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# Analysis of possible risk predictors in patients with coronavirus disease 2019: a retrospective cohort study

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## SUMMARY

**OBJECTIVE:** This study aimed to analyze the clinical-epidemiological profile, possible risk predictors, and outcomes of patients with coronavirus disease 2019 admitted to the ward of a tertiary care hospital in southern Brazil. Specifically, we describe the demographic characteristics, comorbidities, baseline laboratory findings, clinical course, and survival of these patients.

**METHODS:** This is an observational, retrospective cohort study, performed from January to March 2022, on medical records of patients hospitalized between April 2020 and December 2021 in the coronavirus disease 2019 ward of a tertiary hospital in southern Brazil.

**RESULTS:** Data from 502 hospitalized patients were analyzed, of which 60.2% were male, with a median age of 56 years and 31.7% were over 65 years old. The main symptoms presented were dyspnea/respiratory discomfort (69.9%) and cough (63.1%). The most common comorbidities were obesity, systemic arterial hypertension, and diabetes mellitus. A proportion of 55.8% of 493 patients had $PaO_2/FiO_2$<300 mmHg in the first examination performed after admission and 46.0% had a neutrophil/lymphocyte ratio>6.8. Oxygen therapy by Venturi mask or mask with reservoir was used in 34.7% of the patients, and non-invasive ventilation was used in 10.0% of the patients. The majority of the patients (98.4%) used corticosteroids, and the outcome of 82.5% of the hospitalized patients was home discharge.

**CONCLUSION:** After analyzing the clinical and epidemiological profile, it can be concluded that age greater than 65 years and pulmonary involvement >50% are predictors of a worse prognosis for coronavirus disease 2019, as is the need for high-flow oxygen therapy. Corticotherapy, however, proved to be beneficial in the treatment of the disease.

**KEYWORDS:** COVID-19. Risk factors. Prognosis. Disease management.

## INTRODUCTION

A new coronavirus was identified in Wuhan, China, in December 2019, when several cases of severe pneumonia were reported. The disease caused by this virus was later named coronavirus disease 2019 (COVID-19)[1-3].

The clinical picture of COVID-19 is quite variable. Patients may be asymptomatic or may start with a flu-like syndrome that can progress to pneumonia or severe acute respiratory syndrome in a short time[1,4]. Numerous risk factors can contribute to serious diseases, such as comorbidities, advanced age, changes in physiological enzyme levels, and inflammatory markers[1,4-6].

According to the World Health Organization data, among symptomatic patients, about 80% recover without the need for hospital treatment, whereas 15% become seriously ill, requiring oxygen therapy and hospitalization and 5% progress to need for intensive care[1].

Thus, knowing the clinical and epidemiological profile of patients and their main in-hospital outcomes allows for the identification of individuals at risk of a worse prognosis. This allows the institution of a more targeted line of treatment and may contribute to improving the flow of care, avoiding system overload, and leading to a reduction in the rate of mortality.

In this regard, this study aimed to analyze the clinical-epidemiological profile, possible risk predictors, and outcomes of patients with COVID-19 hospitalized in the ward of a tertiary care hospital in southern Brazil. Specifically, we describe the demographic characteristics, comorbidities, baseline laboratory findings, clinical course, and survival of these patients.

## METHODS

This is an observational, retrospective cohort study. Data were obtained from the medical records of patients hospitalized in the COVID-19 ward of a tertiary hospital in southern Brazil, after prior authorization from the institution and approval from the

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The Hospital Infections Control Commission of the hospital in question was asked to provide a list of patients hospitalized due to the disease, from which the inclusion and exclusion criteria of the study were applied. Data were collected from January to March 2022.

Patients over 18 years of age, with a positive diagnosis of COVID-19, hospitalized in the ward from April 2020 to December 2021 were included. Pregnant women and patients in previous palliative care were excluded.

No sample size calculation was performed as this was a census study. All medical records of patients who met the inclusion criteria were analyzed.

The variables analyzed were age, gender, weight, height, symptoms presented at hospital admission, COVID vaccination history, use of medications from the COVID kit (composed of hydroxychloroquine, azithromycin, ivermectin, and corticoid), previous comorbidities presented by the patient, type of oxygen therapy performed during hospitalization in the ward [nasal cannula, Venturi mask or reservoir mask, non-invasive ventilation (NIV), orotracheal intubation (OTI)], the extent of pulmonary impairment on chest tomography, and laboratory tests of an inflammatory, infectious, and thrombotic character, including blood count, C-reactive protein (CRP), lactic dehydrogenase (LDH), D-dimer, and ferritin, in addition to the blood gas test. Regarding drug treatment, the use of antibiotics, corticoids, anticoagulants, and antivirals was evaluated. The length of stay in the ward and the outcome were also analyzed.

The data from this research were initially tabulated in *Google Sheets* and later transferred to the IBM *Statistical Package for the Social Sciences* (SPSS, version 22.0) for statistical analysis.

The results of the characterization of patients' profiles were expressed as mean and standard deviation (±SD) or absolute number (n) and percentage (%). To carry out the statistical inference, the quantitative variables were initially analyzed for their normality using the *Kolmogorov-Smirnov* test. In view of the non-normality, the nonparametric *Mann-Whitney* U test was used. In the association analyses, the outcome was dichotomized into Discharge to Home and Non-Discharge, which included a composite of the need for an intensive care unit (ICU) or death on the ward, with the outcome Non-Discharge characterized as the worse prognosis. For this analysis, the test used was *Pearson's* chi-square ($\chi^2$) or *Fisher's* exact test. When the associations were significant, the analysis of adjusted residuals *(ra)* was performed, considering *ra*>1.96 to indicate the highest prevalence. Variables with p<0.05 from the *Pearson's* chi-square or *Fisher's* exact test were candidates for the model using regression Poisson logistics [prevalence ratio (PR)].

Initially, all variables were analyzed individually – univariate analysis (gross OR) – and following that, the multivariate analysis (adjusted OR) was performed. The model for multivariate analysis was the *backward* selection method, where the least significant variable is removed, one at a time, sequentially and automatically, based on statistical criteria. Only variables with p<0.05 remained in the final model.

## RESULTS

Initially, 754 patients who were hospitalized during the determined period were obtained. After applying the inclusion and exclusion criteria, 210 (27.8%) patients were excluded because they were directed directly to ICU admission, thus not going through the ward beforehand; 28 (3.7%) pregnant women; 10 (1.3%) patients in previous palliative care, and 4 (0.5%) patients younger than 18 years.

Thus, a total of 502 patients were eligible for this study. Patient demographics and clinical data, laboratory data, and therapy instituted are found in Table 1. The outcomes of patients admitted to the ward are given in Table 2.

Table 3 presents the findings of the univariate and multivariate analyses, where it is possible to note the odds ratio of an unfavorable patient outcome, represented by ICU admission or death.

## DISCUSSION

In this study, 502 medical records of patients hospitalized due to COVID-19 in the ward of a tertiary hospital in southern Brazil, in a period of 20 months, which included observation of the patients' demographic, clinical and laboratory data, and the therapy instituted, as well as the outcome obtained by these patients. It was observed that dyspnea/breathing discomfort, cough, and desaturation were the most common symptoms presented by the patients, while the laboratory tests showed that more than half of the patients had a $PaO_2/FiO_2$ <300 mmHg, indicating hypoxemia.

The median age of patients in this study was 56 years. A study that evaluated 25,919 patients from the southern region of Brazil found a median age of 60 years[7], indicating that the analyzed patients were younger than usual. However, the median age was higher for patients who progressed to the need for ICU or death in the ward, when compared with patients who were discharged (65.5 versus 53 years). Age greater than 65 years was considered a risk factor for a worse prognosis of

**Table 1.** Association of possible predictor variables between patients admitted to the COVID ward discharged to home and not discharged (needed ICU or died).

| Variables | Total Median (IQR) or n (%) n=502 | Discharged to home Median (IQR) or n (%) n=414 | Not discharged (ICU or death) Median (IQR) or n (%) n=88 | p-value |
|---|---|---|---|---|
| Age | 56 (43.0–68.0) | 53 (42.0–65.8) | 65.5 (50.8–78.5) | **0.01**[#a] |
| Age >65 years | 159 (31.7) | 114 (27.4)[ra=4.5] | 45 (52.3) | **0.01**[#b] |
| Male | 302 (60.2) | 255 (61.3) | 47 (54.7) | 0.25[b] |
| Vaccinated with one or more doses[d] | 35 (15.7) | 25 (14.2) | 10 (21.3) | 0.24[b] |
| Use of any medication from Kit COVID[e] | 180 (36.5) | 152 (37.0) | 28 (34.1) | 0.63[b] |
| Dyspnea/respiratory discomfort | 351 (69.9) | 286 (68.8) | 65 (75.6) | 0.21[b] |
| Cough | 317 (63.1) | 271 (65.1)[ra=2.0] | 46 (53.5) | **0.04***[b] |
| Oxygen desaturation ($SpO_2$≤94%) | 265 (52.8) | 218 (52.4) | 47 (54.7) | 0.70[b] |
| Fatigue/asthenia | 229 (45.6) | 196 (47.1) | 33 (38.4) | 0.14[b] |
| Fever | 214 (42.6) | 173 (41.6) | 41 (47.7) | 0.30[b] |
| Tachypnea (fR≥24) | 205 (40.8) | 156 (37.5)[ra=3.3] | 49 (57.0) | **0.01**[#b] |
| Pulmonary impairment >50%[f] | 117 (25.0) | 82 (21.1)[ra=4.3] | 35 (44.3) | **0.01**[#b] |
| Obesity (BMI≥30)[g] | 232 (46.7) | 196 (47.3) | 36 (43.4) | 0.51[b] |
| SAH | 222 (44.2) | 168 (40.4)[ra=3.8] | 54 (62.8) | **0.01**[#b] |
| DM | 104 (20.7) | 85 (20.4) | 19 (22.1) | 0.73[b] |
| Dyslipidemia | 58 (11.6) | 44 (10.6) | 14 (16.6) | 0.13[b] |
| Chronic heart disease | 52 (10.4) | 39 (9.4) | 13 (15,1) | 0.11[b] |
| COPD | 24 (4.8) | 18 (4.3) | 6 (7.0) | 0.29[c] |
| Asthma | 20 (4.0) | 14 (3.4) | 6 (7.0) | 0.12[c] |
| CKD | 15 (3.0) | 11 (2.6) | 4 (4.7) | 0.30[c] |
| Neoplasm | 8 (1.6) | 4 (1.0) | 4 (4.7) | **0.03**[c] |
| Absence of comorbidities | 142 (28.3) | 127 (30.5)[ra=2.5] | 15 (17.4) | **0.01**[#b] |
| $PaO_2/FiO_2$<300 mmHg[e] | 275 (55.8) | 217 (53.2)[ra=2.5] | 58 (68.2) | **0.01**[#b] |
| NLR >6,8 | 231 (46.0) | 186 (44.7) | 45 (52.3) | 0.20[b] |
| CRP >100 mg/L[h] | 239 (47.8) | 191 (46.0) | 48 (56.5) | 0.08[b] |
| LDH >250 U/L[i] | 326 (89.8) | 272 (89.8) | 54 (90.0) | 0.96[b] |
| D-dimer >1,000 ng/mL[j] | 72 (19.3) | 54 (17.3)[ra=2.2] | 18 (29.5) | **0.03***[b] |
| Ferritin >500 µg/L[k] | 163 (71.8) | 132 (70.2) | 31 (79.5) | 0.24[b] |
| Oxygen therapy nasal cannula | 405 (80.7) | 343 (82.5)[ra=2.2] | 62 (72.1) | **0.03***[b] |
| Venturi mask or with reservoir | 174 (34.7) | 98 (23.6)[ra=11.5] | 76 (88.4) | **0.01**[#b] |
| NIV | 50 (10,0) | 23 (5.5)[ra=7.3] | 27 (31.4) | **0.01**[#b] |
| OTI | 17 (3.4) | 2 (0.5)[ra=7.9] | 15 (17.4) | **0.01**[#c] |
| Corticotherapy | 494 (98.4) | 412 (99.0)[ra=2.5] | 82 (95.3) | **0.03**[#c] |
| Antibiotic therapy | 393 (78.3) | 328 (78.8) | 65 (75.3) | 0.50[b] |
| Prophylactic anticoagulation[l] | 467 (98.3) | 384 (98.0) | 83 (100.0) | 0.36[c] |
| Full anticoagulation[l] | 8 (1.7) | 8 (2.0) | 0 (0.0) | 0.36[c] |
| Use of antivirals | 69 (13.7) | 51 (12.3)[ra=2.1] | 18 (20.9) | **0.03***[b] |

Statistical method used: [a]*Mann-Whitney* U test; [b]*Pearson's* chi-square test; [c]*Fisher's* exact test. Data are expressed as Median (IQR) or n (%). IQR: interquartile range; n: sample size; SpO2: oxygen saturation; fR: respiratory frequency; BMI: body mass index; SAH: systemic arterial hypertension; DM: diabetes mellitus; COPD: chronic obstructive pulmonary disease; CKD: chronic kidney disease; NLR: neutrophil-to-lymphocyte ratio; CRP: C-reactive protein; LDH: Lactate Dehydrogenase; NIV: non-invasive ventilation; OTI: orotracheal intubation. [#]p<0.01; *p<0.05; [d]223/502; [e]493/502; [f]468/502; [g]497/502; [h]500/502; [i]363/502; [j]374/502; [k]227/502; [l]475/502. Bold indicates statiscally significant p-values.

COVID-19, increasing by 1.85 times the PR of an unfavorable progression, a result similar to that found by Marcolino et al.[6] in a study carried out in 25 Brazilian hospitals.

Males were the most affected, corresponding to 60.2% of hospitalized patients, slightly higher than that found by Ranzani et al.[7] in a study with 254,243 patients admitted to several hospitals in Brazil where the prevalence was 56%. Male patients also had a worse prognosis, and 54.7% were not discharged home and had a higher risk of mortality[8].

Few hospitalized patients had been vaccinated with some dose of the vaccine against COVID-19, and 36.5% of 493 patients had previously used the covid kit, consisting of azithromycin, ivermectin, and hydroxychloroquine. At the beginning of the pandemic, there were still no vaccines available and many drugs have been proposed as therapeutic possibilities against COVID-19, being used on a large scale in Brazil[9]. The use of the covid kit did not result in a better patient outcome.

Among the main signs and symptoms presented by patients are dyspnea/respiratory distress, cough, desaturation, fatigue/asthenia, fever, and tachypnea. Guan et al.[5] found similar symptoms, but in different proportions in their study carried out in China at the beginning of the spread of the disease.

Pulmonary involvement at the first chest tomography was >50% in 25% of 468 patients. This characteristic was also considered a risk factor for an unfavorable outcome, was present in 44.3% of patients who were not discharged home, and increased 1.49 times the risk of ICU admission or death. The most common aspects reported were ground-glass opacities, areas of consolidation, or both, which may be unilateral or bilateral and have greater extension approximately 10 days after the onset of symptoms[2,5]. A study carried out by Santos et al.[10] identified that 55% of patients with pulmonary involvement >50% underwent mechanical ventilation, while only 31% of patients with less than this had the same outcome. The result of our study reinforces this unfavorable outcome.

The main comorbidities presented by the patients were obesity, systemic arterial hypertension (SAH), and diabetes mellitus (DM), similar to what was found by Marcolino et al.[6] It is worth noting that 28.3% of the analyzed patients had no

**Table 2.** Outcomes of patients hospitalized in the COVID ward.

| Variables | Mean±SD or n (%) (n=502) |
|---|---|
| Discharged to home | 414 (82.5) |
| ICU | 68 (13.5) |
| Death | 20 (4.0) |
| Length of stay in the ward | 4.9±3.3 |

Data are expressed as mean±standard deviation or n (%). SD: standard deviation; n: sample size; ICU: intensive care unit.

**Table 3.** Multivariate analysis of factors associated with non-discharge outcome (need for ICU or death) of patients admitted to the COVID ward (n=88).

| Variable | OR (gross) | 95%CI | p-value | OR (adjusted) | 95%CI | p-value |
|---|---|---|---|---|---|---|
| Age >65 years | 2.37 | 1.62–3.46 | **0.01** | 1.85 | 1.30–2.64 | 0.01 |
| Cough | 0.67 | 0.46–0.98 | **0.04** | – | - | - |
| Tachypnea (fR≥24) | 1.92 | 1.30–2.83 | **0.01** | – | - | - |
| Pulmonary impairment>50% | 2.39 | 1.61–3.53 | **0.01** | 1.49 | 1.08–2.05 | 0.01 |
| SAH | 2.13 | 1.43–3.18 | **0.01** | – | - | - |
| Neoplasm | 3.01 | 1.46–6.19 | **0.03** | – | - | - |
| Absence of comorbidities | 0.54 | 0.32–0.90 | **0.02** | – | - | - |
| $PaO_2/FiO_2$<300 mmHg | 1.70 | 1.12–2.59 | **0.01** | – | - | - |
| D-dímero>1,000 ng/mL | 1.76 | 1.08–2.86 | **0.02** | – | - | - |
| Oxygen therapy nasal cannula | 0.62 | 0.41–0.94 | **0.02** | – | - | - |
| Venturi mask or with reservoir | 14.33 | 7.61–26.98 | **0.01** | 9.69 | 4.87–19.26 | 0.01 |
| NIV | 4.13 | 2.91–5.85 | **0.01** | 1.55 | 1.06–2.25 | 0.02 |
| OTI | 6.03 | 4.57–7.94 | **0.01** | 1.86 | 1.27–2.72 | 0.01 |
| Did not use corticotherapy | 3.01 | 1.47 –6.20 | **0.03** | 1.54 | 1.23–1.93 | 0.01 |
| Did not use antivirals | 0.60 | 0.38–0.95 | **0.03** | – | - | - |

OR: odds ratio; CI: confidence interval; fR: respiratory frequency; SAH: systemic arterial hypertension; NIV: non-invasive ventilation; OTI: orotracheal intubation. Bold indicates statiscally significant p-values.

previous comorbidity reported, and this rate is much higher than that found by Ranzani et al.[7] which was 16%.

Regarding laboratory tests, 55.8% of 493 patients had $PaO_2/FiO_2$<300 mmHg, therefore being classified as acute respiratory distress syndrome (ARDS), which can be mild, moderate, or severe[11]. The neutrophil/lymphocyte ratio (NLR) is a parameter used to evaluate the individual's inflammatory state and predicts outcomes in a variety of conditions. In this study, 46.0% of the patients had NLR>6.8. Prozan et al.[12] identified in their study, using an NLR=6.8 as a cut-off point, that for COVID-19, a poor clinical outcome was associated with a higher NLR. In this study, this correlation was not found.

The CRP levels were >100 mg/L in 47.8% of 500 patients, as well as LDH levels >250 U/L in 89.8% of 363, ferritin >500 µg/L in 71.8% of 227, and D-dimer >1,000 ng/mL in 19.3% of 374 patients. Kim and Gandhi[13] identified that the elevation of these markers, above the presented limits, was associated with disease severity, and a CRP≥100 mg/dL was a risk factor for higher mortality[6]. No relationship between these markers and a worse outcome was found in this study.

Individuals who required oxygen therapy by Venturi mask or reservoir bag mask or required NIV or OTI also had a higher risk of not being discharged home, demonstrating that high-flow oxygen therapy to maintain a target $SpO_2$≥90% in adults, refractory hypoxemia requiring NIV, or failure of non-invasive therapies are important factors to an unfavorable outcome for patients admitted to the wards[3,14].

Among these factors, the greatest risk for worse outcomes was found in patients who required oxygen therapy using a Venturi mask or reservoir bag mask. We believe that two factors may have influenced our result. The first is that some patients were very elderly, with many comorbidities, were critically ill, and family members chose not to institute invasive measures in these patients. The second is that the use of the Venturi mask or reservoir mask may have extended beyond a time considered acceptable, delaying a more invasive measure. Some studies have shown that, paradoxically, the use of these measures and the delay in the use of more invasive measures can worsen the patient's respiratory condition, due to the respiratory effort, which leads to self-inflicted lung injury by the patient (PSILI), resulting in worse outcomes[15,16]. However, further studies are needed to confirm this hypothesis.

In drug therapy, 98.4% of patients used corticosteroids, and individuals who did not use corticosteroids had a higher risk of poor prognosis. The use of corticosteroids in low doses for 10 days was recommended during the pandemic for patients hospitalized with COVID-19 using supplemental oxygen[17], and our result corroborates this recommendation.

Among the limitations found, it can be considered that the study was carried out in a single hospital, where some medical records were not very detailed. There were changes in the tests requested according to severity and length of stay, which led to the need to use the relative frequency for the analysis of results. Furthermore, the method for measuring CRP levels only accounts for values up to 159.9 mg/L, with values above these presented as >160 mg/L, so it is not possible to know the accuracy of these values. Vaccination analysis was limited, given that the survey comprises a large period when there were no vaccines against COVID-19 available.

## CONCLUSIONS

Age older than 65 years and a lung involvement extension greater than 50% are predictors of poor prognosis for COVID-19, as well as the need for high-flow oxygen therapy, NIV, and OTI. Corticosteroid therapy, on the contrary, proved to be beneficial in the treatment of the disease.

## AUTHORS' CONTRIBUTIONS

**BN:** Conceptualization, Data curation, Investigation, Methodology, Software, Visualization, Writing – original draft, Writing – review & editing. **MVG:** Conceptualization, Formal Analysis, Project administration, Supervision, Visualization. **FRR:** Methodology, Software, Visualization. **EDM:** Data curation, Visualization. **IS:** Data curation, Visualization. **FP:** Data curation, Visualization. **PSSD:** Conceptualization, Formal Analysis, Investigation, Methodology, Project administration, Supervision, Visualization, Writing – review & editing.

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