSRS grade (≥40) was recorded in 6 of 11 patients (54.5%, 95% CI 27.0–80.0) in the comorbid group and in no patient in either the depression-only group (0/16, 95% CI 0.0–14.3) or the anxiety-only group (0/5, 95% CI 0.0–37.9) (chi-square=14.098, Monte Carlo permutation p=0.003). When the GSRS was dichotomised at the lower threshold of moderate or severe (≥20), the gradient persisted but did not reach significance: 7 of 11 (63.6%, 95% CI 34.8–86.3) in the comorbid group, 6 of 16 (37.5%, 95% CI 17.4–61.7) in the depression-only group, and 1 of 5 (20.0%, 95% CI 2.3–62.9) in the anxiety-only group (Monte Carlo permutation p=0.241). Group distributions for both gastrointestinal instruments are presented in Table 3 and illustrated in Figure 2.

Table 3: Gastrointestinal Symptom Burden by Diagnostic Group

Measure	Total (n = 32)	Anxiety only (n = 5)	Depression only (n = 16)	Comorbid (n = 11)	*p*
IBS-SSS grade, *n* (%)					< .001
Symptom-free (<75)	23 (71.9)	5 (100.0)	15 (93.8)	3 (27.3)	
Mild (75–175)	4 (12.5)	0 (0.0)	0 (0.0)	4 (36.4)	
Moderate (175–300)	4 (12.5)	0 (0.0)	0 (0.0)	4 (36.4)	
Severe (300–500)	1 (3.1)	0 (0.0)	1 (6.2)	0 (0.0)	
IBS-SSS ≥75, *n* (%) [95% CI]	9 (28.1)	0 (0.0) [0.0–37.9]	1 (6.2) [0.7–25.7]	8 (72.7) [43.5–91.7]	< .001
GSRS grade, *n* (%)					.040
Mild (0–19)	18 (56.2)	4 (80.0)	10 (62.5)	4 (36.4)	
Moderate (20–39)	8 (25.0)	1 (20.0)	6 (37.5)	1 (9.1)	
Severe (40–105)	6 (18.8)	0 (0.0)	0 (0.0)	6 (54.5)	
GSRS ≥20, *n* (%) [95% CI]	14 (43.8)	1 (20.0) [2.3–62.9]	6 (37.5) [17.4–61.7]	7 (63.6) [34.8–86.3]	.241
GSRS ≥40, *n* (%) [95% CI]	6 (18.8)	0 (0.0) [0.0–37.9]	0 (0.0) [0.0–14.3]	6 (54.5) [27.0–80.0]	.003

Note. IBS-SSS = Irritable Bowel Syndrome-Symptom Severity Scale; GSRS = Gastrointestinal Symptom Rating Scale; CI = confidence interval. *p* values for ordinal grade are from the Kruskal-Wallis test; *p* values for dichotomised thresholds are from the chi-square test with Monte Carlo permutation. Confidence intervals are Jeffreys intervals.

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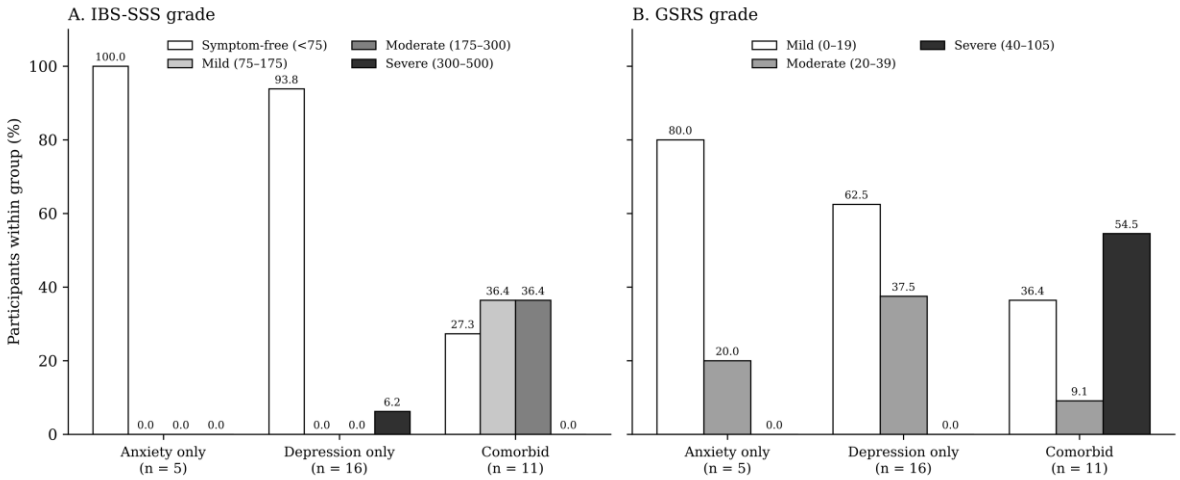


Figure 2: Distribution of Gastrointestinal Symptom Severity Grades by Diagnostic Group

Note. Panel A shows Irritable Bowel Syndrome-Symptom Severity Scale (IBS-SSS) grade; Panel B shows Gastrointestinal Symptom Rating Scale (GSRS) grade. Bars show the percentage of participants within each diagnostic group falling into each severity band. Clinically relevant IBS symptomatology and severe GSRS grades were concentrated in the comorbid group.

Association analyses

Effect estimates are summarised in Table 4. For clinically relevant IBS symptomatology, comorbid status was associated with an OR of 25.10 (95% CI 3.11–202.43; Fisher exact p<0.001) relative to depression alone, corresponding to a prevalence ratio of 11.64 (95% CI 1.69–80.33), and with an OR of 26.71 (95% CI 1.14–624.27; p=0.026) relative to anxiety alone. In Firth penalised logistic regression with comorbid status as the sole predictor, the OR was 33.19 (95% CI 3.91–281.45; p=0.001). After adjustment for age and sex, the estimate was essentially unchanged at 27.36 (95% CI 3.09–241.93; p=0.003); neither age (OR 0.94 per year, 95% CI 0.87–1.03; p=0.173) nor female sex (OR 0.94, 95% CI 0.11–8.03; p=0.958) was independently associated with the outcome.

Table 4: Association Between Comorbid Anxiety and Depression and Gastrointestinal Symptom Burden

Outcome and comparison	Effect measure	Estimate [95% CI]	*p*
IBS-SSS ≥75: comorbid vs depression only	Odds ratio	25.10 [3.11, 202.43]	< .001
IBS-SSS ≥75: comorbid vs depression only	Prevalence ratio	11.64 [1.69, 80.33]	< .001
IBS-SSS ≥75: comorbid vs anxiety only	Odds ratio	26.71 [1.14, 624.27]	.026
IBS-SSS ≥75: comorbid vs non-comorbid (unadjusted)	Odds ratio (Firth)	33.19 [3.91, 281.45]	.001
IBS-SSS ≥75: comorbid vs non-comorbid (adjusted)	Odds ratio (Firth)	27.36 [3.09, 241.93]	.003
Age (per year), same model	Odds ratio (Firth)	0.94 [0.87, 1.03]	.173
Female sex, same model	Odds ratio (Firth)	0.94 [0.11, 8.03]	.958
GSRS ≥40: comorbid vs non-comorbid	Odds ratio	16.15 [2.17, 120.48]	.003
GSRS ≥20: comorbid vs non-comorbid (unadjusted)	Odds ratio (Firth)	3.22 [0.71, 14.70]	.131
GSRS ≥20: comorbid vs non-comorbid (adjusted)	Odds ratio (Firth)	2.98 [0.63, 14.07]	.167

Note. CI = confidence interval; IBS-SSS = Irritable Bowel Syndrome-Symptom Severity Scale; GSRS = Gastrointestinal Symptom Rating Scale. Adjusted models include age and sex. Odds ratios for 2 × 2 comparisons with a zero cell use the

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Haldane-Anscombe correction; *p* values for these comparisons are from the Fisher exact test. Firth estimates are from penalised logistic regression. Confidence intervals are wide throughout, and their upper bounds should not be interpreted as precise.

For a severe GSRS grade, comorbid status compared with all non-comorbid patients combined gave an OR of 16.15 (95% CI 2.17–120.48; Fisher exact p=0.003). At the lower moderate-or-severe GSRS threshold, the Firth-adjusted OR for comorbid status was 2.98 (95% CI 0.63–14.07; p=0.167), with CIs including the null.

Correlations between severity grades are shown in Table 5. GSRS grade correlated moderately with HAM-A grade (Spearman rho=0.490, 95% CI 0.171–0.716; p=0.004) and with PHQ-9 grade (rho=0.443, 95% CI 0.112–0.686; p=0.011). IBS-SSS grade correlated with GSRS grade (rho=0.554, 95% CI 0.255–0.757; p=0.001) but not with HAM-A grade (rho=0.036, 95% CI −0.317 to 0.380; p=0.847) or PHQ-9 grade (rho=0.274, 95% CI −0.083 to 0.568; p=0.130). Duration of illness was not associated with IBS-SSS grade (rho=0.087; p=0.635) or GSRS grade (rho=0.154; p=0.399).

Table 5: Spearman Rank Correlations Between Severity Grades

Variable pair	*rs*	95% CI	*p*
HAM-A grade and IBS-SSS grade	.036	[−.317, .380]	.847
PHQ-9 grade and IBS-SSS grade	.274	[−.083, .568]	.130
HAM-A grade and GSRS grade	.490	[.171, .716]	.004
PHQ-9 grade and GSRS grade	.443	[.112, .686]	.011
IBS-SSS grade and GSRS grade	.554	[.255, .757]	.001
Duration of illness and IBS-SSS grade	.087	[−.270, .423]	.635
Duration of illness and GSRS grade	.154	[−.205, .477]	.399

Note. $N = 32$. *rs* = Spearman rank correlation coefficient; CI = confidence interval, derived from the Fisher *z*-transformation; HAM-A = Hamilton Anxiety Rating Scale; PHQ-9 = Patient Health Questionnaire-9; IBS-SSS = Irritable Bowel Syndrome-Symptom Severity Scale; GSRS = Gastrointestinal Symptom Rating Scale.

DISCUSSION

Key findings

In this cross-sectional study of 32 psychiatric outpatients, patients with comorbid anxiety and depression carried a markedly greater gastrointestinal symptom burden than patients with either condition alone. Clinically relevant IBS symptomatology (IBS-SSS ≥75) was present in 8 of 11 comorbid patients (72.7%, 95% CI 43.5–91.7), compared with 1 of 16 patients with depression alone (6.2%) and none of the 5 patients with anxiety alone (p<0.001), and the comorbid group differed significantly from both single-diagnosis groups in pairwise comparison (Fisher exact p<0.001 and p=0.026, respectively). Severe general gastrointestinal symptoms (GSRS ≥40) were confined entirely to the comorbid group (6 of 11, 54.5%, versus 0 of 21 non-comorbid patients; OR 16.15, 95% CI 2.17–120.48; p=0.003). This gradient was not explained by differences in psychiatric symptom severity: HAM-A (p=0.906) and PHQ-9 (p=0.577) severity distributions were closely similar across the three groups, with identical median grades in every group. The association between comorbid status and IBS symptomatology also persisted after adjustment for age and sex (adjusted OR 27.36, 95% CI 3.09–241.93; p=0.003), with neither covariate independently associated with the outcome.

Comparison with existing literature

These findings are consistent in direction with the broader literature linking psychological distress to disorders of gut-brain interaction. In the Rome Foundation Global Epidemiology Study, clinically relevant psychological distress or somatic symptom severity was associated with more than four-fold higher odds of at least one DGBI, and coexistence of distress and DGBI was the variable most strongly associated with reduced quality of life.[7] Population-level data from the same programme show comparable rates of comorbid anxiety and depression among individuals meeting DGBI criteria in other national settings.[19] Meta-analytic data further indicate that anxiety and depressive symptoms are each common among patients with IBS.[8] The present results extend this picture by approaching the relationship from the psychiatric rather than the gastroenterological side, and by showing that the burden is not distributed evenly across affective presentations.

The observation that comorbid presentations differ from single-diagnosis presentations aligns with a substantial literature on anxious depression. In the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial, patients with anxious major depressive disorder were more likely to be severely depressed, endorsed more somatoform and hypochondriacal symptoms after

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adjustment for depression severity, experienced greater side-effect burden, and had poorer acute treatment outcomes than those with non-anxious depression.[3,4] The finding that the gastrointestinal difference was present despite comparable HAM-A and PHQ-9 grades is compatible with the interpretation, advanced in that literature, that comorbidity indexes something other than simple additive severity.[5]

The findings diverge from parts of this literature in one respect worth noting. Whereas several studies report that somatic symptom burden scales with overall depressive severity, the present analysis found no correlation between IBS-SSS grade and either HAM-A or PHQ-9 grade, although GSRS grade did correlate moderately with both. One plausible explanation is instrument-related: the GSRS captures a broad range of upper and lower gastrointestinal complaints, many of which overlap with the somatic items embedded in anxiety and depression rating scales, whereas the IBS-SSS is anchored to abdominal pain, distension, bowel habit satisfaction, and life interference, and may therefore behave more like a distinct syndromic marker than like a severity gradient.[14,15] A second explanation is the restricted severity range in the sample, in which the majority of participants fell into the two middle HAM-A and PHQ-9 bands, limiting the capacity to detect a dose-response relationship. A third is the small sample, which yields wide CIs around all correlation estimates.

Possible mechanisms

Mechanistically, the pattern is consistent with current models of the gut-brain axis, in which vagal afferent signalling, HPA axis dysregulation, immune activation, and microbial metabolites converge to modulate visceral sensitivity and motility.[9] Anxiety is associated primarily with autonomic arousal and heightened threat monitoring, while depression is associated with altered HPA regulation and reduced descending inhibitory modulation; the co-occurrence of both may combine autonomic and neuroendocrine contributions in a way that neither alone produces. Gastrointestinal-specific anxiety, in which visceral sensations themselves become the object of apprehension, offers a further candidate pathway that would plausibly be strongest where both anxiety and depressive processes are present. The present design cannot test any of these mechanisms, and these interpretations are offered as hypotheses rather than as inferences from the study data.

Clinical implications

Clinically, the findings suggest that diagnostic status at psychiatric assessment may usefully flag patients in whom gastrointestinal enquiry is warranted. In a tertiary outpatient setting with a high patient load, brief screening of patients with comorbid anxiety and depression, rather than of all attendees, would represent an efficient allocation of consultation time. Because gastrointestinal complaints in this group may be attributed to psychotropic adverse effects and may contribute to non-adherence, distinguishing baseline symptom burden from treatment-emergent symptoms is relevant to prescribing decisions. These implications are provisional and require confirmation in larger, preferably longitudinal, samples.

Generalisability

The findings are most directly applicable to adult outpatients aged 18–60 years attending a psychiatry service at a large government tertiary care teaching hospital in north-west India, who carry a DSM-5 diagnosis of an anxiety disorder, a depressive disorder, or both, and who have no medical or other psychiatric comorbidity. Within this frame, several features support external relevance. Participants were recruited consecutively rather than by convenience; the sample spanned urban and rural residence, a wide range of educational attainment, and several income bands, reflecting the socioeconomically diverse catchment of a publicly funded referral hospital; and all four instruments used are internationally established and widely applied, which facilitates comparison with studies in other settings.

Equally, extrapolation beyond this population should be made with caution. Patients reaching a tertiary referral centre are likely to have more severe, more chronic, or more treatment-resistant illness than those managed in primary care or community settings, and the exclusion of medically comorbid patients means that the findings may not extend to older adults or to the large group of psychiatric patients with coexisting physical illness, in whom gastrointestinal symptoms are often more frequent. The anxiety-only group was small and entirely male, so conclusions about that subgroup are particularly tentative. Dietary practices, gut microbial composition, and patterns of help-seeking for somatic symptoms vary across regions, and the magnitude of the association observed in Rajasthan may therefore differ in other Indian states, in other low- and middle-income countries, including those in sub-Saharan Africa, and in high-income settings. The direction of the association is consistent with international population data,[7,19] which suggests that the qualitative finding may be transferable, but the effect sizes reported here should not be applied to other populations without local replication.

Conclusion

In this single-centre cross-sectional study of psychiatric outpatients, comorbid anxiety and depression was associated with substantially greater gastrointestinal symptom burden than anxiety alone or depression alone, on both an IBS-specific and a general gastrointestinal symptom measure. This association was not accounted for by differences in anxiety or depressive symptom severity between groups. Given the small sample, the single-centre

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setting, and the cross-sectional design, these findings should be regarded as hypothesis-generating and require confirmation in larger, multicentre, and longitudinal studies before any recommendation for routine practice can be made.

Limitations

Several limitations must be considered when interpreting these results. First, and most fundamentally, the cross-sectional design establishes co-occurrence at a single point in time and cannot establish temporality. It is not possible to determine whether comorbid affective illness preceded the gastrointestinal symptoms, whether chronic gastrointestinal symptoms contributed to the development of a comorbid affective presentation, or whether both arise from shared antecedent factors. All findings reported here are associations, and no causal inference is warranted.

Second, the sample was small (n=32), with markedly unequal group sizes; the anxiety-only group comprised only five patients. Confidence intervals around the effect estimates are correspondingly wide, and the upper bounds in particular should not be interpreted as meaningful. Where zero cells occurred, estimates depended on continuity corrections and penalised likelihood methods, and remain unstable. No a priori sample size calculation was performed, and the study was not designed to a specified precision.

Third, the study was conducted at a single government tertiary care centre, and referral filters may select for patients with more severe, more chronic, or more somatically prominent illness; the implications of this for generalisability are discussed above.

Fourth, consecutive OPD enrolment does not eliminate selection bias. Patients attending on OPD days during a fixed four-month window may differ systematically from non-attenders, and exclusion of patients unable to complete questionnaires may have removed those with the greatest symptom burden or the poorest functioning.

Fifth, residual and unmeasured confounding is likely. Although patients with medical comorbidity were excluded, current psychotropic medication, dietary patterns, tobacco and alcohol use, physical activity, and prior gastrointestinal diagnoses were either not recorded or not incorporated into the models. History of substance use differed significantly across groups and could not be adjusted for, given the number of events available. The adjusted models included only age and sex; with nine events for the primary outcome, further adjustment would have been uninterpretable.

Sixth, measurement limitations apply. The IBS-SSS, GSRS, HAM-A, and PHQ-9 data were available only as ordered severity categories rather than as continuous total scores, which reduces statistical efficiency, precludes reporting of mean scores and standardised mean differences, and may obscure within-band variation. All four instruments rely on self-report or interview and are subject to recall and social desirability bias. Formal Rome IV diagnostic criteria for IBS were not applied, so the IBS-SSS findings describe symptom burden rather than confirmed diagnosis. Group assignment was based on the recorded DSM-5 diagnosis rather than on a structured research diagnostic interview administered for study purposes.

Finally, multiple outcomes and multiple pairwise comparisons were examined. Although Bonferroni adjustment was applied to pairwise tests, the overall analysis remains exploratory, and the findings require replication.

Recommendations

On the basis of the findings, and bearing in mind the limitations above, the following recommendations are made:

- **Clinical practice:** Psychiatrists and other clinicians assessing outpatients with comorbid anxiety and depression should routinely enquire about gastrointestinal symptoms at the initial psychiatric assessment, using a brief structured tool such as the IBS-SSS or GSRS, rather than relying on spontaneous reporting or later gastroenterological referral.
- **Prescribing and follow-up:** Baseline gastrointestinal symptom burden should be documented before psychotropic medication is started, so that pre-existing symptoms can be distinguished from treatment-emergent adverse effects and adherence can be supported.
- **Integrated care:** Referral pathways between psychiatry, clinical psychology, and gastroenterology services should be strengthened, so that patients with comorbid presentations and prominent gut symptoms receive coordinated assessment, including gut-directed psychological interventions where appropriate.
- **Future research:** Larger, adequately powered, multicentre studies with balanced diagnostic groups are needed, recording continuous instrument scores, applying Rome IV criteria, and measuring psychotropic exposure, diet, and substance use. Longitudinal designs should be used to establish the temporal sequence between comorbid affective illness and gastrointestinal symptoms, and intervention studies should test whether targeted screening and management improve outcomes.
- **Health policy:** Programmes delivering mental health care in India, including the District Mental Health Programme, could consider incorporating simple somatic and gastrointestinal symptom screening for patients with comorbid anxiety and depression, once these findings have been replicated.

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List Of Abbreviations

CI	Confidence interval
df	Degrees of freedom
DGBI	Disorders of gut-brain interaction
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
GI	Gastrointestinal
GSRS	Gastrointestinal Symptom Rating Scale
HAM-A	Hamilton Anxiety Rating Scale
HPA	Hypothalamic-pituitary-adrenal
IBS	Irritable bowel syndrome
IBS-SSS	Irritable Bowel Syndrome-Symptom Severity Scale
IEC	Institutional Ethics Committee
IQR	Interquartile range
OPD	Outpatient department
OR	Odds ratio
PHQ-9	Patient Health Questionnaire-9
RUHS	Rajasthan University of Health Sciences
SD	Standard deviation
SMS	Sawai Man Singh
STAR*D	Sequenced Treatment Alternatives to Relieve Depression
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology

Declarations

Ethics approval and consent to participate

The study was approved by the Institutional Ethics Committee of SMS Medical College, Jaipur. Written informed consent was obtained from all participants.

Consent for publication

Not applicable. The manuscript contains no individual identifying data.

Data availability statement

The de-identified dataset generated and analysed during the current study, together with the analysis code, is available from the corresponding author on reasonable request. Data are not publicly deposited because participant consent did not cover open public release; requests will be considered subject to approval by the Institutional Ethics Committee of SMS Medical College, Jaipur, and a data-sharing agreement that safeguards participant confidentiality.

Conflicts of interest

The authors declare that they have no competing interests.

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Author contributions

Contributions are described according to the CRediT (Contributor Roles Taxonomy) framework.

- **Yogesh Kumar Satija:** Conceptualisation, methodology, supervision, resources, project administration, and writing - review and editing.
- **Niharika Bawankar:** Conceptualisation, methodology, investigation (patient recruitment, clinical assessment, and data collection), data curation, and writing - original draft.
- **Aisha Zubair:** Investigation (administration of psychometric and gastrointestinal symptom instruments), data curation, and writing - review and editing.
- **Vipul Sharma:** Formal analysis, visualisation, literature search, and writing - original draft.
- **Ashish Kumar Shukla:** Formal analysis, validation, literature search, and writing - review and editing.

All authors read and approved the final manuscript and agree to be accountable for all aspects of the work.

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