Received: 4 July 2021 | Revised: 21 August 2021 | Accepted: 30 August 2021

DOI: 10.1002/jmv.27315

RESEARCH ARTICLE

JOURNAL OF MEDICAL VIROLOGY WILEY

# COVID-19 disease in hospitalized young adults in India and China: Evaluation of risk factors predicting progression across two major ethnic groups

Smriti Panda[1] | Sankanika Roy[2,3] | Rohit K. Garg[4] | Gan Hui[5] | Jack Gorard[6] | Mayank Bhutada[1] | Yuanli Sun[5] | Sushma Bhatnagar[7] | Anant Mohan[8] | Lalit Dar[9] | Mao Liu[10]

[1]Department of Otorhinolaryngology, All India Institute of Medical Sciences, New Delhi, Delhi, India

[2]Department of Neurology, Nottingham University Hospitals, Nottingham, UK

[3]Cardiovascular sciences, Leicester Royal Infirmary, University of Leicester, Leicester, UK

[4]Department of Medicine, All India Institute of Medical Sciences, New Delhi, Delhi, India

[5]Department of Allergy, Zhongnan Hospital of Wuhan University, Wuhan University, Wuhan, Hubei, China

[6]Department of Internal Medicine, Lincoln County Hospital, Lincoln, UK

[7]Department of Onco-Anaesthesia, All India Institute of Medical Sciences, New Delhi, Delhi, India

[8]Department of Pulmonary Medicine, All India Institute of Medical Sciences, New Delhi, Delhi, India

[9]Department of Microbiology, All India Institute of Medical Sciences, New Delhi, Delhi, India

[10]Department of Neurology, Tongji Hospital, Tongji Medical College of Huazhong University of Science and Technology, Wuhan, Hubei, China

**Correspondence**
Mao Liu, Department of Neurology, SUNY Downstate Health Sciences University, 450 Clarkson Avenue, Brooklyn, NY 11203, USA.
Email: liumao1987@gmail.com

## Abstract

Data pertaining to risk factor analysis in coronavirus disease 2019 (COVID-19) is confounded by the lack of data from an ethnically diverse population. In addition, there is a lack of data for young adults. This study was conducted to assess risk factors predicting COVID-19 severity and mortality in hospitalized young adults. A retrospective observational study was conducted at two centers from China and India on COVID-19 patients aged 20–50 years. Regression analysis to predict adverse outcomes was performed using parameters including age, sex, country of origin, hospitalization duration, comorbidities, lymphocyte count, and National Early Warning Score 2 (NEWS2) score at admission. A total of 420 patients (172 East Asians and 248 South Asians) were included. The predictive model for intensive care unit (ICU) admission with variables NEWS2 Category II and higher, diabetes mellitus, liver dysfunction, and low lymphocyte counts had an area under the curve (AUC) value of 0.930 with a sensitivity of 0.931 and a specificity of 0.784. The predictive model for mortality with NEWS2 Category III, cancer, and decreasing lymphocyte count had an AUC value of 0.883 with a sensitivity of 0.903 and a specificity of 0.701. A combined predictive model with bronchial asthma and low lymphocyte count, in contrast, had an AUC value of 0.768 with a sensitivity of 0.828 and a specificity of 0.719 for NEWS2 score (5 or above) at presentation. NEWS2 supplemented with comorbidity profile and lymphocyte count could help identify hospitalized young adults at risk of adverse COVID-19 outcomes.

**KEYWORDS**

COVID-19, lymphocyte, lymphopenia, NEWS, NEWS2, prognostic factors, SARS-CoV-2

## 1 | INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic, which began as a cluster of respiratory ailments in Wuhan, China, has now claimed more than 3 million lives around the world.[1] With a current estimate of over 18 million active cases, there is a significant strain over the healthcare system worldwide.[1] Previous studies have shown that 20.7%–31.4% of the infected individuals require hospitalization, 4.9%–11.5% eventually require management in critical care set-ups, and overall the fatality rates being

1.8%–3.4%.[2] It is anticipated, that with the roll-out of vaccines against the virus, there will be a reduction in hospitalization and/or worse disease outcomes. However, given the current vaccination status with the majority of the elderly (age > 50 years) being vaccinated and, with the arrival of new strains and uncertain efficacy of vaccines against them, the probability of hospitalization and severe COVID-19 outcome, especially in the young adults less than 50 years, remains quite high. Therefore, it would be valuable to have validated risk assessment models to triage and identify infected individuals at risk of developing severe COVID pneumonia for optimum care and resource allocation (utilization). The currently available risk assessment models have multiple limitations. First, most of the data amounting to these risk assessment models have a predominance of the elderly population. Individuals above the age of 65 years have a high frailty index owing to reduced physiological reserve and coexisting comorbidities, rendering the generalizability of the existing models to the younger population imprecise.[3,4] Another major lacuna is most data from single institutions focussed on a particular ethnic group with the absence of external validation performed on an ethnically different cohort.[5–7] Studies performed on COVID-19 positive ethnic minorities in the United States have identified increased rates of hospital admission, intensive care unit (ICU) transfers, and mortality in the younger age groups in ethnic minorities compared to non-Hispanic Whites.[8] This study, therefore, aims to analyze potential risk factors and other disease-related predictors involved in disease progression in hospitalized COVID-19 patients across two major (Indian and Chinese) ethnic groups with a focus primarily on younger adult individuals.

## 2 | MATERIALS AND METHODS

### 2.1 | Study cohorts

This study was conducted across two centers, Zhongnan Hospital of Wuhan University, Wuhan University, Wuhan, China (East Asians)—Center A and All India Institute of Medical Sciences, New Delhi, India (South Asians)—Center B. Data were collected retrospectively. The study duration for the Indian cohort was from April 2020 to November 2020. Data were retrieved retrospectively from the Chinese cohort from January to March 2020. All data were retrieved from respective hospital record systems. Patients with definitive evidence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection on reverse transcription-polymerase chain reaction performed on a nasal swab, sputum, bronchoalveolar lavage, or rectal swab were included in the study. Data were collected only for those patients belonging to the age group between 20 and 50 years and with a history of inpatient hospital stay. The study was performed in accordance with the Declaration of Helsinki. Being a retrospective study, this was exempted from the Institutional Ethical Board of respective centers.

### 2.2 | Outcome

The intent of this study was to descriptively analyze the presentation and progression of COVID-19 infection in hospitalized young adults across different ethnic groups and countries. Secondary outcomes were to investigate the possible association of various modifiable and nonmodifiable risk factors and biochemical parameters (as detailed below) with disease severity and progression.

### 2.3 | Demographic parameters

The following demographic details were captured: age, gender, race, comorbidities, oxygen requirement during the stay, ICU admission, duration of stay, and outcome.

Frequency of comorbidities including cardiovascular diseases (coronary artery disease, stroke), hypertension, diabetes, asthma, kidney dysfunction (acute or chronic kidney disease), liver dysfunction, thyroid diseases (hyperthyroidism or hypothyroidism), cancer was compared between the patients admitted to the two medical centers.

### 2.4 | Physiological, hematologic, and biochemical parameters

The National Early Warning Score 2 (NEWS2) was calculated at the first presentation. The NEWS2 is a scoring system based on physiological parameters which include respiration rate, oxygen saturation, systolic blood pressure, pulse rate, level of consciousness or new confusion, and temperature. The total score, as well as individual scores for the various NEWS2 parameters, were included. NEWS2 was categorized as Category I (Score 0), Category II (Score 1–4), Category III (Score 5–6), and Category IV (Score 7 or higher), the increasing score indicates higher severity based on physiological parameters measurements.

### 2.5 | Statistical analysis

All demographic and clinical continuous parameters were presented as mean and standard deviation for normally distributed data and as median and the first as well as the third percentile values for non-normally distributed data. Additionally, each parameter was tested as an independent variable in a univariate regression analysis with ICU admission, death, or higher NEWS2 score (5 or above) as the outcome. Parameters that were significantly associated with each outcome were further included in a multivariate regression analysis. Nonnormally distributed data were transformed into normally distributed data. The odds ratio (OR) of each parameter was calculated, and the power of the predictive model was evaluated by the area under the receiver operating characteristic curve, sensitivity, and specificity. SPSS statistical software (version 22.0) was used for statistical analysis (significance set as $\alpha < 0.05$).

## 3 | RESULTS

### 3.1 | Demographic data

Patient data of the two centers were presented in Table 1. In total, 420 patients (141 females and 279 males) were included. The median age was 37 years old and the median duration of hospitalization was 11 days. The median lymphocyte count was $1.43 \times 10^9$/L. Out of all patients, 13 (3.1%) had cardiovascular diseases, 39 (9.3%) had hypertension, 40 (9.5%) had diabetes, 14 (3.3%) had kidney dysfunction, 14 (3.3%) had thyroid diseases, 12 (2.9%) had liver dysfunction, 10 (2.4%) had cancer, and 5 (1.2%) had asthma. A total of 74 (17.6%) patients were admitted to the ICU and 18 (4.3%) died during hospitalization. The NEWS2 total score ranged from 0 to 17. Of 284 (67.6%), 107 (25.5%), 17 (4.0%), and 12 (2.9%) patients were categorized into NEWS2 Category I, II, III, and IV, respectively.

**TABLE 1** Demographic, clinical, and hematological data of COVID-19 patients from three university hospitals of three countries

| Parameters | China | India | Both |
|---|---|---|---|
| Age (years) | 37.0 [24, 50] | 36.0 [23.2, 49.8] | 37.0 [24, 50] |
| Gender (female, male) | 88, 84 | 53, 195 | 141, 279 |
| Lymphocyte count ($\times 10^9$/L) | 1.44 [0.64, 2.24] | 1.39 [0.63, 2.05] | 1.43 [0.66, 2.20] |
| Hospital stay (days) | 10 [4.3, 15.8] | 10 [7, 13] | 10 [6, 14] |
| Cardiovascular diseases | 3/172 | 11/248 | 14/420 |
| Hypertension | 16/172 | 23/248 | 39/420 |
| Diabetes | 7/172 | 33/248 | 40/420 |
| Asthma | 0/172 | 5/248 | 5/420 |
| Kidney dysfunction | 2/172 | 12/248 | 14/420 |
| Liver dysfunction | 3/172 | 9/248 | 12/420 |
| Thyroid diseases | 1/172 | 13/248 | 14/420 |
| Cancer | 1/172 | 9/248 | 10/420 |
| ICU admission | 6/172 | 68/248 | 74/420 |
| Death | 2/172 | 16/248 | 18/420 |
| NEWS2 total score | 0.5 [0–17][a] | 0 [0–8][a] | 0 [0–17][a] |
| NEWS2 grading (I, II, III, IV) | 86, 79, 2, 5 | 198, 28, 15, 7 | 284, 107, 17, 12 |

*Note*: NEWS2 scores of Categories I, II, III, and IV correspond to 0, 1–4, 5–6, and 7 or more, respectively.

Significant $p$ values are shown in bold.

Abbreviations: COVID-19, coronavirus disease 2019; ICU, intensive care unit; NEWS2, National Early Warning Score 2.

[a]For NEWS total score minimal and maximal values were shown within the square brackets; for all other data 25 and 75 percentile values were shown within the square brackets.

### 3.2 | Univariate regression analysis with ICU admission as the outcome (Table 2)

Compared with Center A, Center B (OR: 10.03, 95% confidence interval [CI]: [4.24–23.75]; $p < 0.001$) had more patients admitted to ICU during hospital stay. Older age (OR: 1.05, 95% CI: [1.01–1.08]; $p = 0.006$), lower lymphocyte count (OR: 0.28, 95% CI: [0.20–0.39]; $p < 0.001$), diabetes (OR: 8.54, 95% CI: [4.11–17.73]; $p < 0.001$), asthma (OR: 15.09, 95% CI: [1.55–147.19]; $p = 0.020$), kidney dysfunction (OR: 12.91, 95% CI: [2.45–67.94]; $p = 0.003$), and liver dysfunction (OR: 10.75, 95% CI: [3.14–36.76]; $p < 0.001$), and cancer (OR: 4.04, 95% CI: [1.06–15.42]; $p = 0.041$) were all associated with a higher risk of ICU admission. Gender ($p = 0.156$), cardiovascular diseases ($p = 0.398$), hypertension ($p = 0.262$), thyroid diseases (0.248), were not associated with a higher risk of ICU admission. Compared with patients of NEWS2 Category I (Score 0), patients of NEWS2 Category II (Score 1–4, OR: 4.94, 95% CI: [2.62–9.32]; $p < 0.001$), of NEWS2 Category III (Score 5–6, OR: 104.61, 95% CI: [22.27–491.42], $p < 0.001$), and of NEWS2 Category IV (Score 7 or higher, OR: 69.94, 95% CI: [14.25–341.27]; $p < 0.001$) were more likely to be admitted to ICU.

### 3.3 | Multivariate regression analysis with ICU admission as the outcome (Table 3)

Among selected independent variables including age, lymphocyte count, diabetes, asthma, kidney dysfunction, liver dysfunction, cancer, and NEWS2 grading, higher NEWS2 grading (Category II, OR: 3.68, 95% CI: [1.69–7.98]; $p = 0.001$; Category III, OR: 69.11, 95% CI: [13.49–353.96]; $p < 0.001$; Category IV, OR: 68.18, 95% CI: [10.19–456.22]; $p < 0.001$), liver dysfunction (OR: 31.47, 95% CI: [5.09–194.48]; $p < 0.001$), diabetes (OR: 10.42, 95% CI: [3.86–28.16]; $p < 0.001$), cancer (OR: 7.79, 95% CI: [1.46–41.53]; $p = 0.016$), lower lymphocyte count (OR: 0.33, 95% CI: [0.22–0.50]; $p < 0.001$) were associated with a higher risk of ICU admission. The combined predictive model had an area under the curve (AUC) value of 0.930 (95% CI: [0.904–0.956]; $p < 0.001$) with a sensitivity of 0.931 and a specificity of 0.784 (Figure S1).

### 3.4 | Univariate regression analysis with death as the outcome (Table 4)

Compared with Center A, more patients from Center B (OR: 5.86, 95% CI: [1.33–25.84]; $p = 0.019$) died during the hospital stay. Lower lymphocyte count (OR: 0.24, 95% CI: [0.14–0.44]; $p < 0.001$), diabetes (OR: 4.77, 95% CI: [1.59–14.28]; $p = 0.005$), liver dysfunction (OR: 8.73, 95% CI: [2.14–35.58]; $p = 0.002$), and cancer (OR: 13.20, 95% CI: [3.01–57.91]; $p = .001$) were all associated with a higher risk

**TABLE 2** Univariate regression analyses with each demographic, clinical, and hematological data from two university hospitals of two countries as independent variable and ICU admission as the outcome

| Parameters | OR | 95% CI | *p* Value |
|---|---|---|---|
| Country | | | |
| China | 1.00 | / | / |
| India | 10.03 | 4.24–23.75 | **<0.001** |
| Gender | | | |
| Female | 1.00 | / | / |
| Male | / | / | 0.156 |
| Age (years) | 1.05 | 1.01–1.08 | **0.006** |
| Lymphocyte count | 0.28 | 0.20–0.39 | **<0.001** |
| Cardiovascular diseases | / | / | 0.398 |
| Hypertension | / | / | 0.262 |
| Diabetes | 8.54 | 4.11–17.73 | **<0.001** |
| Asthma | 15.09 | 1.55–147.19 | **0.020** |
| Kidney dysfunction | 12.91 | 2.45–67.94 | **0.003** |
| Liver dysfunction | 10.75 | 3.14–36.76 | **<0.001** |
| Thyroid diseases | / | / | 0.248 |
| Cancer | 4.04 | 1.06–15.42 | **0.041** |
| NEWS2 grading | | | |
| Category I | 1.00 | / | / |
| Category II | 4.94 | 2.62–9.32 | **<0.001** |
| Category III | 104.61 | 22.27–491.42 | **<0.001** |
| Category IV | 69.94 | 14.25–341.27 | **<0.001** |

*Note*: NEWS2 scores of Categories I, II, III, and IV correspond to 0, 1–4, 5–6, and 7 or more, respectively.

Significant *p* values are shown in bold.

Abbreviations: CI, confidence interval; ICU, intensive care unit; NEWS2, National Early Warning Score 2; OR, odds ratio.

of death. Gender ($p = 0.797$), older age ($p = 0.065$), cardiovascular diseases ($p = 0.640$), hypertension ($p = 0.249$), asthma (0.082), kidney dysfunction ($p = 0.188$), and thyroid diseases (0.060) were not associated with a higher risk of ICU admission. Compared with patients of NEWS2 Category I (Score 0), patients of NEWS2 Category II (Score 1–4; $p = 0.070$) had similar death risk while patients of NEWS2 Category III (Score 5–6, OR: 38.18, 95% CI: [9.40–155.03]; $p < 0.001$) and NEWS2 Category IV (Score 7 or higher, OR: 23.33, 95% CI: [4.54–119.99]; $p < 0.001$) were more likely to die.

## 3.5 | Multivariate regression analysis with death as the outcome (Table 5)

Among selected independent variables including lymphocyte count, diabetes, liver dysfunction, cancer, and NEWS2 grading, NEWS2 Category III (OR: 22.71, 95% CI: [4.84–106.65]; $p < 0.001$), cancer (OR: 44.44, 95% CI: [5.07–322.66], $p < 0.001$), and lower lymphocyte count (OR: 0.25, 95% CI: [0.12–0.53]; $p < 0.001$) were associated with a higher risk of death. The combined predictive model had an AUC value of 0.883 (95% CI: [0.845–0.921]; $p < 0.001$) with a sensitivity of 0.903 and a specificity of 0.701 (Figure S2).

**TABLE 3** Multivariate regression analysis with selected significant demographic, clinical, and hematological parameters from two university hospitals of two countries as independent variables and with ICU admission as the outcome

| Parameters | OR | 95% CI | *p* Value |
|---|---|---|---|
| NEWS2 grading | | | |
| Category I | | / | / |
| Category II | 3.68 | 1.69–7.98 | **0.001** |
| Category III | 69.11 | 13.49–353.96 | **<0.001** |
| Category IV | 68.18 | 10.19–456.22 | **<0.001** |
| Liver dysfunction | 31.47 | 5.09–194.48 | **<0.001** |
| Diabetes | 10.42 | 3.86–28.16 | **<0.001** |
| Cancer | 7.79 | 1.46–41.53 | **0.016** |
| Lymphocyte count | 0.33 | 0.22–0.50 | **<0.001** |

*Note*: NEWS2 scores of Categories I, II, III, and IV correspond to 0, 1–4, 5–6, and 7 or more, respectively.

Significant *p* values are shown in bold.

Abbreviations: CI, confidence interval; ICU, intensive care unit; NEWS2, National Early Warning Score 2; OR, odds ratio.

## 3.6 | Univariate regression analysis with higher NEWS2 score as the outcome (Table 6)

Lower lymphocyte count (OR: 0.56, 95% CI: [0.43–0.74]; $p < 0.001$), diabetes (OR: 2.25, 95% CI: [1.12–4.53]; $p = 0.023$), asthma (OR: 4.96, 95% CI: [2.24–10.98]; $p < 0.001$), and liver dysfunction (OR: 4.90, 95% CI: [1.25–19.19]; $p = 0.023$) were all associated with higher NEWS scores. Gender ($p = 0.265$), older age ($p = 0.328$), cardiovascular diseases ($p = 0.298$), hypertension ($p = 0.356$), kidney dysfunction ($p = 0.437$), thyroid diseases ($p = 0.971$), and cancer ($p = 0.069$) were not associated with higher NEWS scores.

## 3.7 | Multivariate regression analysis with higher NEWS2 score as the outcome (Table 6)

Among selected independent variables including lymphocyte count, asthma, and liver dysfunction, asthma (OR: 13.55, 95% CI: [1.69–108.54]; $p = 0.014$) and lower lymphocyte count (OR: 0.37, 95% CI: [0.24–0.57]; $p < 0.001$) were associated with higher NEWS2 scores. The combined predictive model had an AUC value of 0.768 (95% CI: [0.664–0.872]; $p < 0.001$) with a sensitivity of 0.828 and a specificity of 0.719 (Figure S3).

**TABLE 4** Univariate regression analyses with each demographic, clinical, and hematological data from two university hospitals of two countries as independent variable and death as the outcome

| Parameters | OR | 95% CI | *p* Value |
|---|---|---|---|
| Country | | | |
| China | 1.00 | / | / |
| India | 5.86 | 1.33–25.84 | **0.019** |
| Gender | | | |
| Female | 1.00 | / | / |
| Male | / | / | 0.625 |
| Age (years) | / | / | 0.065 |
| Lymphocyte count | 0.24 | 0.14–0.44 | **<0.001** |
| Cardiovascular diseases | / | / | 0.640 |
| Hypertension | / | / | 0.249 |
| Diabetes | 4.77 | 1.59–14.28 | **0.005** |
| Asthma | / | / | 0.082 |
| Kidney dysfunction | / | / | 0.188 |
| Liver dysfunction | 8.73 | 2.14–35.58 | **0.002** |
| Thyroid diseases | / | / | 0.060 |
| Cancer | 13.20 | 3.01–57.91 | **0.001** |
| NEWS2 grading | | | |
| Category I | 1.00 | / | / |
| Category II | / | / | 0.070 |
| Category III | 38.18 | 9.40–155.03 | **<0.001** |
| Category IV | 23.33 | 4.54–119.99 | **<0.001** |

*Note*: NEWS2 scores of Categories I, II, III, and IV correspond to 0, 1–4, 5–6, and 7 or more, respectively.

Significant *p* values are shown in bold.

Abbreviations: CI, confidence interval; NEWS2, National Early Warning Score 2; OR, odds ratio.

## 4 | DISCUSSION

This is one of the largest multicentric retrospective cohort studies assessing predictive factors including demographic, biochemical, co-morbidities, and NEWS2 score for severe disease leading to ICU admission and mortality in young adults infected with SARS-CoV-2 below the age of 50 years. A predictive model with variables NEWS2 Category II and higher, diabetes mellitus, abnormal liver function tests, any form of malignancy, and low lymphocytes showed a strong predictive value with high sensitivity and moderate specificity for ICU admission as the primary endpoint. The predictive model designed for mortality as the outcome included NEWS2 Category III, coexisting malignancy, and low lymphocyte count showed a high predictive value with very high sensitivity and moderate–high specificity. A combined predictive model with variables of bronchial asthma, and low lymphocyte count showed a good predictive value for a higher NEWS2 score at presentation.

**TABLE 5** Multivariate regression analysis with selected significant demographic, clinical, and hematological parameters from two university hospitals of two countries as independent variables and with death as the outcome

| Parameters | OR | 95% CI | *p* Value |
|---|---|---|---|
| NEWS2 grading | | | |
| Category I | 1.00 | / | / |
| Category II | / | / | 0.229 |
| Category III | 22.71 | 4.84–106.65 | **<0.001** |
| Category IV | / | / | 0.058 |
| Cancer | 44.44 | 5.07–322.66 | **<0.001** |
| Lymphocyte count | 0.25 | 0.12–0.53 | **<0.001** |

*Note*: NEWS2 scores of Categories I, II, III, and IV correspond to 0, 1–4, 5–6, and 7 or more, respectively.

Significant *p* values are shown in bold.

Abbreviations: CI, confidence interval; NEWS2, National Early Warning Score 2; OR, odds ratio.

In the two predictive models with ICU transfer and mortality as the endpoints, advanced NEWS2 category, low lymphocyte count, and any form of malignancy emerged as common consistent independent variables. In fact, in the combined predictive model asthma and low lymphocyte count emerged as a harbinger of a high NEWS2 score on admission. Huang et al.[9] performed a meta-analysis involving 3099 patients from 24 studies to assess risk factors predicting adverse outcomes in COVID-19. Low lymphocyte emerged as the single independent predictor for mortality, ICU admission, severe disease, and acute respiratory distress syndrome. Similar outcomes were obtained when a lymphopenia cut-off of less than 1100 cell/μl was used. The greater impact of lymphopenia was noticed in a subgroup analysis of young patients (age cut-off 55 years). This disparity based on age cut-off was attributed to the relative "immune non-reactivity" in the elderly population. As previously alluded to, this meta-analysis also collated data predominantly from Chinese studies. Tan et al.[10] have studied the kinetics of lymphopenia in COVID-19, namely lymphocyte count at Days 10–12 and Days 17–19. The subgroup of patients that experienced mortality, had a lymphocyte count of 10% at the first time point which later dropped to less than 5% at the second time point. Another parameter of interest related to lymphopenia in COVID-19 is the neutrophil to lymphocyte ratio in predicting adverse COVID-19 outcomes.[11,12] In the study by Zheng et al.[12] neutrophil to lymphocyte ratio with a cut-off of six, held optimum discriminative power in identifying the at-risk group. Another study from China, however, identified neutrophil to lymphocyte ratio of 2.69 as a predictor of systemic inflammatory state in a cohort of 352 COVID-19 patients.[13]

A comprehensive literature search revealed many retrospective studies which evaluated prognostic factors for adverse COVID-19 outcomes.[6,14,15] Factors that emerged to be of prognostic significance in these studies were: age, cerebrovascular disease, chronic kidney disease, malignancy, bacterial or fungal coinfection,

**TABLE 6** Univariate and multivariate regression analyses with each demographic, clinical, and hematological data from two university hospitals of two countries as the independent variable and NEWS2 score[a] as the outcome

| Univariate analysis | | | |
|---|---|---|---|
| **Parameters** | **OR** | **95% CI** | ***p* Value** |
| Country | | | |
| China | 1.00 | / | / |
| India | / | / | 0.056 |
| Gender | | | |
| Female | 1.00 | / | / |
| Male | / | / | 0.265 |
| Age (years) | / | / | 0.328 |
| Lymphocyte count | 0.37 | 0.24–0.57 | **<0.001** |
| Cardiovascular diseases | / | / | 0.298 |
| Hypertension | / | / | 0.356 |
| Diabetes | 3.26 | 1.23-8.63 | **0.018** |
| Asthma | 14.41 | 1.95–106.29 | **0.009** |
| Kidney dysfunction | / | / | 0.437 |
| Liver dysfunction | 4.90 | 1.25–19.19 | **0.023** |
| Thyroid diseases | / | / | 0.971 |
| Cancer | / | / | 0.067 |
| Multivariate analysis | | | |
| Asthma | 13.55 | 1.69, 108.54 | **0.014** |
| Lymphocyte count | 0.37 | 0.24, 0.57 | **<0.001** |

*Note*: Significant *p* values are shown in bold.

Abbreviations: CI, confidence interval; NEWS2, National Early Warning Score 2; OR, odds ratio.

[a]For NEWS2 Scores, 0–4 were defined as low and 5 or more were defined as high.

lymphopenia, thrombocytopenia, neutrophilia, raised C-reactive protein, fibrinogen, interleukin 6, and D-dimer. However, the target population of our present study was adults aged less than 50 years. Hence, results from the literature quoted above cannot be compared with our results. We were able to identify one study from China conducted on patients in the age group between 18 and 50 years ($n = 123$; comparable to our study).[3] Predictive factors for adverse COVID-19 outcomes were age, temperature, anorexia, total leukocyte count, neutrophil count, platelet count, lymphocyte count, C-reactive protein, aspartate transaminase, creatinine kinase, serum albumin, and serum fibrinogen levels. One of the limitations of our study was the nonavailability of sufficient biochemical parameters from the centers. Hence, these parameters could not be included in the prediction model.

Apart from lymphopenia, disease severity measured as NEWS2 emerged as an important prognostic parameter in our study. There is considerable contention surrounding the role of NEWS2 as a prognostic or triage tool in COVID-19. Carr et al.[16] designed a nomogram with a multi-institutional training cohort from United Kingdom and external validation performed on centers from Norway as well as Wuhan. Predictive model designed with NEWS2 +age had poor to moderate discrimination of severe COVID-19 at Day 14. They also designed a supplemental NEWS2 model, where NEWS2 scores were supplemented with $FiO_2$, serum urea, C-reactive protein, glomerular filtration rate, neutrophil count, and neutrophil–lymphocyte ratio. This supplemental NEWS model had an AUC of 0.735. However, our predictive model using NEWS2 score and other factors described above and based on data from two different countries, revealed a higher predictive value for ICU admission and mortality. Richardson et al.[17] in their retrospective cohort of 620 patients, identified NEWS2 score within 24 h of admission to be predictive of mortality risk in COVID-19. The authors have emphasized the added role of serial NEWS2 score assessment, rather than relying only on the baseline value. Of the various scoring systems available for prognostication in a patient admitted to a critical care unit, NEWS was found to have better predictive ability than systemic inflammatory response syndrome and quick sequential organ failure assessment.[18] However, one should be cautious in utilizing only the NEWS2 score for decision making as it is not considered as a good predictor for hypoxemia.[5] Respiratory rate oxygenation index ($SaO_2$/$FiO_2$/respiratory rate) better predicts the need for intubation than NEWS2 scores.[5]

The COVID-19 pandemic is a huge burden for the entire healthcare system throughout the world. Vaccination roll-out provides us with a ray of hope; however, it is still uncertain as to how efficient the vaccines will be and for how long, especially against the new strains that continue to appear. Currently, the younger adults who are yet to be fully vaccinated remain vulnerable and are most prone to hospitalization. Our predictive models can be utilized for future risk stratification and optimization of resource allocation thus help reduce the burden on the healthcare system.

## 4.1 | Strength and limitation

As previously mentioned, this is one of the largest cohorts of young, hospitalized adults evaluating prognostic factors in two major ethnic groups. The limitation lies in the retrospective study design and lack of prospective validation of the prognostic model. Certain laboratory parameters which have an established role in COVID-19 disease severity prognostication could not be included in the model due to lack of data from our centers. Similarly, missing data related to body mass index, smoking status hindered our investigation into its possible role in predicting severity or mortality. Additionally, heterogeneous therapeutic options could have influenced the prognosis of individual patients from China and India and were not included as variables in our statistical analysis. Coherent therapies would have made the interpretation of our findings more convincing. Moreover, there were baseline differences in the admission criteria of the two centers owing to the dynamic nature of the pandemic. This again

differed within the individual centers at different time points during the pandemic. This discrepancy and the lack of duration between symptom onset and hospitalization might have affected our statistical model including both Chinese and Indian patients.

## 5 | CONCLUSION

NEWS2 scores supplemented with lymphocyte count and data pertaining to coexisting diabetes, hepatic impairment, or coexisting malignancy were found to have acceptable discriminative power in identifying individuals at risk for ICU admission or severe COVID-19 and mortality in hospitalized young patients. This model was found to be predictive across two ethnicities in this large cohort study.

### AUTHOR CONTRIBUTIONS

Mao Liu contributed to data analysis. Mao Liu, Sankanika Roy, and Smriti Panda contributed to manuscript writing. Rohit K. Garg and Jack Gorard contributed to manuscript revision. Gan Hui, Mayank Bhutada, Yuanli Sun, Smriti Panda, and Lalit Dar contributed to data acquisition. Mao Liu, Sankanika Roy, Sushma Bhatnagar, Anant Mohan, and Smriti Panda contributed to the study design. Sankanika Roy was responsible for the intellectual content of the study. All authors reviewed and approved the final version.

### DATA AVAILABILITY STATEMENT

Individual patient data can be made available by the corresponding author on request.

### ORCID

*Rohit K. Garg* http://orcid.org/0000-0001-8203-0323
*Gan Hui* http://orcid.org/0000-0002-4960-1507
*Mao Liu* https://orcid.org/0000-0002-1948-0337

### REFERENCES

1. COVID Live Update. 161,470,821 Cases and 3,351,157 deaths from the coronavirus—Worldometer [Internet]; 2021. https://www.worldometers.info/coronavirus/
2. Zhao Q, Meng M, Kumar R, et al. Lymphopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: a systemic review and meta-analysis. *Int J Infect Dis*. 2020;96:131-135.
3. Zhou C, Huang Z, Tan W, et al. Predictive factors of severe coronavirus disease 2019 in previously healthy young adults: a single-center, retrospective study. *Respir Res*. 2020;22(21):157.
4. Zhou Z, Zhang M, Wang Y, et al. Clinical characteristics of older and younger patients infected with SARS-CoV-2. *Aging*. 2020;12:11296-11305.
5. Prower E, Grant D, Bisquera A, et al. The ROX index has greater predictive validity than NEWS2 for deterioration in Covid-19. *EClinicalMedicine*. 2021;35:100828.
6. Zheng Z, Peng F, Xu B, et al. Risk factors of critical & mortal COVID-19 cases: a systematic literature review and meta-analysis. *J Infect*. 2020;81(2):e16-e25.
7. Zhang C, Qin L, Li K, et al. A novel scoring system for prediction of disease severity in COVID-19. *Front Cell Infect Microbiol*. 2020;10:318.
8. Bassett MT, Chen JT, Krieger N. Variation in racial/ethnic disparities in COVID-19 mortality by age in the United States: a cross-sectional study. *PLOS Med*. 2020;17:e1003402.
9. Huang I, Pranata R. Lymphopenia in severe coronavirus disease-2019 (COVID-19): systematic review and meta-analysis. *J Intensive Care*. 2020;8:36.
10. Tan L, Wang Q, Zhang D, et al. Lymphopenia predicts disease severity of COVID-19: a descriptive and predictive study. *Signal Transduct Target Ther*. 2020;5:33.
11. Liu J, Liu Y, Xiang P, et al. Neutrophil-to-lymphocyte ratio predicts critical illness patients with 2019 coronavirus disease in the early stage. *J Transl Med*. 2020;18:206.
12. Zheng Y, Zhang Y, Chi H, et al. The hemocyte counts as a potential biomarker for predicting disease progression in COVID-19: a retrospective study. *Clin Chem Lab Med*. 2020;58:1106-1115.
13. Zeng ZY, Feng SD, Chen GP, Wu JN. Predictive value of the neutrophil to lymphocyte ratio for disease deterioration and serious adverse outcomes in patients with COVID-19: a prospective cohort study. *BMC Infect Dis*. 2021;21:80.
14. Zhang L, Hou J, Ma FZ, Li J, Xue S, Xu ZG. The common risk factors for progression and mortality in COVID-19 patients: a meta-analysis. *Arch Virol*. 2021;166:1-17.
15. Zou L, Dai L, Zhang Y, et al. Clinical characteristics and risk factors for disease severity and death in patients with coronavirus disease 2019 in Wuhan, China. *Front Med*. 2020;7:532.
16. Carr E, Bendayan R, Bean D, et al. Evaluation and improvement of the National Early Warning Score (NEWS2) for COVID-19: a multi-hospital study. *BMC Med*. 2021;19(1):23.
17. Richardson D, Faisal M, Fiori M, Beatson K, Mohammed M. Use of the first National Early Warning Score recorded within 24 hours of admission to estimate the risk of in-hospital mortality in unplanned COVID-19 patients: a retrospective cohort study. *BMJ Open*. 2021;11:e043721.
18. Jang JG, Hur J, Hong KS, Lee W, Ahn JH. Prognostic accuracy of the SIRS, qSOFA, and NEWS for early detection of clinical deterioration in SARS-CoV-2 infected patients. *J Korean Med Sci*. 2020;35(25):e234.

### SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

**How to cite this article:** Panda S, Roy S, Garg RK, et al. COVID-19 disease in hospitalised young adults in India and China: evaluation of risk factors predicting progression across two major ethnic groups. *J Med Virol*. 2022;94:272-278. https://doi.org/10.1002/jmv.27315