ACIN
ASOCIACIÓN COLOMBIANA DE INFECTOLOGÍA

infectio

ARTÍCULO ORIGINAL

Main clinical variables related to long-term mortality in COVID-19

Alirio Bastidas-Goyes[1,2*], Eduardo Tuta-Quintero[1,3], Faure Yezid Rodríguez[1,4], Diego Holguín Riaño[1,5], Aldair Chaar Hernández[1,6], Lorena García Agudelo[1,7], Nicolas Peña Ramos[1,8], Carolina Gómez-Ruiz[1,9], Juan Giraldo-Vásquez[1,10], Doris Pumarejo-Villazón[1,11], María Henríquez-Rodríguez[1,12], Daniela Álvarez-Araujo[1,13], Paola Martínez-Artunduaga[1,14], Paola López Morales[1,15], Yesid Mantilla-Flórez[1,16], Luis F. Reyes[1,17]

Abstract

Objective: To determine relationship between clinical characteristics, laboratory results and treatments with 12 month mortality in COVID-19.

Materials and methods: A retrospective cohort study was conducted in three hospitals in Colombia. Odds ratios (OR) were calculated using multivariate logistic regression analysis with outcome variable mortality at 12 months.

Results: A total of 1194 patients were included out of 4344 potential eligible subjects, average age was 57.7 years. The group of patients who died at 12 months showed a lymphocyte count of 922.6 (SD:572.32) compared to 1200.1 (SD:749.45) in the group of survivors (p<0.001). Hemoglobin averaged 2.1 g/dl less in the patients who died compared to the control group (14.5 vs. 12.4; p<0.001). The blood urea nitrogen (33.3 vs. 19.3; p<0.001) was higher in patients who died at 12-month follow-up compared to the surviving group. Age>70 years OR:7.2 (95%CI:3.9-13.3) and adjusted OR:1.05 (95%CI:1.01-1.08) (p=0.023), Charlson index >4 OR:7.8 (95%CI:4.3-14.1) and adjusted OR:1.35 (95%CI:1.1-1.67) (p=0.005), dexamethasone OR:0.3 (95%CI:0.2-0.6) and adjusted OR:0.3 (95%CI:0.14-0.65) (p=0.002) and pronation OR:0.3 (95%CI:0.1-1) and adjusted OR:0.4 (95%CI:0.08-1.87) (p=0.242).

Conclusions: The increased risk of death 12 months after acute SARS-CoV-2 infection is associated with clinical variables such as age >70 years and Charlson index >4. Use of prone ventilation and dexamethasone were associated with increased survival.

Keywords: COVID-19; SARS-CoV-2; Post-Acute COVID-19 Syndrome; Mortality.

Principales variables clínicas relacionadas con la mortalidad a largo plazo en COVID-19

Resumen

Objetivo: Determinar relación entre características clínicas, resultados de laboratorio y tratamientos con mortalidad a 12 meses en COVID-19.

Materiales y Métodos: Se realizó un estudio de cohorte retrospectivo en tres hospitales de Colombia. Los cocientes de probabilidades (OR) se calcularon mediante un análisis de regresión logística multivariable con la variable de resultado mortalidad a los 12 meses.

Resultados: Se incluyeron un total de 1194 pacientes de 4344 posibles sujetos elegibles, la edad promedio fue de 57,7 años. El grupo de pacientes que fallecieron a los 12 meses presentó un recuento de linfocitos de 922,6 (DE:572,32) frente a 1200,1 (DE:749,45) en el grupo de supervivientes (p<0,001). La hemoglobina promedió 2,1 g/dl menos en los pacientes que fallecieron en comparación con el grupo control (14,5 vs. 12,4; p<0,001). El nitrógeno ureico en sangre (33,3 frente a 19,3; p<0,001) fue mayor en los pacientes que fallecieron a los 12 meses de seguimiento en comparación con el grupo de supervivientes. Edad>70 años OR:7,2 (IC95%:3,9-13,3) y OR ajustado:1,05 (IC95%:1,01-1,08) (p=0,023), índice de Charlson >4 OR:7,8 (IC95%:4,3- 14,1) y OR ajustada: 1,35 (IC 95%: 1,1-1,67) (p=0,005), dexametasona OR: 0,3 (IC 95%: 0,2-0,6) y OR ajustada: 0,3 (IC 95%: 0,14-0,65) (p=0,002) y pronación OR:0,3 (IC95%:0,1-1) y OR ajustada:0,4 (IC95%:0,08-1,87) (p=0,242).

Conclusión: El aumento del riesgo de muerte 12 meses después de la infección aguda por SARS-CoV-2 se asocia con variables clínicas como la edad > 70 años y el índice de Charlson > 4. El uso de ventilación en decúbito prono y dexametasona se asoció con una mayor supervivencia.

Palabras clave: COVID-19; SARS-CoV-2; Síndrome Post-Agudo de COVID-19; Mortalidad.

1 School of Medicine, Universidad de La Sabana. Chía. Colombia.
2 https://orcid.org/0000-0002-8873-9779
3 https://orcid.org/0000-0002-7243-2238
4 https://orcid.org/0000-0002-1807-0221
5 https://orcid.org/0000-0003-0639-6061
6 https://orcid.org/0000-0001-9180-7114
7 https://orcid.org/0000-0003-1604-6911
8 https://orcid.org/0000-0003-2915-3388
9 https://orcid.org/0000-0003-4058-4517
10 https://orcid.org/0000-0003-3425-5549
11 https://orcid.org/0000-0003-1976-7124
12 https://orcid.org/0000-0002-3998-3281
13 https://orcid.org/0000-0002-9099-6571
14 https://orcid.org/0000-0003-1291-0952
15 https://orcid.org/0000-0001-6618-914X
16 https://orcid.org/0000-0002-6276-7544
17 Clínica Universidad de La Sabana. Chía. Colombia. https://orcid.org/0000-0003-1172-6539
* Autor para correspondencia:
Correo electrónico: alirio.bastidas@unisabana.edu.co

Recibido: 14/03/2023; Aceptado: 09/07/2023

Cómo citar este artículo: A. Bastidas-Goyes, *et al.* Main clinical variables related to long-term mortality in COVID-19. Infectio 2023; 27(3): 159-164

Introduction

In late 2019, a new coronavirus was identified as the cause of pneumonia in Wuhan, a city in China's Hubei province[1,2]. It spread rapidly, resulting in a China-wide epidemic and subsequently a pandemic. In February 2020, the disease was designated COVID-19 (coronavirus disease 2019) by the World Health Organization and was found to be caused by a virus named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)[1,3]. An enveloped positive-stranded RNA virus belonging to the subgenus betacoronavirus like severe acute respiratory syndrome virus (SARS) and Middle East respiratory syndrome virus (MERS)[4-6]. The spectrum of COVID-19 ranges from asymptomatic infection to severe, life-threatening conditions. According to estimates by the Chinese center for disease control and prevention, 81% are mild infections, 14% are severe (dyspnea, hypoxia, or pulmonary compromise on imaging >50% within 24 to 48 hours), 5% are critical (respiratory failure, shock or multiorgan dysfunction) and 2.3% of patients die[6]. Multiple long-term complications of COVID-19 and its main sequelae have been described, including asthenia, adynamia, respiratory distress, chronic chest pain, and dyspnea, among others. Therefore, the need to understand and respond to long-term effects of COVID-19 is increasingly urgent[7,8].

Long-term COVID-19 encompasses physical, medical, and cognitive sequelae with a reported prevalence of between 30% and 54%[7-9]. Huang et al[10], described persistent signs and symptoms at 6 months and 12 months later in 1,276 COVID-1 survivors, including fatigue, muscle weakness, limited mobility, and anxiety or depression. Motloch et al[11], described biomarkers such as troponin and vascular cell adhesion molecule-1 associated with hospital and long-term mortality in patients with a history of COVID 19. However, the risk factors for long-term morbidity and mortality in patients with a history of SARS-CoV-2 infection are unknown. In addition, there are limited data describing the main variables associated with mortality in small cohorts, mostly hospitalized COVID-19 cases and compared with the population without the infection[5-9]. Given that the increased risk of mortality after COVID-19 requires multidisciplinary and specific interventions to prevent these deaths, we have developed this study that aims to determine the relationship between clinical characteristics, laboratory results and the treatments used with mortality at 12 months in patients with COVID-19.

Methods

Design

Retrospective cohort study in three hospitals in Colombia, Clínica Universidad de la Sabana (Chía, Cundinamarca), Clínica Palermo (Bogotá D.C.) and Hospital Regional De La Orinoquía (Yopal, Casanare) in patients who attended these institutions between March 2020 and March 2021, with a 12-month follow-up after hospital discharge.

Criteria eligibility

Patients over 18 years of age and whose discharge status was "alive" were included. The diagnosis of COVID-19 was made by polymerase chain reaction (PCR) in a respiratory sample. Patients who were referred to other institutions were excluded. Twelve months after hospital discharge, follow-up was performed to establish survival.

Variables

Several variables were obtained, including demographic characteristics, clinical forms of presentation of COVID-19, laboratory test results, treatment, and condition at the end of hospitalization. The primary outcome investigated was the 12-month mortality after hospitalization.

Data sources/measurement

Data were obtained from clinical records of the information systems from hospital centers. One year after discharge, the status was obtained from the Administradora de los Recursos del Sistema General de Seguridad Social en Salud (ADRES) database and through telephone calls. Qualitative variables were summarized in frequencies and percentages and quantitative variables in mean and standard deviations if the distribution was normal or in medians and interquartile ranges if the distribution did not respect normality.

Biases

There was variability in the units of measurement in which some laboratory results were reported, so these measurements were converted to unify them into the same one. Patients whose survival status could not be established were excluded from the outcome to be evaluated.

Sample size

The sample size was calculated using the Hosmer-Lemeshow formula for logistic regression. Considering the entry of 10 parameters for the regression, a minimum number of 10 cases per parameter, a 10% frequency of the death event and one year of follow-up, finally requiring 1000 subjects[12].

Statistical methods

Data were analyzed using the SPSS 25 program licensed by the Universidad de La Sabana. Qualitative variables were summarized in frequencies and percentages, quantitative variables in averages and standard deviations if the distribution was normal, or medians and interquartile ranges if the distribution was not normal. A bivariate was performed comparing the quantitative variables using a student's t-test if they were normally distributed. If the distribution was not normal, the Mann-Whitney U test was used. Qualitative variables were compared with Chi-square or Fisher's test. Crude and adjusted odds ratios were calculated using multivariate logistic regression analysis with the outcome variable mortality at 12 months, considering a statistically significant $p < 0.05$.

Results

Population characteristics

A total of 1194 patients were included out of 4344 potential eligible subjects Figure 1. The average age of the general population was 57.7 years, and 58.7 % (n=701) were male. Death occurred in 50 individuals in the study (4.2 %), which was more common in older subjects with a mean of 73 years (SD ±12,91). 36.6 % of the patients presented arterial hypertension, and 93.6% of the patients used antihypertensives. Table 1 shows the characteristics of the cohort.

Laboratory exams and treatment

The group of patients who died at 12 months showed a lymphocyte count of 922.6 (SD: 572.32) compared to 1200.1 (SD: 749.45) in the group of survivors (p<0.001) table 2. Hemoglobin averaged 2.1 g/ dl less in the patients who died compared to the control group (14.5 vs. 12.4; p<0.001). The blood urea nitrogen (BUN) (33.3 vs. 19.3; p<0.001) and d-dimer (2252.0 vs. 1273.1; p=0.029) were higher in patients who died at 12-month follow-up compared to the surviving group. Table 3 shows the different treatments used.

Odds ratio and multivariate analyzes

Age > 70 years OR: 7.2 (95% CI: 3.9-13.3) and adjusted OR: 1.05 (95% CI: 1.01-1.08) (p=0.023), Charlson index >4 OR: 7.8 (95% CI: 4.3-14.1) and adjusted OR: 1.35 (95% CI: 1.1-1.67) (p=0.005), dexamethasone OR: 0.3 (95% CI: 0.2-0.6) and adjusted OR: 0.3 (95% CI: 0.14-0.65) (p=0.002) and pronation OR: 0.3 (95% CI: 0.1-1) and adjusted OR: 0.4 (95% CI: 0.08-1.87) (p=0.242) Table 4.

Discussion

These results show the variables associated with mortality at 12 months after acute SARS-CoV-2 infection. In the adjusted analysis, it was shown that age > 70 years and Charlson index > 4 were risk factors, and pronation and the use of dexamethasone were protective factors for mortality. A higher frequency of lymphopenia was observed, as well as a higher neutrophil/lymphocyte (N/L) ratio in the group of patients who died at 12 months. In addition, increased BUN concentration and creatinine were correlated with increased mortality in the subjects tested.

We found that an increase in some acute phase reagents that have previously been associated with increased early lethality, such as C-reactive protein, D-dimer, ferritin, among others, are correlated with decreased long-term survival. In addition, in our cohort, we found certain laboratory test abnormalities that are more frequently found in subjects with a fatal outcome. These results are novel and useful in the po-

Table 1. General characteristics of the population.

	Overall patients n= 1194	Dead at 12 months n= 50	Alive at 12 months n= 1144	*p value*
Age years, m(SD)	57.1 (15.76)	73.0 (12.91)	57.1 (15.76)	<0.001
Male, n (%)	701 (58.7)	32 (64.0)	669 (58.5)	0.438
Epidemiological nexus, n (%)	828 (69.3)	38 (76.1)	790 (69.1)	0.297
Close contact with positive COVID-19, n (%)	307 (25.7)	7 (14.1)	300 (26.2)	0.053
Previous hospitalization, n (%)	32 (2.7)	3 (6.9)	29 (2.5)	0.138
Arterial hypertension, n (%)	437 (36.6)	22 (44.7)	415 (36.3)	0.267
Smoking, n (%)	26 (2.2)	1 (2.5)	25 (2.2)	0.930
Previous smoking, n (%)	95 (8.0)	4 (8.4)	91 (8.0)	0.991
Myocardial infarction, n (%)	30 (2.5)	1 (2.3)	29 (2.5)	0.813
Heart failure, n (%)	24 (2.0)	3 (6.7)	21 (1.8)	0.040
Stroke, n (%)	18 (1.5)	2 (4.4)	16 (1.4)	0.140
Dementia, n (%)	20 (1.7)	3 (6.2)	17 (1.5)	0.015
COPD, n (%)	66 (5.5)	10 (20.9)	56 (4.9)	<0.001
Asthma, n (%)	35 (2.9)	(0.0)	35 (3.1)	0.740
Antihypertensive, n (%)	1118 (93.6)	41 (82.3)	1077 (94.1)	<0.001
ACE inhibitor, n (%)	65 (5.4)	2 (4.3)	63 (5.5)	0.646
ARA-II, n (%)	297 (24.9)	11 (22.2)	286 (25.0)	0.631
Charlson index, m(SD)	1.9 (1.91)	4.6 (2.56)	1.8 (1.79)	<0.001

Abbreviations: m: average, SD: standard deviation; COPD: Chronic obstructive pulmonary disease; ACE: Angiotensin converter enzyme; ARA-II: Angiotensin II receptor antagonist.

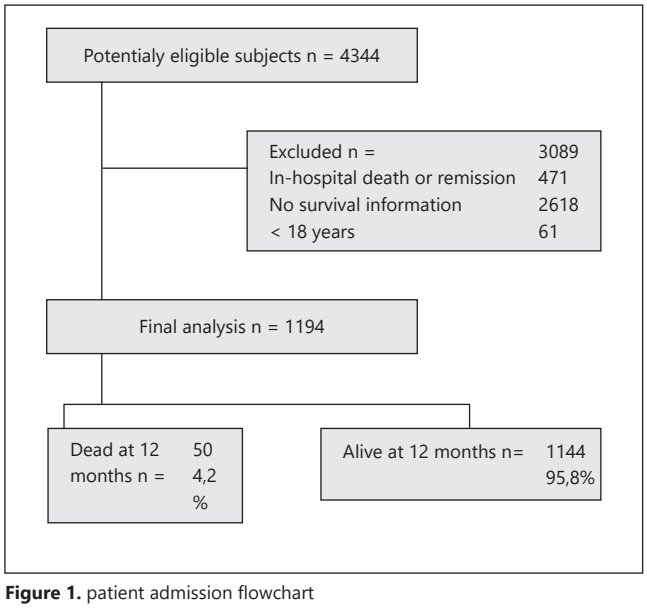

Figure 1. patient admission flowchart

Table 2. Laboratory results on admission

	Overall patients n= 1194	Dead at 12 months n= 50	Alive at 12 months n= 1144	p value
Leucocyte 10^9 cells/L, m (SD)	8698.5 (4290.44)	8673.4 (5465.57)	8699.6 (4233.83)	0.973
Neutrophils 10^9 cells/L, m (SD)	7017.6 (4051.87)	7270.7 (5087.79)	7006.3 (4001.88)	0.717
Lymphocytes 10^9 cells/L, m (SD)	1188.3 (744.67)	922.6 (572.32)	1200.1 (749.45)	<0.001
N/L ratio, m (SD)	7.9 (7.01)	10.5 (8.32)	7.8 (6.92)	0.008
Hemoglobin g/dl, m (SD)	14.4 (2.29)	12.4 (2.78)	14.5 (2.23)	<0.001
Hematocrit %, m (SD)	42.8 (6.49)	37.9 (7.62)	43.0 (6.35)	<0.001
Platelets 10^9/L, m (SD)	248.4 (97.76)	244.0 (109.76)	248.6 (97.24)	0.743
Sodium mEq/L, m (SD)	136.8 (6.2)	137.2 (5.19)	136.8 (6.25)	0.577
Creatinine mg/dl, m (SD)	1.3 (1.45)	2.3 (2.51)	1.2 (1.37)	0.004
BUN mg/dl, m (SD)	19.9 (12.94)	33.3 (22.57)	19.3 (12.08)	<0.001
Glucose mg/dl, m (SD)	143.3 (72.77)	118.9 (38.46)	144.3 (73.75)	<0.001
Albumin g/l, m (SD)	3.1 (0.51)	3.1 (0.37)	3.1 (0.54)	0.989
Ferritin ng/mL, m (SD)	1188.7 (2047.89)	977.2 (1629.45)	1196.5 (2062.23)	0.358
LDH mg/dl, m (SD)	391.5 (233.71)	336.2 (182.97)	394.0 (235.55)	0.031
AST U/L, m (SD)	51.8 (56.76)	44.8 (44.95)	52.1 (57.23)	0.265
ALT U/L, m (SD)	55.8 (66.53)	43.1 (66.62)	56.4 (66.51)	0.165
TB mg/dl, m (SD)	0.7 (0.49)	0.8 (0.75)	0.7 (0.47)	0.151
DB mg/dl, m (SD)	0.3 (0.34)	0.5 (0.57)	0.3 (0.32)	0.049
IB mg/dl, m (SD)	0.3 (0.24)	0.3 (0.25)	0.3 (0.24)	0.861
Procalcitonin ng/mL, m (SD)	1.4 (6.23)	0.1 (0.09)	1.5 (6.33)	<0.001
CRP mg/L, m (SD)	111.8 (96.86)	101.4 (89.59)	112.2 (97.18)	0.441
Troponin ng/mL, m (SD)	1.8 (37.65)	8.9 (36.74)	1.5 (37.68)	0.173
D-dimer ng/mL, m (SD)	1311.6 (3095.64)	2252.0 (3180.67)	1273.1 (3087.68)	0.029

Notes: m: average, SD: standard deviation; N/L: Neutrophil to lymphocyte; BUN: Blood ureic nitrogen; LDH: Lactic dehydrogenase; AST: Aspartate transaminase; ALT: Alanine transaminase; TB: Total bilirubin, DB: Direct bilirubin; IB: Indirect bilirubin; CRP: C-reactive protein.

pulation of low- and middle-income countries because they evaluate clinical variables and laboratory tests that are easy to collect during acute hospitalization and clinical follow-up at hospital discharge in patients with COVID-19[9,13-15].

Oxygen deprivation due to lung injurie and low hemoglobin levels leads to a greater oxygen deficit in the tissues, thus potentially increasing long-term morbidity and mortality[16-19]. Regarding the treatments received, it is important to mention that at the beginning of the study, the patients received different medications based on the national guidelines for managing patients with COVID-19, which were modified according to the results of the evidence that was published. In July 2020, the preliminary results of the RECOVERY study were published[13,17-19]. From that time on, dexamethasone became widespread, which is reflected in our cohort. We found a clear difference in its use with the outcomes in the population. The analysis adjusted for confounding variables showed a lower mortality in patients treated with dexamethasone, corroborating the positive impact on mortality from COVID-19.

This study presents important strengths and limitations. The strengths include the use of a reliable and unified database in each institution for the follow-up of the patients; in them, information was obtained on their survival, clinical evolution and laboratory results over time. Likewise, validatedudy and standardized molecular biology diagnostic tests were used to include the subjects in the st, giving greater internal validity to our work. We analyzed variables already demonstrated as predictors of severity (lymphocyte count, N/L ratio, BUN, creatinine, among others). Additionally, knowledge of 12-month mortality in patients with COVID-19 gives an idea of the long-term impact of the disease on the population as well as its impact in terms of quality of life and overall disease burden, the latter related to premature death[17,18].

Relevant limitations of our work include the fact that the data are observational. However, it serves as a basis for the development of intervention studies with which to corroborate our results. Although we have an important sample of patients in our study, obtained information represents three institutions and therefore, it is difficult to generalize the results to the entire population. More clinical studies are needed that include a larger number of patients over a prolonged period to better describe the causes of death in patients, and that are not related to sequelae derived from COVID-19.

Table 3. Treatment used.

	Overall patients n= 1194	Dead at 12 months n= 50	Alive at 12 months n= 1144	p value
Lopinavir/ritonavir, n (%)	3 (0.3)	(0)	3 (0.3)	0.939
Chloroquine, n (%)	3 (0.3)	(0)	3 (0.3)	0.939
Hydroxychloroquine, n (%)	2 (0.2)	(0)	2 (0.2)	0.951
Ivermectin, n (%)	93 (7.8)	1 (2.1)	92 (8.2)	0.119
Colchicine, n (%)	56 (4.7)	1 (2.1)	55 (4.8)	0.358
Dexamethasone, n (%)	780 (65.3)	20 (40)	760 (66.4)	<0.001

Table 4. Odds ratios for each variable related to mortality 12 months.

	OR (95% CI)	OR* (95% CI)	p value
Age >70 years	7.2 (3.9-13.3)	1.05 (1.01-1.08)	0.023
Female	0.8 (0.4-1.4)	0.61 (0.28-1.34)	0.220
Charlson index > 4	7.8 (4.3-14.1)	1.35 (1.1-1.67)	0.005
Initial Glasgow <12 ingreso	9.5 (1.8-50.2)	0.87 (0.65-1.17)	0.348
Initial Ph <7.4	3.6 (1.9-6.6)	0.57 (0-153.81)	0.845
Initial N/L ratio >10 ingreso	2.9 (1.6-5.1)	1.02 (0.98-1.07)	0.277
Initial Hemoglobin <12 g/dL	6.9 (3.8-12.4)	0.83 (0.71-0.97)	0.017
Initial Creatinine ≥1.5 mg/dl	4.9 (2.6-9.1)	1.03 (0.85-1.25)	0.754
Dilation of cavities	7.2 (1.9-27.2)	3.59 (0.33-38.8)	0.292
Dexamethasone	0.3 (0.2-0.6)	0.3 (0.14-0.65)	0.002
Pronation	0.3 (0.1-1)	0.4 (0.08-1.87)	0.242

Abbreviations: N/L: Neutrophil to lymphocyte; OR: Odds ratio; OR: adjusted Odds ratio.

In conclusion, increased risk of death from COVID-19 is not limited to acute illness. Lymphopenia, anemia, and elevation of BUN, creatinine, and d-dimer occurred more frequently in patients who died at 12-month follow-up after COVID-19. The increased risk of death 12 months after acute SARS-CoV-2 infection is associated with clinical variables such as age > 70 years and Charlson index > 4. Use of prone ventilation and dexamethasone were associated with increased survival in this population.

Ethical considerations

Patients were not involved in the development of the research question, design, recruitment, or intervention burden assessed; no patient advisors were required, and data were analyzed anonymously. This study was approved by the research committee of the Universidad de La Sabana and the institutional ethics committee of the Clínica Universidad de La Sabana, as registered on Act Minute Nº 526 of January 29, 2021. We consider it to be an investigation without risk according

to resolution 8430 of 1993 and to respect the protection of personal data according to the habeas data law 1266 of 2008; therefore, obtaining informed consent is not required.

The authors declare that for the elaboration of this project, no experiments with humans or animals were carried out.

Confidentiality of the data. The authors declare that they have followed the protocols of the institution of origin of the patients on the publication of data, the document does not contain data that allows them to be identified.

Financing. This work was supported by Universidad de La Sabana grant number MEDMSc-69-2023.

Conflicts of interest. The authors declare that they have no conflict of interest.

Acknowledgments. The study was carried out at the Universidad de La Sabana.

Author contributions. LFR , FYR, DHR, ACH, LGA, NPR, CGR, JGV, DPV, MHR, DAA, PMA, PLM, YMF, ETQ and LFR contributed to the conception and design. LFR and LFR supervised the whole process. FYR, DHR, ACH, LGA, NPR, MHR, DAA, PMA and PLM contributed to data collection. ABG, CGR, JGV, DPV and LFR analyzed and interpreted the patient data. ABG and ETQ wrote major parts of the manuscript. ABG and LFR revised the manuscript. All authors read and approved the final manuscript.

References

1. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497-506. DOI: 10.1016/S0140-6736(20)30183-5.
2. Bell ML, Catalfamo CJ, Farland LV, Ernst KC, Jacobs ET, Klimentidis YC, et al. Post-acute sequelae of COVID-19 in a non-hospitalized cohort: Results from the Arizona CoVHORT. PLoS One. 2021 ;16(8):e0254347. DOI: 10.1371/journal.pone.0254347.
3. World Health Organization. WHO coronavirus (COVID-19) dashboard [Internet]. [accessed on 26 January 2023]. Available: https://covid19.who.int/.
4. Gallo Marin B, Aghagoli G, Lavine K, Yang L, Siff EJ, Chiang SS, et al. Predictors of COVID-19 severity: A literature review. Rev Med Virol. 2021 Jan;31(1):1-10. DOI: 10.1002/rmv.2146.
5. Abdelghany TM, Ganash M, Bakri MM, Qanash H, Al-Rajhi AMH, Elhussieny NI. SARS-CoV-2, the other face to SARS-CoV and MERS-CoV: Future predictions. Biomed J. 2021;44(1):86-93. DOI: 10.1016/j.bj.2020.10.008.
6. Yadaw AS, Li YC, Bose S, Iyengar R, Bunyavanich S, Pandey G. Clinical features of COVID-19 mortality: development and validation of a clinical prediction model. Lancet Digit Health. 2020 ;2(10):e516-e525. DOI: 10.1016/S2589-7500(20)30217-X.
7. Bellan M, Soddu D, Balbo PE, Baricich A, Zeppegno P, Avanzi GC, et al. Respiratory and Psychophysical Sequelae Among Patients With COVID-19 Four Months After Hospital Discharge. JAMA Netw Open. 2021 ;4(1):e2036142. DOI: 10.1001/jamanetworkopen.2020.36142.
8. Haberland E, Haberland J, Richter S, Schmid M, Hromek J, Zimmermann H, et al. Seven Months after Mild COVID-19: A Single-Centre Controlled Follow-Up Study in the District of Constance (FSC19-KN). Int J Clin Pract. 2022 ;2022:8373697. DOI: 10.1155/2022/8373697.
9. Groff D, Sun A, Ssentongo AE, Ba DM, Parsons N, Poudel GR, et al. Short-term and Long-term Rates of Postacute Sequelae of SARS-CoV-2 Infection: A Systematic Review. JAMA Netw Open. 2021 ;4(10):e2128568. DOI: 10.1001/jamanetworkopen.2021.28568.
10. Huang L, Yao Q, Gu X, Wang Q, Ren L, Wang Y, et al. 1-year outcomes in hospital survivors with COVID-19: a longitudinal cohort study. Lancet. 2021 ;398(10302):747-758. DOI: 10.1016/S0140-6736(21)01755-4.
11. Motloch LJ, Jirak P, Gareeva D, Davtyan P, Gumerov R, Lakman I, et al. Cardiovascular Biomarkers for Prediction of in-hospital and 1-Year Post-discharge Mortality in Patients With COVID-19 Pneumonia. Front Med (Lausanne). 2022 ;9:906665. DOI: 10.3389/fmed.2022.906665.
12. Hosmer DW, Lemeshow S, Sturdivant RX. Special Topics. In: Hosmer DW, Lemeshow S, Sturdivant RX, editors. Applied Logistic Regression, 3rd ed. New York, NY: John Wiley & Sons, Inc; 2013. p. 401-408.
13. Horby P, Lim WS, Emberson JR, Mafham M, Bell JL, Linsell L, et al. dexamethasone in hospitalized patients with Covid-19. N Engl J Med 2021;384:693–704. DOI: 10.1056/NEJMoa2021436.
14. Mainous AG 3rd, Rooks BJ, Wu V, Orlando FA. COVID-19 Post-acute Sequelae Among Adults: 12 Month Mortality Risk. Front Med (Lausanne). 2021 ;8:778434. DOI: 10.3389/fmed.2021.778434
15. Desai AD, Lavelle M, Boursiquot BC, Wan EY. Long-term complications of COVID-19. Am J Physiol Cell Physiol. 2022 ;322(1):C1-C11. DOI: 10.1152/ajpcell.00375.2021
16. Mainous AG 3rd, Rooks BJ, Orlando FA. The Impact of Initial COVID-19 Episode Inflammation Among Adults on Mortality Within 12 Months Post-hospital Discharge. Front Med (Lausanne). 2022 ;9:891375. DOI: 10.3389/fmed.2022.891375
17. Akbarialiabad H, Taghrir MH, Abdollahi A, Ghahramani N, Kumar M, Paydar S, et al. Long COVID, a comprehensive systematic scoping review. Infection. 2021;49(6):1163-1186. DOI: 10.1007/s15010-021-01666-x.
18. LaVergne SM, Stromberg S, Baxter BA, Webb TL, Dutt TS, Berry K, et al. A longitudinal SARS-CoV-2 biorepository for COVID-19 survivors with and without post-acute sequelae. BMC Infect Dis. 2021 ;21(1):677. DOI: 10.1186/s12879-021-06359-2.
19. Ahmad MS, Shaik RA, Ahmad RK, Yusuf M, Khan M, Almutairi AB, et al. "LONG COVID": an insight. Eur Rev Med Pharmacol Sci. 2021;25(17):5561-5577. DOI: 10.26355/eurrev_202109_26669.