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MORTALITY FROM COVID-19 IN AN INTENSIVE CARE UNIT IN THE SEYCHELLES ISLANDS

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SUMMARY

Objectives: *to identify the significance or impact of epidemiological factors and the selected treatment on the mortality in the population of patients suffering from COVID-19.*

Method: *design, frame of reference and patients: An observational, analytical case-control study was carried out in critically ill patients diagnosed with COVID-19, who were admitted to the Intensive Care Unit of H.H Sheikh Khalifa Bim Zayed al Nahyan. Hospital in the period from January 2021 to September 2021.*

Results: *the variables that turned out to have a statistically significant impact on mortality were "presence of vasoactive drugs" (21,5 times more likely) and "age over 65 years" (5,4 times more likely).*

Conclusions: *mortality in the study population, affected with COVID-19 was higher in older adult patients and those who required vasoactive support during their stay in the intensive care unit, with the majority presenting with acute respiratory insufficiency.*

Keywords: *acute Respiratory Distress Syndrome, Mechanical Ventilation, vasoactive drugs.*

INTRODUCTION

Understanding the direct and indirect impact that COVID-19 has had on mortality, is of the utmost importance in all health management. In principle, these deductions allows not only to know the magnitude of the disease itself, but also because it brings us closer to understanding the level of performance that health systems have had in planning and executing the response to this pandemic[1].

Taking into account that seven of the ten leading causes of death worldwide are chronic non-communicable diseases, it is remarkable to show that coronavirus infection has changed the statistics of mortality in the general population over the last 10 years[2].

The presence of comorbidities in hospitalized patients with COVID-19 is common and can negatively affect their prognosis, posingthem at a higher fatality risk. It has been reported that chronic noncommunicable diseases associated with this viral infection, as well as the extent of lung damage, extra-pulmonary complications, secondary infections, and quality of care could increase the risk of developing serious complications, increasing mortality[3].

In addition to age and sex, various factors have been associated with a worse evolution of the disease [4]. However, these factors are sometimes contradictory; they may differ in older people, the population group where the highest mortality is recorded, and could be influenced by the type of population studied [5].

Studies suggest that mortality

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in older adults is attributable to characteristics of the aging process; infection in the elderly can present atypically and its severity is linked to frailty, cardio-metabolic and respiratory diseases and diabetes. Expression of the ACE2 gene, which encodes the SARS-CoV-2 receptor, has been linked to specific immune signatures in older adult men; gene expression is age-related[6].

Natural aging appears to be a risk factor for SARS-Cov2 infection. Recent investigations have shown, under the chronological analysis of cases in older adults, mortality of up to 11 % for men and 6,5 % in women, for the global elderly population, the fatality rate would be 9,1 %; Regarding age, mortality is higher in people aged 80 and over [6].

Most patients admitted to the Intensive Care Unit (ICU) with COVID-19 develop bilateral interstitial pneumonia/ Acute Respiratory Distress Syndrome (ARDS) with hypoxemic acute respiratory failure and multiple organ failure. Depending on the duration of the disease, they may also present hemodynamic instability that requires volume resurrectmethods and/or vasoactive drugs once the differential diagnosis has been made [7,8].

Currently there is not enough evidence in the bibliography about specific hemodynamic support in COVID-19 patients, and most of the recommendationsareextrapolations from the usual management of critically ill patients, especially the recommendations of the Surviving Sepsis Campaign: International Journals for Management of Sepsis and Septic Shock: 2016 [7, 8].

Even though most cases of COVID-19 are mild or present only minor symptoms, 5-10% of patients require hospital admission and oxygen therapy and a large number of patients presented severe respiratory failure, requiring respiratory support and admission in an ICU, exceeding in many cases their capacities and turning COVID-19 into a challenge for health systems around the world[9].

The Seychelles Islands are not spared from the multiple challenges caused by the pandemic. For this reason that the group of researchers that works in the ICU of the H.H Sheikh Khalifa Bim Zayed Al Nahyan Hospital (Seychelles Family Hospital), caring for seriously and critically ill patients affected by COVID-19, proposed to identify the impact of selected epidemiological, diagnostic and treatment factors on mortality in the population of patients suffering from COVID-19.

MATERIALS AND METHOD

A study was carried out that classified as observational, analytical of cases and controls, (10) (cases and controls nested in a cohort) [11].

The population was made up of a cohort of patients infected with SARSCov-2, who developed the COVID-19 disease, in its serious and critical state, aged 18 years or older, of both sexes and who were cared for in the ICU of this Hospital), who gave their consent to voluntary participation in the research, through the informed consent of them or their relatives and, for whom, sufficient information on the empirical data of interest was found in the clinical histories.

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A randomized sample of 74 patients, discharged from the aforementioned hospital institution, was selected based on the availability of human, material and logistical resources, which allowed achieving the knowledge proposed in the research [12, 13].

In order to know the causal weight of the different variables in the explanation of the risk of dyingin the cohort of interest, a total of 15 variables was initially selected, which after a process of deep and detailed theoretical review of the updated bibliography on the subject of mortality, attributable to this new infectious disease, was reduced to six (independent) explanatory variables, namely: "older age equal to or greater than 65 years"; "presence of comorbidities (personal pathological history)"; "presence of altered D-dimer"; "presence of vasoactive drug prescription"; "presence of invasive mechanical ventilation prescription" and "presence of being vaccinated against the disease, (having received at least one dose)".

In order to achieve greater discrimination of the variables that are causally associated with mortality in the cohort of patients suffering from COVID-19, a Principal Component Analysis was applied to reduce the dimensionality of the set of selected variables [14].

The model's significant or ideal parameters were taken into account, namely: The Kaiser-Meyer-Olkin (KMO) sample adequacy measure and Bartlett's sphericity test [14].

The most appropriate number keeping of components was selected according to the Kaiser Criterion, which indicates that the main components whose eigenvalues are greater than unity 14 must be kept. In order to achieve optimal discrimination of the factorial saturations of the variables, according to the components retained in the process for dimensionality reduction, the Varimax method of rotation of the data matrix was applied. In addition, the sedimentation graph obtained in the extraction process of the components is presented; (Appendix 1) [14].

Subsequently, based on the design of cases and controls gathered in a cohort, previously stated, two random samples of patients from said cohort were selected: the sample of cases (patients discharged deceased; n1= 45) and the sample of controls (discharges alive; n2= 29).

The information for the explanatory analysis of mortality was based on the construction of a multivariate logistic regression model, with a binary response, according to the following logistic function: [15]

P (y= 1) = 1/1 + Exp – (□ + □1x1 +: □2x2 + □3x3 +……+ □kxk), where:

P (y= 1) = Probability of death on discharge.

□= Constant.

X1…xk= Independent variables.

□1...□k= Coefficients of the independent variables.

The dependent variable was the presence or absence of mortality at discharge, coded as "1" and "0", respectively, and the explanatory (independent) variables turned out to be the four identified in the selection process, which offered the Principal Components Analysis; namely: "presence of vasoactive drug prescription"; "presence of altered D-dimer"; "age equal to or greater than 65 years"

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and "presence of comorbidities (Past Medical History)"; coded as presence: "1" and absence: "0".

The construction of the model was carried out through the "Introduce" method (Appendix 2), which allowed to mitigate the undesired effect of the collinearity of the independent variables. The collinearity analysis between the variables was performed using the multiple correlation matrix.

The fit of the constructed model was considered satisfactory and was carried out through the analysis of the value of the Nagelkerke R2 Determination coefficient, the Hosmer-Lemeshow statistical significance test (calibration) and the analysis of the magnitude of the overall percentage of agreement between the results. (15) Observed and predicted values of the variable dependent (mortality), obtained by the model; (Appendix 2).

Odds ratios were estimated using the exponentials of the regression coefficients, with their respective 95% confidence intervals. The patient's risk of dying in the presence of mortality predictors was calculated using the formula: [exp([illegible]) - 1] *100. (15)

For the collection of the primary data, a database was built in Excel®; version 2010, of Microsoft Word®. Data processing was performed using the SPSS/PC® statistical processor; version 21.0. The results were presented in statistical tables.

RESULTS

The study revealed that out of 74 patients admitted to the ICU, 45 of them (60,8 %) were discharged dead, and 29 patients (39,2 %) were discharged alive. A total of 21 patients (28,4 %) were above 65 years of age, there were 6 patients (8,1 %) out of the study population were vaccinated with only one dose, and the rest of study population had received the recommended 2 doses. Also 20 patients (27,0 %) of the total of they, had a unremarkable previous medical history.

It was shown that 31 patients (41,8 %) had a normal D-dimer level. In addition, 60 patients (81,1 %) and 56 out of the total (75,7 %) received invasive ventilatory support and vasoactive support respectively.

The results of the Principal Components Analysis, which later led to the construction of the binary logistic model, are presented below:

A positive matrix was obtained, with a Determinant equal to 0.207, which indicated that the selected variables are linearly related and the analysis is pertinent.

The adjustment parameters of this procedure were based on the Kaiser-Meyer-Olkin (KMO) and Bartlett's sphericitytests(14). The first estimated a result of 0,54, higher than 0,5; which indicated a good magnitude, which asserts that the correlations between the pairs of variables can be explained by other variables.

Subsequently, the results of the Bartlett's sphericity test (p= 0,000) are specified, which means that the state of the associations between the six selected variables is strong enough to continue the analysis, that is, the correlation matrix does not is an identity matrix, therefore the model is relevant.

Then the commonalities are made explicit, which are nothing more than the magnitudes of the variability of the variables introduced in the analysis, explained by the extracted components. Es important to know that the variables that are explaining the greatest proportions of variability of all the data entered into the analysis are "the presence of being vaccinated", "the presence of vasoactive support" and "the presence of mechanical ventilation", with values of 0,84; 0,90 and 0,87; respectively; (Appendix 1).

Three main components were extracted, being those that presented an eigenvalue equal to or greater than unity (Kaiser Criterion). The first component accumulated 34,81% of the total explained variance; the second, 20,93 % and the third, 16,88 %; in that order, which accumulated a total percentage of variance explained by the three extracted components of 72,64 %.

The results are illustrated through the sedimentation graph, which serves as an illustrative rule for determining the optimal number of factors that must be present in the solution; (Appendix 1).

The matrix of the components rotated by the Varimax method [14] shows that the highest factorial saturations of the first component rotated are that of the variables "presence of vasoactive support: (0,94)", followed by "presence of VAM: (0,93)" and " Altered D-dimer: (0,40)". Of the first two variables mentioned above, it was decided to retain the variable "presence of vasoactive support" for the analysis of the logistic regression model, since they are intensely correlated, with a value of Pearson's linear correlation coefficient greater than 0,85; [14] which means that both variables practically explain the same in terms of the magnitude of the variability of the data, so it was decided to choose the one that presented the highest factor load in the first component extracted, which is the component that explains the highest percentage of total variability (34,81 %).

The variable "presence of vasoactive support" being retained for the subsequent causal analysis, with a factorial load in this first rotated component of 0,94. Similarly, the variable "presence of altered D-dimer" was selected, which is the third in factorial weight in this first component.

For the second rotated component, with total explained variability of 20,93 %, it was observed that the highest factor loads were represented by the variables "presence of age equal to or greater than 65 years: (0,79)"; and the "presence of comorbidities: (0,76)"; which were included in the causal model of Logistic regression. Finally, the highest factorial load of the third component extracted was provided by the "presence of vaccination", with a factorial saturation magnitude of 0,91.

It was necessary to exclude this last variable from the logistic regression model, since the latter requires _in order to obtain optimal results_, that at least 10 or more subjects must be classified with the presence or absence of any of the independent variables that are introduced. In the model; however, when the frequency analysis for this variable was carried out, only six patients had been vaccinated, a value much lower than 10 subjects; Consequently, to avoid possible

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aberrations in the estimates of the regression coefficients and their exponentials (Odds ratio), [15] it was necessary to exclude the variable "presence of vaccination" when building the logistic model, which tries to offer a causal explanation of the risk of mortality in the cohort of patients of interest.

As a final result of the ¨Principal Components Analysis, of the six variables that had initially been selected based on clinical judgment, the theoretical-referential framework and the personal experience of the authors of this research report, only they were determined, from the point of view of theoretical and statistical view, the following variables: "vasoactive support prescription", "age equal to or greater than 65 years", "the presence of altered D-dimer" and "the presence of comorbidities (Past Medical History)".

Regarding the logistic model, the four independent variables that were selected from the previous principal components analysis and that were expected to elucidate the magnitude and significance of their participation in the causal explanation of death in the population were included using the "Introduce" method of patients suffering from COVID-19, graduated from the ICU.

A moderately acceptable fit was obtained (Nagelkerke's R square= 0,40); although the statistical test of Hosmer and Lemeshow turned out to be optimal; which means that the observed observations did not differ significantly from the observations predicted by the model; (p= 0,54) [14].

A high global explanation percentage of 77,0 % was estimated; (Appendix 2), which was interpreted as a good explanation of the model, by the variables included in it, of their participation in the explanation of mortality at discharge in the cohort of patients. The correct percentage of model classification for discharged patients deceased was 93,3 %, but for living graduates it was 51,7 %; (Appendix 2).

Finally, the variables (factors) that turned out to have a statistically significant causal explanation in the explanation of mortality (Table 1) were the "presence of the support prescription with vasoactive drugs" and "age over 65 years", that is, in other words, it is 21,5 times more likely [95 % CI: 4,080 - 113,446] that a patient suffering from covid-19 will die if a vasoactive drug is prescribed than if it is not prescribed. Similarly, it is 5,4 times more likely [95% CI: 1,091 - 27,628] that a patient with covid-19 will die if they are 65 years of age or older than if they are younger. When the rest of the variables remain constant in both cases.

DISCUSSION

The behaviour and magnitude of the pandemic worldwide has been evidently different across the globe, being shaped by different socioeconomic factors. It is also worth noting that the in those countries whose population censuses and death records have been more transparent, the analytical comparison of mortality in short periods has been allowed, making it possible to observe the evolution of the phenomenon with greater precision and, above

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all, its behavior according to sociodemographic and clinical factors with whom they are related[16].

It was possible to observe in the general results of this investigation, that the majority of the patients admitted to the intensive care room, where this study was carried out, showed that most of the patients who passed away had associated comorbidities, were not vaccinated and had elevated D-dimer levels at the time of hospital admission, requiring a large part of them during their stay, invasive mechanical artificial support and vasoactive support, showing a worst outcome in elderly patients. (More than 60 years).

According to others researchers, sociodemographic factors such as sex and marital status have no relevance for COVID-19 mortality, but age does, since it is significantly related to it, highlighted by the fact that 30,80 % of deaths occurred in age group above 65 years. These results are consistent with the fact that Spain reports a mean age of deaths of 81,50 years, with more than 50 % of this population with comorbidity associated with COVID-19 [16].

However, these results are different from the real reports, although they are true, found that in the patients over the age 65 years, only 25 % of said population died from COVID-19 [16].

Most of the authors agree that all diseases seen in adults affect old age. Therefore, one cannot speak of diseases of old age, but of diseases in old age. The decrease in the functional reserve in the organs and systems, its changes with aging and the lack of adaptation capacity determine that in many cases the expression of the signs and symptoms of the disease in the elderly is different from that of the younger adult [17].

Aging is genetically conditioned, with modifications in the genes themselves that promote or delay changes throughout the organism. A series of environmental factors act on these genetic factors, many of them determined by lifestyle, which accelerate or delay the changes of aging. Depending on the determinants of this process, it can develop without disease or, if the factors affect more aggressively, manifestations in the form of age-related chronic diseases can occur[18, 19].

It is generally accepted that the elderly is more vulnerable to infections than the young population and that infectious diseases constitute one of the main causes of morbidity and mortality in the geriatric population. The increased susceptibility to infections has been attributed to the process of anatomical, physiological and immunological aging and the higher prevalence in them of chronic diseases, especially cardiovascular and pulmonary diseases and diabetes mellitus, which predispose to infection[20].

This data is previously known through various prospective studies, carried out in recent years and contribute to better understand the clinical epidemiology of the most serious infectious diseases in the elderly population, such as pneumonia, meningitis and bacteraemia [20].

Age is one of the main predictors of mortality of the patients with Community Acquired Pneumonia

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(CAP) and is the most important factor in predicting 30 day mortality on the fine scale. In patients older than 65 years, the overall mortality of CAP is between 15 and 26% [20].

According to the researcher, there are differences in the clinical presentation of patients with bacteremia according to age group, unlike other researchers who have found that very elderly patients with bacteremia present more often without fever, but with leukocytosis and left shift, and more frequently develop septic shock, respiratory failure, acute renal failure, and altered mental status [20].

It's important to consider the overall state of health rather than chronological age when making the decision on whether the patient can benefit from intensive treatment that can improve the prognosis in the most serious cases. This and other decisions regarding indications for diagnostic and therapeutic procedures in elderly patients with severe infections will become more frequent in our hospital as the population ages. Fortunately, in developed countries, aging is accompanied by an increasingly better quality of life for the elderly, with better expectations of control of chronic diseases and recovery after acute processes [20].

As is known, the pathophysiology of this disease favors older patients with associated comorbidities to have a worse clinical evolution, given that the immune response induces an uncontrolled production of pro-inflammatory cytokines (tumor necrosis factor ⍰, interleukin 1⍰, interleukin 6, interleukin 8, interleukin 12, interferon gamma-inducible protein 10, macrophage inflammatory protein 1-alpha, and monocyte chemoattractant protein 1. This phenomenon is called cytokine storm and has been linked to the genesis of Distress Syndrome. Acute Respiratory Disease (ARDS) and multi-organ failure [21,22].

Critically ill patients from COVID-19 suffer from states of macro vascular and microvascular thrombosis. In this regard, the following have been reported: pulmonary thromboembolism, deep vein thrombosis, catheter-related thrombosis, ischemic cerebrovascular disease, acrosyndromes, and capillary leak syndrome in organs such as the lungs, kidneys, and heart [22].

Data from clinical laboratory tests indicate the presence of an increase in D-dimer, prolongation of prothrombin time, and a modest decrease in platelet count. These changes are part of the genesis of multiple organ failure and are the reason why coagulopathy in patients with COVID-19 becomes a factor that increases the risk of death [22].

Hypoxia causes vasoconstriction which reduces flow and increases endothelial damage. In addition, it promotes alteration of the early growth response protein gene, changing the phenotype of the endothelium towards a pro-inflammatory and pro-coagulant stat[22].

As has been analyzed in this research, the patients with high mortality were those who needed, at some point during their stay in the ICU, hemodynamic support with vasactive drugs, in patients over 65 years of age. Due to the fact that

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the state of shock was present for the most part, contributing to the clinical worsening and showing a torpid evolution during his stay in the ward, he cares for the critically ill patient. Perhaps aggravated by his personal pathological history, by the hypoxemia typical of this new infectious disease.

Numerous mechanisms contribute to vasodilatory shock in sepsis. They highlight the increased expression induced by cytokines of the inducible nitric oxide synthase. This enzyme produces nitric oxide (NO), a potent endogenous vasodilator, in high concentrations. Other stimuli present in shock, such as cellular hypoxia, acidosis, and NO itself, activate ATP-sensitive potassium channels (23).

These channels induce hyperpolarization of the membrane, which prevents an increase in cytoplasmic calcium, which leads to vasodilation. Other mechanisms, such as the presence of adrenal insufficiency, inappropriately low vasopressin and elevated adrenomedullin plasma levels, or oxidation and inactivation of catecholamines contribute to the pathophysiology of septic shock (SS) (23).

Sometimes a component of myocardial dysfunction is associated due to inflammation that can further aggravate the shock condition, complicating both the prognosis and management. Therefore, even in the presence of a picture of SS of clear etiology, there may be multiple components that contribute to refractory circulatory collapse (23).

Septic shock (SS) is defined as that situation of sepsis in which the underlying circulatory, cellular and metabolic alterations are profound enough to increase mortality. It includes the need for vasopressor treatment to maintain a mean arterial pressure (MAP) ≥ 65 mmHg together with the presence of lactate levels > 2 mmol/L (23,24).

This situation is associated with a mortality of 30 to 40 %. However, there are situations of SS in which, despite the initiation of high-dose vasoactive therapy, it is not possible to achieve MAP ≥ 65 mmHg. This situation is called refractory septic shock (RSS) and although there is no universally established definition, NA doses > 0,5 mcg/kg/min or the need for rescue therapy with vasopressin have been considered by various authors as criteria for SRH ???. And are associated with mortality figures ranging between 50 and 94 % (23, 25).

In the COVID-19 patient, it is known that the cytokine storm is the cause of organic dysfunction, since this massive release of cytokines facilitates vascular permeability and fluid extravasation, actively participating in the pathophysiology of arterial hypotension, thereby that generates the hypothesis that a viral process causes immune dysregulation, causing insufficiency organic, resulting in the current concept of sepsis, only in this case the source is a virus (viral sepsis) (26).

Sepsis is the most frequent cause of acute respiratory failure, this due to a respiratory infection focus (pneumonia) that causes increased vascular permeability and endothelial injury, which causes the most serious expression of respiratory failure called ARDS that also occurs in the SARS-CoV-2

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infection. There is information in this regard, on the similarity of inflammatory behavior in both cases of AIDS, both from COVID-19 and in that of septic origin [26].

For example, the results published by Sosa MA. Who sought to compare the inflammatory response between the two, finding that the main cytokines, such as: IL-1β, IL-1RA, IL-6, IL-8, IL-18 and TNF-α, were similar between an ARDS due to sepsis and in COVID-19 [26].

Another feature shared by these two conditions (cytokine storm and sepsis) is undoubtedly the role of nitric oxide synthase activation, which is inducible in macrophages and other cells during the bacterial and viral infectious event, resulting in increased oxide release nitric, with subsequent vasodilation and reduction in systemic blood pressure with decreased response of vascular smooth muscle cells to non-adrenergic stimulation, exacerbating shock [26].

The researcher, De la Torre Fonseca, states that during the COVID-19 infection, the binding of the virus to the angiotensin-converting enzyme 2 (ACE2) receptors, the invasion of lung cells and their replication, has triggered multiple manifestations in the organism. From the aforementioned cytokine storm, severe hypoxia, endothelial dysfunction, or the imbalance between supply and demand, there are multiple mechanisms that attempt to demonstrate why COVID-19 infection causes myocardial injury in infected patients [27].

The estimated fatality rate for this disease has varied from 3 to 7%, depending on the region, the spread of the virus and the affected populations. Cardiovascular risk factors, diabetes mellitus and smoking have had a direct relationship with the number of deaths and complications of all kinds. The early detection of this myocardial damage and the rational use of treatments and therapeutic measures constitute a key point for controlling the pandemic and minimizing its sequelae [27].

Being able to this mentioned above, contribute to the appearance and perpetuation of the state of shock in this population studied and contributing to the need for vasoactive support, to try to improve the supply and demand needs caused by this disease.

CONCLUSIONS

Mortality in the population subject to study, with COVID-19 infection, is higher in the older adult patients and those who required vasoactive support during their stay in the intensive care unit, most of whom presented with acute respiratory failure.

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RESUMEN

Objetivos: *identificar el peso causal de factores epidemiológicos, diagnósticos y del tratamiento seleccionado, en la explicación de la mortalidad en la población de enfermos aquejados de covid-19, egresados del servicio de atención al paciente grave.*

Método: *diseño, marco de referencia y pacientes: Se llevó a cabo un estudio observacional, analítico de casos y controles, en pacientes graves diagnosticados de COVID-19, que ingresaron en la Unidad de Cuidados Intensivos del H.H Sheikh Khalifa Bim Zayed Al Nahyan Hospital en el período comprendido desde enero del 2021 hasta septiembre del 2021.*

Resultados: *finalmente, las variables (factores) que resultaron tener una explicación causal estadísticamente significativa en la explicación de la mortalidad fueron la "presencia de drogas vasoactivas" (21,5 veces más probable) y la "edad superior a los 65 años"(5,4 veces más probable).*

Conclusiones: *la mortalidad en la población sujeta a estudio, enferma de COVID-19, afectó más de forma general a los pacientes adultos mayores y a los que durante su estadía en la unidad de cuidados intensivos necesitaron apoyo vasoactivo, estando presente en su mayoría la insuficiencia respiratoria aguda.*

Palabras claves: *síndrome Distres Respiratorio Agudo; Ventilación Mecánica; drogas vasoactivas.*

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Table 1. Predictive factors for mortality in patients with covid-19.

Independent variables	Dependent variable (Mortality)		O.R	Interval of Confidence 95% EXP (ß)		
	Alive (n/ %)	Deaths (n/ %)		low limit	Upper Limit	Prob.
Prescription of vasoactive drugs	18/ 24,3 %	56/ 75,7 %	21,5	4,0	113,4	0,000
Age equal to or greater than 65 years	53/ 71,6 %	21/ 28,4 %	5,4	1,0	27,6	0,039
Presence of comorbidities	15/ 20,3 %	59/ 79,7 %	0,384	0,06	2,13	0,274
Altered D-Dimer	30/ 40,5 %	44/ 59,5 %	1,7	0,5	5,5	0,366

Appendix 1

Principal component analysis

Matrix of correlations

		Age 2 (65 and over)	Vaccinated	D-dimer	Past medical History	Presence of vasoactive support	Presence of mechanical artificial ventilation
Correlation	Age2 (65 and over)	1,000	,077	-,030	,243	,008	-,002
	vaccinated	,077	1,000	-,144	-,027	-,053	-,017
	D-dimer	-,030	-,144	1,000	-,006	,302	,234
	PMH(comorbidities)	,243	-,027	-,006	1,000	,263	,186
	Presence of vasoactive support	,008	-,053	,302	,263	1,000	,852
	Presence of mechanical artificial ventilation	-,002	-,017	,234	,186	,852	1,000
Sig. (Unilateral)	Age2 (65 and over)		,257	,401	,019	,475	,493
	vaccinated	,257		,110	,411	,327	,443
	D-dimer	,401	,110		,481	,004	,023
	PMH(comorbidities)	,019	,411	,481		,012	,057
	Presence of vasoactive support	,475	,327	,004	,012		,000
	Presence of mechanical artificial ventilation	,493	,443	,023	,057	,000	

a. Determinant = ,207

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KMO and Bartlett's test

Kaiser-Meyer-Olkin measure of sampling adequacy		**0,541**
Bartlett's test of sphericity	Approximate chi-square	110,428
	gl	15
	Sig.	,000

Appendix 1.(Cont.)

Communalities		
	Initial	Extraction
Age2 (65 and over)	1,000	,652
vaccinated	1,000	,848
D-dimer	1,000	,441
PMH(comorbidities)	1,000	,636
Presence of vasoactive support	1,000	,905
Presence of mechanical artificial ventilation	1,000	,876

Extraction method: Principal Component Analysis.

Total explained variance

Component	Initial eigenvalues			Addition of the square saturations of the extraction			Addition of squared saturations of rotation		
	Total	% variance	% accumulated	Total	% variance	% accumulated	Total	% variance	% accumulated
1	2,089	34,819	34,819	2,089	34,819	34,819	1,989	33,155	33,155
2	1,256	20,935	55,755	1,256	20,935	55,755	1,252	20,870	54,025
3	1,013	16,886	72,641	1,013	16,886	72,641	1,117	18,616	72,641
4	,838	13,972	86,613						
5	,663	11,049	97,662						
6	,140	2,338	100,000						

Extraction method: Principal Component Analysis.

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Appendix 1 (Cont)

Component matrix[a]

	Component		
	1	2	3
Presence of vasoactive support	,937	-,029	,159
Presence of mechanical artificial ventilation	,903	-,042	,245
D-dimer	,466	-,394	-,260
Age2 (65 and over)	,072	,749	-,291
PMH(comorbidities)	,396	,618	-,312
vaccinated	-,126	,393	,823

Extraction method: Principal component analysis.

a. 3 extractedcomponents

Matrix of RotatedComponents[a]

	Component		
	1	2	3
Presence of vasoactive support	,941	,115	-,078
Presence of mechanical artificial ventilation	,934	,059	-,003
Age2 (65 and over)	-,091	,797	,093
APP presence	,225	,763	-,057
vaccinated	,082	-,040	,916
D-dimer	,406	-,129	-,509

Extraction method: Principal component analysis.

Rotation method: Varimax normalization with Kaiser.

a .The rotation has converged in 5 iterations.

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Appendix 2

Logistic Regression Analysis

Block 1: Method = Enter

ModelSummary

Step	-2 log likelihood	Cox and Snell R squared	Nagelkerke's R-squared
1	72,815[a]	,299	,405

a. The estimation finished at iteration number 5 because the parameter estimates have changed by less than .001.

Hosmer and Lemeshow test

Step	Chi squared	gl	Sig.
1	5,014	6	,542

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Contingency table for the Hosmer and Lemeshow test						
		Status at discharge = 0		Status at discharge = 1		Total
		Observed	Expected	Observed	Expected	
Step 1	1	5	5,577	1	,423	6
	2	7	5,799	0	1,201	7
	3	3	3,624	2	1,376	5
	4	4	4,737	7	6,263	11
	5	8	6,715	14	15,285	22
	6	0	1,171	7	5,829	7
	7	1	,606	4	4,394	5
	8	1	,771	10	10,229	11

Appendix 2. (cont)

Classificationtable[a]					
Observed			Predicted		
			Status at discharge		Correctpercentage
			0	1	
Step 1	Status at discharge	0	15	14	51,7
		1	3	42	93,3
	Global percentage				77,0
a. The cutoff value is,500					

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Classificationtable[a]					
Observed			Predicted		
			Status at discharge		Correctpercentage
			0	1	
Step 1	Status at discharge	0	15	14	51,7
		1	3	42	93,3
	Global percentage				77,0

a. The cutoff value is,500