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ORIGINAL ARTICLE

FACTORS ASSOCIATED WITH MORTALITY DUE TO COVID-19 IN ADULTS AND OLDER PEOPLE IN A PUBLIC HOSPITAL IN CHILE: A RETROSPECTIVE COHORT STUDY

FACTORES ASOCIADOS A MORTALIDAD DE ADULTOS Y PERSONAS MAYORES POR COVID-19 EN UN HOSPITAL PÚBLICO CHILENO: ESTUDIO DE COHORTE RETROSPECTIVO

FATORES ASSOCIADOS À MORTALIDADE EM ADULTOS E IDOSOS POR COVID19 EM UM HOSPITAL PÚBLICO CHILENO: ESTUDO DE COORTE RETROSPECTIVO

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ABSTRACT

Introduction: Many countries are studying the risk factors associated with death in patients with COVID-19, due to the impact that the SARS-CoV-2 pandemic has had globally. Although there are several studies on this disease in our country, research that explores the risk factors associated with COVID-19-related mortality in people who were hospitalized for this pathology is scarce. **Objective:** To determine the risk factors that could influence mortality in patients who were hospitalized for COVID-19 in Hospital de Quillota. **Methods:** Retrospective cohort study. All adult patients hospitalized with a main diagnosis of COVID-19 during 2020 and the first semester of 2021 were included. Five risk factors were analyzed: age over 60 years, male gender, high blood pressure, type 2 diabetes, and obesity. **Results:** The sample consisted of 428 subjects, with a mean age of 58.8 years, where 50.7% were older than 60 years, 56% were men, and 63.4% presented some comorbidity. Hospital fatality was 26.6%. People over 60 years of age had a 40% risk of mortality, with 3 times

more risk of death than those younger than 60 years. No significant statistical relationship was observed between the remaining factors and the risk of death. **Conclusion:** It was found that age greater than 60 years is a risk factor that could influence mortality in patients hospitalized for COVID-19.

Keywords: COVID-19; Mortality; Risk Factors.

RESUMEN

Introducción: Los factores de riesgos asociados a la mortalidad por COVID-19 están siendo estudiados en múltiples países dado el impacto de la pandemia alrededor del mundo. Si bien, en Chile hay investigaciones relacionadas con la enfermedad, aún son escasos los estudios que hayan expuesto cuáles son los factores de riesgo que se podrían asociar a la mortalidad por COVID-19 en personas que fueron hospitalizadas por esta patología. Objetivo: Determinar cuáles son los factores de riesgo que podrían incidir en la mortalidad en personas que fueron hospitalizados por COVID-19 en el Hospital de Quillota. Métodos: Estudio de cohorte retrospectivo. Se incluyó a la totalidad de pacientes adultos con diagnóstico principal de hospitalización por COVID-19 durante el año 2020 y el primer semestre del año 2021. Se midieron cinco factores de riesgo: edad mayor a 60 años, sexo hombre, hipertensión arterial, diabetes mellitus tipo 2 y obesidad. Resultados: La muestra estudiada fue de 428 sujetos. 50,7% personas mayores de 60 años, 56% hombres y 63,4% presentaba alguna comorbilidad. La letalidad hospitalaria fue de un 26,6%. Las personas mayores de 60 años tuvieron un 40% de riesgo de fallecer y a su vez, tendrían 3 veces más riesgo de fallecer en relación con los menores de 60 años. No se mostró una asociación estadística significativa para afirmar que los otros factores estudiados constituyeran un riesgo de muerte. Conclusiones: Se identificó que la edad mayor a 60 años es un factor de riesgo que podría incidir en la mortalidad en pacientes hospitalizados por COVID-19.

Palabras claves: COVID-19; Mortalidad; Factores de Riesgo.

RESUMO

Introdução: Os fatores de risco associados à mortalidade por COVID-19 estão sendo estudados em vários países, devido ao impacto da pandemia de SARS-CoV-2 em todo o mundo. Apesar de, em nosso meio, existirem diversas investigações relacionadas à doenca, ainda são pouços os estudos que expuseram os fatores de risco que poderiam estar associados à mortalidade por COVID-19 em pessoas que foram hospitalizadas por esta patologia. Objetivo: Determinar quais são os fatores de risco que podem afetar a mortalidade em pacientes hospitalizados por COVID-19 no Hospital de Quillota. Métodos: Estudo de coorte retrospetivo. Foram incluídos todos os pacientes adultos com diagnóstico primário de internação por COVID-19 durante 2020 e primeiro semestre de 2021. Foram medidos 5 fatores de risco: idade acima de 60 anos, sexo masculino, hipertensão arterial, diabetes mellitus tipo 2 e obesidade. Resultados: A amostra estudada foi de 428 sujeitos. 50,7% eram pessoas com mais de 60 anos, 56% homens e 63,4% apresentavam alguma comorbidade. A mortalidade hospitalar foi de 26,6%. Pessoas com mais de 60 anos tinham 40% de risco de morrer e, por sua vez, teriam 3 vezes mais risco de morrer em relação aos menores de 60 anos. Nenhuma associação estatística significativa foi mostrada para confirmar que os outros fatores estudados constituíam risco de morte. Conclusões: Identificou-se que a idade acima de 60 anos é um fator de risco que pode afetar a mortalidade em pacientes internados por COVID-19.

Palavras-chave: COVID-19; Mortalidade; Fatores de Risco.

INTRODUCTION

The World Health Organization (WHO) defines Coronavirus Disease (COVID-19) as an illness caused by a new kind of coronavirus called Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). The organization first became aware of the virus on December 31, 2019, upon being informed of a cluster of viral pneumonia cases in Wuhan, China.¹ This infectious agent can manifest in several ways, ranging from common cold symptoms to more severe conditions such as Severe Acute Respiratory Distress Syndrome.²

In Chile, the Ministry of Health confirmed the first case of COVID-19 on March 3, 2020, involving a 33-year-old individual who had arrived in the country after traveling to Southeast Asia, specifically Singapore, a nation experiencing an outbreak of the disease.³ In the same month, on March 11, 2020, the World Health Organization (WHO) declared COVID-19 a pandemic.⁴ Subsequently, by mid-2023, over 750 million cases and 6 million deaths have been reported globally.⁵

Thousands of cases have been reported in our country, surpassing five million confirmed cases as of the second month of 2023. The number of deaths is particularly concerning, exceeding 60,000 confirmed cases of COVID-19-related deaths, making it the leading cause of death in 2020.⁶⁻⁷

The SARS-CoV-2 virus, responsible for Severe Acute Respiratory Syndrome (SARS), is highly transmissible, rendering the entire population susceptible to infection. However, the majority of individuals with the disease experience mild symptoms, with only approximately 15% progressing to severe pathology requiring hospitalization and 5% requiring admission to an Intensive Care Unit (ICU).¹

Hospitalizations due to COVID-19 in Chile resulted in a significant strain on healthcare facilities, particularly impacting emergency units and ICUs. Nationally, ICU bed occupancy reached 97% in 2021.⁸ As of early 2023, over 200,000 individuals have been reported to require hospitalization due to this disease. The highest incidence rates of COVID-19 cases reported among hospitalized individuals are observed in those aged 60 and above, with prevalent comorbidities including hypertension, diabetes, and obesity.⁹

While the entire population is susceptible to COVID-19, it is noteworthy that individuals of advanced age and/or with chronic comorbidities may be more prone to experiencing severe manifestations of the disease.¹⁰ In this context, various international studies assert that age is a factor associated with a higher risk of death in hospitalized COVID-19 patients, as older individuals are more likely to develop critical or fatal conditions.¹¹⁻¹³ Other studies indicate that, in addition to age, comorbidities such as hypertension, type 2 diabetes mellitus, and obesity also increase the risk of mortality.¹⁴⁻¹⁸ Furthermore, some works describe that characteristics such as being male may be associated with an increased risk of mortality due to COVID-19.¹⁹⁻²¹

Research has also been conducted on this matter in Chile. A study carried out at *Clínica Indisa* in Santiago indicates that age and diabetes are included as independent risk factors for mortality in hospitalized COVID-19 patients, among others.²² Another national study involving patients with acute SARS-CoV-2 infection concludes that the primary predictors of hospitalization and admission to critical care units are age and pre-existing conditions, especially hypertension, diabetes mellitus, dyslipidemia, obesity, chronic neurological disease, immunosuppression, and depression.²³

Despite this valuable information, there is a scarcity of information in Chile regarding the comorbidities present in deceased COVID-19 patients and other potentially associated factors. Based on the aforementioned, the objective of this study is to determine the risk factors that may influence mortality in individuals hospitalized for COVID-19 in a Chilean public hospital.

METHODOLOGY

This is a retrospective cohort study with secondary analysis of information.

The research was conducted at the San Martín de Quillota Hospital, a high-complexity public hospital in the Valparaiso region that serves the population of 12 municipalities in the area, encompassing approximately 310,000 residents.²⁴

The study population comprised 763 individuals who were hospitalized. Intentional sampling was used, aiming to include all individuals hospitalized with a COVID-19 diagnosis from March 29, 2020 (the date of the first case received) to June 30, 2021. Participants had to meet the following eligibility criteria:

- Inclusion Criteria: Hospitalized individuals with a primary diagnosis of COVID-19, meeting the definition of 'confirmed case' established by the Ministry of Health (MINSAL),²⁵ and aged 18 years or older.
- Exclusion Criteria: Individuals who contracted COVID-19 during their hospitalization, patients hospitalized for COVID-19 who were referred to other healthcare centers, whether public or private, and patients hospitalized for a different diagnosis who also presented with COVID-19.

The independent variable in this study is identified as the risk factors that are studied, while the dependent variable is represented by individuals who passed away due to COVID-19 during their hospitalization.

The risk factors considered for this study are a) male gender, b) age over 60 years, c) history of hypertension, d) history of type 2 diabetes mellitus, and e) history of obesity. The first two factors were defined as personal characteristics, and the latter three were considered elements of the medical history present in clinical records, all of which could negatively impact the progression of COVID-19.

The research hypothesis posits that male gender, age over 60 years, hypertension, type 2 diabetes mellitus, and obesity are risk factors that may influence mortality in individuals hospitalized for COVID-19 during the study period.

Regarding data collection, access was granted to an anonymized Excel database created by the head of the Diagnosis-Related Groups (DRG) unit at the hospital. This database included the risk factors being analyzed. Subsequently, a review of the spreadsheet was conducted, followed by the creation of a new spreadsheet containing only the data relevant to this study.

Concerning data processing and analysis, descriptive statistics for categorical variables included frequency and percentage analyses, while mean and standard deviation were calculated for continuous variables. Due to the predominance of categorical variables, the Chi-square test was used to conduct bivariate comparisons. This test was chosen for its ability to analyze the association between such variables. Additionally, the Fisher's exact test was employed to determine the presence of a significant association between two specific categorical variables that showed low frequencies in the cells of their respective contingency table. This is to provide a more accurate and reliable approximation in such scenarios. Given the analysis of categorical variables, these tests, which do not rely on normality assumptions, were deemed appropriate.

Binary logistic regression models were used to analyze the association between independent and dependent variables. Measures of effect were employed in this study since they make it possible to quantify disparities in the occurrence of an event in groups that differ in the presence or absence of certain characteristics. The measures used were the absolute risk (AR), which allows for obtaining

the probability of developing the event of interest in a given time, and the relative risk (RR), representing the strength of the association between exposure and the event. In this case, it indicates the probability of death in individuals exposed to a risk factor, compared to the group of those not exposed. Statistical significance was considered at a p-value < 0.05, with a 95% confidence interval (CI). Data analysis was conducted using the STATA® software.

Regarding ethical considerations, the study adhered to the principles of the Declaration of Helsinki. Additionally, the research was approved by the Bioethics Committee of the Faculty of Medicine at Universidad de Valparaíso, documented in Act No. 21/2021. Authorization was also obtained from the Director of Hospital de Quillota.

RESULTS

Descriptive Analysis

In the analyzed period, a total of 763 individuals with COVID-19 received medical assistance. Of these, 335 were excluded for not meeting the inclusion and exclusion criteria. Thus, the final sample comprised 428 individuals.

Table 1 presents the main personal characteristics and comorbidities of the participants. The majority were individuals over 60 years of age and predominantly male. Hypertension was the most prevalent comorbidity. The hospital fatality rate was 26.6%. Among patients with hypertension, this rate was 32.8%, decreasing to 23.2% and 18.5% for patients with type 2 diabetes mellitus and obesity, respectively.

| Characteristics | Total % (n=428) | Alive (n=314) | Deceased (n=114) |
|--|-----------------|----------------------|------------------|
| Age Ranges | | | |
| Over 60 years old | 50.7% (217) | 41.4% (130) | 76.3% (87) |
| Under 60 years old | 49.3% (211) | 58.6% (184) | 23.7% (27) |
| Sex | | | |
| Man | 56% (239) | 53.8% (169) | 61.4% (70) |
| Woman | 44% (189) | 46.2% (145) | 38.6% (44) |
| Number of Comorbidities | | | |
| 0 | 36.6% (157) | 37.6% (118) | 34.2% (39) |
| 1 | 33.1% (142) | 31.2% (101) | 35.9% (41) |
| 2 | 24.7% (106) | 23.9% (75) | 27.2% (31) |
| 3 | 5.3% (23) | 6.3% (20) | 2.6% (3) |
| Arterial Hypertension | 45.6% (195) | 67.2% (131) | 32.8% (64) |
| Type 2 Diabetes Mellitus | 29.2% (125) | 76.8% (96) | 23.2% (29) |
| Obesity | 24.0% (103) | 81.5% (84) | 18.5% (19) |
| | Total | Minimum | Maximum |
| Average number of hospitalization days | 16.6 | 1 day | 145 days |
| Average age for both sexes | 58.8 | 19 years | 92 years |

Table 1. Personal characteristics, comorbidities, and average length of stay for hospitalized COVID-19 patients.

Source: Own Elaboration.

Table 2 displays the percentages of comorbidities observed in the deceased patients. Hypertension was the most prevalent disease in this group, with 56.1%. This differed from type 2 diabetes mellitus and obesity, where more patients without these pathologies than those with them died. Other conditions were not included, regardless of whether they were present or not

| Comorbidities | Presence / Absence | Deceased (n=114) | |
|---------------|----------------------------|------------------|--|
| | With Arterial Hypertension | 56.1% (64) | |
| Hypertension | Without Arterial | 43.9% (50) | |
| | Hypertension | | |
| Diabetes | With type 2 Diabetes | 25.4% (29) | |
| | Without type 2 Diabetes | 75.6% (85) | |
| Obesity | With Obesity | 16.7% (19) | |
| | Without Obesity | 83.3% (95) | |
| | Source: Own Elaboration. | . , | |

Table 2. Percentage of comorbidities in deceased patients.

Chart 1 shows the distribution of deceased patients according to the studied risk factors. More male patients, over 60 years of age, and those with hypertension passed away due to the illness. Conversely, more patients without type 2 diabetes mellitus or obesity died than those without these diseases.

Chart 1. Distribution of deceased patients according to risk factors.



Source: Own Elaboration.

Association Analysis

Figure 1 presents the Fisher's exact test conducted to analyze deceased individuals based on the number of comorbidities (qualitative variables). The figure shows that there is no association between the number of deceased patients and the number of comorbidities. This is evidenced by the decreasing trend in the number of deceased patients as the number of comorbidities increases.



Figure 1. Fisher's Test for the Analysis of Deceased Patients

Source: Own Elaboration.

Tables 3 and 4 present the logistic regression with relative risk that was conducted for the studied risk factors. Individuals over 60 years old had 3 times more risk of mortality compared to younger individuals. The remaining factors did not show a statistically significant association. Additionally, individuals over 60 years old had a 40.09% risk of mortality, compared to those under 60 years old, who had a 12.79% risk of mortality, with a statistically significant association. Similarly, individuals with hypertension had a 32.82% risk of mortality compared to those without hypertension.

| | C C | , | | |
|-------------------------------|----------------------|------|-----------------------|--|
| Variables | Relative Risk | Р | CI 95% | |
| | (RR) | | (Confidence Interval) | |
| Sex (Man) | 1.24 | 0.16 | [0.91-1.69] | |
| Age (Older than 60 years old) | 3.17 | 0.00 | [2.11-4.77] | |
| Arterial Hypertension | 1.04 | 0.78 | [0.75-1.44] | |
| Type 2 Diabetes Mellitus | 0.69 | 0.05 | [0.48-1.00] | |
| Obesity | 0.80 | 0.08 | [0.97-1.00] | |

Table 3. Relative Risk according to the risk factors.

Source: Own Elaboration.

| Variables | Sub-variables | Absolute Risk (AR) | Р | CI 95% (Confidence Interval) |
|----------------------|---------------|-----------------------|------|---------------------------------|
| Sex | Men | 29.28% | 0.16 | [0.90-1.74] |
| 2011 | Women | 23.28% | | |
| Age | Age >60 years | 40.09% | 0.00 | [2.12-4.61] |
| | Age <60 years | 12.79% | | |
| Arterial | Yes | 32.82% | 0.00 | [1.11-2.10] |
| Hypertension | No | 21.45% | | |
| Type 2 | Yes | 23.20% | 0.30 | [0.57-1.19] |
| Diabetes Mellitus | No | 28.05% | | |
| Obesity | Yes | 18.44% | 0.03 | [0.40-0.97] |
| | No | 29.23% | | |

Table 4. Absolute Risk according to risk factors.

Source: Own Elaboration.

DISCUSSION

The findings reveal that age is a significant risk factor, as individuals over 60 years hospitalized for COVID-19 had a 40% risk of mortality compared to 12.7% in those under 60 years. Additionally, individuals over 60 years old were three times more likely to die than those under 60 years. These results align with evidence from various countries, including the United States, Mexico, Peru, and our own, indicating that age is associated with an increased risk of death. ^{11-13,22-23}

On the other hand, regarding male gender, there is no statistically significant association to assert that it is a risk factor influencing mortality in patients hospitalized for COVID-19. It's important to note that 61.4% of the deceased patients in the study were male, but this was not considered a risk factor for death, unlike what is found in various international studies.¹⁹⁻²¹ This could be explained by the coexistence of other variables and characteristics associated with male gender, not necessarily biological conditions.

Concerning comorbidities, individuals with hypertension had a 32.8% risk of mortality compared to 21.4% in those without hypertension. However, there was no statistically significant association to establish it as a relative risk factor, similar to type 2 diabetes and obesity, which did not show a statistically significant association as risk factors for death in this study. This is similar to what had been found in countries like Peru, where age was the only factor associated with death from COVID-19, among various factors and comorbidities.²⁶ Nonetheless, this result contradicts international and national research indicating that the presence of these pathologies is indeed associated with a higher risk of death from COVID-19. ^{14-18, 22, 23} This discrepancy may be related to specific characteristics of the studied population, including socioeconomic, cultural, and environmental factors, as well as the medical control individuals with these comorbidities seek, which may have an impact beyond the mere presence of these chronic diseases.

The main limitation of this study was its retrospective nature, which meant the anonymized Excel spreadsheet did not include relevant data such as the administration of any COVID-19 vaccine to the

participants. This could have impacted the scope of the results of this research, as it was not possible to differentiate between those who may have received a vaccine and those who did not.

CONCLUSIONS

Similar to what can be found in various studies, age was identified as a risk factor that could influence the mortality of individuals hospitalized due to COVID-19. Those aged over 60 had a 40% risk of death and were three times more likely to die from COVID-19 compared to individuals under 60 years old.

The COVID-19 pandemic posed a significant challenge for healthcare facilities in providing timely and quality care. Although there is a decreasing trend in confirmed cases and consequently fewer patients requiring hospitalization, this study contributes significantly to the knowledge of healthcare teams working directly with this population in inpatient care. Understanding the risk factors that may affect mortality in hospitalized COVID-19 patients allows for focused and specific actions, anticipating the course of the disease and its potential complications.

Further research is necessary to confirm whether being male and having hypertension, type 2 diabetes mellitus, or obesity are indeed risk factors for mortality in hospitalized COVID-19 patients. Additionally, it is essential to explore other relevant comorbidities, such as chronic kidney disease, chronic obstructive pulmonary disease, and the presence of tumors or cancer, among others, to identify pathologies associated with an increased risk of death from COVID-19.

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AUTHORSHIP:

CCA: Conceptualization, Methodology, Research, Writing - Original Draft. PG: Formal analysis, Validation, Writing.

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