

Clinical Profile and Severity Spectrum of COVID-19 Patients with and without Comorbidities Admitted to a Tertiary Care Hospital in India

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ABSTRACT

Background: COVID-19 severity is influenced by age, sex and chronic comorbidities; therefore, unadjusted comparisons may overestimate the independent effect of comorbidity.

Objective: This revised analysis aimed to compare the clinical profile and disease severity of hospitalized COVID-19 patients without comorbidity, with a single comorbidity and with multiple comorbidities, and to determine whether comorbidity status remained associated with severe disease after adjustment for age and sex.

Methods: A retrospective record-based cross-sectional study was conducted among 255 adult RT-PCR/RAT-confirmed COVID-19 patients admitted to a tertiary care hospital in Ratlam, Madhya Pradesh, India, from January to March 2021. Patients were categorized as non-comorbid (n=127), single-comorbidity (n=78) and multiple-comorbidity (n=50). Descriptive statistics, chi-square testing, independent t-test and multivariable binary logistic regression were applied.

Results: The mean age was higher in comorbid than non-comorbid patients (62.4 ± 12.1 vs 46.2 ± 15.9 years; $p < 0.001$), whereas sex distribution showed no statistically significant difference ($p = 0.069$). Fever (65.49%), cough (53.72%) and dyspnea (33.72%) were the predominant symptoms. Hypertension (71.87%), diabetes mellitus (34.37%) and cardiac disease (12.50%) were the leading comorbidities. Severe disease occurred in 10.23% of non-comorbid patients, 24.36% of single-comorbidity patients and 42.00% of patients with multiple comorbidities ($p < 0.001$). In adjusted analysis, age ≥ 60 years [adjusted odds ratio (OR) 3.28, 95% confidence interval (CI) 1.62-6.64; $p = 0.001$], male sex (adjusted OR 1.41, 95% CI 0.70-2.86; $p = 0.338$), single comorbidity (adjusted OR 2.05, 95% CI 0.89-4.72; $p = 0.092$) and multiple comorbidities (adjusted OR 3.86, 95% CI 1.56-9.55; $p = 0.004$) were evaluated as predictors of severe disease.

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Conclusion: Comorbidity burden showed a graded association with COVID-19 severity, particularly among patients with multiple chronic conditions. However, interpretation should account for the confounding effect of age and the limitations of retrospective single-centre data.

Keywords: COVID-19, comorbidities, disease severity, clinical profile, hypertension, diabetes mellitus, logistic regression.

INTRODUCTION

The emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in late 2019 precipitated a global health crisis of unprecedented magnitude, fundamentally transforming healthcare delivery systems worldwide (1). Since its initial identification in Wuhan, China, coronavirus disease 2019 (COVID-19) has affected hundreds of millions of individuals across all continents, with clinical manifestations ranging from asymptomatic carriage to fulminant respiratory failure and death (2). The pandemic has highlighted the vulnerability of specific population subgroups, necessitating detailed characterization of risk factors associated with adverse outcomes.

The pathophysiological mechanisms underlying COVID-19 involve viral entry through angiotensin-converting enzyme 2 (ACE-2) receptors expressed on respiratory epithelium and multiple organ systems (3). This receptor-mediated entry, coupled with subsequent inflammatory cascades and immunological dysregulation, produces a spectrum of clinical presentations that have challenged clinicians globally. Understanding the factors that determine disease trajectory remains important for optimizing therapeutic interventions and resource allocation.

Accumulating evidence from international studies has demonstrated that pre-existing comorbidities influence COVID-19 prognosis (4). Chronic conditions including hypertension, diabetes mellitus, cardiovascular disease, chronic respiratory disorders and malignancies have been associated with increased hospitalization rates, intensive care requirements and mortality (5). The biological underpinnings of this association include chronic inflammatory states, endothelial dysfunction, impaired immune responses

and metabolic derangements that compromise the host response to viral infection (6).

Early pandemic data from China revealed that hypertension was present in approximately one-quarter of hospitalized patients, with diabetes affecting 10-20% of cases requiring admission (7). Subsequent large-scale investigations from the United States documented even higher comorbidity burdens, with hypertension having been identified in over half of hospitalized patients and diabetes in approximately one-third (8). These observations prompted recognition that individuals with chronic diseases constituted particularly vulnerable populations requiring targeted preventive and therapeutic strategies.

India, home to a substantial proportion of the global burden of non-communicable diseases, faced unique challenges during the pandemic (9). The intersection of a large diabetic and hypertensive population with limited healthcare resources created conditions conducive to adverse outcomes. Despite substantial national case numbers, epidemiological data characterizing clinical profile and outcomes from different Indian regions remain heterogeneous (10). Regional variations in population demographics, health-seeking behaviour and infrastructure require location-specific investigations to inform clinical practice (11).

Earlier evidence has quantified higher risk among patients with hypertension, diabetes and cardiovascular disease (12). Nevertheless, the association between comorbidities and severe COVID-19 cannot be interpreted adequately without considering age and sex, because chronic diseases cluster strongly in older populations and both age and male sex are established prognostic factors (13, 14). Therefore, studies based only on crude group comparisons may exaggerate or misattribute the effect of comorbidities

unless homogeneity testing and adjusted analyses are performed.

The present study was revised to address this methodological concern. Instead of treating comorbidity as a simple binary exposure alone, the analysis additionally differentiates patients with no comorbidity, a single comorbidity and multiple comorbidities. This approach provides better clinical interpretation of comorbidity burden and avoids pooling patients with one chronic disease together with those having multiple associated conditions.

This study was undertaken to evaluate the clinical profile and severity spectrum of hospitalized COVID-19 patients admitted to a government tertiary care hospital in Central India. The primary objective was to compare disease severity across non-comorbid, single-comorbidity and multiple-comorbidity groups. Secondary objectives were to characterize symptom patterns, identify predominant comorbid conditions and assess whether comorbidity status remained associated with severe disease after adjustment for age and sex. 

MATERIALS AND METHODS

Study design and setting

This retrospective record-based cross-sectional study was conducted in a government medical college hospital in Ratlam, Madhya Pradesh, India. The institution served as a designated COVID-19 treatment centre during the pandemic, providing care across the disease severity spectrum. The study was designed to evaluate clinical characteristics, comorbidity patterns and admission severity among eligible adult patients.

Study duration and population

The study encompassed COVID-19 positive patients admitted to the facility between January 2021 and March 2021, corresponding to the period preceding the severe second wave in India. This three-month duration was selected to capture a temporally comparable cohort under broadly similar admission and treatment protocols.

Eligibility criteria

Patients were included if they met the following criteria: 1) confirmed SARS-CoV-2 infection by reverse transcription-polymerase chain reaction

(RT-PCR) or rapid antigen test (RAT); 2) age 18 years or above; and 3) admission to the study institution during the defined period. Exclusion criteria comprised: 1) patients younger than 18 years; 2) individuals with negative COVID-19 testing; and 3) pregnant women, given the distinct physiological considerations applicable to this population.

Data collection procedures

Data were extracted retrospectively from the Medical Records Department using a pre-designed standardized proforma. Variables included sociodemographic characteristics, presenting symptoms, duration of illness before admission, comorbidity type, number of comorbidities and admission severity category. Data extraction was performed by trained personnel and cross-checked for completeness and internal consistency.

Exposure group definitions

To address the reviewer's concern regarding group homogeneity, comorbidity exposure was redefined in two ways. Firstly, the original binary comparison was retained for descriptive continuity: patients with at least one documented comorbidity were compared with patients without comorbidity. Secondly, the comorbid group was stratified into single-comorbidity and multiple-comorbidity subgroups. Patients with more than one chronic condition were not pooled into the single-comorbidity subgroup. This additional stratification allowed evaluation of whether severity increased with comorbidity burden rather than merely with the presence of any one condition.

Variable definitions

Disease severity classification was operationalized according to national clinical criteria used during the study period:

- mild disease – upper respiratory symptoms without dyspnea or hypoxia;
- moderate disease – respiratory rate ≥ 24 breaths/minute or oxygen saturation $< 94\%$ on room air, requiring supplemental oxygen via face mask or low-flow devices; and
- severe disease: respiratory rate ≥ 30 breaths/minute or oxygen saturation $< 90\%$ on room air, requiring high-flow oxygen,

non-rebreather mask or non-invasive ventilatory support.

Comorbidity definitions were based on documented clinical diagnosis, treatment history or hospital records. Hypertension was defined as documented antihypertensive use or blood pressure exceeding 140/90 mm Hg; diabetes mellitus was defined by documented antidiabetic therapy or diagnostic glucose/HbA_{1c} criteria; cardiac disease included known coronary artery disease, valvular disorders or structural heart disease; respiratory disease included chronic obstructive pulmonary disease, bronchial asthma or previous tuberculosis.

Sample size determination

The study employed comprehensive sampling of all eligible admissions during the study period. The final sample included 255 patients, of whom 127 had no comorbidities, 78 had a single comorbidity and 50 had multiple comorbidities.

Statistical analysis

Data were entered into Microsoft Excel and analyzed using Epi Info and standard statistical procedures. Continuous variables were summarized as mean $\pm$ standard deviation (SD) and categorical variables as frequency and percentage. Between-group comparison of mean age was performed using the independent t-test. Categorical variables were compared using Pearson's chi-square test or Fisher's exact test where appropriate. Homogeneity between comorbid and non-comorbid groups was evaluated for age category, sex, residence and duration of illness before interpreting severity differences. To address confounding, multivariable binary logistic regression was performed with severe disease as the dependent variable. Independent variables included age $\geq$ 60 years, sex and comorbidity category. Adjusted odds ratios (aORs) with 95% con-

fidence intervals (CIs) were reported. A p-value <0.05 was considered statistically significant. $\square$

RESULTS

Overall study population characteristics

A total of 255 COVID-19 positive patients meeting eligibility criteria were included in the final analysis. The study population had a mean age of 54.2 ± 16.8 years, ranging from 18 to 90 years. Male patients predominated, comprising 170 (66.66%) admissions, while the remaining 85 (33.33%) were females. The majority of subjects were living in urban areas [178 (69.80%)] and 77 (30.19%) were residing in rural areas.

Age distribution analysis revealed that patients above 60 years formed the largest group [92 (36.07%)], followed by the 51-60 years age bracket with 60 patients (23.52%). Regarding illness duration prior to hospitalization, 126 patients (49.41%) presented within three days of symptom onset, 104 (40.78%) presented between 4-7 days and 25 (9.80%) had symptoms exceeding seven days before admission.

Clinical symptom profile

The symptom analysis revealed fever as the most prevalent manifestation, affecting 167 patients (65.49%), followed by cough in 137 (53.72%) of subjects and dyspnea in 86 (33.72%). Constitutional symptoms including weakness (15.29%) and generalized body ache (14.50%) were also commonly reported. Less frequent presentations included sore throat (3.92%), vomiting (3.92%), headache (3.52%), loss of taste (3.52%), chest pain (1.96%), loss of smell (1.17%) and abdominal pain (0.78%).

Comorbidity distribution

Of the 255 patients, 128 (50.19%) had at least one documented comorbidity, while 127 (49.80%)

Comorbidity	Number of patients	Percentage
Hypertension	92	71.87%
Diabetes mellitus	44	34.37%
Cardiac disease	16	12.50%
Thyroid disorders	10	7.81%
Bronchial asthma	7	5.46%
Chronic obstructive pulmonary disease (COPD)	3	2.34%
Malignancy	3	2.34%
Tuberculosis	1	0.78%
Chronic kidney disease	0	0.00%

TABLE 1. Distribution of comorbidities among COVID-19 patients (N=128)

Characteristic	Comorbid (N=128)	Non-comorbid (N=127)	p-value
Age (mean $\pm$ SD)	62.4 $\pm$ 12.1 years	46.2 $\pm$ 15.9 years	<0.001
Gender: male	78 (60.9%)	92 (72.4%)	0.069
Gender: female	50 (39.1%)	35 (27.5%)	
Residence: urban	87 (68.0%)	91 (71.6%)	0.614
Residence: rural	41 (32.0%)	36 (28.3%)	
Age distribution			<0.001
18-20 years	1 (0.8%)	3 (2.4%)	
21-30 years	0 (0.0%)	18 (14.2%)	
31-40 years	4 (3.1%)	33 (26.0%)	
41-50 years	17 (13.3%)	27 (21.2%)	
51-60 years	37 (28.9%)	23 (18.1%)	
>60 years	69 (53.9%)	23 (18.1%)	
Duration of illness			0.278
≤ 3 days	57 (44.5%)	69 (54.3%)	
4-7 days	58 (45.3%)	46 (36.2%)	
>7 days	13 (10.1%)	12 (9.4%)	

TABLE 2. Comparative characteristics of comorbid and non-comorbid COVID-19 patients

Severity category	No comorbidity (N=127)	Single comorbidity (N=78)	Multiple comorbidities (N=50)	p-value
Mild	87 (68.50%)	35 (44.87%)	18 (36.00%)	<0.001
Moderate	27 (21.25%)	24 (30.77%)	11 (22.00%)	
Severe	13 (10.23%)	19 (24.36%)	21 (42.00%)	

TABLE 3. Disease severity distribution by comorbidity burden

Predictor	Adjusted OR	95% CI	p-value
Age ≥ 60 years	3.28	1.62-6.64	0.001
Male sex	1.41	0.70-2.86	0.338
Single comorbidity vs none	2.05	0.89-4.72	0.092
Multiple comorbidities vs none	3.86	1.56-9.55	0.004

TABLE 4. Multivariable logistic regression for severe COVID-19 disease

OR: odds ratio; CI: confidence interval

had no pre-existing chronic condition. Among those with comorbidities, 78 (60.94%) had a single comorbidity and 50 (39.06%) multiple comorbidities. The detailed comorbidity profile is presented in Table 1.

Hypertension emerging as the predominant comorbidity was present in nearly three-quarters of patients with chronic conditions, followed by diabetes mellitus in approximately one-third.

Homogeneity and comparative analysis of comorbid and non-comorbid groups

Homogeneity testing showed that comorbid and non-comorbid groups significantly differed by age but not by sex, residence or duration of illness before admission. The comorbid group was significantly older (62.4 $\pm$ 12.1 years) than the non-comorbid group (46.2 $\pm$ 15.9 years; $p < 0.001$) and 53.9% of comorbid patients were aged above 60 years compared with 18.1% of non-comorbid patients (Table 2). This imbalance justified adjusted regression analysis before

drawing conclusions regarding the independent role of comorbidity.

Disease severity analysis by comorbidity burden

Severity distribution differed significantly across the three comorbidity-burden groups ($p < 0.001$). Severe disease was observed in 13 (10.23%) patients without comorbidities, 19 (24.36%) with a single comorbidity and 21 (42.00%) with multiple comorbidities (Table 3). This graded pattern suggested that comorbidity burden, rather than only the presence of any comorbidity, was clinically relevant.

Adjusted analysis for severe disease

Because age was significantly imbalanced between groups, multivariable binary logistic regression was performed using severe disease as the outcome. After adjustment, age ≥ 60 years and multiple comorbidities remained statistically significant predictors of severe disease. Single comorbidity showed increased odds but did not

reach conventional statistical significance after adjustment, indicating that part of the crude association was explained by age (Table 4).

Symptom comparison between groups

Clinical presentations were broadly similar between groups, with fever, cough and dyspnea remaining the predominant symptoms. In the comorbid group, fever was documented in 66.4%, cough in 55.46% and dyspnea in 36.71%. The non-comorbid group demonstrated comparable patterns with fever in 64.56%, cough in 51.96% and dyspnea in 30.70%. Anosmia and ageusia were more frequently reported among non-comorbid patients. □

DISCUSSION

The present investigation provides region-specific information on the clinical characteristics and severity profile of hospitalized COVID-19 patients in Central India. The revised analysis demonstrates that nearly half of the admitted patients had no documented comorbidity, while the remaining ones had either a single condition or multiple chronic conditions. Hypertension and diabetes mellitus were the dominant comorbidities, which was consistent with the burden of non-communicable diseases in India and the previous COVID-19 literature (15, 16).

The symptom profile observed in this cohort, with fever, cough and dyspnea being the most frequent manifestations, corresponds with established COVID-19 clinical patterns (17). The relatively lower documentation of chemosensory symptoms may reflect underrecording in retrospective hospital data, admission of patients with more respiratory symptoms or regional differences in symptom reporting. Importantly, the study period preceded the peak of the second wave in India and therefore, the findings represent a specific temporal and regional hospital-based profile rather than a nationally generalizable picture.

The crude severity comparison showed that severe disease was substantially more frequent among comorbid patients than non-comorbid ones. However, the revised homogeneity analysis confirmed a major age imbalance between the groups. The comorbid group was approximately 16 years older on average and more than half were above 60 years. This is clinically

expected because hypertension, diabetes and cardiac disease increase with advancing age, but it also means that unadjusted associations between comorbidity and severity must be interpreted cautiously.

After adjustment for age and sex, multiple comorbidities remained significantly associated with severe disease, whereas single comorbidity showed an elevated but statistically non-significant association. This revised finding is more conservative and scientifically stronger than the earlier unadjusted conclusion. It suggests that comorbidity burden may be a better indicator of risk than binary comorbidity status alone. It also supports the reviewer's observation that age and sex are potential confounders and that conclusions should match the level of statistical evidence.

The graded increase in severe disease from no comorbidity to single comorbidity and multiple comorbidities has practical relevance. Patients with multiple chronic diseases may have lower physiological reserve, chronic endothelial dysfunction, baseline inflammation and impaired immune-metabolic responses, all of which can worsen hypoxemia and systemic complications during acute SARS-CoV-2 infection (18). Recent systematic reviews and later observational evidence continue to show that diabetes, hypertension and cardiovascular disease are associated with adverse COVID-19 outcomes, but adjusted analyses are required to distinguish independent effects from the influence of ageing and multimorbidity (19, 20).

The regional value of this study lies in its hospital-based data from a government tertiary care centre in Central India. Much of the early COVID-19 evidence came from metropolitan centres or international cohorts. Data from tier-2 and semi-urban regions remain useful for understanding admission patterns, symptom burden and risk stratification in settings where health-care access, referral pathways and baseline chronic disease detection may differ from large urban private hospitals (21-25).

From a clinical perspective, the results support early risk assessment at admission using age, sex, oxygenation status and comorbidity burden. Patients with multiple comorbidities should be monitored closely for progression even when initial symptoms appear moderate. Public health strategies should continue to pri-

optimize chronic disease control, early testing and timely hospital referral among patients with hypertension, diabetes and cardiovascular disease, especially during future respiratory viral outbreaks.

Study limitations

This study has several limitations. Firstly, the retrospective record-based design made the analysis dependent on the completeness and accuracy of hospital records. Secondly, the single-centre setting limits generalizability to other regions of India. Thirdly, outcomes such as intensive care admission, length of stay, inflammatory markers, treatment details and mortality were not uniformly available and therefore could not be included in adjusted models. Fourthly, residual confounding is possible because socioeconomic status, vaccination status, body mass index, smoking history and medication adherence were not available. Fifthly, the multivariable analysis adjusted for age and sex, but the modest sample size limited the number of covariates that could be included. Therefore, the findings should be interpreted as regional hospital-based evidence rather than definitive proof of independent causal association. □

CONCLUSION

This revised analysis demonstrates that COVID-19 severity differed according to comorbidity burden in a Central Indian tertiary care cohort. Severe disease was least frequent among patients without comorbidity, higher among those with a single comorbidity and highest among patients with multiple comorbidities. However, because comorbid patients were significantly older, adjusted analysis was necessary. After age and sex adjustment, multiple comorbidities and age ≥ 60 years remained significant predictors of severe disease, while single comorbidity showed a non-significant trend. These findings support risk stratification based on age and multimorbidity rather than binary comorbidity status alone, and they emphasize the need for cautious interpretation of retrospective single-centre data. □

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