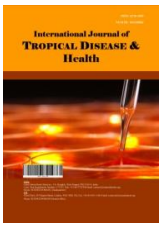

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Mortality Due to COVID-19 in the Elderly: Integrative Literature Review

Dayara de Nazaré Rosa de Carvalho[1*], Viviane Ferraz Ferreira de Aguiar[2], Dandara de Fátima Ribeiro Bendelaque[3], Lorena Nayara Alves Neves[4], Celice Ruanda Oliveira Sobrinho[4], Jaqueline Dantas Neres Martins[5], Rafael Everton Assunção Ribeiro da Costa[6], Susi dos Santos Barreto de Souza[7], Mônica Custódia do Couto Abreu Pamplona[8], Marcia Helena Machado Nascimento[8], Antônia Margareth Moita Sá[8], Elisa da Silva Feitosa[9] and Ivonete Vieira Pereira Peixoto[8]

[1]Program in Nursing at the State University of Pará (PPGENF / UEPA), Belém-Pará, Brazil.
[2]Program in Tropical Diseases, Center for Tropical Medicine, Federal University of Pará (PPGdt/UFPA), Nursing Faculty/ICS/UFPA and University Center UNIFAMAZ, Belém, Pará, Brazil.
[3]Paraense Teaching College (FAPEN), Belém, Pará, Brazil.
[4]Metropolitan University Center of the Amazon (UNIFAMAZ), Belém, Pará, Brazil.
[5]State University of Pará, Belém, Pará, Brazil.
[6]Medical Academic, State University of Piauí (UESPI), Teresina, Piauí, Brazil.
[7]Oncology from the Federal University of Pará (UFPA), Belém, Pará, Brazil.
[8]Graduate Program in Nursing, State University of Pará (PPGENF / UEPA), Belém, Pará, Brazil.
[9]Federal University of Santa Catarina (UFSC), Faculdade Pan Amazônica (FAPAN), Belém, Pará, Brazil.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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**Corresponding author: Email: dayara_twain@hotmail.com;*

ABSTRACT

Aims: Explore national and international literature about mortality in elderly caused by COVID-19.
Methodology: An integrative literature review was performed using the databases: Virtual Health Library (VHL), PubMed/Medline (National Library of Medicine and National Institutes of Health/Medical Literature Analyzes Sand Retrieval System Online) and Cochrane Library. The selection of articles occurred from the combination of the descriptors: “Coronavirus Infections”; “Aged” and “Mortality” mediated by the Boolean operator “AND”. After evaluating and synthesizing the articles, the data were analyzed using the IRaMuTeQ software, a program that is anchored in the R software.
Results: After analyzing the identification of textual domains and interpretation, 4 classes emerged: 1) The importance of tests for the control and good prognosis of infection in the elderly; 2) Predictors related to high mortality in the elderly; 3) Comorbidities associated with a high mortality rate; 4) The reasons for the transmission of the virus are more worrying in the elderly.
Conclusion: The elderly population presents different risks for mortality, an example of physiological changes such as immune senescence, critical, social and psychological factors and the presence of comorbidities.

Keywords: Coronavirus; infections; mortality; elderly.

1. INTRODUCTION

COVID-19 is an infectious disease, caused by the new coronavirus that had its first cases recorded in December 2019 in Wuhan, China. It brings clinical manifestations of fever, tiredness and dry cough, as well as symptoms such as pain, nasal congestion, runny nose, sore throat or diarrhea [1].

Considered by the World Health Organization as a pandemic in March 2019, COVID-19 presents new cases in constant growth, presenting daily updates. Currently, there are more than 7,000,000 cases of COVID-19 and 403,000 deaths worldwide. In Brazil, a total of 710,887 cases and 37,312 deaths were confirmed until June 8, 2020 [2].

There are so-called risk groups, in which COVID-19 affects more severely, increasing vulnerability and the chances of mortality. The elderly population is part of this group, with comorbidities such as diabetes mellitus, systemic arterial hypertension, cardiovascular diseases, lung and kidneys, neurological diseases, being treated for cancer, patients with immune suppression, among others and patients with frailty syndrome [3].

The greater involvement of pathologies and weaknesses can occur due to immune senescence, characterized by quantitative changes and affected by molecular and cellular components, resulting in irregular activities of the immune system. Because of this, the elderly have a more frequent response to external factors [4]. In addition, we have other factors such as: the presence of multimorbidities, including cardiovascular disease, diabetes mellitus, arterial hypertension, among others, such as changes in the respiratory system due to functional reserve, fewer patients and greater use of hospital care, making them more vulnerable to the development of a severe structure [5].

Due to greater vulnerability to health problems, the elderly are at higher risk of mortality. Patients aged 60-70 years have a 0.4% probability of dying, those aged 70 to 80 years old have 1.3% and those over 80 years old, 3.6% [6].

Data from China show that the elderly, especially those with serious underlying health conditions, are at greater risk of serious illness and death associated with COVID-19 than young people. Approximately 80% of deaths occurred in the elderly ≥60 years; only one (0.1%) death occurred in a person aged ≤ 19 years [7].

Therefore, based on the above, an Integrative Literature Review (RIL) was developed with the aim of analyzing in the national and international literature on the mortality of elderly people caused by COVID-19 between the months of December 2019 and May 2020, regardless considering that measuring the number of deaths in the elderly is extremely important for the creation of public health policies and for the knowledge of professionals.

2. MATERIALS AND METHODS

It is descriptive, qualitative research, of the type Integrative Literature Review (RIL). At RIL, it is carried out in six distinct stages, as follows: 1) Identification of the theme, research problem and object of study; 2) Establishment of search criteria in the main databases; 3) Categorization of studies and data collection using an instrument; 4) Evaluation of studies and data collection; 5) Presentation of results; 6) Discussion and presentation of the Integrative Literature Review [8].

From the object of study, the following research question was elaborated: What is the mortality due to COVID-19 in the elderly in the national and international scientific literature? Data collection occurred through online access in the following databases: Virtual Health Library (VHL), PubMed / Medline (National Library of Medicine and National Institutes of Health / Medical Literature Analyzes Sand Retrieval System Online) and Cochrane Library. In order to optimize and refine the search and guarantee the direction for all relevant works on the theme, the selection of articles occurred from the combination of three controlled descriptors and registered in the DeCS (Health Sciences Descriptors), respectively: "Coronavirus Infections"; "Aged" and "Mortality" mediated by the Boolean operator "AND", aiming to expand the number of studies.

The inclusion criteria established for the elaboration of the RIL were: scientific articles published in the period from 2019 to 2020, from free full journals in Portuguese and English, and which presented significance regarding the subject of study. Articles outside the defined period, editorials, letters to the editor, incomplete articles, paid articles, reflective studies and those that did not address the theme suggested by the authors were excluded.

The articles were categorized based on the level of evidence. The levels of evidence are: level 1, the evidence is provided by a systematic review or meta-analysis of randomized controlled trials or those originating from guidelines; level 2, evidence from a randomized controlled clinical trial is well designed; level 3, evidence obtained from well-designed clinical trials without randomization; level 4, evidence from cohort and case-control studies; level 5, evidence derived from a systematic review of descriptive and qualitative studies; level 6, evidence derived from descriptive or qualitative research; level 7, evidence from the opinion of authorities and / or expert committee reports [9].

After evaluating and synthesizing the studies, the data were analyzed using the IRaMuTeQ *software* (R Interface for Analyzes Multidimensionnelles de Textes et de Questionnaires), which originated in France; The program is anchored in the R *software* that allows several forms of statistical analysis on the textual corpus and word tables [10]. For the analysis of the data obtained through the IRaMuTeQ software, we opted for the Descending Hierarchical classification method (CHD), proposed by Reinert, in which this analysis aims to obtain classes of text segments that will present themselves with similar words to each other and also words that are different from segments of other classes. However, in order for the method (CDH) to be used, it is necessary that the text segments analyzed through the textual corpus have an utilization equal to or above 75% [11].

At the end of the data collection, a total of 448 articles were obtained in the referred databases and database. After this phase, the articles underwent an evaluation regarding the title and abstract, and of this total, 349 were excluded from the screening process. The assessment during this phase was intended to discard irrelevant articles. At the end of the screening process, the final sample of 24 articles emerged, which were evaluated according to the title of the article, country, authors, year of publication and database, types of study, level of evidence [12], objective and synthesis of the results and those who answered the guiding question of the research. The selection process for the selected articles is shown in the following prism diagram (Fig. 1).

3. RESULTS AND DISCUSSION

At the end of this stage, the final sample came up, consisting of 24 publications, which met the stipulated criteria, as noted below (Chart 1).

From the final sampling, the analysis was performed using IRaMuTeQ *software* (Interface for R pour les Multidimensional Analyzes de Textes et de Questionnaires) that assimilated the content through the Descending Hierarchical Classification (CHD) and characterized 4 classes. Class 1 corresponds to 20.3% of the words in the corpus, class 2 corresponds to 24.1% of the words, class 3 corresponds to

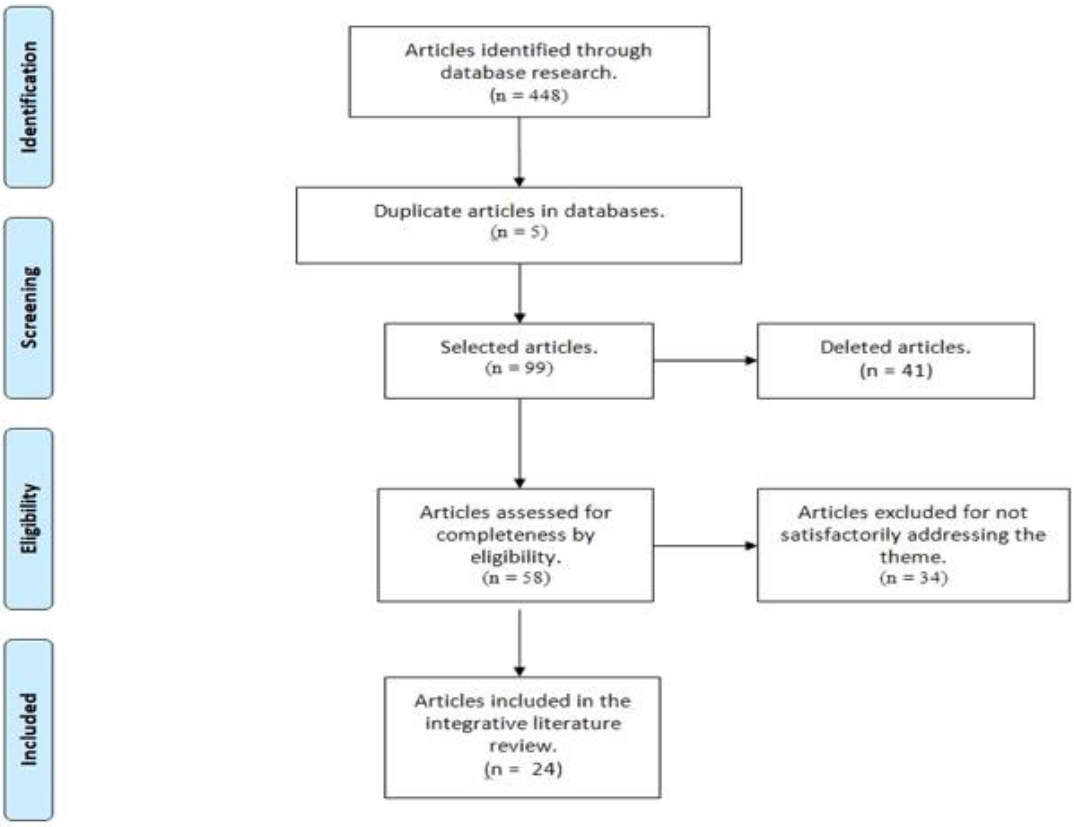

Fig. 1. Prism diagram for selecting the articles included in this integrative review study, PRISMA Group (2009)

Source: Research authors, 2020

34.3% of the word association in the corpus and class 4 corresponds to 21.2% of word association in the corpus. In the association of the classes with the fixed variables of the study, the following was taken into account: database; journal and year of publication [13].

Through the Descending Hierarchical Classification (CHD), the IRaMuTeQ *software* constructed the dendogram of the classes obtained from the text corpus. For the construction of the Dendogram, the words that obtained a frequency equal to or higher than the registered average were organized into classes, being represented by the most significant words and their associations. After analyzing the identification of textual domains and interpretation, we tried to name their respective meanings in the classes described below: 1) The importance of tests for the control and good prognosis of infection in the elderly; 2) Predictors related to high mortality in the elderly; 3) Comorbidities associated with a high mortality rate; 4) The reasons for the transmission of the virus are more worrying in the elderly [13]. The class dendogram is shown below (Fig. 2).

3.1 Discussion

3.1.1 CLASS 1 - The importance of testing for the control and good prognosis of infection in the elderly

Although testing and control does not inhibit the spread of the pathology, it is worth noting that both are essential for monitoring the progress / decline of the disease, therefore important for public health, epidemiological surveillance for observing the disease's behavior and means that facilitate its spread transmission, as well as monitoring of most vulnerable groups. Through testing and control actions implemented early in Brazil and in other countries, it was possible to support the planning, control, evaluation and execution of actions for potential risk publics and those with greater vulnerability to disease [14].

Chart 1. Articles included in the integrative review

Title of the article parents	Authors year and database	Type of study and level of evidence	Objective	Summary of results
1-Clinical course and outcome of 107 patients infected with the novel coronavirus, SARS-CoV-2, discharged from two hospitals in Wuhan, China. China.	WANG D, YIN Y, HU C, LIU X, ZHANG X, ZHOU S et al. 2020. PubMed. [43]	Study of case series. Level 6.	Describe clinical courses and prognosis in patients with COVID-19.	The clinical course of COVID-19 was presented as a three-phase pattern. The symptoms of the disease were characterized by fever, cough, dyspnoea, lymphopenia and multilobar radiological pulmonary infiltrates.
2-Clinical predictors of mortality of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infection: A cohort study. Saudi Arabia.	ALFARAJ SH, TAWFIQ JAA, ASSIRIG AY, ALZAHRANIA NA, ALANAZIA AA, MEMISHH ZA. 2019. PubMed. [44]	Cohort study. Level 3.	Examine clinical predictors of mortality from infection by the Middle East Respiratory Syndrome (MERS).	A total of 314 symptomatic patients with MERS-CoV. The following parameters were associated with increased mortality, age, leukocytes, neutrophil count, serum albumin level, use of continuous renal replacement therapy (CRT) and use of corticosteroids. The odd ratio for mortality was higher for CRRT and the use of corticosteroids (4.95 and 3.85, respectively).
3- Effect of High vs Low Doses of Chloroquine Diphosphate as Adjunctive Therapy for Patients Hospitalized With Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection. A Randomized Clinical Trial. Brazil	BORBA MGS, VAL FFA, SAMPAIO VS, ALEXANDRE MAA, MELO GC, BRITO M et al. 2020. PubMed. [45]	Randomized clinical study. Level 2.	To evaluate the safety and efficacy of 2 doses of QC in patients with severe COVID-19.	Viral RNA was detected in 31 of 40 (77.5%) and 31 of 41 (75.6%) patients in the low and high dose groups, respectively. Lethality until the 13th was 39.0% in the high-dose group (16 of 41) and 15.0% in the low-dose group (6 of 40).
4-Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. China.	CHEN T, WU D, CHEN H, YAN W, YANG D, CHEN G et al. 2020. PubMed. [46]	Cohort study. Level 3.	Outline the clinical characteristics of 2019 coronavirus disease patients (covid-19) who died.	Overall, 71 (63%) patients who died and 62 (39%) who recovered had at least one chronic medical condition. Hypertension, cardiovascular disease and cerebrovascular disease were much more frequent among deceased patients (54 (48%), 16 (14%) and 4 (4%)) than among recovered patients (39 (24%), 7 (4%) and 0 (0%)).
5-Kidney disease is associated with in-hospital death of patients with COVID-19. China.	CHENG Y, LUO R, WANG K, ZHANG M, WANG Z, DONG L et al. 2020. PubMed. [47]	Cohort study. Level 3.	To determine the prevalence of AKI in patients with COVID-19 and to define the association between markers of kidney disease and	The Kaplan-Meier analysis revealed a significantly higher in-hospital mortality rate for patients with renal abnormalities, including high baseline serum creatinine, high baseline BUN,

Title of the article parents	Authors year and database	Type of study and level of evidence	Objective	Summary of results
			death in patients infected with COVID-19.	proteinuria, hematuria and AKI (P <0.001). Cox's univariate regression analysis showed that age over 65 years, male gender and severe COVID-19 disease were associated with hospital death.
6- Analysis on 54 Mortality Cases of Coronavirus Disease 2019 in the Republic of Korea from January 19 to March 10, 2020. Korea	SCI JKM. 2020. PubMed. [48]	Cross-sectional study. Level 3.	Summarize the morality data from February 19, when the first mortality occurred at 12:00 am, March 10, 2020, in Korea, compared to other countries.	Since the last report on the epidemiology of the Korean outbreak 1 on March 2, 2020, when the number of fatal cases was 22 patients, the number of deaths has increased to 54 cases on March 10, 2020.
7-Novel coronavirus 2019 (COVID-19) A case report and review of treatments. United States.	DOUEDI S, MISKOFF J. 2020. PubMed. [64]	Case report study. Level 7.	To present a case of elderly woman who presented fever, cough and shortness of breath, considered positive for COVID-19.	She remained seriously ill and ended up receiving care according to the family's wishes and died.
8-Predictors of Mortality for Patients with COVID-19 Caused pneumonia by SARS-CoV-2: A Prospective Cohort Study. China.	DU RH, LIANG LR, YANG CQ, WANG W, CAO TZ, LI M et al. 2020. PubMed. [49]	Prospective cohort study. Level 3.	Identify the clinical and laboratory parameters associated with mortality in patients with COVID-19 pneumonia.	The mean age was 57.6 years (SD, 13.7 years; range: 18–87 years) and 97 (54.2%) were men. Of the 179 patients, 21 (11.7%) worsened in a short period of time and died of multiple organ failure, mainly respiratory failure and heart failure, and the average hospital stay until death was 13.7 days.
9-Potential lethal outbreak of coronavirus disease (COVID-19) among the elderly in retirement homes and long-term facilities, France, March 2020. France.	ETARD JF, VANHEMS P, ATLANI-DUAULT L, ECOCHARD R. 2020. PubMed. [50]	Restrospective cohort study Level 3.	Present the impact of the worst-case scenarios on French institutions, using a specific age structure and age-related mortality ratios.	The resulting number of deaths in these institutions may be equal to the national annual number of deaths caused by seasonal influenza in people over 65 years old (9,025 deaths on average between 2000 and 2009) or may well exceed that figure, depending on the final AR and the proportion of infected institutions.
10- Systematic review of the efficacy and safety of antiretroviral drugs against SARS, MERS or COVID-19: initial assessment. Switzerland.	FORD N, VITORIA M, RANGARAJ A, NORRIS SL, CALMY A, DOHERTY M. 2020. PubMed. [51]	Systematic Review Study Level 1.	Analyze the clinical results of using antiretroviral drugs for the prevention and treatment of coronavirus and plan clinical trials.	From an initial screen of 433 titles, two randomized controlled trials and 24 observational studies provided clinical outcome data on the use of antiretroviral drugs; most studies have reported results using LPV / r as treatment. Of the 21 observational studies that reported treatment results, there were three studies among patients with SARS, six studies among

Title of the article parents	Authors year and database	Type of study and level of evidence	Objective	Summary of results
				patients with MERS and 12 studies among patients with COVID-19
11- Prognostic value of NT-proBNP in patients with severe COVID-19. China.	GAO L, JIANG D, WEN XS, CHENG XC, SUN M, HE B et al. 2020. PubMed. [52]	Cohort study Retrospective Level 3.	Investigating prognostic markers for critically ill patients provides insights into early therapeutic strategies.	The present study showed for the first time the relationship between the plasma level of NT-proBNP and the risk of hospital death in critically ill patients with COVID-19
12- Epidemiological analysis of the early 38 fatalities in Hubei, China, of the coronavirus]disease 2019. China.	CHEN Y, ZHAO M, WU Y, ZANG S. 2020. PubMed.	Prospective cohort study Level 3.	Analyze the first set of death cases, with the aim of increasing the current evidence and reducing panic in the population.	Among the 38 fatalities, 71.05% were male and 28.95% female, with an average age of 70 years (interquartile range (IQR) = 65-81). People aged 66 to 75 represented the largest share. Twenty-five cases had a history of chronic illness.
13-Acute Hyperglycemic Crises with Coronavirus Disease-19: Case Reports. Korea.	KIM NY, HA E, LUA JS, LEE YH, CHOI EY. 2020. PubMed. [53]	Systematic review study. Level 1.	Describe two cases of COVID-19 compromised with acute hyperglycemic crises - CAD and HHS - during the outbreak in Daegu, South Korea	People with comorbidities, especially with DM, are susceptible to COVID-19 infection.
14-Regulation and Trust: 3-Month Follow-up Study on COVID-19 Mortality in 25 European Countries. Finland.	OKSANEN A, KAAKINEN M, LATIKKA R, SAVOLAINEN L, SAVELA N, KOIVULA A. 2020. PubMed.	Case series study. Level 6.	Examine country variations in COVID-19 mortality in Europe.	The spread of the COVID-19 epidemic has been rapid everywhere, but the results revealed significant differences between countries in COVID-19 mortality. The perceived sociability predicted a higher mortality due to COVID-19. The main differences between the 25 countries were found in the times of reaction to the crisis.
15-Current epidemiological status of Middle East respiratory syndrome coronavirus in the world from 1.1.2017 to 17.1.2018: a cross-sectional study. Iran.	MOBARAKI K, AHMADZADEH J. 2019. PubMed. [54]	Cross-sectional study Level 5.	Describe the current epidemiological status of MERS-CoV in the world.	The occurrence of the disease was higher among men than women. Variables such as comorbidities and exposure to MERS-CoV cases were significantly associated with mortality in people affected by MERS-CoV infections.
16-Emerging SARS-CoV-2 mutation hot spots include a novel RNA-dependent-RNA polymerase variant. United States.	PACHETTI M, MARINI B, BENEDETTI F, GIUDICI F, MAURO E, STORICI P. 2020 PubMed. [55]	Systematic Review Study.. Level 1	Assess whether new viral variants were spreading across countries.	The presence of additional “conserved mutations” was found in all geographic areas, taking into account only those that occur more than 10 times in our database.
17-Association of the insulin resistance marker	REN H, YANG Y, WANG F, YAN Y, SHI X, DONG K, YU X, ZHANG	Cohort study. Level 3	To evaluate the association of the TyG index with the severity and	The TyG index was significantly associated with an increased risk of severe case and mortality.

Title of the article parents	Authors year and database	Type of study and level of evidence	Objective	Summary of results
TyG index with the severity and mortality of COVID-19. China	S. 2020. PubMed. [56]		mortality of coronavirus 2019 (COVID-19)	The associations were not statistically significant for subsequent adjustment of inflammatory factors.
18-Sex-Specific SARS-CoV-2 Mortality: Among Hormone-Modulated ACE2 Expression, Risk of Venous Thromboembolism and Hypovitaminosis D. Italy,	VIGNERA SL, CANNARELLA R, CONDORELLI RA TOWER F, AVERSA A, CALOGERO AE. 2020 PubMed. [57]	Systematic Review Study Level 1.	Speculate the factors involved in different sex-related susceptibility.	Vitamin D deficiency, regardless of testosterone levels, in elderly men may be worthy of an additional epidemiological assessment to better understand the different susceptibilities and lethality between the sexes.
19-Updated understanding of the outbreak of 2019 novel coronavirus (2019-nCoV) in Wuhan, China. China.	WANG W, TANG J, WEI F. 2020. PubMed. [58]	Systematic Review Study Level 1.	Help health professionals and the public to recognize and deal with the disease quickly, effectively and calmly.	The first official announcement by the Wuhan Municipal Health Commission, 1 a total of 27 patients were diagnosed with viral pneumonia (later confirmed as 2019-related pneumonia) - nCoV) until December 31, 2019.
20- Clinical characteristics of patients with 2019 coronavirus disease in a non-Wuhan area of Hubei Province, China: a retrospective study. China.	ZHAO XY, XU XX, YIN HS, HU QM, XIONG T, TANG YY et al. 2020. PubMed. [59]	Case control study Level 4.	Conduct a comprehensive exploration of the epidemiology and clinical features of 91 confirmed patients with COVID-19 admitted to Jingzhou Central Hospital in Jingzhou, one of the most severely affected cities in Hubei province.	Older patients with chronic illnesses were more likely to become seriously ill and negative qPCR results could not safely exclude virus infection at the onset of symptoms.
21-Correlation between Heart fatty acid binding protein and severe COVID-19: A case-control study. China.	YIN L, MOU H, SHAO J, ZHU Y, PANG X, YANG J et al. 2020. PubMed. [60]	Case control study. Level 4.	Analyze the epidemiological, clinical and laboratory characteristics of patients with COVID-19.	Three patients with COVID-19 who tested positive for HFABP in serum changed from mild to severe during hospitalization.
22-Clinical characteristics and outcomes of patients with severe covid-19 with diabetes. China.	YAN Y, YANG Y WANG F, REN H, ZHANG S, SHI X et al. 2020. PubMed. [61]	Retrospective cohort study. Level 3.	It explores the clinical characteristics of patients with diabetes with severe covid-19.	Patients with severe covid-19 with diabetes had higher levels of leukocyte count, neutrophil count, highly sensitive protein C, procalcitonin, ferritin, interleukin receptor (IL) 2, IL-6, IL-8, necrosis factor a tumor, D-dimer, fibrinogen, lactic dehydrogenase and pro-cerebral N-terminal natriuretic peptide.
23-Association of radiologic findings with mortality of patients infected with	YUAN M, YIN W, TAO Z, TAN W, HU Y. 2020.	Retrospective cohort study. Level 3	Summarize the clinical and radiological characteristics of 27	The comorbidity rate in the mortality group was significantly higher than in the survival group

Title of the article parents	Authors year and database	Type of study and level of evidence	Objective	Summary of results
2019 novel coronavirus in Wuhan, China. Germany.	PubMed. [63]		confirmed cases and analyze the association of radiological findings with cases of mortality.	(80% vs 29%, P = 0.018), especially comorbid hypertension, diabetes and heart disease.
24- Successful treatment of COVID-19 using extracorporeal membrane oxygenation, a case report. China	ZHAN WQ, LI MD, XU M, LU YB. 2020. PubMed. [62]	Case report study. Level 7.	Report a successful example of a seriously ill patient with COVID-19 with extracorporeal membrane oxygenation (ECMO) technology in our hospital.	Experience has shown that the early application of ECMO can dramatically promote the recovery of critically ill patients with COVID-19.

Source: Research authors, 2020

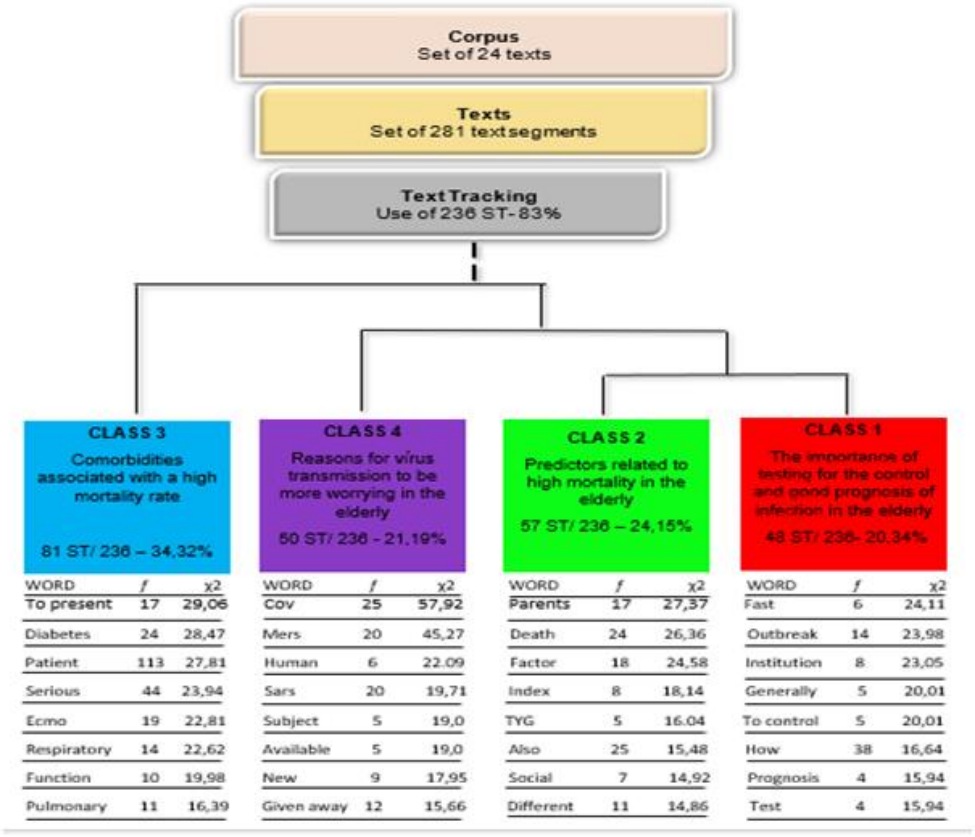

Fig. 2. Dendogram of classes created by IRaMuTeQ
Source: Research authors, 2020

Thus, the test is a strategy which allows the knowledge of the approximate number of cases and the evaluation of the morbidity and mortality of the disease in the elderly, being recommended by the World Health Organization (WHO) with the isolation of cases [15,16].

Among the usufruct of carrying out the tests was the discovery of the elderly as one of the most vulnerable groups of the disease and with the most severe clinical evolution, as it is often one of the groups with the greatest need for invasive procedures and the Intensive Care Unit. In this context, in view of these possibilities, norms on clinical management, risk classification and guidelines for the protection of the elderly emerged, both in the home and in health institutions [16].

Another potential benefit advanced with a test was the early detection of COVID-19 in the elderly and / or their family members and the implementation of protective actions and damage control. Survival is greater when the pathology is detected early by laboratory, clinical and radiological follow-up actions [17].

3.1.2 CLASS 2 - Predictors related to high mortality in the elderly

Knowledge of the pathology of COVID-19 in the body of the elderly is essential to interpret the presence or absence of clinical findings. It is known that senility and senescence have a significant influence on the postponement process by COVID-19. Facing this prerogative, it is important to pay attention to the aspects that can predict higher chances of mortality in the elderly, evidenced by the results of radiographs, laboratories and clinics [18].

One of the most important predictors of mortality in the elderly in the sample of this research was presence of previous comorbidities, such as: pulmonary, cardiovascular, renal diseases, obesity, arterial hypertension, diabetes mellitus, since it was observed in several studies at least one of these factors related to death. In addition,

even if the elderly does not have any of these risk factors, the physio-anatomy, the organofunctional weakness of the elderly determined the capacity of exposure / adaptation / coping with the disease, which may be insufficient, producing irreparable tissue damage such as heart failure and failure organic [19].

A multicentre study in China demonstrated these results: mortality was higher in people with a history of chronic diseases or with irreparable functional damage related to the cardiopulmonary system [20] Another survey in Beijing demonstrates the same results, the presence of higher mortality in patients aged advanced and chronic diseases [21].

Other relevant predictors are also radiographic and laboratory findings respectively, such as: ground glass, cardiac-pulmonary damage, elevation of cardiac troponin, lymphopenia, thrombocytopenia, alteration of C-reactive protein and D-dimer, increase in lactate, leukocytosis, hypoalbuminemia and change in procalcitonin [22,23].

In a multicentre survey conducted in China to evaluate right ventricular tension in patients with COVID-19, it was observed that the patients with the highest mortality were those with distended right ventricle and decreased function in addition to the increase in pulmonary artery pressure [24].

Other studies have also described the age factor as independent for mortality from disease. This fact occurs due to the process of physiological organic changes in the elderly, such as decreased lung compliance, decreased pneumocytes, cardiomyocytes, presence of fibrosis and low / inadequate defense response capacity. In surveys conducted by Tian and Zhou, they describe that elderly people independent or not of diseases and predictors have a higher risk of mortality, ICU admission. In addition, the authors contribute by adding other factors that potentiate mortality from the disease in the elderly, such as those acquired during the course of the pathology such as cardiac injury, kidney injury and respiratory impairment [25].

Outras pesquisas concordam com os resultados dos preditores laboratoriais descritos neste estudo: Altos níveis de troponina, D-dímero alterado, procalcitonina, interleucina, linfopenia, leucocitose [26,27].

A cohort study carried out in China, on risk factors for mortality in elderly patients, described the presence of dyspnea, chest pain and discomfort (3 to 6 times more frequent in the group of elderly people with the disease who died in comparison with surviving elderly) as one of the most common symptoms in patients who died, in addition, patients in the death group were less susceptible to fever [28].

Therefore, advanced age is considered a risk factor for mortality due to COVID-19, in which other chronic conditions can aggravate it and potentiate lethality, given that clinical, laboratory and radiographic predictors are important to perform the control and evolution of disease to establish strategies relevant to the situation presented [28,29].

3.1.3 CLASS 3 - Comorbidities associated with high mortality rates

It was observed that patients with underlying chronic diseases and over 65 years of age are more likely to have disease deterioration and a higher risk of mortality. This fact has been mainly associated with decreased immunity in the elderly, especially those with underlying diseases, which directly make the elderly more likely to be in a fragile state and more vulnerable to infections and, subsequently, aggravate the disease [30].

Mortality from COVID-19 covers patients with hypertension and / or diabetes, representing the largest share, which can be explained by the fact that these pathologies are at the top of the table of chronic diseases worldwide. This fact can be explained by the fact that the COVID-19 virus uses the receptor of the renin-angiotensin system to enter target cells, exactly the same as SARS-CoV [31].

The COVID-19 virus can also have a negative effect on people with pre-existing diabetes, due to the damage suffered in the islets, leading to an increased risk of death. A previous study evaluated that of 113 patients with severe covid-19, 48 (24.9%) had diabetes. When compared to patients with severe COVID-19 without diabetes, patients with diabetes were older, susceptible to mechanical ventilation and admission to the ICU and had higher mortality [32].

The greater susceptibility of diabetic patients to complications and greater risk of death can be explained due to the presence of pulmonary dysfunction, in which the low performance of this function is perceived. They also have a greater

severe inflammatory response and need for mechanical ventilation and admission to Intensive Care Units [33].

In addition, some evidence points to the vulnerability of renal patients to being affected by COVID-19 and a higher risk of mortality. It was observed in cases in a hospital in Wuhan, China found a high prevalence of kidney disease in patients hospitalized with COVID-19. It was found that more than 40% of them had evidence of kidney disease, with high serum creatinine and urea in more than 13% of them. Surprisingly, the presence of kidney disease was associated with increased hospital mortality [32].

A possible explanation for the high prevalence of chronic kidney patients is because they have a pro-inflammatory state with functional defects in the populations of innate and adaptive immune cells and are known to present a higher risk of upper respiratory tract infection and pneumonia, presenting greater vulnerability for evolve to death [34].

3.1.4 CLASS 4 - Reasons for virus transmission to be of more concern in the elderly

The elderly population became prominent in the COVID-19 pandemic, mainly due to changes due to senescence and/or senility. The pandemic reinforced the need to attend to the health of the elderly person, mainly due to the risk potential of this population, with targeting actions and strategies of social distance specifically for this group [35,36].

Immunosenescence is a natural aging process in which there is a decrease in the effectiveness and production of defense cells, increasing the vulnerability of the elderly to contract infectious diseases such as influenza, common colds and COVID-19. When the elderly have comorbidities (diseases such as diabetes, high blood pressure, heart disease and lung diseases), the risk of infection and complications increases [37].

In addition, the involution of lymphoid organs such as the thymus and defective production of lymphoid precursors are trademarks of the aging process. This leads to a decrease in T lymphocytes in Organs lymphoid organs. Humoral immunity is also functionally compromised in the elderly, since there is less antibody response [38]. All this causes the most severe form of the disease to end up affecting this age group in a greater proportion, above all, elderly people who have heart diseases such as hypertension, in addition to diabetes, kidney diseases, lung diseases, cancer and situations of immune suppression [39].

The data referring to the new coronavirus indicate a higher mortality rate among people aged 80 or over, of whom 14.8% of those infected died, compared to 8.0% among the elderly aged 70 to 79 and 8, 8% among those 60 to 69 years old (rate 3.82 times higher than the general average), reinforcing concerns about this age group. It is known that the risk of dying from COVID-19 is exacerbated with age, since the majority of deaths from the disease around the world were in the elderly, especially those with chronic diseases [40,41,42].

4. CONCLUSION

This integrative review enabled a greater understanding of COVID-19 mortality in the elderly, and it is possible to conclude that this population presents different risks to the worsening of the disease, such as physiological changes such as immunosenescence, structural, social and psychological factors and the presence of comorbidities, which in conjunction with the COVID-19 infection lead to high mortality rates.

Thus, it is essential to produce new research that addresses the mortality of the elderly, in addition to protocols and guidelines aimed at reducing these cases, so that assistance is carried out according to the specificities of the elderly population and in a holistic way, aiming at the decrease in the mortality rate.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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