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Prevalence of death and ICU admission in individuals hospitalized at a University Hospital in Amazonas: Crosssectional study

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Keywords— Coronavirus, Prevalence, Mortality, Cross-Sectional Studies, Amazonas. Abstract— Objective: To estimate the prevalence of intensive care admission and deaths among inpatients suspected to have COVID-19 in Hospital Universitário Getúlio Vargas (HUGV). Methods: Cross-sectional study with secondary data from discharged patients or deaths of those that had positive RT-PCR for COVID-19. Prevalence ratio and Confidence Interval were calculated using Poisson Regression. Results: The study included 87 individuals. Men (65,5%), elderly \geq 60 years (47%) and multimorbidity (46%). Women had less association with admission to intensive care (PR= 0.75%; 95%CI: 0.41-1.36) and deaths (PR= 0.57; 95%CI: 0.24-1.34). The time of hospitalization was death protecting factor. Conclusion: Men had a more severe outcome and contributed to higher mortality. Adequate medical records are necessary for a better understanding of suspected cases and to support the most appropriate health policies.

I. INTRODUCTION

The new coronavirus, SARS-CoV-2, the etiological agent of coronavirus disease (COVID-19), was initially discovered in December 2019 by Chinese authorities, thus identifying a new virus. Highly contagious, it quickly spread to all continents, being declared a pandemic by the World Health Organization (WHO) in March 2020 [1].

Currently with several variants, it is responsible for about 395 million cases of contamination and more than 5.7 million deaths worldwide.[2] The pandemic also had a negative influence on socioeconomic factors, due to the need of social distancing in order to reduce the transmission rates of the virus, such a prolonged action resulted in increased levels of poverty and unemployment in several regions of the world. [3].

In Brazil, the first diagnosed and confirmed case of COVID-19 took place at the end of February 2020, at Hospital Israelita Albert Einstein in the state of São Paulo [4]. The contamination soon spread to the country's regions, capitals, and municipalities, in part due to the lack of adequate policies to contain the virus. As of mid-March 2022, Brazil had more than 26,473,273 confirmed cases and 657,998 deaths caused by the new coronavirus [2].

Amazonas, with an estimated population of 3,483,985 [5], was one of the brazilian states most affected by the coronavirus pandemic. The first wave of COVID-19, peaked in May 2020, causing a meltdown on the funeral system which did not expect such demand. After 6 months, a second wave was even more serious, this time resulting in a complete collapse of the public and private health system due to lack of hospital beds, Intensive Care Unit (ICU), and lack of oxygen in hospitals. Until mid-February 2022, Amazonas had 549,076 confirmed cases of COVID-19 and 14,024 deaths [6].

Because it is a disease of severity and lethality that is constantly evolving, there is a need for a systematic search for knowledge about its epidemiology and its negative outcomes in the population in different contexts. In this sense, this study aimed to estimate the prevalence of hospitalization in the ICU and death in individuals hospitalized with suspected COVID-19 at the Hospital Universitário Getúlio Vargas (HUGV) in Manaus, Amazonas, Brazil.

II. METHOD

2.1 Study design and context

This is a cross-sectional study with data from electronic medical records of individuals suspected of having COVID-19 hospitalized at Hospital Universitário Getúlio Vargas, in Manaus, Amazonas. HUGV is a tertiary hospital that acted as a backup in the care of individuals suspected of having COVID-19, receiving patients previously treated by other health units. Data from this study are part of a multicenter study "Artificial intelligence algorithms to predict outcomes related to covid-19", carried out through a partnership with the Faculty of Public Health of the University of São Paulo (FSP/USP) and the Laboratory of Big Data and Predictive Analysis in Health (LABDAPS), of the State of São Paulo. HUGV was one of the partner centers to carry out the initial phase of data collection.

2.2 Participants

Individuals who had already been discharged or died, who underwent a positive RT-PCR test for COVID-19, were included in the study. Individuals whose clinical information was not found in the electronic medical record, within the 24-hour window before and after the RT-PCR, were excluded.

2.3 Data collect

A preliminary list containing 144 records of suspected COVID-19 hospitalizations was obtained for screening participants. After selection, data from participants were collected anonymously from March to August 2020, through the Management Application for University Hospitals. At this stage, the medical prescription and hospitalization modules were used. Clinical data collection was performed based on a 24-hour window before or after the RT-PCR test was performed, since it was the main objective of the Project "Artificial intelligence algorithms to predict outcomes related to covid-19".

2.4 Variables

Study outcomes were ICU admission and death from COVID-19, dichotomized (yes or no). The demographic variables collected were categorized: sex (male and female); age group (16 to 29 years, 30 to 59 years and ≥ 60 years); race/skin color (white, brown and undeclared); education (higher education, high school, elementary school, elementary school or less and undeclared). Clinical variables were: temperature, O2 saturation, systolic blood pressure, diastolic blood pressure, mean blood pressure, heart rate and respiratory rate; use of vasoactive drugs; dialysis; mechanical ventilation and chronic diseases (hypertension, diabetes, vascular disease. chronic obstructive pulmonary disease - COPD, chronic renal failure, bronchial asthma and asthmatic bronchitis, heart disease, hypercholesterolemia, lupus, stroke, and cancer). Multimorbidity was categorized into (no disease, one disease, and two or more diseases per individual); hospitalization, was categorized into (1 to 5 days, 6 to 15 days, 10 to 35 days and 36 or more) of hospitalization.

2.5 Statistical analyses

Initially, the descriptive statistics of the variables measured in the study were obtained by calculating their frequency and stratification by ICU admission and death. In this step, eventual differences among the proportions were identified by Pearson's χ^2 calculation. Subsequently, bivariate analyses were performed between all independent and dependent variables to calculate the prevalence ratio (PR) and confidence intervals 95% (CIs), using Poisson regression [7]. The difference in mean and 95% CI of clinical variables stratified by sex was obtained by the t-test. Data analysis was carried out Stata V.14.2 (Stata).

2.6 Ethical considerations

The project "Artificial intelligence algorithms to predict outcomes related to covid-19", was approved by the Research Ethics Committee of the Faculty of Public Health USP/SP with CAAE 32872920.4.1001.5421. Through an amendment to the project, the participation of the Hospital Universitario Getúlio Vargas was approved, through opinion 4,202,536.

III. III. RESULT

3.1 Participant characteristics

Table 1 shows the demographic and clinical characteristics of the individuals. Of the 144 records of individuals hospitalized for suspected COVID-19, 87 individuals who performed PCR-RT were included in the study. The sample consisted of 65,5% male, elderly \geq 60 years old (47.1%), brown skin color (92%), had high school education (29.9%), multimorbidity (two or more diseases) was identified in 46% of the records, hospitalization for 36 days or more (18.4%), about half of

the individuals required vasoactive drugs and mechanical ventilation was required in 49.4% of the hospitalized individuals.

3.2 Prevalence of ICU admission and death

The prevalence of ICU admission was 60.9%. More than half of the individuals who required ICU admission were male (66.7%), elderly \geq 60 years (65.8%), with higher education (69.2%) and 62.5% had multimorbidity.

Prevalence of death was 34.5% and was more frequent in males (40.3%) compared to females (23.3%), individuals aged between 30 and 59 years (37%) had a higher frequency of mortality as well as those without any preexisting comorbidities (42.8%) (Table 1).

 Table 1 Demographic and clinical characteristics of COVID-19 patients, stratified by ICU admission and death at HUGV.

 Manaus- Amazonas, 2020.

| Vasiahla | n | % | Prevalence % | | | |
|--------------------------------|----|------|--------------|----------------------|-------|----------------------|
| variable | | | ICU | p-value ^a | Death | p-value ^a |
| Total | 87 | | 60,9 | | 34,5 | |
| Sex | | | | 0,130 | | 0,112 |
| Male | 57 | 65,5 | 66,7 | | 40,3 | |
| Female | 30 | 34,5 | 50,0 | | 23,3 | |
| Age groups (years) | | | | 0,464 | | 0,833 |
| 16 to 29 | 11 | 12,6 | 45,4 | | 27,3 | |
| 30 to 59 | 35 | 40,2 | 60,0 | | 37,1 | |
| ≥60 | 41 | 47,1 | 65,8 | | 34,1 | |
| Race/Color | | | | 0,332 | | 0,709 |
| White | 5 | 5,7 | 80,0 | | 20,0 | |
| Brown | 80 | 92,0 | 58,7 | | 35,0 | |
| Not reported ^b | 2 | 2,3 | 100 | | 50,0 | |
| Education | | | | 0,569 | | 0,135 |
| Higher education | 13 | 14,9 | 69,2 | | 15,4 | |
| High school | 26 | 29,9 | 65,4 | | 50,0 | |
| Elementary school | 15 | 17,2 | 66,7 | | 40,0 | |
| Less than elementary school | 20 | 22,9 | 45,0 | | 20,0 | |
| Not reported ^b | 13 | 14,9 | 61,5 | | 38,5 | |
| Multimorbidity | | | | 0,918 | | 0,644 |
| None | 21 | 24,1 | 57,1 | | 42,8 | |
| 1 disease | 26 | 30,0 | 61,5 | | 30,7 | |
| 2 or more diseases | 40 | 46,0 | 62,5 | | 32,5 | |
| Length of hospital stay (days) | | | | 0,157 | | 0.406 |
| 1 to 5 | 17 | 19,0 | 47,0 | | 47,0 | |

| 6 to 15 | 30 | 34,5 | 53,3 | | 26,7 | |
|-------------------------------|----|------|------|--------|------|--------|
| 10 to 35 | 24 | 27,6 | 66,7 | | 29,2 | |
| 36 or more | 16 | 18,4 | 81,2 | | 43,7 | |
| Use of Mechanical ventilation | 43 | 49,4 | 93,0 | <0,001 | 62,8 | <0,001 |
| Use of vasoactive drugs | 40 | 46,0 | 90,0 | <0,001 | 67,5 | <0,001 |
| Use of dialysis | 27 | 31,0 | 74,0 | 0,064 | 57,2 | 0,002 |
| | | | | | | |

^a Pearson's chi-square test; ^b there was no record in the medical report

3.3 Factors associated with ICU admission and death

In the bivariate analysis (Table 2), women had a lower association with ICU admission (RP=0.75; 95%CI:0.41-1.36) and death (RP=0.57; 95%CI:0.24-1.34). Elderly people ≥ 60 years (PR=1.44; 95%CI: 0.55-3.76) were more associated with ICU compared to young people aged 16 to 29 years. The presence of two or more chronic diseases (PR=1.09; 95%CI:0.54-2.17) and 36 days or more of hospitalization (PR=1.72; 95%CI:0.71-4.16) had a greater association with ICU admission, respectively,

compared with those who had no disease and 1 to 5 days of hospitalization.

Regarding the outcome of death, individuals aged 30 to 59 years were more associated (PR=1.36; 95%CI: 0.38-4.77) than those aged ≥ 60 years (PR=1.25; IC95%:0.35-4.35). Individuals who used mechanical ventilation (RR=9.20; 95%CI: 2.79-30.35), vasoactive drugs (RR=10.57; 95%CI:3.20-34.85) and dialysis (RR=2.40; 95%CI: 1.17-4.93) were more associated with negative outcomes. Duration of hospitalization of 36 days or more had a lower association with death than 1 to 5 days of hospitalization.

 Table 2 Prevalence Ratio of factors associated with ICU and death, in patients of COVID-19, hospitalized at HUGV.

 Manaus- Amazonas, 2020

| Variables | n | 0/ | Prevalence% | | | | |
|-----------------------------|----|------|-------------|----------------------|-------|----------------------|--|
| variables | | %0 | ICU | p-value ^a | Death | p-value ^a | |
| Total | 87 | | 60,9 | | 34,5 | | |
| Sex | | | | 0,130 | | 0,112 | |
| Male | 57 | 65,5 | 66,7 | | 40,3 | | |
| Female | 30 | 34,5 | 50,0 | | 23,3 | | |
| Age groups (years) | | | | 0,464 | | 0,833 | |
| 16 to 29 | 11 | 12,6 | 45,4 | | 27,3 | | |
| 30 to 59 | 35 | 40,2 | 60,0 | | 37,1 | | |
| ≥60 | 41 | 47,1 | 65,8 | | 34,1 | | |
| Race/Color | | | | 0,332 | | 0,709 | |
| White | 5 | 5,7 | 80,0 | | 20,0 | | |
| Brown | 80 | 92,0 | 58,7 | | 35,0 | | |
| Not reported ^b | 2 | 2,3 | 100 | | 50,0 | | |
| Education | | | | 0,569 | | 0,135 | |
| Higher education | 13 | 14,9 | 69,2 | | 15,4 | | |
| High school | 26 | 29,9 | 65,4 | | 50,0 | | |
| Elementary school | 15 | 17,2 | 66,7 | | 40,0 | | |
| Less than elementary school | 20 | 22,9 | 45,0 | | 20,0 | | |
| Not reported ^b | 13 | 14,9 | 61,5 | | 38,5 | | |

| Multin | norbidity | | | | 0,918 | | 0,644 |
|--------|---------------------------|----|------|------|--------|------|--------|
| | None | 21 | 24,1 | 57,1 | | 42,8 | |
| | 1 disease | 26 | 30,0 | 61,5 | | 30,7 | |
| | 2 or more diseases | 40 | 46,0 | 62,5 | | 32,5 | |
| Lengtl | h of hospital stay (days) | | | | 0,157 | | 0.406 |
| | 1 to 5 | 17 | 19,0 | 47,0 | | 47,0 | |
| | 6 to 15 | 30 | 34,5 | 53,3 | | 26,7 | |
| | 10 to 35 | 24 | 27,6 | 66,7 | | 29,2 | |
| | 36 or more | 16 | 18,4 | 81,2 | | 43,7 | |
| Use of | Mechanical ventilation | 43 | 49,4 | 93,0 | <0,001 | 62,8 | <0,001 |
| Use of | vasoactive drugs | 40 | 46,0 | 90,0 | <0,001 | 67,5 | <0,001 |
| Use of | dialysis | 27 | 31,0 | 74,0 | 0,064 | 57,2 | 0,002 |

^a Pearson's chi-square test; ^b there was no record in the medical report

3.4 Mean clinical parameters stratified by sex

In Table 3, the mean difference stratified by sex, shows that men in comparison to women presented on average higher heart rates (93.49 \pm 18.54), respiratory rate (25.00 \pm 8.00), more use of vasoactive drugs (0.54 \pm 0.50), use of

dialysis (0.36 \pm 0.48), mechanical ventilation (0.56 \pm 0.50), and ICU admission (0.66 \pm 0.47). While women had higher mean O2 saturation (95.00 \pm 6.25), longer hospital stay (23.56 \pm 28.43 days), and higher mean presence of some chronic diseases (1.73 \pm 0.94).

Table 3 Mean of clinical parameters stratified by sex in COVID-19 patients hospitalized at HUGV. Manaus-Amazonas,

2020.

| Variables | Mean ± SD (CI95%) | | | | | |
|----------------------------------|--|--|--|--|--|--|
| variables | Women | Men | | | | |
| Heart rate | 83,73 ± 23,79 (74,11 - 93,34) | $93,\!49 \pm 18,\!54 \; (88,\!27 - 98,\!70)$ | | | | |
| Respiratory rate | 21,60 ± 5,73 (19,12 - 24,08) | $25{,}00\pm 8{,}00\ (22{,}70-27{,}29)$ | | | | |
| Systolic pressure | 130,25 ± 22,78 (120,62 –139,87) | $129,\!26\pm31,\!30~(120,\!27-138,\!25)$ | | | | |
| Diastolic pressure | 78,37 ± 16,59 (71,36 - 85,38) | $76,85 \pm 16,97\;(71,98-81,73)$ | | | | |
| MAP | $76{,}51\pm41{,}66\ (60{,}96-92{,}07)$ | 81,07 ± 37,05 (71,24 - 90,90) | | | | |
| O ₂ Saturation | 95,00 ± 6,25 (92,22 - 97,77) | $93,\!29 \pm 10,\!01 \; (90,\!38 - 96,\!19)$ | | | | |
| Use of vasoactive drugs | $0,30 \pm 0,46 \; (0,12 - 0,47)$ | $0{,}54\pm0{,}50\;(0{,}41-0{,}67)$ | | | | |
| Use of dialysis | $0,23 \pm 0,43 \; (0,07 - 0,39)$ | $0,\!36\pm0,\!48\;(0,\!23-0,\!49)$ | | | | |
| Use of Mechanical ventilation | $0,\!36\pm0,\!49\;(0,\!18-0,\!54)$ | $0{,}56\pm0{,}50\;(0{,}42-0{,}69)$ | | | | |
| ICU admission | $0,50 \pm 0,50 \; (0,31 - 0,68)$ | $0{,}66\pm 0{,}47\;(0{,}54-0{,}79)$ | | | | |
| Days of hospitalization | 23,56 ±28,43 (12,94 - 34,18) | 22,36 ± 26,57(15,31 - 29,41) | | | | |
| Presence of some chronic disease | 1,73 ± 0,94 (1,38 – 2,08) | 1,36 ± 1,33 (1,01 – 1,72) | | | | |

SD: Standard Deviation; CI_{95%:} 95% confidence interval, MAP: mean blood pressure

IV. DISCUSSION

This is an observational study with electronic medical record data from March to August 2020, during the first wave of COVID-19 in Manaus, Amazonas. The results of the study reveal that 34.5% of hospitalized individuals died and 60.9% were admitted to the ICU. Of the 87 hospitalized individuals, 65.5% were male and had worse negative clinical outcomes

We identified a relatively high frequency of mortality and hospitalization in ICU compared to national data. A longitudinal cohort conducted in Brazil using secondary data from 398,063 medical reimbursement authorization records classified as COVID-19 hospitalization, describes a 21.7% death rate and a 26.07% rate of ICU admissions, and 55.5% of the hospitalizations of males.[8] A retrospective study of 250,000 COVID-19 admissions in the country also shows that the northern region outperformed the other Brazilian regions in hospital death rate (50%), and in the hospitalization of males (60%) [9].

Other studies conducted with similar outcomes in individuals hospitalized in the states of Rio de Janeiro, Espírito Santo and Bahia also support that men, age over 60 years, and the presence of multimorbidity were conditions more associated with a higher risk of ICU admissions and deaths [10]–[12].

In other Contexts such as China the mortality frequency ranged from 1.4% to 4.3% in the year 2020 (13,14), in Seattle and New York in the United States, a mortality frequency of 33% and 39% respectively was identified [13], [14], in Mexico, there was a variation of 1% to 20% in mortality rates between health institutions [15], in Italy, in the Lombardy region, the overall hospital mortality rate was 53.4% in one of the worst pandemic moments in that country [16], while in the region of Aragon in Spain, a mortality rate of 3.84 deaths per 100,000 people per day in the year 2020 has been identified [17].

A higher frequency of negative COVID-19 outcomes, such as ICU admission and deaths in males, elderly (60 years and older), and presence of multimorbidity is supported by strong evidence that reinforces our findings. A meta-analysis carried out in 2020 showed that males, advanced age, presence of chronic diseases were considered risk factors for death among patients with COVID-19 [18].

Two systematic reviews conducted in 2020, including more than 350,000 individuals, found that men had a higher risk of developing the outcomes of death and ICU admission compared to women [19], [20], as well as individuals who have some chronic health condition. Studies conducted in 2020, in European countries such as, (Spain, Italy, England, Belgium, Greece, Denmark and the Netherlands) showed a male to female ratio for death in confirmed cases of COVID-19 equal to or greater than 1.7 [21]. Suggesting that women may be less likely to develop severe complications of COVID-19 leading to death [22].

The reasons for lower lethality from COVID-19 in women are still uncertain. Previous studies report that women have a greater perception of their health status, and they seek more health care services [23], This can help women identify the symptoms of the disease and seek assistance more quickly. While men tend to seek health services at a more advanced stage of the disease, when in general therapeutic supports for care are more limited.

There are also studies that suggest that the difference in lethality between men and women may be related to sexual dimorphism, which plays a central role in the genetic and hormonal regulation of immune responses, mainly in the regulation of Angiotensin Converting Enzyme 2 (ACE2), which is the main receptor used by SARS-CoV-2 to enter cells [24].

We identified an average time of two days more in the hospital and almost twice as many chronic diseases in women when compared to men, but these factors apparently did not contribute to greater severity or lethality in women. While in men, more severe outcomes were identified, such as changes in heart rate, respiratory rate, use of mechanical ventilation and vasoactive drugs.

A meta-analysis conducted in 2021, demonstrated that oxygen saturation lower than 93% is associated with more severe outcomes in patients with COVID-19, [24] A mean oxygen saturation of (93.29 ± 10.01) in men was observed in our study, which was lower than the mean observed in women (95.00 ± 6.25) , which may justify the presence of more reserved outcomes for that group.

Our study detected that the risk of death was nine times higher in individuals on mechanical ventilation, when compared to those who did not use mechanical ventilation, as well as those who used vasoactive drugs had a ten-time increased risk of death compared to those who did not need to receive vasoactive drugs during hospitalization. In Brazil, mortality rates ranging from 59.5% to 82.98% were observed in patients on mechanical ventilation [25], [26], and in developed countries, the mortality rate was 45%, and that points to a meta-analysis including data from 23 countries [27]. The use of vasoactive drugs was also associated with mortality in patients with COVID-19 [28].

The difficulties in obtaining this data were significant, mainly due to the need to search for the information in the electronic medical record where access is restricted to the hospital's employees, the release of data by the competent sectors and the academic unavailability, as there was no legal support for the access of students to the hospital premises, out of respect to state decrees since the state of Amazonas was in lockdown. And the restricted time of the researcher to access the electronic medical records.

The pandemic has imposed great challenges to all of us, including conducting research. The very structure and team of the hospital where this study was conducted, as it had to adapt physical spaces, personnel, equipment, and supplies to become a back-up hospital in facing COVID-19 in the state of Amazonas.

Other limitations to this research are those common to the cross-sectional study design, which are due to the nonprobabilistic design and the use of secondary data, with the possibility of registration errors, missing data, and incomplete information. The information on comorbidities was self-reported, and some patients' hospitalization time for diagnosis was limited, often considering only the family member's information and this may favor overestimation or underestimation of some diseases.

The records can be related to more severe patients because it is a back-up hospital, which received patients only by transfer. In any way this study points out similarity with previous research and provides a support to identify the profile of individuals hospitalized with suspected COVID-19 in Amazonas, and outline strategies for supportive public policies in the study region.

V. CONCLUSION

The new coronavirus has imposed great challenges to the population of Amazonas, as well as to its authorities. In this study, more than half of the hospitalized individuals suspected of COVID-19, required ICU admission and more than a third died. Men had more severe outcomes and contributed to higher mortality, according to the electronic medical records of the researched hospital. Adequate reporting and recording in medical records are of great importance for a better understanding of suspected cases of COVID-19, as well as providing high quality studies to evaluate and inform health policies in the region.

AUTHOR CONTRIBUTIONS

Araújo MEA, contributed to the study design, analysis and writing of the manuscript. Castro JO, Araújo TA and Aguiar TL contributed to the writing of the manuscript and review. All authors have approved the final version of the manuscript and are responsible for the integrity and accuracy of the article.

REFERENCES

- A. DG *et al.*, "Current Status of Epidemiology, Diagnosis, Therapeutics, and Vaccines for Novel Coronavirus Disease 2019 (COVID-19)," *J. Microbiol. Biotechnol.*, vol. 30, no. 3, pp. 313–324, 2020, doi: 10.4014/JMB.2003.03011.
- [2] WHO, "WHO Coronavirus (COVID-19) Dashboard | WHO Coronavirus (COVID-19) Dashboard With Vaccination Data," Feb. 07, 2022. https://covid19.who.int/ (accessed Feb. 07, 2022).
- [3] A. Martin, M. Markhvida, S. Hallegatte, and B. Walsh, "Socio-Economic Impacts of COVID-19 on Household Consumption and Poverty," *Econ. Disasters Clim. Chang.* 2020 43, vol. 4, no. 3, pp. 453–479, Jul. 2020, doi: 10.1007/S41885-020-00070-3.
- [4] V. D. Teich *et al.*, "Epidemiologic and clinical features of patients with COVID-19 in Brazil," *Einstein (Sao Paulo).*, vol. 18, p. eAO6022, 2020, doi: 10.31744/EINSTEIN_JOURNAL/2020AO6022.
- [5] IBGE, "Brasil. Instituto Brasileiro de Geografia e Estatistica (IBGE). Censo demográfico de 2010.," 2010. .
- [6] FVS, "Fundação de Vigilância em Saúde do Amazonas. Centro de Informações Estratégicas em Vigilância em Saúde do Amazonas (CIEVS/FVS-AM)BOLETIM DIÁRIO COVID-19 NO AMAZONAS," Feb. 2022. Accessed: Feb. 07, 2022. [Online]. Available: https://www.fvs.am.gov.br/media/publicacao/07_02_22_BO LETIM_DIARIO_DE_CASOS_COVID-19.pdf.
- [7] A. J. Barros and V. N. Hirakata, "Alternatives for logistic regression in cross-sectional studies: an empirical comparison of models that directly estimate the prevalence ratio," *BMC Med. Res. Methodol. 2003 31*, vol. 3, no. 1, pp. 1–13, Oct. 2003, doi: 10.1186/1471-2288-3-21.
- [8] I. R. Zimmermann *et al.*, "Trends in COVID-19 case-fatality rates in Brazilian public hospitals: A longitudinal cohort of 398,063 hospital admissions from 1st March to 3rd October 2020," *PLoS One*, vol. 16, no. 7, p. e0254633, Jul. 2021, doi: 10.1371/JOURNAL.PONE.0254633.
- [9] R. OT *et al.*, "Characterisation of the first 250,000 hospital admissions for COVID-19 in Brazil: a retrospective analysis of nationwide data," *Lancet. Respir. Med.*, vol. 9, no. 4, pp. 407–418, Apr. 2021, doi: 10.1016/S2213-2600(20)30560-9.
- [10] C. C. Escosteguy, T. de A. Eleuterio, A. G. L. Pereira, M. R. V. E. Marques, A. D. Brandão, and J. P. M. Batista, "COVID-19: estudo seccional de casos suspeitos internados em um hospital federal do Rio de Janeiro e fatores associados ao óbito hospitalar," *Epidemiol. e Serviços Saúde*, vol. 30, no. 1, p. e2020750, 2021, doi: 10.1590/S1679-49742021000100023.
- [11] C. L. T. de Andrade, C. C. de A. Pereira, M. Martins, S. M. L. Lima, and M. C. Portela, "COVID-19 hospitalizations in Brazil's Unified Health System (SUS)," *PLoS One*, vol. 15, no. 12, p. e0243126, Dec. 2020, doi: 10.1371/JOURNAL.PONE.0243126.
- [12] M. KC, V. ACBC, S. ASS, M. WD, B. VG, and M. ELN, "COVID-19 hospitalization and death and relationship with social determinants of health and morbidities in Espírito

Santo State, Brazil: a cross-sectional study," *Epidemiol. e Serv. saude Rev. do Sist. Unico Saude do Bras.*, vol. 30, no. 3, pp. 1–11, 2021, doi: 10.1590/S1679-49742021000300004.

- [13] B. FS et al., "Clinical Features and Outcomes of 105 Hospitalized Patients With COVID-19 in Seattle, Washington," Clin. Infect. Dis., vol. 71, no. 16, pp. 2167– 2173, Oct. 2020, doi: 10.1093/CID/CIAA632.
- [14] M. J. Cummings *et al.*, "Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study," *Lancet (London, England)*, vol. 395, no. 10239, p. 1763, Jun. 2020, doi: 10.1016/S0140-6736(20)31189-2.
- [15] H. Najera and A. G. Ortega-Avila, "Health and Institutional Risk Factors of COVID-19 Mortality in Mexico, 2020," Am. J. Prev. Med., vol. 60, no. 4, pp. 471–477, Apr. 2021, doi: 10.1016/J.AMEPRE.2020.10.015.
- [16] G. Grasselli *et al.*, "Risk Factors Associated With Mortality Among Patients With COVID-19 in Intensive Care Units in Lombardy, Italy," *JAMA Intern. Med.*, vol. 180, no. 10, p. 1, Oct. 2020, doi: 10.1001/JAMAINTERNMED.2020.3539.
- [17] B. Poblador-Plou *et al.*, "Baseline Chronic Comorbidity and Mortality in Laboratory-Confirmed COVID-19 Cases: Results from the PRECOVID Study in Spain," *Int. J. Environ. Res. Public Heal. 2020, Vol. 17, Page 5171*, vol. 17, no. 14, p. 5171, Jul. 2020, doi: 10.3390/IJERPH17145171.
- [18] F. M. Noor and M. M. Islam, "Prevalence and Associated Risk Factors of Mortality Among COVID-19 Patients: A Meta-Analysis," *J. Community Health*, vol. 45, no. 6, p. 1, Dec. 2020, doi: 10.1007/S10900-020-00920-X.
- [19] J. Li *et al.*, "Epidemiology of COVID-19: A systematic review and meta-analysis of clinical characteristics, risk factors, and outcomes," *J. Med. Virol.*, vol. 93, no. 3, pp. 1449–1458, Mar. 2021, doi: 10.1002/JMV.26424.
- [20] X. Fang *et al.*, "Epidemiological, comorbidity factors with severity and prognosis of COVID-19: a systematic review and meta-analysis," *Aging (Albany NY)*, vol. 12, no. 13, p. 12493, 2020, doi: 10.18632/AGING.103579.
- [21] C. Penna, V. Mercurio, C. G. Tocchetti, | Pasquale Pagliaro, and C. G. Tocchetti, "Sex-related differences in COVID-19 lethality," 2020, doi: 10.1111/bph.15207.
- [22] C. Penna, V. Mercurio, C. G. Tocchetti, | Pasquale Pagliaro, and C. G. Tocchetti, "Sex-related differences in COVID-19 lethality," *Br J Pharmacol*, vol. 177, no. 19, pp. 4375–4385, 2020, doi: 10.1111/bph.15207.
- [23] M. E. A. Araujo, M. T. Silva, T. F. Galvao, and M. G. Pereira, "Prevalence of health services usage and associated factors in the Amazon region of Brazil: A population-based cross-sectional study," *BMJ Open*, vol. 7, no. 11, 2017, doi: 10.1136/bmjopen-2017-017966.
- [24] A. Booth *et al.*, "Population risk factors for severe disease and mortality in COVID-19: A global systematic review and meta-analysis," *PLoS One*, vol. 16, no. 3, Mar. 2021, doi: 10.1371/JOURNAL.PONE.0247461.
- [25] F. S. H. de Souza, N. S. Hojo-Souza, B. D. de O. Batista, C. M. da Silva, and D. L. Guidoni, "On the analysis of mortality risk factors for hospitalized COVID-19 patients: A

data-driven study using the major Brazilian database," *PLoS One*, vol. 16, no. 3, p. e0248580, Mar. 2021, doi: 10.1371/JOURNAL.PONE.0248580.

- M. S. Marcolino *et al.*, "Clinical characteristics and outcomes of patients hospitalized with COVID-19 in Brazil: Results from the Brazilian COVID-19 registry," *Int. J. Infect. Dis.*, vol. 107, pp. 300–310, Jun. 2021, doi: 10.1016/J.IJID.2021.01.019.
- [27] L. ZJ et al., "Case Fatality Rates for Patients with COVID-19 Requiring Invasive Mechanical Ventilation. A Metaanalysis," Am. J. Respir. Crit. Care Med., vol. 203, no. 1, pp. 54–66, Jan. 2021, doi: 10.1164/RCCM.202006-2405OC.
- [28] Z. Qian, S. Lu, X. Luo, Y. Chen, and L. Liu, "Mortality and Clinical Interventions in Critically ill Patient With Coronavirus Disease 2019: A Systematic Review and Meta-Analysis," *Front. Med.*, vol. 8, p. 635560, Jul. 2021, doi: 10.3389/FMED.2021.635560.