Ther Adv Infectious Dis
2021, Vol. 8: 1–12
DOI: 10.1177/20499361211040325



# Impact of preemptive hospitalization on health outcomes at the temporary COVID-19 hospital in Mexico City: a prospective observational study

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***Abstract***

**Introduction:** In response to the evolution of the coronavirus disease 2019 (COVID-19) pandemic, the admission protocol for the temporary COVID-19 hospital in Mexico City has been updated to hospitalize patients preemptively with an oxygen saturation ($SpO_2$) of >90%.

**Methods:** This prospective, observational, single-center study compared the progression and outcomes of patients who were preemptively hospitalized *versus* those who were hospitalized based on an $SpO_2$ ⩽90%. We recorded patient demographics, clinical characteristics, COVID-19 symptoms, and oxygen requirement at admission. We calculated the risk of disease progression and the benefit of preemptive hospitalization, stratified by CALL Score: age, lymphocyte count, and lactate dehydrogenase (<8 and ⩾8) at admission.

**Results:** Preemptive hospitalization significantly reduced the requirement for oxygen therapy (odds ratio 0.45, 95% confidence interval 0.31–0.66), admission to the intensive care unit (ICU) (0.37, 0.23–0.60), requirement for invasive mechanical ventilation (IMV) (0.40, 0.25–0.64), and mortality (0.22, 0.10–0.50). Stratification by CALL score at admission showed that the benefit of preemptive hospitalization remained significant for patients requiring oxygen therapy (0.51, 0.31–0.83), admission to the ICU (0.48, 0.27–0.86), and IMV (0.51, 0.28–0.92). Mortality risk remained significantly reduced (0.19, 0.07–0.48).

**Conclusion:** Preemptive hospitalization reduced the rate of disease progression and may be beneficial for improving COVID-19 patient outcomes.

***Keywords:*** COVID-19, SARS-CoV-2, Mexico, preemptive hospitalization, temporary hospital, pulse oximetry, HFNC, IMV, CALL score

Received: 7 June 2021; revised manuscript accepted: 30 July 2021.

## Introduction

As of 20 May 2021, there have been over 163.8 million confirmed coronavirus disease 2019 (COVID-19) cases globally, of which more than 65.1 million cases have been detected in the Americas.[1] In Mexico, more than 2.3 million COVID-19 cases have been confirmed as of 20 May 2021, with more than 220,000 patient deaths reported due to COVID-19.[2] Even though the pandemic has been ongoing since March

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2020, there are still no established standards of care being applied across the globe.[3] At present, the Government of Mexico has applied pandemic management practices based on the recommendations of the World Health Organization (WHO).[3] The WHO approach is dependent on disease severity, with hospitalization generally reserved for severely ill patients; this has been recommended primarily to avoid overburdening healthcare systems. Venous thromboembolism prophylaxis and antithrombotic therapy are started for these patients, although this is dependent on contraindications.

To reduce the burden on healthcare facilities as well as mitigate the impact of the COVID-19 pandemic in Mexico City's metropolitan area, a synergistic public–private partnership among a group of foundations, the Government of Mexico City, and the National Autonomous University of Mexico, funded, designed, developed, and currently operate an intermediate-care, dedicated COVID-19 hospital in the heart of Mexico City. This was made possible by rapidly converting the largest convention center in Latin America into a temporary hospital along with the concomitant development of a referral network that comprises dedicated respiratory triage community centers and 40 federal and state primary care clinics and hospitals. The operations of the temporary COVID-19 hospital (TCH) include a streamlined process of admission, treatment, clinical monitoring, discharge, and household follow-up.

The TCH is dedicated to patients with a mild or moderate severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and who require oxygen therapy. Admission is only by referral through our network of dedicated respiratory triage community centers, hospitals, and primary care centers. With a continually evolving pandemic and the steady release of newly emerging data related to this illness, it has been necessary to update and adapt the management and care protocols used in the TCH. Accordingly, the TCH protocol of referral and admission was revised to provide a preemptive approach to hospitalization for patients with COVID-19.

Preemptive hospitalization aims to prevent progression to severe disease, reduce the onset of complications, and improve patient outcomes. Furthermore, by ensuring a hospital stay during the period of contagion, this approach is likely to prevent spread in the community. Thus, rather than admitting patients with an oxygen saturation ($SpO_2$) level of $\leqslant$90%, referred patients are now being admitted based on $SpO_2$ >90%, as measured by pulse oximetry. This $SpO_2$ level also takes into consideration the geographical and atmospheric factors of Mexico City due to its high altitude (approximately 2250 m above sea level).[4] In this prospective observational study, we report our analysis and outcomes of preemptive hospitalization of patients with COVID-19 who were referred and admitted to the TCH in Mexico City. Furthermore, we compare these patients against those who were admitted with an $SpO_2$ $\leqslant$90% according to the previous protocol for referral to the TCH.

## Methods

### *Study design*

This prospective, observational, single-center study was conducted between 1 June 2020 and 6 November 2020 at the TCH in Mexico City. This study aimed to compare the progression and outcomes between patients who underwent preemptive hospitalization [hereafter known as the preemptive hospitalization (PH) group] and patients who did not undergo preemptive hospitalization [hereafter known as the non-preemptive hospitalization (NPH) group]. The objective was to compare hospitalized patients' characteristics and outcomes by stratifying both groups using a comorbidities, age, lymphocyte count, and lactate dehydrogenase (CALL) score cut-off of <8 and $\geqslant$8 at admission, which represents a moderate risk of disease.[5]

This study adhered to the Declaration of Helsinki as well as local laws and regulations. The need for informed consent was waived as the data were collected retrospectively and deidentified prior to analysis. The study protocol was approved by an independent ethical review board at the National Autonomous University of Mexico (FM/DI/099/2020).

### *Patients*

The analysis included information from all men and non-pregnant women aged $\geqslant$18 years, referred from community respiratory triage centers, with a confirmed COVID-19 diagnosis by polymerase chain reaction (PCR), who were admitted to the

TCH from 1 June 2020 and discharged by 6 November 2020, without a history of hospitalization for COVID-19, and who had known outcomes and complete laboratory data. We excluded information from those patients without an advance directive document that permitted transfer to the TCH, pregnant women, patients who refused the prescribed treatment, and those with incomplete outcome assessment data.

### *Procedures and treatment*

On admission, patients underwent a physical examination and routine laboratory tests, including hematology, blood chemistry, arterial blood gas analysis, D-dimer, and ferritin.[6] The triage screening of patients on arrival was conducted using the national early warning score (NEWS), a scoring method based on physiological parameters that allows the standardized assessment of acute-illness severity.[7] A green status (NEWS $<5$) indicates that patients are either provided with regular follow-up by a general practitioner, or, during the early stage of the disease, are hospitalized to prevent spread in the community. An orange status (NEWS 5 or 6) indicates the patient has symptoms of concern and requires a specialist's priority care. A red status (NEWS $>6$) indicates a severe condition, and patients are immediately provided with respiratory therapy and are either admitted for intensive care or counter-referred to another hospital.

The operational definition of preemptive hospitalization was based on the following criteria: COVID-19 diagnosis as confirmed by PCR and with an $SpO_2$ $>90\%$ as measured by pulse oximetry. Furthermore, the TCH also used the CALL score to predict the risk of progression in patients with COVID-19 pneumonia.[5] For this analysis, patients with a CALL score $>8$ were considered at higher risk of progression, and those with a CALL score $<8$ were deemed to have a lower risk of progression. The treatment prescribed for hospitalized patients at the TCH follows the Government of Mexico's recommendations and is focused on the control of comorbidities, oxygen therapy, anticoagulation, and immunomodulation.[3]

### *Data sources and variables*

We collected data from patient medical charts and the COVID360 Digital Health platform. We evaluated the following variables: demographics and clinical characteristics of patients at admission; respiratory status at admission [i.e. whether patients required supplemental oxygen, use of high-flow nasal cannula (HFNC), bilevel positive airway pressure (BiPAP), or invasive mechanical ventilation (IMV)]; treatment prescribed at admission; signs and symptoms at admission; and laboratory test results. We also routinely evaluated patients' NEWS,[7] CALL score,[5] and Charlson comorbidity index.[8] Hospitalization outcomes included the timing of symptom onset before admission, use of HFNC, admission to the intensive care unit (ICU), length of hospital stay, and clinical outcome.

### *Statistical methods*

The sample size considered all patients admitted to the TCH who met the inclusion criteria during the study period. For descriptive group comparisons, we used a two-sided Student's *t*-test or the Wilcoxon rank-sum test for quantitative variables and Fisher's exact test or chi-square test for categorical variables, depending on the variable distribution.

To evaluate the impact of preemptive hospitalization on patient outcomes we used a multiple logistic regression model and adjusted by sex, age, diabetes, hypertension, obesity, prior dexamethasone use, D-dimer levels, and ferritin levels to control for differences between groups at the time of hospitalization admission. We also stratified patients by risk of progression using the CALL score at admission ($<8$ points and $\geqslant 8$ points). We reported odds ratios (ORs) with 95% confidence intervals (CIs) for different hospitalization outcomes and a *p*-value of $<0.05$ was considered statistically significant. Statistical analysis was conducted using STATA version 15 (StataCorp LLC, Texas, USA) and R package version 1.3.1073.

## Results

### *Patients*

A total of 2265 patients were included, of which 1988 were preemptively hospitalized ($SpO_2$ $>90\%$), and 277 were hospitalized ($SpO_2 \leqslant 90\%$). In the PH group, there were significantly more women (53.1% *versus* 38.6%; $p<0.0001$) and patients were significantly younger (median age 48 *versus* 53 years; $p<0.0001$) compared with the NPH group (Table 1).

**Table 1.** Patient demographics at admission.

| Characteristic | Total | Preemptive hospitalization | Non-preemptive hospitalization | *p*-Value |
|---|---|---|---|---|
| | ***N*** **= 2265** | ***n*** **= 1988 (87.8%)** | ***n*** **= 277 (12.2%)** | |
| Sex, *n* (%) | | | | |
| Female | 1162 (51.3) | 1055 (53.1) | 107 (38.6) | <0.0001 |
| Male | 1103 (48.7) | 933 (46.9) | 170 (61.4) | |
| Age (years), median (IQR) | 49 (37–58) | 48 (36–57) | 53 (45–63) | <0.0001 |
| Age >60 years | 446 (19.7) | 365 (18.4) | 81 (29.2) | <0.0001 |
| BMI, *n* (%) | | | | |
| Normal | 390 (17.2) | 350 (17.6) | 40 (14.4) | 0.14 |
| Overweight | 849 (37.5) | 744 (37.4) | 105 (37.9) | |
| Obese | 851 (37.6) | 730 (36.7) | 121 (43.7) | |
| No record | 175 (7.7) | 164 (8.3) | 11 (4.0) | |
| Active smoking, *n* (%) | 680 (30.0) | 580 (29.2) | 100 (36.1) | 0.004 |
| Active alcoholism, *n* (%) | 831 (36.7) | 717 (36.1) | 114 (41.2) | 0.05 |
| Oxygen saturation (%) | 93.6 ± 3.2 | 94.5 ± 1.8 | 87.6 ± 4.3 | <0.0001 |
| Respiratory rate (breaths per minute) | 20.4 ± 3.3 | 20.3 ± 3.1 | 21.5 ± 4.5 | <0.0001 |
| Heart rate (bpm) | 82.2 ± 14.8 | 81.9 ± 14.8 | 84.1 ± 14.3 | 0.02 |
| Body temperature | 36.6 ± 1.4 | 36.6 ± 1.5 | 36.5 ± 0.4 | 0.01 |
| Systolic blood pressure (mmHg) | 121.1 ± 15.6 | 121.2 ± 15.7 | 120.3 ± 15.2 | 0.29 |
| Diastolic blood pressure (mmHg) | 76.3 ± 10.8 | 76.4 ± 10.8 | 75.4 ± 10.4 | 0.12 |
| Occupation, *n* (%) | | | | |
| Employed | 1418 (62.6) | 1234 (62.1) | 184 (66.4) | 0.02 |
| Unemployed | 170 (7.5) | 148 (7.4) | 22 (7.9) | |
| Retired | 126 (5.6) | 105 (5.3) | 21 (7.6) | |
| Disability | 3 (0.1) | 3 (0.2) | 0 | |
| Nursing home resident | 341 (15.1) | 312 (15.7) | 29 (10.5) | |
| Student | 81 (3.6) | 79 (4.0) | 2 (0.7) | |
| Other | 120 (5.3) | 101 (5.1) | 19 (6.9) | |
| No record | 6 (0.3) | 6 (0.3) | 0 | |

Data are mean ± standard deviation unless otherwise stated.
BMI, body mass index; bpm, beats per minute; IQR, interquartile range.

Analysis of risk factors for COVID-19 progression showed that there were significantly fewer patients in the PH group who were >60 years of age (18.4% *versus* 29.2%) and had ⩾1 point in the Charlson comorbidity index [low risk (1–2 points): 33.7% *versus* 40.4%; high risk (⩾3 points): 4.7% *versus* 11.6%], and patients in the PH group had lower CALL scores (6.4 *versus* 7.7) compared with the NPH group (all $p < 0.0001$) (Table 2). Patients in the PH group were also significantly more likely than those in the NPH group to have a NEWS <5 (80.1% *versus* 70.0%), whereas patients in the PH group were significantly less likely to have a NEWS of 5 or 6 (12.3% *versus* 18.8%, respectively), or a score of ⩾7, (2.7% *versus* 8.7%, respectively) than those in the NPH group (all $p < 0.0001$).

Furthermore, significantly more patients in the NPH group had not received any treatment prior to admission compared with the PH group (57.0% *versus* 44.3%; $p < 0.0001$) (Table 2). Of note, 36.3% ($n = 821$) of patients overall were prescribed steroids before arriving at the triage centers; significantly more patients in the PH group received steroids than in the NPH group (37.1% *versus* 30.0%; $p = 0.02$).

### *Respiratory status at admission*

At admission, it was observed that significantly fewer patients in the PH group required oxygen supplementation compared with the NPH group (45.4% *versus* 80.9%; $p < 0.0001$) (see Supplemental Table 1 online). Compared with the NPH group, the PH group also had significantly fewer patients receiving oxygen supplementation by simple nasal cannula (40.4% *versus* 59.6%), simple mask (1.5% *versus* 3.3%), reservoir mask (1.2% *versus* 2.9%), or HFNC (2.3% *versus* 14.8%) (all $p < 0.0001$). One patient in the PH group received BiPAP therapy, and one patient in the NPH group received IMV at admission.

### *Signs and symptoms of patients with COVID-19*

The most common symptoms (>40%) of patients referred from the triage centers were headache (59.3%), cough (55.9%), myalgia (51.4%), fever (46.7%), and pharyngodynia (40.3%), as shown in Supplementary Table 2 online. Most of these symptoms were significantly more common in the NPH group, including cough (65.7% *versus* 54.5%; $p < 0.0001$), fever (60.3% *versus* 44.8%; $p < 0.0001$), myalgia (58.1% *versus* 50.4%; $p = 0.02$), and arthralgia (45.9% *versus* 37.2%; $p < 0.01$).

### *Laboratory test results at admission*

The main laboratory test results obtained from the referred patients at the time of admission showed that the absolute lymphocyte count in the PH group was significantly higher than that in the NPH group ($1452.3 \pm 702.7$ *versus* $1085.7 \pm 512.8$; $p < 0.0001$) (Table 3). Furthermore, a higher proportion of patients in the NPH group had lymphocyte counts <18% (55.3% *versus* 33.4%; $p < 0.0001$) as well as platelet counts $<150 \times 10^3/\mu L$ (16.4% *versus* 10.8%; $p < 0.01$) compared with the PH group. A higher proportion of patients in the NPH group also had elevated lactate dehydrogenase (LDH) levels (>233 UI/L) compared with the PH group (52.9% *versus* 27.9%; $p < 0.0001$). Significant differences were also noted between different levels of D-dimer [500–1000 ng/mL, 27.3% *versus* 22.2%; >1000 to <1500 ng/mL, 8.2% *versus* 7.7%; and >1500 ng/mL, 12.9% *versus* 6.4% (all $p < 0.0001$)] and ferritin [>336.2 µg/dL, 52.2% *versus* 33.5% ($p < 0.0001$)] in the NPH and PH groups, respectively.

### *Hospitalization outcomes*

Patients in the NPH group had significantly longer hospital stays than those in the PH group (13.4 days *versus* 10.5 days; $p < 0.0001$) (Table 4). Furthermore, more patients in the NPH group required HFNC (33.2% *versus* 10.7%; $p < 0.0001$), were transferred to the ICU (16.3% *versus* 5.5%; $p < 0.0001$), required IMV (15.5% *versus* 5.3%; $p < 0.0001$), and had higher mortality rates (6.9% *versus* 1.4%; $p < 0.0001$) compared with patients in the PH group. The most common causes of death (⩾10%) were septic shock (37.0% *versus* 36.8%), acute respiratory failure syndrome (18.5% *versus* 26.3%), and viral pneumonia (11.1% *versus* 10.5%), respectively.

### *Hospitalization outcomes by progression risk*

Patients with a CALL score ⩾8 were at a significantly greater risk of disease progression, requiring HFNC, admission to ICU, requiring IMV,

**Table 2.** Clinical characteristics at admission.

| Characteristic | Total | Preemptive hospitalization | Non-preemptive hospitalization | *p*-Value |
|---|---|---|---|---|
| | ***N*** **= 2265** | ***n*** **= 1988 (87.8%)** | ***n*** **= 277 (12.2%)** | |
| NEWS at admission | 3.1 ± 1.8 | 3.0 ± 1.7 | 4.1 ± 1.9 | <0.0001 |
| Green, *n* (%) | 1786 (78.9) | 1592 (80.1) | 194 (70.0) | <0.0001 |
| Yellow, *n* (%) | 296 (13.1) | 244 (12.3) | 52 (18.8) | |
| Red, *n* (%) | 77 (3.4) | 53 (2.7) | 24 (8.7) | |
| CALL score at admission | 6.6 ± 2.4 | 6.4 ± 2.4 | 7.7 ± 2.4 | <0.0001 |
| Comorbidities, *n* (%) | | | | |
| Diabetes mellitus | 525 (23.2) | 435 (21.9) | 90 (32.5) | <0.0001 |
| Uncontrolled diabetes mellitus[a] | 275 (52.4) | 232 (53.3) | 43 (47.8) | 0.34 |
| Hypertension | 592 (26.1) | 494 (24.9) | 98 (35.4) | <0.0001 |
| Uncontrolled hypertension[b] | 135 (6.0) | 118 (5.9) | 17 (6.1) | 0.16 |
| Charlson index, *n* (%) | | | | |
| Absence (0 points) | 1358 (60.0) | 1225 (61.6) | 133 (48.0) | <0.0001 |
| Low comorbidity (1–2 points) | 781 (34.5) | 669 (33.7) | 112 (40.4) | |
| High comorbidity (⩾3 points) | 126 (5.6) | 94 (4.7) | 32 (11.6) | |
| Days from symptom onset to admission | 7.5 ± 5.0 | 7.3 ± 5.0 | 8.6 ± 4.9 | <0.0001 |
| Treatment prior to admission, *n* (%) | | | | |
| None | 1038 (45.8) | 880 (44.3) | 158 (57.0) | <0.0001 |
| Hydroxychloroquine | 11 (0.5) | 10 (0.5) | 1 (0.4) | 0.75 |
| Chloroquine | 8 (0.4) | 7 (0.4) | 1 (0.4) | 0.98 |
| Azithromycin | 313 (13.8) | 259 (13.0) | 54 (19.5) | <0.01 |
| Lopinavir/ritonavir | 1 (0) | 1 (0.1) | 0 | 1 |
| Steroid treatment | 821 (36.3) | 738 (37.1) | 83 (30.0) | 0.02 |

Data are mean ± standard deviation unless otherwise stated.
[a]Uncontrolled diabetes mellitus was defined as a random blood glucose level of >10 mmol/L.
[b]Uncontrolled hypertension was defined as >140 mmHg systolic blood pressure and >100 mmHg diastolic blood pressure.
CALL, comorbidities, age, lymphocyte count, and lactate dehydrogenase; NEWS, national early warning score.

**Table 3.** Laboratory results of patients at admission.

| | Total | Preemptive hospitalization | Non-preemptive hospitalization | *p*-Value |
|---|---|---|---|---|
| | ***N*** **= 2265** | ***n*** **= 1988** | ***n*** **= 277** | |
| Lymphocytes (%), *n* = 2114 | 22.9 ± 11.1 | 23.6 ± 11.0 | 17.9 ± 10.0 | <0.0001 |
| <18%, *n* (%) | 764 (36.1) | 619 (33.4) | 145 (55.3) | <0.0001 |
| Absolute lymphocyte, *n* = 2114 | 1406.9 ± 692.6 | 1452.3 ± 702.7 | 1085.7 ± 512.8 | <0.0001 |
| ⩾800 per µL, *n* (%) | 1701 (80.5) | 1521 (82.1) | 180 (68.7) | <0.0001 |
| 400–<800 per µL, *n* (%) | 356 (16.8) | 289 (15.6) | 67 (25.6) | <0.0001 |
| <400 per µL, *n* (%) | 57 (2.7) | 42 (2.3) | 15 (5.7) | <0.0001 |
| Platelets ($10^3$/µL), *n* = 2114 | 240.6 ± 88.2 | 241.1 ± 86.4 | 237.1 ± 99.7 | 0.05 |
| <150 × $10^3$/µL, *n* (%) | 243 (11.5) | 200 (10.8) | 43 (16.4) | 0.008 |
| Alkaline phosphatase (IU/L), *n* = 1694 | 87.4 ± 41.2 | 88 ± 42.7 | 83.4 ± 29.1 | 0.35 |
| Lactate dehydrogenase (IU/L), *n* = 1946 | 215.1 ± 89.9 | 209.5 ± 88.3 | 254.4 ± 91.4 | <0.0001 |
| >233 IU/L, *n* (%) | 603 (31.0) | 476 (27.9) | 127 (52.9) | <0.0001 |
| Inspired fraction of oxygen (%), *n* = 1453 | 29.1 ± 16.7 | 27.9 ± 14.9 | 36 ± 22.8 | <0.0001 |
| PaFi ($PaO_2/FiO_2$) (mmHg), *n* = 1453 | 279.9 ± 83.8 | 285.2 ± 81.7 | 251.1 ± 89.1 | <0.0001 |
| D-dimer (ng/mL), *n* = 1850 | 767 ± 1666.3 | 712.2 ± 1495.2 | 1108.2 ± 2455.8 | <0.0001 |
| <500 ng/mL, *n* (%) | 1147 (62.0) | 1015 (63.7) | 132 (51.6) | <0.0001 |
| 500–1000 ng/mL, *n* (%) | 424 (22.9) | 354 (22.2) | 70 (27.3) | <0.0001 |
| >1000–<1500 ng/mL, *n* (%) | 144 (7.8) | 123 (7.7) | 21 (8.2) | <0.0001 |
| ⩾1500 ng/mL, *n* (%) | 135 (7.3) | 102 (6.4) | 33 (12.9) | <0.0001 |
| Ferritin (µg/L), *n* = 1584 | 376.5 ± 489.4 | 356.5 ± 487.9 | 509.5 ± 479.5 | <0.0001 |
| >336.2 µg/L, *n* (%) | 569 (35.9) | 461 (33.5) | 108 (52.2) | <0.0001 |

Data are mean ± standard deviation unless otherwise stated.
$FiO_2$, fractional inspired oxygen; PaFi, PaO2/FiO2 ratio; $PaO_2$, arterial oxygen tension.

**Table 4.** Hospitalization outcomes.

| | Total | Preemptive hospitalization | Non-preemptive hospitalization | *p*-Value |
|---|---|---|---|---|
| | ***N*** **= 2265** | ***n*** **= 1988** | ***n*** **= 277** | |
| Use of HFNC, *n* (%) | 305 (13.5) | 213 (10.7) | 92 (33.2) | <0.0001 |
| Days with HFNC | 10.0 ± 7.4 | 10.4 ± 7.6 | 9.1 ± 6.9 | 0.21 |
| Admission to ICU, *n* (%) | 155 (6.8) | 110 (5.5) | 45 (16.3) | <0.0001 |
| Length of stay in ICU, days | 13.7 ± 11.5 | 13.5 ± 12.3 | 14.2 ± 9.3 | 0.33 |
| IMV required, *n* (%) | 149 (6.6) | 106 (5.3) | 43 (15.5) | <0.0001 |
| Days intubated | 25.1 ± 14.5 | 26.2 ± 15.7 | 22.2 ± 10.9 | 0.13 |
| Length of hospital stay, days | 10.8 ± 7.9 | 10.5 ± 7.7 | 13.4 ± 8.8 | <0.0001 |
| Deaths, *n* (%) | 46 (2.0) | 27 (1.4) | 19 (6.9) | <0.0001 |

Data are mean ± standard deviation unless otherwise stated.
HFNC, high-flow nasal cannula; ICU, intensive care unit; IMV, invasive mechanical ventilation.

prolonged hospital stay, and death (all $p < 0.0001$) (Table 5). A logistic regression analysis showed that preemptive hospitalization reduced the mortality rate by 78% (adjusted OR 0.22, 95% CI 0.10–0.50), requiring IMV by 60% (adjusted OR 0.40, 95% CI 0.25–0.64), requiring HFNC by 55% (adjusted OR 0.45, 95% CI 0.31–0.66), and ICU admission by 63% (adjusted OR 0.37, 95% CI 0.23–0.60) (Table 6). Among patients at high risk of progression of disease severity (CALL score ⩾8), preemptive hospitalization reduced the likelihood of death by 81% (OR 0.19, 95% CI 0.07–0.48). In patients with a lower risk of progression (CALL score <8), the likelihood of requiring IMV was reduced by 69% (adjusted OR 0.31, 95% CI 0.12–0.80), the likelihood of requiring HFNC was reduced by 54% (adjusted OR 0.46, 95% CI 0.23–0.91), and the likelihood of admission to ICU decreased by 72% (adjusted OR 0.28, 95% CI 0.10–0.73).

## Discussion

This prospective observational study aimed to evaluate the importance of preemptive hospitalization by comparing patients with an $SpO_2$ >90% with those who were previously admitted with an $SpO_2$ ⩽90% according to the previous referral protocol. During this study, 2265 patients were referred to the TCH from our dedicated respiratory triage community centers. Overall, most patients were middle-aged with approximately 20% of patients older than 60 years. The most common comorbidities were diabetes mellitus and hypertension; however, over two-thirds of patients were classified as either overweight or obese.

As expected, the PH group had a significantly shorter mean time from onset of symptoms to admission than the NPH group (7.3 *versus* 8.6 days; $p < 0.0001$). Patients in the PH group presented with significantly fewer severe respiratory symptoms, as shown by fewer patients needing oxygen supplementation by simple nasal cannula, simple mask, reservoir mask, or HFNC. No patient in the PH group required the use of IMV at admission. Furthermore, predictive markers associated with poor outcomes,[9–12] such as LDH, D-dimer, and ferritin levels, were all abnormal and at significantly higher levels in a larger proportion of patients in the NPH group compared with the PH group. Notably, the main difference between the groups in terms of risk factors for progression was that a significantly higher proportion of patients in the NPH group were aged 60 years or older, had a high Charlson comorbidity index score, had diabetes mellitus or hypertension, and had higher CALL scores compared with the PH group at admission (all $p < 0.0001$). This is consistent with previous findings in Mexico where it has been reported that patients with COVID-19 and comorbidities such as hypertension, diabetes mellitus, and obesity are associated

**Table 5.** Distribution of patient outcomes as stratified by the CALL score at admission.

| Characteristic | Preemptive hospitalization | | *p*-Value | Non-preemptive hospitalization | | *p*-Value |
|---|---|---|---|---|---|---|
| | *N* = 1788 | | | *N* = 263 | | |
| | CALL score <8 (*n* = 1276) | CALL score ⩾8 (*n* = 512) | | CALL score <8 (*n* = 125) | CALL score ⩾8 (*n* = 138) | |
| HFNC | | | | | | |
| Yes, *n* (%) | 86 (6.7) | 119 (23.2) | <0.0001 | 29 (23.2) | 61 (44.2) | <0.0001 |
| Mean (SD) days with HFNC | 10.8 ± 6.8 | 10.1 ± 8.0 | 0.4 | 9.9 ± 5.9 | 8.7 ± 7.4 | 0.39 |
| Admission to ICU | | | | | | |
| Yes, *n* (%) | 32 (2.5) | 65 (12.7) | <0.0001 | 8 (6.4) | 33 (23.9) | <0.0001 |
| Mean (SD) days in ICU | 12.4 ± 13.4 | 15 ± 11.7 | 0.06 | 8.6 ± 5.6 | 16.4 ± 9.5 | 0.05 |
| IMV required | | | | | | |
| Yes, *n* (%) | 32 (2.5) | 61 (11.9) | <0.0001 | 8 (6.4) | 31 (22.5) | <0.0001 |
| Mean (SD) days with IMV | 27.6 ± 16.9 | 26.8 ± 15.0 | 0.84 | 22.1 ± 7.6 | 23 ± 11.2 | 0.88 |
| Length of hospital stay | | | | | | |
| Mean days (SD) | 9.2 ± 6.2 | 14.2 ± 9.9 | <0.0001 | 11.4 ± 6.6 | 15.3 ± 10 | 0.001 |
| Deaths | | | | | | |
| Yes, *n* (%) | 6 (0.5) | 21 (4.1) | <0.0001 | 1 (0.8) | 18 (13) | <0.0001 |

CALL, comorbidities, age, lymphocyte count, and lactate dehydrogenase; HFNC, high-flow nasal cannula; ICU, intensive care unit; IMV, invasive mechanical ventilation; SD, standard deviation.

with worse outcomes.[13] Interestingly, it was shown in a Swiss tertiary care setting that disease progression was not significantly affected by the presence of comorbidities or by age, with these parameters providing little prognostic information. However, the small sample size as well as an older cohort (median of 67 years) in that study may have masked some associations. Finally, our study also reports that thrombotic and inflammatory markers are prognostic characteristics of poorer outcomes, which has also been reported in several other studies.[10,14,15]

Treatment administered in the TCH follows the recommendations of the Government of Mexico,[3] which is based on the recommendations provided by the WHO. Although significantly more patients in the PH group had received treatment before admission, no significant differences were observed between groups regarding the types of treatments received before admission. Of note, over 35% of patients, most of whom were in the PH group, had previously been treated with steroids. This is not consistent with the current recommendations, which state that steroids should only be prescribed under careful supervision in an in-hospital setting and for no longer than 10 days.[3] Although there is a biological rationale for off-label steroid treatment during this pandemic, patients are at an increased risk of drug–drug interactions, especially patients with high-risk comorbidities.[16,17] As such, it is unknown if prior steroid treatment had any effect on patient outcomes once admitted to the TCH.

Although there is substantial heterogeneity in COVID-19 symptomatology, the most common symptoms reported at the TCH were headache, cough, myalgia, fever, and pharyngodynia, which is in line with the existing literature.[18,19] In our study, patients in the NPH group, who were more likely to present with disease progression, frequently reported headache, myalgia, and arthralgia in addition to cough and fever. Of note,

**Table 6.** Impact of preemptive hospitalization on patient outcomes as stratified by the CALL score at admission.

| | All patients | | CALL score <8 | | CALL score ⩾8 | |
|---|---|---|---|---|---|---|
| | *N* = 1285 | | *n* = 773 | | *n* = 425 | |
| | Adjusted OR[a] (95% CI) | *p*-Value | Adjusted OR[a] (95% CI) | *p*-Value | Adjusted OR[a] (95% CI) | *p*-Value |
| HFNC required | 0.45 (0.31–0.66) | <0.0001 | 0.46 (0.23–0.91) | 0.03 | 0.51 (0.31–0.83) | <0.01 |
| ICU admission | 0.37 (0.23–0.60) | <0.0001 | 0.28 (0.10–0.73) | <0.01 | 0.48 (0.27–0.86) | 0.01 |
| IMV required | 0.40 (0.25–0.64) | <0.0001 | 0.31 (0.12–0.80) | 0.02 | 0.51 (0.28–0.92) | 0.03 |
| Death | 0.22 (0.10–0.50) | <0.0001 | 0.06 (0.002–1.77) | 0.11 | 0.19 (0.07–0.48) | <0.0001 |

[a]Adjusted for sex, age, diabetes, hypertension, obesity, prior dexamethasone treatment, D-dimer levels, and ferritin levels.
CALL, comorbidities, age, lymphocyte count, and lactate dehydrogenase; CI, confidence interval; HFNC, high-flow nasal cannula; ICU, intensive care unit; IMV, invasive mechanical ventilation; OR, odds ratio.

specific symptoms such as loss of a patient's sense of smell and taste were only reported in approximately 20% of patients, without any differences between the groups.

Patients in each group were stratified by CALL score at admission, which is a risk factor scoring system based on a patient's age, presence of comorbidities, lymphocyte count, and serum LDH levels. These characteristics have previously been identified as risk factors that are associated with poor prognosis at an early stage of disease.[12,20] It has been shown that the CALL score is an accurate and easy to use model for predicting the risk of progression in patients with COVID-19.[5,21] Therefore, we evaluated the effect preemptive hospitalization had on patient outcomes when stratifying patients by CALL score. In patients at a higher risk of disease progression (CALL score ⩾8), there were significantly fewer patients requiring HFNC (23.2% *versus* 44.2%), admission to the ICU (11.9% *versus* 23.9%) or IMV (11.9% *versus* 22.5%) when compared with patients who were not preemptively hospitalized.

When stratifying by a CALL score of <8 (low risk of progression) and ⩾8 (high risk of progression), preemptive hospitalization reduced the likelihood of death by 94% and 81%, respectively. Furthermore, preemptive hospitalization reduced the likelihood of requiring IMV (69% and 49%), HFNC (54% and 49%), or admission to the ICU (72% and 52%), respectively. These findings show that preemptive hospitalization prevented progression to a more severe form of disease compared with patients who were not preemptively hospitalized. An additional benefit of preemptive hospitalization may be a reduction in community and household contagiousness.

The study's main limitations are the observational, single-center, retrospective study design, the heterogeneous population, and possible selection bias.

## Conclusion

Preemptive hospitalization, based on $SpO_2$, may result in a lower rate of progression to severe disease and may be beneficial for improving outcomes in patients with COVID-19. In addition, our results show that it is important to triage patients by CALL score at admission as those with a CALL score ⩾8 are more likely to require HFNC or IMV, be admitted to the ICU, and have a higher mortality risk.

## Authors' contributions

All authors conceived of and designed the study. HGR, JLG, RSM, LAMJ, and LMJ acquired and interpreted the data. HGR, JLG, LMJ, LAMJ, and RTC drafted the manuscript; acquired, analyzed, and interpreted the data; contributed to writing the sections of the manuscript dealing with data analysis; and revised the manuscript for important intellectual content. All authors read and approved the final version to be published and agree to be accountable for all aspects of the work.

## Conflict of interest statement

The Carlos Slim Foundation funded this study. The funding source was involved in the design of

the study, analysis, interpretation of data, and in writing the manuscript. The authors HGR, JLG, RSM, LAMJ, and RTC are employees of the Carlos Slim Foundation in Mexico. RRVV, RVB, LMJ, MAA, STB, RVAW, ESL, MDNO, AGR, LMBR, PEC, LERG, ACS, JBM, AGR, APC, HHB, LVA, and RARL are employed full-time by the temporary COVID-19 hospital. The authors declare no other outside funding from any other organizations and declare no further conflicts.

## Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: The authors would like to thank Keyra Martinez Dunn and James Graham of Edanz for providing medical writing support, which was funded by the Carlos Slim Foundation.

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## Availability of supporting data

The data that support the findings of this study will be made available on reasonable request to the corresponding author.

## Supplemental material

Supplemental material for this article is available online.

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