RESEARCH PAPER

ANXIETY AND DEPRESSION ACROSS GOLD STAGES IN STABLE COPD: A CROSS-SECTIONAL HADS-BASED STUDY FROM RURAL SOUTH INDIA

Chittin N Swamy[1]*, Chirag KC[2], Bommeri Nandakishore[3], Deepu CC[4], Harshini Jagalur[5], Shabaresh KM[6]

[1]*Postgraduate, Department of Respiratory Medicine, Adichunchanagiri Institute of Medical Sciences, Mandya, Karnataka, India*
[2]*Assistant Professor, Department of Respiratory Medicine, Adichunchanagiri Institute of Medical Sciences, Mandya, Karnataka, India*
[3]*Postgraduate, Department of Respiratory Medicine, Adichunchanagiri Institute of Medical Sciences, Mandya, Karnataka, India*
[4]*Professor and Head, Department of Respiratory Medicine, Adichunchanagiri Institute of Medical Sciences, Mandya, Karnataka, India*
[5]*Postgraduate, Department of Dermatology, Adichunchanagiri Institute of Medical Sciences, Mandya, Karnataka, India*
[6]*Postgraduate, Department of Respiratory Medicine, Adichunchanagiri Institute of Medical Sciences, Mandya, Karnataka, India*
Corresponding author: Dr. Chittin N. Swamy, chittin.n.swamy@bgsaims.edu.in

ABSTRACT

Background: Anxiety and depression are common comorbidities of chronic obstructive pulmonary disease (COPD), with the GOLD 2025 report recommending routine screening; however, data from rural South India combining spirometric GOLD staging with a formal dose-response analysis remain scarce.

Methods: This hospital-based, cross-sectional study enrolled 53 consecutive stable COPD patients at a rural tertiary center in Karnataka, India. Patients were staged by post-bronchodilator spirometry (GOLD 2025) and assessed with a study-specific Kannada translation of the Hospital Anxiety and Depression Scale (HADS); scores ≥11 defined caseness. The dose-response across ordered GOLD stages was evaluated by the Cochran-Armitage trend test; 2×2 associations by Fisher's exact test with Cramer's V and Wilson 95% confidence intervals; Firth-penalized logistic regression adjusted for sex served as a pre-specified sensitivity analysis.

Results: Of 53 patients (mean age 61.0 ± 8.9 years; 77.4% male), 58.5% (95% CI 45.1-70.7) screened positive for anxiety and 52.8% (39.7-65.6) for depression. A strong monotonic dose-response was observed (Cochran-Armitage $Z = 4.36$ for anxiety, $Z = 5.65$ for depression; both $p < 0.001$): anxiety caseness rose from 25.0% in Stage 1 to 100% in Stage 4, and depression from 0% to 100%. Each one-stage GOLD increment independently predicted higher odds of anxiety caseness (adjusted OR 4.97, 95% profile CI 2.26-14.13) and depression caseness (adjusted OR 37.18, 95% profile CI 11.79-316.10).

Conclusions: Anxiety and depression are highly prevalent in rural Indian COPD and scale strongly with spirometric severity. Brief HADS screening at every GOLD Stage 3-4 visit, with structured psychiatric referral for positive screens, operationalizes GOLD 2025 recommendations in resource-limited rural settings.

Keywords: Anxiety, Biomass fuel exposure, Chronic obstructive pulmonary disease, COPD, Depression, GOLD, Hospital Anxiety and Depression Scale (HADS), Psychiatric comorbidity, Rural India, Spirometry

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is the third leading cause of death globally and one of the largest contributors to the non-communicable disease burden in India [1,2]. India accounts for approximately one-third of the global chronic respiratory disease burden, with more than 55 million prevalent COPD cases [2]. Among the extrapulmonary manifestations of this multisystem disorder, anxiety and depression are pervasive yet under-recognized in clinical practice.

The relationship between COPD and mental health is bidirectional. Dyspnea, functional limitation, and social withdrawal contribute to the development of mood disorders; these, in turn, impair medication adherence, increase exacerbation frequency, and increase healthcare utilization [3]. Global prevalence estimates place depression or anxiety in 25-50% of COPD patients, though figures vary widely by geographic and socioeconomic context [3,4]. A recent narrative synthesis re-emphasized that psychological comorbidities remain largely overlooked in routine COPD assessment despite clear guideline recommendations [5]. Non-detection in turn contributes to poor self-management, exacerbations, hospitalizations, and excess mortality [5].

In rural India, this burden is compounded by limited access to healthcare, low health literacy, and region-specific risk factors - particularly biomass-fuel smoke from household cooking, which disproportionately affects women and is linked to a distinct COPD phenotype with potentially different systemic inflammatory profiles [6-8]. COPD in never-smokers - driven substantially by biomass combustion, occupational dust, and early-life respiratory insults - is now a well-characterized phenotype globally, with substantial prevalence documented in Indian women [7,9]. Biomass-exposed Indian women have been reported to carry an elevated risk of depressive symptoms,

hypothesized to relate to altered serotonergic activity and chronic particulate exposure [10].

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2025 report explicitly recommends screening for anxiety and depression at diagnosis and during follow-up, highlights that COPD patients are approximately twice as likely to die by suicide as the general population, and endorses pulmonary rehabilitation as an intervention with documented benefits for mood [1]. Indian studies have reported psychiatric comorbidity rates of 47-64% using a variety of instruments (MINI, HAM-A/D, PHQ-9, HADS) [11-16], but have rarely combined spirometry-confirmed GOLD staging with a validated psychiatric screen and a formal dose-response analysis in a rural South Indian tertiary setting. The present study aimed to (i) estimate the prevalence of clinically significant anxiety and depression in spirometry-confirmed stable COPD patients in a rural South Indian tertiary care setting, (ii) test the dose-response relationship between GOLD 2025 stage and psychiatric morbidity, and (iii) explore associations with gender, biomass-fuel exposure, and smoking status.

MATERIALS AND METHODS

Study design and setting

This was a hospital-based, cross-sectional observational study conducted at the Department of Respiratory Medicine of a rural tertiary care center in Karnataka, South India, over three months (July-September 2025).

Study population

All eligible patients presenting during the study period were enrolled by consecutive sampling (n = 53).

Inclusion criteria: age ≥ 40 years; COPD confirmed per GOLD 2025 spirometric criteria (post-bronchodilator FEV1/FVC < 0.70); clinically stable (no acute exacerbation in the preceding four weeks); and written informed consent.

Exclusion criteria: active pulmonary tuberculosis; interstitial lung disease; bronchial asthma; lung malignancy; pre-existing psychiatric disorder currently on treatment; and inability to comprehend the study questionnaire.

Sample size was determined by complete enumeration of all eligible patients presenting during the predefined three-month window; no a priori power calculation was performed. The study is therefore framed as hypothesis-generating: a post-hoc calculation (N = 53, alpha = 0.05, power = 80%) indicates a minimum detectable Cramer's V of approximately 0.38, sufficient for moderate-to-large but not small effects in the absence of a published psychometric validation. This sample is broadly comparable to several published Indian COPD-psychiatric-comorbidity studies (n = 50-100) [11-15]. The implications for the gender, biomass, and smoking subgroup analyses are discussed in the Limitations.

Data collection

Sociodemographic data (age, sex, socioeconomic status using the Modified Kuppuswamy Scale) and clinical data (smoking history, biomass-fuel exposure) were collected using a structured proforma. Spirometry was performed per the 2019 American Thoracic Society / European Respiratory Society standardization update [17]. Severity was operationalized as the GOLD 2025 spirometric grade (1-4) [1]; the ABE assessment was not used because systematic exacerbation history was not available for all participants. Symptom burden was characterized by mMRC and CAT (Table 1).

Table 1. Sociodemographic and clinical characteristics of the study population (N = 53).

Variable	Category	Frequency (n)	Percentage (%)
Age (years)	Mean ± SD	61.02 ± 8.93	—
Gender	Male	41	77.4
	Female	12	22.6
Socioeconomic status (Modified Kuppuswamy)	Class II (Upper Middle)	7	13.2
	Class III (Lower Middle)	12	22.6
	Class IV (Upper Lower)	19	35.8
	Class V (Lower)	15	28.3
Smoking status	Current smoker	22	41.5
	Former smoker	21	39.6
	Never smoker	10	18.9
Biomass-fuel exposure	Present	10	18.9
	Absent	43	81.1
mMRC dyspnoea grade	Grade 1	4	7.5
	Grade 2	18	34.0
	Grade 3	20	37.7
	Grade 4	11	20.8
CAT score	Mean ± SD	18.45 ± 7.43	—
COPD severity (GOLD 2025)	Stage 1 (Mild)	8	15.1
	Stage 2 (Moderate)	16	30.2
	Stage 3 (Severe)	18	34.0
	Stage 4 (Very Severe)	11	20.8
HADS-A score	Mean ± SD	10.49 ± 3.85	—
HADS-D score	Mean ± SD	10.60 ± 4.68	—

Psychiatric morbidity was assessed using the Hospital Anxiety and Depression Scale (HADS), administered in a study-specific Kannada translation (described below). The HADS comprises 14 items (seven each for anxiety [HADS-A] and depression [HADS-D]), scored 0-3, yielding subscale scores of 0-21 [18].

Scores were categorized as Normal (0-7), Borderline (8-10), and Abnormal/Case (≥ 11). The ≥ 11 threshold was selected as the primary cut-off because it offers approximately 80% sensitivity and specificity for clinically significant anxiety and depression in non-psychiatric medical populations [19] and is the threshold most widely adopted in COPD-specific HADS literature, facilitating direct comparison with prior Indian and international cohorts. “Case” status was defined as Abnormal only; Borderline cases were reported separately and were not pooled with

Abnormal for 2×2 testing. A pre-specified sensitivity analysis using the broader ≥ 8 cut-off (any positivity, combining Borderline and Abnormal) was conducted alongside the primary analysis.

In the absence of a published psychometric validation of the HADS in Kannada at the time of the study, the instrument was prepared by standard forward-backward translation with consensus reconciliation and a comprehensibility pilot (pilot participants excluded), consistent with published Malayalam and Marathi HADS adaptations [20,21]. All HADS interviews were conducted by a single trained research interviewer (B.N.), blinded to the participant's spirometric results at the time of administration. Ongoing national work on culturally adapted Kannada anxiety screens informed item-level review for idiomatic fidelity [22]. Internal consistency of the study-specific Kannada HADS was assessed in the present sample by Cronbach's alpha for each subscale.

Statistical analysis

The primary outcomes were the prevalence of HADS-A and HADS-D caseness (score ≥ 11) and their relationship with GOLD stage. Data were entered into Microsoft Excel and analyzed in Python 3.11 (pandas, SciPy, statsmodels) and SPSS v26.0. Continuous variables are expressed as mean ± standard deviation (SD); categorical variables as frequencies and percentages. Prevalence estimates are reported with 95% confidence intervals (CIs) calculated using the Wilson score method.

The primary test of the dose-response relationship between ordered GOLD stages (1-4) and HADS caseness was the Cochran-Armitage trend test, implemented in the standard binomial-variance (score-test) form following Armitage (1955) - equivalent to R's prop.trend.test() and to the trend option in SAS PROC FREQ. Integer stage scores (1, 2, 3, 4) were assigned to GOLD Stages 1 through 4, respectively. For the descriptive 4×3 cross-tabulation of GOLD stage by HADS category, expected cell counts fell below 5 in the majority of cells; the chi-square statistic is therefore reported alongside a Monte Carlo-simulated exact p-value (20,000 replicates). Associations between categorical variables in 2×2 comparisons were assessed using Fisher's exact test (two-tailed). Effect sizes for 2×2 associations are reported as Cramer's V, interpreted by conventional thresholds (small ~ 0.10, moderate ~ 0.30, large ~ 0.50). A two-tailed p-value < 0.05 was considered statistically significant.

Two primary tests were pre-specified (one Cochran-Armitage trend test per outcome); secondary subgroup p-values are interpreted descriptively.

Because all 11 GOLD Stage 4 patients met caseness on both subscales, standard maximum-likelihood logistic regression was subject to quasi-complete separation. Firth's penalized maximum-likelihood logistic regression [23,24] was therefore used, adjusting for female sex, with profile-likelihood 95% confidence intervals. The model was intentionally restricted to GOLD stage plus sex for three reasons: (i) with 28-31 events, the conventional events-per-variable threshold of 10 supports a maximum of approximately three predictors, making additional covariates inadvisable even under Firth penalization; (ii) mMRC dyspnea grade and CAT score are strong correlates of GOLD stage - adjusting for them alongside the primary exposure constitutes over-adjustment by conditioning on variables that lie near the causal pathway from GOLD stage to mood outcomes; and (iii) age showed no significant univariate association with either HADS outcome in this sample, and SES variance was insufficient to act as a meaningful confounder (Classes IV-V, 64.1% of the cohort). Smoking status and biomass-fuel exposure were additionally excluded because of collinearity with each other and with disease severity. A supplementary sensitivity analysis adding age (continuous) to the GOLD stage + sex model confirmed that the GOLD stage odds ratio was not materially affected. A parallel Firth-penalized model was fitted at the broader HADS ≥ 8 cut-off as an additional sensitivity analysis. Linear regression on the continuous HADS subscale scores was performed alongside as a corroborative analysis.

Ethics and reporting

The study protocol was approved by the Institutional Ethics Committee of Adichunchanagiri Institute of Medical Sciences (study approval number AIMS/IEC/209/2025; IEC registration number EC/NEW/INST/2023/KA/0382; approved 18 June 2025) and conducted in accordance with the Declaration of Helsinki (2013 revision). Written informed consent was obtained from every participant.

RESULTS

Table 2. Prevalence of anxiety and depression (HADS Abnormal, score ≥ 11) by COPD severity, gender, biomass-fuel exposure, and smoking status.

Variable	N	Anxiety cases, n (%) [95% CI]	Depression cases, n (%) [95% CI]	Test statistic (anxiety / depression)
Overall population	53	31 (58.5) [45.1-70.7]	28 (52.8) [39.7-65.6]	—
COPD severity (dichotomised)				V = 0.62 / 0.81; p < 0.001 / < 0.001
Mild-Moderate (Stage 1-2)	24	6 (25.0) [12.0-44.9]	2 (8.3) [2.3-25.8]	
Severe-Very Severe (Stage 3-4)	29	25 (86.2) [69.4-94.5]	26 (89.7) [73.6-96.4]	
COPD severity (per stage)				
Stage 1 (Mild)	8	2 (25.0) [7.1-59.1]	0 (0.0) [0.0-32.4]	
Stage 2 (Moderate)	16	4 (25.0) [10.2-49.5]	2 (12.5) [3.5-36.0]	
Stage 3 (Severe)	18	14 (77.8) [54.8-91.0]	15 (83.3) [60.8-94.2]	
Stage 4 (Very Severe)	11	11 (100.0) [74.1-100.0]	11 (100.0) [74.1-100.0]	
Cochran-Armitage trend (Stage 1->4)	53	Z = 4.36; p < 0.001	Z = 5.65; p < 0.001	—
Gender				V = 0.09 / 0.06; p = 0.740 / 0.750
Male	41	23 (56.1)	21 (51.2)	
Female	12	8 (66.7)	7 (58.3)	
Biomass-fuel exposure*				V = 0.02 / 0.03; p = 1.000 / 1.000
Present	10	6 (60.0)	5 (50.0)	
Absent	43	25 (58.1)	23 (53.5)	
Smoking status				V = 0.38 / 0.59; p = 0.010 / < 0.001
Current smokers	22	8 (36.4)	4 (18.2)	
Non-/former smokers	31	23 (74.2)	24 (77.4)	

Sociodemographic and clinical characteristics

Of 53 patients included (mean age 61.0 ± 8.9 years; 77.4% male), the majority belonged to lower socioeconomic classes (Classes IV and V: 64.1%). Current smokers constituted 41.5% (n = 22), former smokers 39.6% (n = 21), and never-smokers 18.9% (n = 10). Biomass-fuel exposure was present in 18.9% of participants (n = 10). A structural feature of the cohort was that biomass exposure was perfectly collinear with never-smoker status (all 10 biomass-exposed patients were never-smokers and vice versa). Ten of 12 women were biomass-exposed never-smokers; the remaining 2 women were ever-smokers without biomass exposure; all 41 men were current or former smokers without biomass exposure. GOLD stage distribution was: Stage 1, 15.1% (n = 8); Stage 2, 30.2% (n = 16); Stage 3, 34.0% (n = 18); Stage 4, 20.8% (n = 11). Mean CAT score was 18.5 ± 7.4. Full characteristics appear in Table 1.

SD, standard deviation; mMRC, modified Medical Research Council; CAT, COPD Assessment Test; GOLD, Global Initiative for Chronic Obstructive Lung Disease; HADS, Hospital Anxiety and Depression Scale. In this cohort all 10 biomass-exposed patients were never-smokers (biomass exposure was perfectly collinear with never-smoker status). Ten of the 12 female patients were biomass-exposed never-smokers; 2 women were ever-smokers without biomass exposure. All 41 male patients were current or former smokers without biomass exposure.

Item-level data were complete: all 53 participants completed every HADS item (no missing data). Internal consistency of the study-specific Kannada HADS was high in the present sample, with Cronbach's alpha = 0.91 for the seven HADS-A items and 0.85 for the seven HADS-D items.

Prevalence of anxiety and depression

Overall, 31/53 patients (58.5%; 95% CI 45.1-70.7) screened positive for clinically significant anxiety (HADS-A ≥ 11); 10 (18.9%) were Borderline and 12 (22.6%) Normal. For depression, 28/53 (52.8%; 95% CI 39.7-65.6) screened positive (HADS-D ≥ 11); 10 (18.9%) were Borderline and 15 (28.3%) Normal. Mean subscale scores fell within the Borderline range and were closely matched between the two outcomes (HADS-A 10.5 ± 3.9; HADS-D 10.6 ± 4.7).

Association between COPD severity and psychiatric morbidity

Figure 1 illustrates the per-stage distribution across HADS categories; full per-stage proportions and confidence intervals are presented in Table 2.

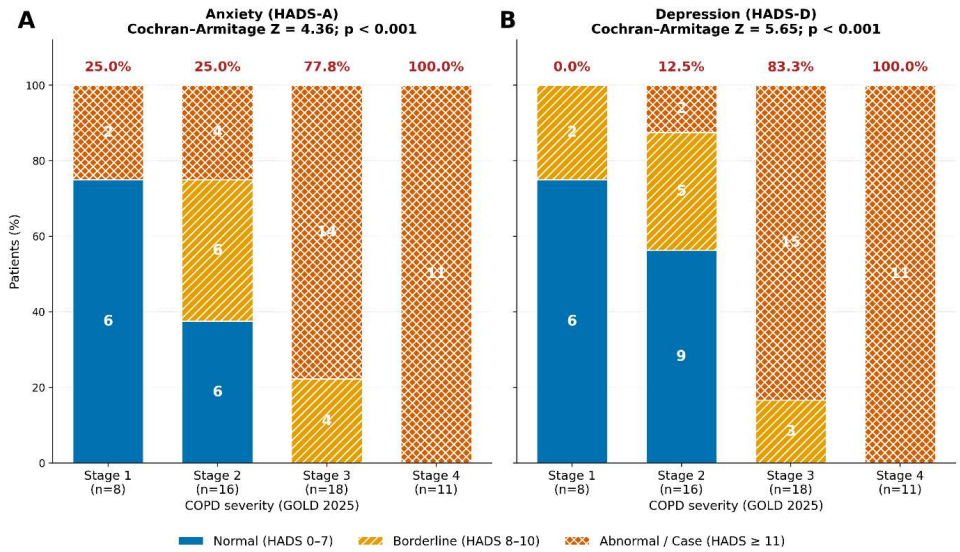

Figure 1: Stacked-bar plot of HADS-A (panel A) and HADS-D (panel B) categories (Normal / Borderline / Abnormal) by GOLD 2025 stage (1-4), illustrating the monotonic dose-response between spirometric severity and psychiatric caseness. Cochran-Armitage trend test: Z = 4.36 (anxiety) and 5.65 (depression); both p < 0.001. Numbers within bars denote absolute case counts; percentages above bars denote the proportion of patients meeting HADS Abnormal/Case status (≥ 11) within each GOLD stage.

The Cochran-Armitage trend test confirmed a strong monotonic dose-response across ordered GOLD stages 1-4 (anxiety: Z = 4.36, p < 0.001; depression: Z = 5.65, p < 0.001). Dichotomizing severity as Mild-Moderate (Stages 1-2) versus Severe-Very-Severe (Stages 3-4), caseness rose from 25.0% to 86.2% for anxiety and from 8.3% to 89.7% for depression; both Fisher's exact comparisons were significant at p < 0.001, with large effect sizes (Cramer's V = 0.62 for anxiety; 0.81 for depression). A Monte Carlo-simulated exact p-value < 0.0001 for the 4×3 cross-tabulation of GOLD stage by HADS category corroborated these findings for both outcomes. Results are summarized in Table 2.

HADS, Hospital Anxiety and Depression Scale; CI, confidence interval (Wilson score method); V, Cramer's V effect size. P-values from two-tailed Fisher's exact test for 2×2 comparisons. The Cochran-Armitage trend test was computed across ordered GOLD Stages 1, 2, 3, and 4. In this cohort, biomass exposure was perfectly collinear with never-smoker status (all 10 biomass-exposed patients were never-smokers and vice versa). Ten of the 12 female patients were biomass-exposed never-smokers; 2 women were ever-smokers without biomass exposure. All 41 male patients were current or former smokers without biomass exposure. Subgroup comparisons (gender, biomass exposure, smoking status) are presented as exploratory; given structural collinearities and small subgroup sizes, univariate p-values and effect sizes should not be interpreted as estimates of independent effects. See Results text.

Sensitivity analysis: broader HADS cut-off (≥ 8)

In a sensitivity analysis using the broader HADS ≥ 8 cut-off (any positivity, combining Borderline and Abnormal), 41/53 patients (77.4%; 95% CI 64.5-86.5) screened positive for anxiety and 38/53 (71.7%; 95% CI 58.4-82.0) for depression. Cochran-Armitage trend tests remained highly significant (anxiety Z = 4.45, p < 0.001; depression Z = 4.70, p < 0.001), and all 29 patients in the Severe-Very-Severe stratum met the ≥ 8 threshold on both subscales (Fisher's exact p < 0.001 for both). The principal conclusion is therefore robust to the choice of HADS cut-off.

Sensitivity analysis: Firth-penalized multivariable regression

In Firth-penalized logistic regression of HADS subscale caseness on GOLD stage adjusted for female sex, each one-stage increment in GOLD severity independently predicted markedly higher odds of HADS-A caseness (adjusted OR 4.97, 95% profile CI 2.26-14.13; p = 0.0005) and HADS-D caseness (adjusted OR 37.18, 95% profile CI 11.79-316.10; p = 0.0002). The wide upper bound of the depression confidence interval reflects the inherent uncertainty arising from the small number of patients in the highest GOLD stage, all of whom met caseness; the odds ratio is best interpreted as evidence of a very steep gradient rather than a precise multiplier. Female sex was not independently associated with either outcome (anxiety adjusted OR 0.78, 95% profile CI 0.16-3.69, p = 0.76; depression adjusted OR 0.28, 95% profile CI 0.02-2.10, p = 0.25). At the broader ≥ 8 cut-off, where no separation arose, estimates were more compact and concordant in direction (anxiety adjusted OR 6.96, 95% profile CI 2.45-19.97, p = 0.002; depression adjusted OR 8.98, 95% profile CI 3.06-28.40, p < 0.001). Linear regression on continuous HADS scores corroborated the gradient (HADS-A: beta = +3.22 per stage, p < 0.001, R-squared = 0.68; HADS-D: beta = +4.26 per stage, p < 0.001, R-squared = 0.78).

Exploratory subgroup descriptions

Subgroup comparisons are exploratory; structural collinearities and small subgroup sizes preclude interpretation as independent effects (Table 2).

Gender. Anxiety caseness was numerically higher in women (8/12; 66.7%) than men (23/41; 56.1%), and depression similarly so (7/12; 58.3% vs. 21/41; 51.2%); neither difference reached statistical significance (Fisher's exact p = 0.740 and 0.750; Cramer's V = 0.09 and 0.06). The direction of the point estimates is consistent with the wider Indian community-based literature on rural female mental health [25,26] but the present comparison is too underpowered to be informative.

Biomass-fuel exposure. Univariate prevalence was near-identical between exposed and unexposed strata (anxiety 60.0% vs.58.1%; depression 50.0% vs.53.5%; p = 1.000 for both).

Smoking status. Current smokers had numerically lower prevalence of both outcomes than non- and former-smokers combined (anxiety 36.4% vs.74.2%; depression 18.2% vs.77.4%; Fisher's exact p = 0.010 and p < 0.001; Cramer's V = 0.38 and 0.59). Smoking status, however, is collinear with severity (83.3% of mild-moderate patients vs.6.9% of severe-very-severe were current smokers).

DISCUSSION

This study quantifies a substantial burden of clinically significant anxiety and depression among stable COPD patients in a rural

tertiary care setting in South India. Approximately three in five patients screened positive for anxiety (58.5%) and one in two for depression (52.8%) - figures at or above the upper range of published global estimates of 25-50% [3-5] and consistent with Indian tertiary-care series reporting 47-64% psychiatric morbidity in stable COPD [11-16]. The near-parity of the two outcomes contrasts with some published series in which anxiety predominates [3] and supports parallel rather than sequential screening for both conditions. The present cohort - spirometry-confirmed, rurally recruited, and analyzed with a formal dose-response test across all four GOLD stages - adds granularity that has been rare in the Indian literature on this topic [12-15].

The principal finding is a strong, monotonic dose-response between GOLD stage and psychiatric morbidity, reaching 100% caseness on both subscales among GOLD Stage 4 patients, with large effect sizes (Cramer's V = 0.62 for anxiety; 0.81 for depression). These findings closely echo, and extend, those of Chaudhary et al. and Dar et al., who reported increasing psychiatric comorbidity with worsening airflow limitation in North Indian tertiary cohorts [13,14], and of Jose et al., who documented 51.9% anxiety and 39.7% depression prevalence in a South Indian tertiary sample [15]. Mechanistically, worsening airflow limitation drives progressive dyspnea, functional decline, and social withdrawal [3,5], and aligns with the systemic-inflammatory hypothesis that has been proposed to link advanced COPD to depression via elevated IL-6 and TNF-alpha [27].

Gender was not significantly associated with either anxiety ($p = 0.740$) or depression ($p = 0.750$), though point estimates in women were numerically higher on both subscales (anxiety 66.7% vs.56.1%; depression 58.3% vs.51.2%). The small female subgroup (n = 12) leaves the study substantially underpowered to detect modest gender differences. Community-based rural Indian data, including the National Mental Health Survey 2015-16 [28], suggest an excess burden of common mental disorders in rural women [25,26] and a higher prevalence of depression in rural than urban middle-aged and older Indian populations [29], which is consistent with the direction of the point estimates observed here.

Biomass-fuel exposure showed no univariate association with either outcome. This stands in apparent tension with literature linking biomass exposure to depressive symptoms in Indian women [10] and to a distinct COPD phenotype [6-8]. Cohort-structural collinearity (biomass x never-smoker x female sex) precludes univariate disentanglement; the null is best read as no independent biomass effect over and above disease severity. Across the pre-specified sensitivity analyses, the direction and magnitude of the dose-response gradient were concordant. Larger multi-site studies with adequate representation of female smokers and male biomass-exposed patients are required to isolate independent contributions.

A striking and counter-intuitive univariate pattern was observed for smoking status: current smokers had lower rates of both anxiety (36.4%) and depression (18.2%) than non- and former-smokers combined (anxiety 74.2%; depression 77.4%). This cannot be taken at face value. Within the mild-moderate GOLD stratum, 83.3% of patients were current smokers, whereas within the severe stratum only 6.9% were still smoking - the classic "sick-quitter" pattern, in which patients with advanced COPD are more likely to have stopped smoking on clinical advice and are also more likely to exhibit psychiatric symptomatology. A recent North Indian case-control study similarly found higher psychiatric morbidity among COPD patients despite complex interactions with tobacco exposure history [30]. Smoking status in this sample is therefore collinear with disease severity, and the apparent protective association of continued smoking is most plausibly explained by severity-based confounding rather than by any true effect of continued tobacco use. Isolating any independent effect of smoking would require multivariable analysis in a substantially larger cohort.

Within-sample internal consistency of the Kannada HADS was high (Cronbach's alpha = 0.91 [HADS-A], 0.85 [HADS-D]), comparable with the original English instrument [19] and Indian-language adaptations [20,21]. This is not a formal psychometric validation, which - informed by ongoing Kannada anxiety-instrument work [22] - remains a priority for future methodological work in this language community.

Limitations

Several limitations should be acknowledged. First, the sample size (n = 53) was determined by complete enumeration over a fixed three-month window rather than by a priori power calculation; the resulting confidence intervals - particularly in subgroup comparisons - are wide, and the study is best viewed as hypothesis-generating. Second, the cohort's structural collinearities (perfect overlap of biomass exposure with never-smoker status, and substantial overlap with female sex) precluded full multivariable adjustment to disentangle the contributions of sex, biomass exposure, smoking status, and GOLD stage. Third, the cross-sectional design precludes causal inference regarding the direction of the COPD-mood-disorder relationship; longitudinal evidence suggests this relationship is bidirectional [3,5]. Fourth, the HADS is a screening instrument - positive screens require formal psychiatric evaluation for diagnosis. Fifth, recruitment at a tertiary referral center may have over-represented patients at the severe end of the disease spectrum, and the cohort accordingly skews toward Stages 3-4 (29/53; 54.7%); although this distribution is broadly consistent with other Indian tertiary-care COPD series [12-14], external validity to community or primary-care COPD populations - where Stages 1-2 predominate - remains to be established. Sixth, single-center recruitment may further limit generalizability, as case-mix and biomass-exposure patterns vary across Indian states [2]. Seventh, severity in this analysis is captured by the GOLD spirometric grade alone. The GOLD 2025 ABE assessment, which integrates symptom burden and exacerbation history, was not used because annualized exacerbation history was not systematically recorded for all participants. Whether the steep dose-response observed across spirometric grades would be preserved, attenuated, or strengthened under the ABE framework - particularly given that ABE upweights symptom-driven and exacerbation-prone phenotypes that may themselves correlate with mood - is a question for future work in cohorts where complete exacerbation histories are available. Finally, the Kannada HADS used in this study was produced by forward-backward translation for this project; a formal psychometric validation in Kannada remains to be published. Eighth, the structured proforma did not capture comorbidity burden (e.g., cardiovascular disease, diabetes, osteoporosis), current COPD pharmacotherapy or psychoactive medication use, time since COPD diagnosis, or formal social-support measures. All four variables can plausibly influence HADS scores independently of GOLD stage, and their omission limits the attribution of observed psychiatric burden to disease severity alone. A future prospective study should incorporate standardized comorbidity indices (e.g., the Charlson Comorbidity Index), complete medication records, time-since-diagnosis, and a validated social-support measure.

CONCLUSIONS

Anxiety and depression are highly prevalent in this rural South Indian COPD cohort, affecting 58.5% and 52.8% of the study population respectively, and scale strongly with GOLD stage in an unambiguous monotonic dose-response. These findings align with the GOLD 2025 recommendation to screen for and treat anxiety and depression as important but under-diagnosed comorbidities of COPD. A pragmatic, low-cost screening algorithm is implementable within existing rural respiratory outpatient services: brief HADS administration at every spirometry-confirmed clinic visit for GOLD Stage 3 or 4 patients, with structured psychiatric referral for those screening positive. Where available, integration with pulmonary rehabilitation - which has documented benefits for both physical fitness and mood - would further strengthen this approach.

AUTHOR CONTRIBUTIONS

Concept and design: Chittin N. Swamy, Bommeri Nandakishore, Chirag K C, Deepu Changappa, Shabaresh K M. Acquisition, analysis, or interpretation of data: Chittin N. Swamy, Harshini Jagalur, Nandakishore Bommeri, Chirag K C, Shabaresh K M. Drafting of the manuscript: Chittin N. Swamy, Harshini Jagalur, Nandakishore Bommeri, Chirag K C, Deepu Changappa, Shabaresh K M. Critical review of the manuscript for important intellectual content: Chittin N. Swamy, Harshini Jagalur, Nandakishore Bommeri, Chirag K C, Deepu Changappa, Shabaresh K M. Supervision: Deepu Changappa.

ETHICS AND DISCLOSURES

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. The Institutional Ethics Committee of Adichunchanagiri Institute of Medical Sciences issued approval AIMS/IEC/209/2025 (IEC registration number EC/NEW/INST/2023/KA/0382), approved in the meeting held on 18 June 2025. Animal subjects: All authors have confirmed that this study did not involve animal subjects or tissue. Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare that no financial support was received for the submitted work, that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work, and that there are no other relationships or activities that could appear to have influenced the submitted work.

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