Saúde e Pesquisa
DOI: 10.17765/2176-9206.2024v17n1.e12198

Initial symptoms of COVID-19 and their relationship with mortality in patients hospitalized in the state of Paraná

Sintomas iniciais da COVID–19 e sua relação com a mortalidade em pacientes internados no Paraná

Danielle Bordin[1*], Jessica Cardozo[1], Midiã Vanessa dos Santos Spekalski[2], Geiza Rafaela Bobato[3], Péricles Martim Reche[1], Carla Luiza da Silva[1]

[1] Department of Nursing, State University of Ponta Grossa (UEPG), Ponta Grossa (PR), Brazil,[2] Postgraduate Program in Nursing, Federal University of Paraná (UFPR), Curitiba (PR), Brazil, [3] Postgraduate Program in Molecular and Morphofunctional Biology, Institute of Biology, State University of Campinas (UNICAMP), Campinas (SP), Brazil.

***Autor correspondente**: Danielle Bordin – *E-mail*: dbordin@uepg.br

ABSTRACT
To analyze the initial symptoms of COVID-19 and associate them with the death of adult patients and older people hospitalized in the state of Paraná. A cross-sectional study carried out with data from the Paraná notification system. The study population was made up of individuals infected with SARS-CoV-2 in the state of Paraná. The clinical outcome (discharge and death) was used as the dependent variable and the independent the clinical signs. The chi-square and logistic regression were performed. Sample of 15,492 individuals, of which 66.5% were discharged from the hospital. Individuals with low oxygen saturation, dyspnea, irritability or confusion, and nasal flaring were 2.09, 1.68, 1.65 and 2.37, respectively, more likely to die ($p<0.001$). Headache (OR=0.82), myalgia (OR=0.76), and dysgeusia (OR=0.78) were presented as protective factors against mortality ($p\leq0.001$). Death from COVID-19 was associated with low oxygen saturation, dyspnea, irritability or confusion, and nasal flaring.

Keywords: COVID-19. Death. Signs and symptoms.

RESUMO
Analisar os sintomas iniciais da COVID-19 e associar ao óbito de pacientes adultos e pessoas idosas internadas no estado do Paraná. Estudo transversal, realizado com dados do sistema de notificação do Paraná. A população de estudo foi composta por indivíduos que contraíram SARS-CoV-2 no estado do Paraná. Como variável dependente utilizou-se o desfecho clínico (alta e óbito) e independentes os sinais clínicos. Realizou-se qui-quadrado e regressão logística. Amostra de 15.492 indivíduos, com 66,5% alta hospitalar. Indivíduos com baixa saturação de oxigênio, dispneia, irritabilidade ou confusão e batimento de asas nasais apresentaram 2,09, 1,68, 1,65 e 2,37, respectivamente, mais chances de vir a óbito ($p<0,001$). Indivíduos com cefaleia (OR=0,82), mialgia (OR=0,76) e disgeusia (OR=0,78) apresentaram-se como fator de proteção à mortalidade ($p\leq0,001$). O óbito pela COVID-19 esteve associado à saturação de oxigênio baixa, dispneia, irritabilidade ou confusão e batimento de asas nasais.

Palavras-chave: COVID-19. Óbito. Sinais e Sintomas.

INTRODUCTION

The severe acute respiratory syndrome coronavirus (SARS-CoV-2) is the etiological agent of COVID-19, a disease that, in addition to causing social, economic, cultural, political, and environmental impacts, revealed the fragility of healthcare systems in several countries[1]. Worldwide, as of June 26, 2023, 768,187,096 confirmed cases and 6,945,714 deaths have been recorded[2]. Brazil, being the subset of the global panorama, accounted for 37,656,050 infected people and 703,719 fatal outcomes[2]. Of these, 2,933,804 cases and 46,168 deaths corresponded to the state of Paraná[2].

Since the beginning of the pandemic, there has been much discussion about the characteristic signs and symptoms of the new respiratory disease. Currently, national and international literature defines that the clinical condition of COVID-19 can vary from asymptomatic infection to severe cases that require hospitalization in intensive care units[3]. According to the Ministry of Health (2023), the most frequently reported signs and symptoms are cough, sore throat, runny nose, fever, myalgia, headache, ageusia, anosmia, and fatigue[4]. Critical cases are generally treated in Intensive Care Units (ICU) and characterized by the presentation of sepsis, acute respiratory distress syndrome, severe respiratory failure, multiple organ dysfunction, severe pneumonia, and the need for ventilatory support[5]. These definitions are extremely relevant for hospital management of the disease.

A study carried out in China indicated that the most frequent symptoms among deaths were dyspnea, chest tightness, loss of consciousness, tachycardia, tachypnea, low oxygen saturation (≤93%), lymphopenia, and leukocytosis[6]. A Brazilian retrospective cohort study found that dyspnea contributed to the outcome of death, while sore throat and headache were symptoms associated with survival[7]. These clinical signs are directly linked to respiratory failure and associated with the progression to multiple organ failure, considered one of the main reasons for mortality from COVID-19[8].

However, the factors associated with the clinical outcomes of patients infected with COVID-19 must be analyzed with caution as they can vary considerably according to the demographic composition and health service offered. Therefore, given the strong impacts caused by COVID-19, it is necessary to identify and monitor signs and symptoms in addition to correct clinical management to prevent the disease from getting worse. Another important aspect to be mentioned is disease prevention. Primary Health Care (PHC) must assume a guiding role in the global response in order to provide health education to prevent the transmission of COVID-19 and offer resolute care[9] since the disease still has no cure. Therefore, the present study aimed to analyze the initial symptoms of COVID-19 and associate them with the death of adult patients and older people hospitalized in the state of Paraná.

METHODOLOGY

This was a cross-sectional, quantitative study carried out with secondary data from the Paraná notification system.

The study population was composed of individuals infected with SARS-CoV-2 in the state of Paraná (n=56,205). The following inclusion criteria were adopted: being 18 years old or over; having been infected with SARS-CoV-2 between March and December 2020; having been notified in Paraná's "Notifica COVID-19" system; having been admitted to a ward and/or ICU; presenting outcome data (discharge or death). The exclusion criterion was not having information about the outcome of the discharge or death of the individuals.

Data were collected using cases reported in Notifica COVID-19 (COVID-19 notification

system in the state of Paraná) in September 2021, consisting of two stages. The first consisted of collecting raw data and determining the variables that would be part of the study; in the second stage, the database was cleaned, and the data was categorized.

The clinical outcome (discharge and death) was considered as a dependent variable and, as independent variables, all clinical signs presented by the individual upon notification available in the notification system, namely fever, cough, sore throat, myalgia, arthralgia, diarrhea, nausea or vomiting, headache, runny nose, irritability and/or confusion, adynamia, sputum, chills, nasal congestion, conjunctival congestion, difficulty swallowing, red spots, infarcted lymph nodes, nasal flaring, low oxygen saturation, dyspnea, dysgeusia or anosmia.

To investigate the association between the researched items, the non-parametric Chi-Square test was initially applied. Logistic regression analysis was carried out using the stepwise method. The variables that presented values of $p \leq 0.20$ were considered to be included in the model, remaining in the final model, only the variables that presented p-value ≤ 0.05 to assume the hypothesis that there was an association between the studied variables. The model was adjusted by age (numerical variable), supported by clinical justification, and during the analysis, the Omnibus Tests of Model Coefficients evidenced that the adjusted model was better than the raw model ($p < 0.001$).

RESULTS

The final sample was made up of 15,492 individuals, the majority of whom were male (56.1%), with a mean age of 60.4±16.6 years, median of 60 years, and white (44.1%) (Table 01).

Table 1. Demographic characteristics of individuals hospitalized for COVID-19 in the state of Paraná. Paraná, Brazil, 2020 (n=15,492)

Variables		Total n (%)
Sex	Female	6,850(43.9)
	Male	8,746(56.1)
Age	Mean (±SD)	60.4(±16.6)
Color	White	6,871(44.1)
	Brown	1,156(7.4)
	Yellow	801(5.1)
	Black	259(1.7)
	Indigenous	14(0.1)
	Not informed	6,495(41.6)

Source: prepared by the authors, 2023.

The most prevalent clinical outcome was hospital discharge, 66.5%. Headache, myalgia, dysgeusia, and anosmia were the symptoms associated with this better prognosis. At the same time, the mortality rate was 33.5%, with an association between death and the following variables: low oxygen saturation (56.6%), dyspnea (65.0%), fever (49.5%), cough (82.5%), and myalgia (30.3%) (Tables 02 and 03).

Table 2. Presence of initial severe symptoms of COVID-19 in hospitalized individuals, according to clinical outcome. Paraná, Brazil, 2020 (n=15,492)

		Clinical outcome			
Variables		**Discharge n(%)**	**Death n(%)**	**Total n (%)**	**p-value**
Clinical outcome		10,376(66.5)	5,220(33.5)	15,596(100)	
Irritability and/or confusion	No	6,723(64.8)	3,008(57.6)	9,731(62.4)	**p<0.001**
	Yes	286(2.8)	288(5.5)	574(3.7)	
	Not informed	3,367(32.4)	1,924(36.9)	5,291(33.9)	
Nasal flaring	No	6,886(66.4)	3,136(60.1)	10,022(64.3)	**p<0.001**
	Yes	60(0.6)	99(1.9)	159(1.0)	
	Not informed	3,430(33.1)	1,985(38.0)	5,415(34.7)	
O_2 Saturation	No	4,548(43.8)	1,190(22.8)	5,738(36.8)	**p<0.001**
	Yes	3,442(33.2)	2,954(56.6)	6,396(41.0)	
	Not informed	2,386(23.0)	1,076(20.6)	3,462(22.2)	
Dyspnea	No	3,363(32.4)	891(17.1)	4,254(27.3)	**p<0.001**
	Yes	5,103(49.2)	3,393(65.0)	8,496(54.5)	
	Not informed	1,910(18.4)	936(17.9)	2,846(18.2)	
Dysgeusia or anosmia	No	5,032(48.5)	2,568(49.2)	7,600(48.7)	**p<0.001**
	Yes	1,610(15.5)	509(9.8)	2,119(13.6)	
	Not informed	3,734(36.0)	2,143(41.1)	5,877(37.7)	
Arthralgia	No	6,228(60.0)	2,920(55.9)	9,148(58.7)	**0.003**
	Yes	877(8.5)	337(6.5)	1,214(7.8)	
	Not informed	3,271(31.5)	1,963(37.6)	5,234(33.6)	
Adynamia	No	4,494(43.3)	2,031(38.9)	6,525(41.8)	0.312
	Yes	3,160(30.5)	1,489(28.5)	4,649(29.8)	
	Not informed	2,722(26.2)	1,700(32.6)	4,422(28.4)	
Infarcted lymph nodes	No	6,896(66.5)	3,200(61.3)	10,096(64.7)	0.179
	Yes	31(0.3)	21(0.4)	52(0.3)	
	Not informed	3,449(33.2)	1,999(38.3)	5,448(34.9)	

Source: prepared by the authors, 2023.

Table 3. Presence of mild initial symptoms of COVID-19 in hospitalized individuals, according to clinical outcome. Paraná, Brazil, 2020 (n=15,492)

(Continua)

		Clinical outcome			
Variables		**Discharge n(%)**	**Death n(%)**	**Total n (%)**	**p-value**
Sore throat	No	4,819(46.4)	2,574(49.3)	7,393(47.4)	**p<0.001**
	Yes	3,069(29.6)	995(19.1)	4,064(26.1)	
	Not informed	2,488(24.0)	1,651(31.6)	4,139(26.5)	
Myalgia	No	3,477(33.5)	2,049(39.3)	5,526(35.4)	**p<0.001**

(Conclusão)

		Clinical outcome			
Variables		**Discharge n(%)**	**Death n(%)**	**Total n (%)**	**p-value**
	Yes	4,642(44.7)	1,584(30.3)	6,226(39.9)	
	Not informed	2,257(21.8)	1,587(30.4)	3,844(24.6)	
Nausea or vomiting	No	5,688(54.8)	2,707(51.9)	8,395(53.8)	**p<0.001**
	Yes	1,737(16.7)	675(12.9)	2,412(15.5)	
	Not informed	2,951(28.4)	1,838(35.2)	4,789(30.7)	
Headache	No	3,826(36.9)	2,329(44.6)	6,155(39.5)	**p<0.001**
	Yes	4,175(40.2)	1,183(22.7)	5,358(34.4)	
	Not informed	2,375(22.9)	1,708(32.7)	4,083(26.2)	
Runny nose	No	5,057(48.7)	2,570(49.2)	7,627(48.9)	**p<0.001**
	Yes	2,478(23.9)	881(16.9)	3,359(21.5)	
	Not informed	2,841(27.4)	1,769(33.9)	4,610(29.6)	
Chill	No	5,588(53.9)	2,756(52.8)	8,344(53.5)	**p<0.001**
	Yes	1,770(17.1)	547(10.5)	2,317(14.9)	
	Not informed	3,018(29.1)	1,917(36.7)	4,935(31.6)	
Nasal congestion	No	6,057(58.4)	2,984(57.2)	9,041(58.0)	**p<0.001**
	Yes	1,185(11.4)	311(6.0)	1,496(9.6)	
	Not informed	3,134(30.2)	1,925(36.9)	5,059(32.4)	
Cough	No	1,794(17.3)	912(17.5)	2,706(17.4)	0.070
	Yes	7,278(70.1)	4,306(82.5)	11,584(74.3)	
	Not informed	1,304(12.6)	2(0.0)	1,306(8.4)	
Diarrhea	No	5,703(55.0)	2,739(52.5)	8,442(54.1)	**0.001**
	Yes	1,808(17.4)	742(14.2)	2,550(16.4)	
	Not informed	2,865(27.6)	1,739(33.3)	4,604(29.5)	
Adynamia	No	4,494(43.3)	2,031(38.9)	6,525(41.8)	0.312
	Yes	3,160(30.5)	1,489(28.5)	4,649(29.8)	
	Not informed	2,722(26.2)	1,700(32.6)	4,422(28.4)	
Sputum	No	6,429(62.0)	2,973(57.0)	9,402(60.3)	0.951
	Yes	630(6.1)	290(5.6)	920(5.9)	
	Not informed	3,317(32.0)	1,957(37.5)	5,274(33.8)	
Conjunctiva congestion	No	6,768(65.2)	3,153(60.4)	9,921(63.6)	**0.024**
	Yes	178(1.7)	59(1.1)	237(1.5)	
	Not informed	3,430(33.1)	2,008(38.5)	5,438(34.9)	
Difficulty swallowing	No	6,534(63.0)	3,031(58.1)	9,565(61.3)	0.964
	Yes	502(4.8)	232(4.4)	734(4.7)	
	Not informed	3,340(32.2)	1,957(37.5)	5,297(34.0)	
Red spots	No	6,908(66.6)	3,209(61.5)	10,117(64.9)	0.958
	Yes	51(0.5)	24(0.5)	75(0.5)	
	Not informed	3,417(32.9)	1,987(38.1)	5,404(34.6)	
	No	3,185(30.7)	1,471(28.2)	4,656(29.9)	0.391
Fever	Yes	5,404(52.1)	2,582(49.5)	7,986(51.2)	
	Not informed	1,787(17.2)	1,167(22.4)	2,954(18.9)	

Source: prepared by the authors, 2023.

Regarding COVID-19 symptoms associated with mortality, individuals admitted to the hospital with low oxygen saturation, dyspnea, irritability or confusion, and nasal flaring were 2.09 (95%CI =1.87-2.34), 1.68 (95%CI =1.49-1.89), 1.65 (95%CI =1.29-2.12) and 2.37 (95%CI =1.50-3.72), respectively, more likely to die than individuals without these symptoms (p<0.001). On the other hand, individuals hospitalized with initial symptoms of headache (0.82; 95%CI: 0.72-0.92) and dysgeusia or anosmia (0.78; 95%CI: 0.67-0.90) presented mortality protection factor (p≤0.001), that is, patients with these symptoms were more likely to be discharged from the hospital (Table 04).

Table 4. Explanatory models of COVID-19 symptoms associated with mortality in hospitalized older adults. Paraná, Brazil, 2020 (n=15,492)

Death				**Death**	
Variables		**OR_{crude} (95%CI)**	**p-value**	**$OR_{adj.}$ (95%CI)**	**p-value**
O_2 Saturation	No	1.00	**p<0.001**	1.00	**p<0.001**
	Yes	2.50(2.24-2.78)		2.09(1.87-2.34)	
Dyspnea	No	1.00	**p<0.001**	1.00	**p<0.001**
	Yes	1.62(1.45-1.82)		1.68(1.49-1.89)	
Irritability or confusion	No	1.00	**p<0.001**	1.00	**p<0.001**
	Yes	2.12(1.68-2.69)		1.65(1.29-2.12)	
Nasal flaring	No	1.00	**p<0.001**	1.00	**p<0.001**
	Yes	2.39(1.55-3.71)		2.37(1.50-3.72)	
Myalgia	No	1.00	**p<0.001**	1.00	**p<0.001**
	Yes	0.72(0.65-0.81)		0.76(0.68-8.85)	
Headache	No	1.00	**p<0.001**	1.00	**0.001**
	Yes	0.68(0.61-0.76)		0.82(0.0.72-0.92)	
Dysgeusia or anosmia	No	1.00	**p<0.001**	1.00	**0.001**
	Yes	0.70(0.61-0.80)		0.78(0.67-0.90)	
Sore throat	No	1.00	**p<0.001**	1.00	0.369
	Yes	0.79(0.66-0.95)		0.95(0.84-1.07)	
Chill	No	1.00	**0.032**	1.00	0.080
	Yes	0.85(0.74-0.99)		0.87(0.75-1.01)	
Nasal congestion	No	1.00	**0.011**	1.00	0.098
	Yes	0,79(0,70-0,89)		0,85(0,71-1,03)	

$OR_{adj.}$= Odds Ratio adjusted to age. CI= Confidence Interval

Crude Model: Explanatory power of the model= 70.7%; -2 Log likelihood=9,590.8; R^2 Cox & Snell=0.16.

Adjusted Model: Explanatory power of the model= 73.3%; -2 Log likelihood=8,907.9; R^2 Cox & Snell=0.18.

Source: prepared by the authors, 2023.

DISCUSSION

Worldwide, by November 2023, more than 770 million confirmed cases of COVID-19 had been recorded, with 38,022,277 confirmed cases and more than 707 thousand deaths[2] only in Brazil. Paraná presented 2,966,772 confirmed cases, of which 46,509 resulted in death[2]. In the present study, 1/3 of the Paraná population notified with COVID-19 in the database used for analysis, and who were hospitalized due to the disease, died in 2020. These comprehensive numbers reveal the significance and potential impact of the virus.[10]

Regarding the initial symptoms of COVID-19 associated with death in adults and older people hospitalized in the state of Paraná, in the present study, individuals who presented dyspnea, low oxygen saturation, irritability/confusion, and nasal flaring showed a higher probability of death. On the other hand, symptoms such as headache, myalgia, dysgeusia, or anosmia were shown to be protective factors against mortality.

Individuals who manifested dyspnea were more likely to die compared to eupneic individuals. A condition also observed in studies demonstrating that patients with dyspnea were more likely to die.[11,12]

Dyspnea suggests impaired lung function since the virus, through its mechanism of action, compromises the efficiency of pulmonary hematosis.[3] Furthermore, the process involving lung dysfunction results in the release of cytokines, a condition that damages lung tissue.[13] Therefore, dyspnea can worsen the condition of individuals, which can lead to death.

Another condition that was also associated with an increased chance of death was low oxygen saturation. Corroborating the present findings, other studies[11] reported that patients with oxygen saturation lower than 95% were more likely to die. Another study also pointed out that oxygen saturation lower than 95% increased the risk of death[12]. Each hemoglobin molecule can carry up to four oxygen molecules; this state of full occupancy is referred to as "saturated" with oxygen. When all binding sites in the hemoglobin molecule are occupied by oxygen, 100% saturation is achieved, which is described in the literature as ideal.[13] However, in an individual with COVID-19, gas exchange is impaired, and oxygen saturation tends to decrease, being insufficient to meet metabolic needs, increasing the risk of death.[13] Therefore, continuous monitoring of oxygen saturation levels in patients with COVID-19 is crucial.

The presence of the physical sign defined by the opening and closing of the nose wing during the inspiration and expiration of the respiratory cycle, known as "nasal flaring", revealed a significant increase in the chance of death. This phenomenon occurs as a response to hypoxemia caused by the virus, in which the body activates physiological mechanisms trying to reduce upper airway resistance and respiratory effort, aiming to increase the current volume.[14] Therefore, a relevant finding to be observed in patients with COVID-19. Furthermore, the sign of nasal flaring is generally linked to dyspnea and reduced oxygen saturation, reinforcing its association with the clinical outcome of death.

The presence of mental confusion or irritability is also associated with a greater risk of death. This finding is not yet fully understood. However, it is known that the systemic inflammatory response can affect the functioning of the central nervous system, which can generate neurological symptoms, including confusion, disorientation, difficulty concentrating, and changes in the mental state of infected individuals.[15] Furthermore, mental confusion can also be associated with a lack of oxygenation, which can cause a lowering of the level of consciousness.[16]

Symptoms associated with a better prognosis (headache, myalgia, dysgeusia, and anosmia) are highlighted in the literature as

characteristic factors of early-stage COVID-19.[4] In a cohort study carried out in 2020, headache, myalgia, dysgeusia, and anosmia were also associated with a greater chance of survival.[7] In other words, individuals who presented these symptoms were less likely to die.[7] These symptoms are related to mild cases of COVID-19, generally not progressing to complications, such as septic shock, respiratory failure, or multiple organ failure.[4]

Given the findings, a constant and broad discussion is essential regarding the association between the signs and symptoms of COVID-19 and mortality in hospitalized patients. In this way, health professionals, especially the nursing staff, which stands out as the class of professionals that most assist in patient care, can recognize the initial signs and symptoms of the disease to work as part of a multidisciplinary team and intervene to prevent new deaths.

Furthermore, this study makes it possible to present suggestions for new studies on this important topic, as the signs and symptoms of COVID-19 can result in different severe clinical outcomes among the population, such as mortality.

The limitations of the study are related to the use of secondary data, which are likely to suffer from information bias, as some relevant information may not be collected or be recorded as "ignored." As occurred in the present study, there was a large portion of the independent variables without information, a condition that could interfere with the results.

Furthermore, in the present study, only the initial symptoms presented in the notification form were taken into consideration, adjusted by age (due to higher mortality in the older population), and other clinical variations during the hospitalization period were not taken into account.[1] However, these limitations do not exclude the relevance of the study in understanding the initial signs and symptoms related to mortality from COVID-19.

CONCLUSION

In conclusion, death due to COVID-19 in adults and older people was associated with low oxygen saturation, dyspnea, irritability or confusion, and nasal flaring. In turn, individuals who presented headache, myalgia, dysgeusia, and anosmia as clinical signs of COVID-19 were more likely to be discharged from the hospital. The findings are important for defining interventions aimed at preventing new deaths.

REFERENCES

1. dos Santos IL, Zimmermann IR, Donalísio MR, Santimaria MR, Sanchez MN, de Carvalho JLB, et al. Social vulnerability, survival, and hospital lethality by COVID-19 in patients aged 50 years and over: retrospective cohort of cases in Brazil in 2020 and 2021. Cad Saude Publica. 2022;38(11):1–14. doi: 10.1590/0102-311XPT261921.

2. Secretaria de Saúde do Estado do Paraná. Coronavírus - COVID-19. 2023;1–72. Disponível em: https://www.saude.pr.gov.br/Pagina/Coronavirus-COVID-19.

3. Iser BPM, Sliva I, Raymundo VT, Poleto MB, Schuelter-Trevisol F, Bobinski F. Suspected COVID-19 case definition: A narrative review of the most frequent signs and symptoms among confirmed cases. Epidemiol e Serv Saude. 2020;29(3):1–11. doi: 10.5123/S1679-49742020000300018.

4. Brasil. Ministério da saúde. Boletim Epidemiológico Nº 152 - Boletim COE Coronavírus. 2023;1–39. Disponível em: https://www.gov.br/saude/pt-br/centrais-de-conteudo/publicacoes/boletins/epidemiologicos/covid-19/2023/boletim-epidemiologico-no-152-boletim-coe-coronavirus/view

5. Costa TMS, Santos KVG, Oliveira SE, Silva BVS, Melo EBB, Dantas RAN, et al. Characterization of Covid-19 Cases in Critically Ill Patients: Scoping Review.

Ciencia, Cuid e Saude [Internet]. 2021;20:1–10. doi: 10.4025/ciencuidsaude.v20i0.57572.

6. hen T, Wu D, Chen H, Yan W, Yang D, Chen G, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: Retrospective study. BMJ. 2020;368. doi: 10.1136/bmj.m1091.

7. Prado PR, Gimenes FRE, Lima MVM, Prado VB, Soares CP, Amaral TLM. Risk factors for death due to COVID-19, in the state of Acre, Brazil, 2020: a retrospective cohort study. Epidemiol e Serv Saude. 2021;30(3):1–10. doi: 10.1590/S1679-49742021000300018.

8. Vincent JL, Taccone FS. Understanding pathways to death in patients with COVID-19. Lancet Respir Med. 2020;8(5):430–2. doi: 10.1016/S2213-2600(20)30165-X.

9. Nedel JL, Silveira EF, Vivian AG. Qualidade de vida no trabalho de profissionais que atuaram na atenção primária à saúde durante a pandemia da COVID-19. Saúde e Pesqui. 2023;16(e-11570). doi: 10.17765/2176-9206.2023

10. Pimentel M, Magalhães APA, Novak CV, May BM, da Rosa LGB, Zimerman LI. Cardiac arrhythmias in patients with covid-19. Arq Bras Cardiol. 2021;117(5):1010–5. doi: 10.36660/abc.20200963.

11. Farias AG, Brito AAC, Silva JV, Cunha ATR, Queiroz JM, Freitas KOR, et al. Perfil epidemiológico dos pacientes hospitalizados com Covid-19 no município de Mossoró-RN. Rev Ciência Plur. 2022;8(3):1–18.

12. Carvalho AD, Deusa AAF, Tassiany Caroline Souza Trindade TCS, Tittonia AA. Perfil epidemiológico dos casos e óbitos por síndrome respiratória aguda grave confirmados para COVID-19. Rev Baiana Saúde Pública Artig. 2021;45(1):19-32. doi:10.22278/2318-2660.2021.v45.NEspecial_1.a3252.

13. Rodrigues SS, Galli RA. Análise fisiopatológica das manifestações clínicas respiratórias em pessoas infectadas pelo vírus SARS-CoV-2. Rev Médica Minas Gerais. 2022;32. doi: 10.5935/2238-3182.2022e32201.

14. Avena MJ, Pedreira M da LG, Gutiérrez MGR de. Conceptual validation of the defining characteristics of respiratory nursing diagnoses in neonates. Acta Paul Enferm. 2014;27(1):76–85.

15. Neto ARS, Carvalho ARB, Oliveira EMN, Magalhães LBR, Moura MEB, Freitas DRJ. Symptomatic manifestations of the disease caused by coronavirus (COVID-19) in adults: systematic review. Rev Gauch Enferm. 2021;42(spe):1–11. doi: 10.1590/1982-0194201400015.

16. Barioni EMS, Nascimento CS, Amaral TLM, Neto JMR, Prado PR. Clinical indicators, nursing diagnoses, and mortality risk in critically ill patients with COVID-19: a retrospective cohort. Rev da Esc Enferm. 2022;56:1–7. doi: 10.1590/1980-220X-REEUSP-2021-0568en.