

# Risk Factors Associated with Prolonged Nasopharyngeal Carriage of SARS-CoV-2 and Length of Stay among Patients Admitted to a COVID-19 Referral Center in Manila, Philippines

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## ABSTRACT

**Objective.** Prolonged nasopharyngeal carriage of SARS-CoV-2 has been linked to prolonged hospital stay and delayed radiologic recovery. To determine if clinical risk factors are associated with prolonged nasopharyngeal carriage or longer hospital stay, we performed a descriptive analysis of 169 moderate to severe COVID-19 patients admitted at the Philippine General Hospital from March to June 2020.

**Methods.** Length of nasopharyngeal RT-PCR positivity and clinical demographic data were extracted from existing patient records. Chi-square test, Mann-Whitney U test, and regression analysis were performed to describe the association of clinical risk factors with prolonged nasopharyngeal carriage and length of hospital stay.

**Results.** The median duration of carriage was 19 days (IQR 12.0-30.0 days). No comorbidities or inflammatory markers had a statistically significant association with prolonged nasopharyngeal carriage defined as >24 days of nasopharyngeal RT-PCR positivity. Characteristics associated with a statistically significant longer hospital stay included chronic kidney disease stages 3-5, severe disease, and use of empiric antibiotics on admission. Prolonged carriage >24 days, hsCRP, and D-dimer at admission, also had a statistically significant but weak correlation with length of stay.

**Conclusion.** Among patients with moderate disease, comorbidities and inflammatory markers were not associated with prolonged COVID-19 nasopharyngeal carriage. Prolonged nasopharyngeal carriage >24 days was associated with longer hospital stay, while D-dimer and hsCRP levels at admission, also had statistically significant but small effects on increasing the hospital length of stay.

**Keywords:** COVID-19, nasopharyngeal carriage, inflammatory markers, length of stay

## INTRODUCTION

The 2019 coronavirus disease (COVID-19) drew global attention when pneumonia cases of then unknown etiology began to sweep across Wuhan, China in late December 2019.<sup>1</sup> The growing number of similarly ill patients across the mainland spurred the isolation and characterization of the causative virus: the 2019 novel coronavirus, initially dubbed novel coronavirus (NCOV) and later SARS-CoV-2, and its associated disease, COVID-19. By the end of January, cases of COVID-19 had begun to appear worldwide, likely signaling the beginning of the current pandemic. Case fatality rate was then calculated to be 2.2%. As of July 2022, SARS-CoV-2 has affected more than 552 million people and has resulted in more than 6 million deaths worldwide, with numbers still increasing.<sup>2</sup> In the Philippines, more than 3.7



eISSN 2094-9278 (Online)  
Published: December 18, 2023  
<https://doi.org/10.47895/amp.vi0.5764>

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million have been infected, resulting in more than 60,000 deaths.<sup>3</sup> Because of its rising toll on healthcare systems worldwide, studies on the pathobiology and clinical behavior of COVID-19 continue to be the subject of a growing body of research.

As a means of dealing with a novel and foreign pathogen, there have been a growing number of studies, mostly dealing with experiences on the epidemiological and clinical features of inpatients with COVID-19. Based on currently available data, COVID-19 has an incubation period of 5.2 days on average.<sup>4</sup> Among those with severe disease, the time from onset to worsening of symptoms and eventual death is highly variable, ranging from 6 to 41 days, with a median of 14 days. This is the basis for the previously protocolized quarantine period of 14 days for those with significant exposure to the virus.<sup>5</sup> More recently, quarantine recommendations were revised following studies on the behavior and transmissibility of COVID-19, given the introduction of vaccines and the appearance of new viral strains. Infectiousness was noted to peak during the first week of symptom onset, hence recent guidelines have shortened the quarantine period to five days with an additional five days of continued masking.<sup>6</sup> Diagnosis remains largely made based on RT-PCR of oropharyngeal and nasopharyngeal secretions.

Preliminary observational studies have shown that the duration of viral carriage as evidenced by RT-PCR positivity is variable, and may depend on the severity of illness, ranging from 10 days in mild illness to up to 42 days in severe disease, with reported medians of 20 to 31 days.<sup>7,8</sup> Studies in mild cases show that the highest SARS-CoV-2 RNA levels are detected and could be isolated within the first week of illness. Beyond 7 days, the majority of patients continue to shed viral RNA, which could not be grown in culture and are likely nonviable.<sup>9,10</sup> Even so, neither viral carriage nor viral load necessarily equates to infectiousness. The variability of its clinical course has previously been associated with age, and experts have also hypothesized associations with the quality of immune response. According to the CDC, in patients who continue to have viral shedding three days after recovery, RNA levels are generally below the level at which infectious particles can be isolated. Other studies have also found RT-PCR positivity in saliva, urine, and stool, but studies are incomplete on whether these are capable of transmission.<sup>11</sup>

COVID-19 symptoms are similar to other etiologies of pneumonia, and patients usually present with fever, cough, sputum production, hemoptysis and other nonspecific symptoms such as headache and fatigue. Patients may also present with diarrhea, which is rarer among patients with MERS-CoV and SARS-CoV1. Mason and colleagues describe three phases in COVID-19 infection. Stage 1 describes an asymptomatic stage wherein the virus binds and fuses with ciliated airway cells. At this point, RT-PCR will be able to detect the virus in nasopharyngeal secretions. The viral load is noted to be low, but the patient is nevertheless infectious. Stage 2 heralds the symptomatic stage where

the virus propagates in the airway and activates the innate immune response, producing symptoms of upper respiratory tract infection. About 80% of COVID-19 patients will manifest with only mild symptoms restricted to the upper and conductive airways. Stage 3 occurs in the remaining 20% of patients, where investigators believe that viral propagation and resulting inflammation reaches the lower airways and alveoli. Pulmonary infiltrates appear subpleurally, reflecting the propensity of SARS-CoV-2 for the type II alveolar cells which are located peripherally. Radiologic findings such as peripheral ground glass opacities are widely associated with COVID-19, but are nonspecific, and may also occur with other viral pneumonia. Epithelial cells are destroyed, fueling the immune response, causing further damage to the surrounding tissue in a vicious cycle that may lead to acute respiratory distress syndrome and cytokine storm. Clinical experience shows that there may be significant overlap between these stages, as many asymptomatic patients presumably in stage 1, also exhibit signs of lower airway involvement as evidenced by pulmonary infiltrates on chest CT scan. Several studies have proposed certain laboratory markers as indicators for the risk of cytokine storm, but much remains to be learned about the patient profile and characteristics that would predispose to the development of more severe disease. At the beginning of the pandemic, most cases of COVID-19 were observed in the elderly. Early studies showed associations between older age, higher SOFA score, elevated D-dimer levels, presence of comorbidities (such as diabetes, coronary artery disease, and hypertension), with in-hospital mortality.<sup>12-16</sup>

More relevant to today's global management of the pandemic are channels of human-to-human transmission. Observations show that transmission likely occurs through direct contact, droplet spread, and in recent times, airborne transmission.<sup>17</sup> Case studies that report vertical transmission specifically during the third trimester have also been published,<sup>18</sup> but it is unclear whether this occurs only through the hematogenous route in the prenatal period or if it may also occur perinatally during transit through the vaginal canal.

This study aims to determine clinical risk factors that are associated with prolonged nasopharyngeal RNA carriage among COVID patients in our institution. The second objective is to determine whether these clinical characteristics and prolonged nasopharyngeal carriage are associated with a longer hospital stay. Once these factors are known, efforts can be made to seek interventions that target these factors and reduce carriage and length of stay. For mild or moderate cases of COVID-19, local guidelines at this time no longer recommend repeat RT-PCR prior to discharge. However, for certain populations, such as immunocompromised patients, patients undergoing chronic dialysis, and patients on long-term immunosuppression among others, RT-PCR continues to be a requirement prior to treatments and hospital admissions.<sup>19</sup> The findings of this study can contribute to the evolving science of COVID-19 pathogenesis and

transmission, as well as help shape the landscape for policy-making and optimization, especially among the vulnerable populations described.

## MATERIALS AND METHODS

### Study Setting

The investigators performed a chart review of COVID-19 patients admitted at the Philippine General Hospital COVID-19 wards and intensive care units from March 2020 to June 2020. During this period, patients with at least one positive nasopharyngeal swab RT-PCR test for SARS-CoV-2 were admitted to the designated COVID-19 wards and intensive care units. Discharge criteria at that time required that patients had at least one negative nasopharyngeal RT-PCR test.

An RT-PCR assay was used for qualitative detection of SARS-CoV-2-specific RNA in nasopharyngeal and oropharyngeal specimens, which were collected by trained medical personnel. The assay has been evaluated through analytical validation, with 100% positivity at 0.25 genomic equivalents/microliter. There was no noted cross-reactivity with bacteria or common viral pathogens. On clinical evaluation, the RT-PCR assay used in the study yielded 100% concordant results with another EUA-approved RT-PCR detection kit. Notable causes of false-negative results include improper specimen collection, transport, or handling, presence of RT-PCR inhibitors such as heparin, timing of sample collection, or new viral mutations. False-positive results may be due to sample contamination or cross-reactivity with other coronaviruses.

### Study Participants

Patient cases included in the study were those who met the following criteria: 1) adults aged at least 18 years of age, 2) had at least one positive nasopharyngeal swab RT PCR, 3) at least one negative nasopharyngeal swab RT PCR after an initial positive result, 4) moderate to critical COVID-19 as classified by existing national interim guidance on the clinical management of adult patients with suspected or confirmed COVID-19 infection published last July 2020.<sup>19</sup> Exclusion criteria included: 1) pregnant or postpartum patients, 2) patients previously infected with COVID-19, 3) patients with no negative nasopharyngeal swab RT-PCR for any reason, such as those transferred to step-down quarantine facilities or those who died. The calculated minimum sample size required to describe the target population (n=524) with a 95% confidence interval and 10% margin of error was 82 samples, which was met by the 169 patient samples that fulfilled our inclusion criteria (Figure 1).

### Data Collection

We reviewed the charts of patients admitted at PGH COVID wards and intensive care units between March and June 2020 through convenience sampling in the order

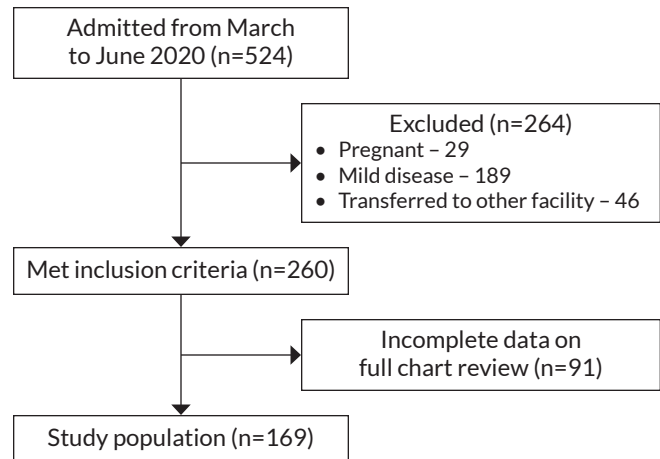


Figure 1. Study flow chart showing selection process.

of admission. The selection of this time frame is due to the change in hospital policy implemented in July 2020, which no longer required a negative RT-PCR for discharge in non-immunocompromised patients. The investigators and research assistant collected data from physical patient charts and electronic medical records, including patient demographics, comorbidities, the severity of COVID-19, and laboratory parameters on admission (serum ferritin, lactate dehydrogenase, high-sensitivity C reactive protein, procalcitonin, D-dimer, WBC count). The severity of COVID-19 was determined by the attending physicians prior to this study through assessment of clinical presentation, laboratory values, and radiologic findings as per recommendations by Philippine Society For Microbiology And Infectious Diseases (PSMID).<sup>19</sup> Patient charts which did not indicate the dates for at least one positive and at least one negative nasopharyngeal RT-PCR were considered incomplete, and excluded from the analysis. Data were entered in an excel file, which was imported and analyzed on statistics software JASP version 0.16.

This study was submitted to the University of the Philippines Manila Research Ethics Board and underwent expedited review and approval (UPMREB Code 2020-559-01). Waiver of written informed consent was sought and granted during the ethics review due to the retrospective and descriptive nature of the study, with no personal identifying data being collected.

### Statistical Analysis

Length of nasopharyngeal carriage was calculated by determining the number of days from first positive RT-PCR to first negative RT-PCR. Descriptive statistics were generated for baseline demographics and clinical characteristics of patients. The continuous variables were assessed using the Shapiro-Wilk test for normalcy of distribution, Levene's test for homogeneity of variance, and residual plots were observed for homoscedasticity. Normally-distributed variables were described using means, while non-normally distributed

variables were described with median values. The association of categorical variables with prolonged nasopharyngeal carriage defined as >24 days of RT-PCR positivity, was tested using the Chi-square test. Prolonged carriage was defined as >24 days, since this was the most conservative estimate for median length of carriage in existing studies, where other median durations were 7 days and 20 days.<sup>7-10</sup>

To determine association with prolonged nasopharyngeal carriage, age and laboratory parameters upon admission were entered into multiple logistic regression analysis via entry method. The regression coefficient of each covariate and p-values were reported. The Mann-Whitney U test was used to test if prolonged nasopharyngeal carriage, comorbidities, and clinical characteristics affected length of hospital stay. Continuous variables were entered into multivariable linear regression analysis to assess correlation with hospital stay. For all statistical tests, a p-value of <0.05 was considered significant.

## RESULTS

### Patient Characteristics

A total of 169 patients were included in this study with a mean age of 56.3 years (IQR 48.0-66.0 years), with males comprising 54.4% of the study subjects. Median length of nasopharyngeal carriage was 19 days (IQR 12.0-30.0 days), while the median length of hospital stay was 25 days (IQR 16.0-37.0 days). Majority of the patients (N=153, 90.5%) had at least one comorbidity. Table 1 shows the comorbidities and clinical characteristics identified among the patient population and their association with prolonged nasopharyngeal carriage.

### Clinical characteristics correlated with nasopharyngeal carriage

The most common comorbidities were hypertension (N=110, 65.1%), bacterial pneumonia (N=80, 47.3%), and diabetes mellitus (N=58, 34.3%). Majority of the patients

**Table 1.** Baseline clinical characteristics and outcomes, and their association with prolonged nasopharyngeal carriage

| Demographic characteristic             | Total (n=169)<br>n (%)              | Median length of<br>carriage in days<br>(IQR) | Duration of nasopharyngeal carriage |                         | p-value |
|--|-------------------------------------|---|-------------------------------------|-------------------------|---------|
|  |                                     |   | n=110<br><24 days, n (%)            | n=59<br>≥24 days, n (%) |         |
| <b>Age</b>                             | Mean: 56.3 years<br>(IQR 48.0-66.0) | Overall median:<br>19 (12.0-30.0)             | Mean: 56.9 years                    | Mean: 55.2 years        |         |
| <b>Age &gt;60 years</b>                | 70 (41.4%)                          | 18 (13.3-27.8)                                | 46 (41.2%)                          | 24 (40.7%)              | 0.89    |
| <b>Male</b>                            | 92 (54.4%)                          | 20 (14.0-31.3)                                | 59 (53.6%)                          | 33 (55.9%)              | 0.87    |
| <b>Clinical characteristics</b>        |                                     |   |                                     |                         |         |
| No comorbidities                       | 16 (9.5%)                           | 18.5 (11.0-34.3)                              | 10 (9.1%)                           | 6 (10.2%)               | 0.81    |
| Hypertension                           | 110 (65.0%)                         | 18 (12.3-29.5)                                | 72 (65.5%)                          | 38 (64.4%)              | 0.89    |
| Hypertension on RAS blocker            | 50 (29.6%)                          | 17.5 (8.3-27.5)                               | 34 (30.9%)                          | 16 (27.1%)              | 0.61    |
| Diabetes mellitus                      | 58 (34.3%)                          | 18.5 (13.0-29.5)                              | 39 (35.5%)                          | 19 (32.2%)              | 0.67    |
| Diabetes mellitus on insulin           | 16 (9.5%)                           | 16.5 (10.5-30.3)                              | 10 (9.1%)                           | 6 (10.2%)               | 0.64    |
| Chronic kidney disease                 | 25 (14.8%)                          | 21 (14.0-28.0)                                | 15 (13.6%)                          | 10 (16.9%)              | 0.56    |
| Chronic kidney disease on hemodialysis | 21 (12.4%)                          | 21 (17.0-34.0)                                | 12 (10.9%)                          | 9 (15.3%)               | 0.50    |
| Heart failure                          | 19 (11.2%)                          | 21 (7.0-27.5)                                 | 11 (10.0%)                          | 8 (13.6%)               | 0.49    |
| Prior cerebrovascular disease          | 8 (4.7%)                            | 17 (12.5-30.0)                                | 5 (4.5%)                            | 3 (5.1%)                | 0.88    |
| Bacterial pneumonia                    | 80 (47.3%)                          | 18.5 (14.0-28.0)                              | 51 (46.4%)                          | 29 (49.2%)              | 0.73    |
| Chronic obstructive pulmonary disease  | 4 (2.4%)                            | 10.5 (7.5-16.3)                               | 3 (2.7%)                            | 1 (1.7%)                | 0.67    |
| Bronchial asthma                       | 10 (5.9%)                           | 18 (8.3-25.5)                                 | 7 (6.4%)                            | 3 (5.1%)                | 0.74    |
| Pulmonary tuberculosis                 | 19 (11.2%)                          | 20 (14.5-27.5)                                | 13 (1.2%)                           | 6 (10.2%)               | 0.75    |
| <b>COVID-19 severity</b>               |                                     |   |                                     |                         |         |
| Moderate                               | 141 (83.4%)                         | 19 (12.0-30.0)                                | 90 (81.8%)                          | 51 (86.4%)              | -       |
| Severe                                 | 28 (16.6%)                          | 18 (12.5-27.3)                                | 20 (18.2%)                          | 8 (13.6%)               | 0.44    |
| Critical                               | 0                                   | -   | -                                   | -                       | -       |
| <b>Treatment</b>                       |                                     |   |                                     |                         |         |
| Empiric antibiotic use                 | 112 (66.9%)                         | 19 (13.0-30.0)                                | 72 (65.4%)                          | 40 (67.7%)              | 0.76    |
| Use of investigational drugs           | 14 (8.3%)                           | 15 (8.5-24.0)                                 | 10 (9.1%)                           | 4 (6.8%)                | 0.60    |
| Oxygen-requiring                       | 87 (51.5%)                          | 20 (14.0-29.0)                                | 55 (50.0%)                          | 32 (54.2%)              | 0.60    |
| High-flow nasal cannula                | 7 (4.1%)                            | 24 (9.0-31.0)                                 | 4 (3.6%)                            | 3 (5.1%)                | 0.65    |
| Mechanical ventilation                 | 6 (3.5%)                            | 21.5 (13.5-41.5)                              | 3 (2.7%)                            | 3 (5.1%)                | 0.43    |
| <b>Outcome</b>                         |                                     |   |                                     |                         |         |
| Discharged                             | 160 (94.7%)                         | 19 (12.3-30.0)                                | 101 (91.2%)                         | 59 (100%)               | 0.024*  |
| Expired                                | 9 (5.3%)                            | 10 (7.0-13.0)                                 | 9 (8.2%)                            | 0                       | -       |

\*comparisons done through chi-square test



included in the population had moderate COVID-19 (N=141, 83.4%) and most patients received empiric antibiotics upon admission (N=112, 66.9%). The most common presenting symptom was cough (24.9%), followed by dyspnea (22.5%) and fever (17.8%).

There was a longer median length of carriage among the male sex (median 20 days), those with chronic kidney disease on hemodialysis (median 21 days), heart failure (median 21 days), and pulmonary tuberculosis, including both clinically-diagnosed and bacteriologically-confirmed cases (median 20 days). The requirement of oxygen supplementation (20 days), use of high-flow nasal cannula (24 days), and mechanical ventilation (21.5 days) also led to longer median length of carriage. However, none of these differences were statistically significant.

Regarding outcome, data showed that patients who died had a significantly shorter median duration of nasopharyngeal carriage (10 days). This suggests that prolonged nasopharyngeal carriage is not necessarily associated with poor outcomes. Conversely, the patients in our study who died did so despite already having a negative nasopharyngeal RT-PCR result. On review of the cases of these patients, majority were being treated for nosocomial infections from multi-drug resistant organisms and died from septic shock. Logistic regression analysis of continuous variables such as age and inflammatory markers upon admission was done via entry method to explore their correlation with prolonged nasopharyngeal carriage (Table 2). The confidence intervals for the odds ratios of these independent variables all included 1.0, hence none of these variables were statistically associated with prolonged nasopharyngeal carriage.

**Clinical characteristics correlated with length of hospital stay**

Clinical characteristics associated with a statistically significant longer hospital stay included chronic kidney disease stages 3-5 (including dialytic patients), severe disease, and use of empiric antibiotics upon admission. Prolonged nasopharyngeal carriage had a statistically significant effect on the hospital length of stay with a p-value of <0.001 (Table 3). Linear regression analysis of laboratory markers upon

admission showed that the CRP and D-dimer at admission had a statistically significant positive correlation with length of hospital stay (Table 4). However, the regression coefficients for CRP (0.06) and D-dimer (1.06) were small and were unlikely to be clinically significant.

**DISCUSSION**

In the descriptive analysis we performed, a large proportion of patients had moderate disease (83.4%). There was only a small group of patients with severe disease, and no patient had critical illness. This could be attributed to the high mortality rate among patients with severe to critical disease, especially during the early days of the pandemic. These severely ill patients were no longer able to undergo a repeat RT-PCR swab, thus we could not obtain data on their RT-PCR status and whether SARS-CoV-2 continued to replicate in their nasopharyngeal tissue. Because of this survivorship bias, the data we collected largely represents patients with moderate disease.

In our patient population, the median duration of RT PCR positivity – that is, the duration before a patient had a negative RT-PCR – was 19 days, which is consistent with previously available data. Studies on nasopharyngeal viral carriage had a variety of definitions for “prolonged” carriage, ranging from more than 7 to more than 23 days.<sup>20,21</sup> Studies are still lacking regarding the correlation of RT-PCR positivity with infectiousness, with some studies postulating that prolonged positivity may only be due to shedding of nonviable viral remnants.

Though it may not necessarily indicate infectiousness, observational studies have shown that prolonged carriage is associated with prolonged hospital stay and delayed radiologic recovery of pneumonia. Investigations on the risk factors that are associated with prolonged length of RT-PCR positivity have identified the following factors to have statistically significant association: age, male sex, delayed time to admission (>5 days from onset to admission), invasive mechanical ventilation, malignant disease, and lymphopenia.<sup>20-22</sup>

In our study, none of the comorbidities observed in this study seemed to affect the duration of nasopharyngeal carriage among patients with moderate COVID-19. Many of these comorbidities have been shown in other studies to worsen the severity and outcomes of COVID-19. Notably, in these studies, severe cases constituted a larger proportion of cases – ranging from 28.3% to 32.1%, whereas only 16.6% of our study population had severe disease. Another significant finding is that majority of our study population (90.5%) had at least one comorbidity, indicating a relatively ill population. Due to these factors, it is difficult to ascertain the true impact of individual comorbidities on nasopharyngeal carriage, since almost all patients had one or several comorbidities.

Inflammatory markers upon admission also did not correlate with the length of nasopharyngeal carriage. Our findings are consistent with the recommendations of the

**Table 2.** Multivariate Logistic Regression of patient characteristics and laboratory markers with prolonged nasopharyngeal carriage

| Variable      | OR   | 95% CI           | p-value |
|---------------|------|------------------|---------|
| Age           | 0.99 | [-0.09 - 0.08]   | 0.85    |
| LDH           | 1.00 | [-0.01 - 0.004]  | 0.33    |
| WBC           | 0.92 | [-0.38 - 0.21]   | 0.58    |
| procalcitonin | 0.22 | [-4.8 - 1.84]    | 0.38    |
| CRP           | 1.02 | [-0.01 - 0.04]   | 0.29    |
| ferritin      | 1.00 | [-0.003 - 0.002] | 0.77    |
| D-dimer       | 0.68 | [-1.18 - 0.42]   | 0.35    |

**Table 3.** Clinical characteristics and association with length of hospital stay

| Demographic characteristic              | Total (n=169), n (%)         | Median hospital stay in days (IQR) | p-value |
|---|------------------------------|------------------------------------|---------|
| <b>Age</b>                              | Mean: 56.3 years (22.0-83.0) | Overall median: 25 (16.0-37.0)     | -       |
| <b>Age&gt;60 years</b>                  | 70 (41.4%)                   | 23.5 (15.3-37.0)                   | 0.26    |
| <b>Male</b>                             | 92 (54.4%)                   | 26 (19.0-39.0)                     | 0.07    |
| <b>Clinical characteristics</b>         |                              |                                    |         |
| No comorbidities                        | 16 (9.5%)                    | 25 (18.5-41.3)                     | 0.74    |
| Hypertension                            | 110 (65.0%)                  | 24.5 (16.0-37.0)                   | 0.55    |
| Hypertension on RAS blocker             | 50 (29.6%)                   | 23.5 (15.0-36.3)                   | 0.55    |
| Diabetes mellitus                       | 58 (34.3%)                   | 24 (16.0-36.8)                     | 0.49    |
| Diabetes mellitus on insulin            | 16 (9.5%)                    | 26.5 (18.8-31.0)                   | 0.86    |
| Chronic kidney disease                  | 25 (14.8%)                   | 31 (26.0-42.0)                     | 0.001*  |
| Chronic kidney disease on hemodialysis  | 21 (12.4%)                   | 32 (29.0-43.0)                     | 0.04*   |
| Heart failure                           | 19 (11.2%)                   | 26 (12.5-36.0)                     | 0.99    |
| Prior cerebrovascular disease           | 8 (4.7%)                     | 29 (25.8-33.0)                     | 0.35    |
| Bacterial pneumonia                     | 80 (47.3%)                   | 26 (18.8-34.3)                     | 0.27    |
| Chronic obstructive pulmonary disease   | 4 (2.4%)                     | 25 (17.5-28.3)                     | 0.58    |
| Bronchial asthma                        | 10 (5.9%)                    | 25 (17.8-31.0)                     | 0.82    |
| Pulmonary tuberculosis                  | 19 (11.2%)                   | 29 (20.5-36.5)                     | 0.37    |
| <b>COVID-19 severity</b>                |                              |                                    |         |
| Moderate                                | 141 (83.4%)                  | 24 (16.0-36.0)                     | -       |
| Severe                                  | 28 (16.6%)                   | 29.5 (22.8-40.3)                   | 0.04*   |
| Critical                                | 0                            | -                                  | -       |
| <b>Treatment</b>                        |                              |                                    |         |
| Empiric antibiotic use on admission     | 112 (66.9%)                  | 27 (19.8-37.0)                     | 0.004*  |
| Use of investigational drugs            | 14 (8.3%)                    | 29 (20.8-38.5)                     | 0.21    |
| Oxygen-requiring                        | 87 (51.5%)                   | 25 (17.0-37.0)                     | 0.74    |
| High-flow nasal cannula                 | 7 (4.1%)                     | 28 (24.0-33.5)                     | 0.54    |
| Mechanical ventilation                  | 6 (3.5%)                     | 31 (25.8-51.3)                     | 0.19    |
| <b>Outcome</b>                          |                              |                                    |         |
| Discharged                              | 160 (94.7%)                  | 25 (16.0-37.0)                     | 0.70    |
| Died                                    | 9 (5.3%)                     | 26 (22.0-34.0)                     | -       |
| <b>Prolonged carriage (&gt;24 days)</b> | 59 (34.9%)                   | 39 (28.0-45.5)                     | <0.001* |

\*comparisons done through Mann-Whitney test

**Table 4.** Multivariate linear regression analysis of laboratory markers with length of hospital stay

| Variable      | Coefficient | p-value |
|---------------|-------------|---------|
| Age           | -0.15       | 0.28    |
| LDH           | -0.01       | 0.29    |
| WBC           | 0.02        | 0.81    |
| procalcitonin | 0.88        | 0.24    |
| CRP           | 0.06        | 0.05*   |
| ferritin      | -0.002      | 0.45    |
| D-dimer       | 1.06        | 0.03*   |

PSMID 2020 interim guidance on COVID-19 care,<sup>19</sup> wherein these markers are suggested only for patients with severe to critical disease and for monitoring disease progression.

It is also interesting to note that none of the patients who died during their admission (n=9) had prolonged nasopharyngeal carriage. Their median length of carriage was

10 days, which was shorter than the overall median length of carriage of 19 days. On review, these patients were being treated for nosocomial infections from multi-drug resistant organisms and died from septic shock. This is a significant finding because analysis also showed empiric use of antibiotics to be associated with longer hospital stay. These associations suggest that a portion of the mortality burden of COVID-19 admissions could be related to the use of empiric antibiotics on admission, potentially leading to subsequent infections with multi-drug resistant organisms. Further studies would need to be done to shed more light on the collateral damage dealt by empiric antibiotic usage among patients with COVID-19.

This study was limited by the evolving recommendations on the inclusion of RT-PCR testing in the institutional protocol for discharge. Data was also lacking for severe and critical patients who died, since these patients also did not have a repeat RT-PCR. Furthermore, the study was based on qualitative testing and data did not include quantitative measures of viral yield (i.e. cycle threshold), which could have provided additional information on viral pathogenesis. While

our data suggested that laboratory markers only weakly or do not correlate with length of hospital stay or length of viral carriage, further studies should be done on whether their usage has an impact on other important outcomes, such as mortality and cost-effectivity of care.

## CONCLUSION

In our descriptive analysis of COVID-19 patients admitted at the Philippine General Hospital from March to June 2020, we found that common comorbidities and several inflammatory markers were not associated with prolonged nasopharyngeal carriage. The median duration of nasopharyngeal carriage was 19 days, which is longer than the current quarantine period for moderate cases – 14 days. Clinical characteristics associated with a statistically significant longer hospital stay included chronic kidney disease stages 3-5, severe disease, and use of empiric antibiotics upon admission. Prolonged nasopharyngeal carriage >24 days was associated with longer hospital stay. While D-dimer and hsCRP levels at admission also had statistically significant effects, their coefficients were small and would have minimal impact on increasing the hospital length of stay. Moreover, prolonged nasopharyngeal carriage was not associated with mortality, and patients who died did so from infections with multi-drug resistant organisms.

## Statement of Authorship

All authors contributed to the conceptualization of work, acquisition and analysis of data, drafting and revising, and approval of the final version submitted.

## Author Disclosure

All authors declared no conflicts of interest.

## Funding Source

None.

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