Comorbidities and risk factors identified in people who died from Severe Acute Respiratory Syndrome caused by Covid-19

Comorbidades e fatores de risco identificados em pessoas que vieram a óbito por Síndrome Respiratória Aguda Grave por Covid-19

Comorbilidades y factores de riesgo identificados en personas que fallecieron por síndrome respiratorio agudo severo por Covid-19

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RESUMO

Objetivo: Analisar a frequência de registros de casos de comorbidades e fatores de riscos relacionados aos óbitos de Síndrome Respiratória Aguda Grave (SRAG) por Covid-19 até a Semana Epidemiológica (SE) 40, no recorte geográfico formado pelo "Brasil", no recorte histórico formado pelo ano de "2021". **Método:** Estudo exploratório, descritivo e de abordagem quantitativa. Os dados foram adquiridos junto ao Sistema de Informação da Vigilância Epidemiológica da Gripe (SIVEP-Gripe) do Ministério da Saúde (MS). **Resultados:** Foi identificado o universo de 386.094 registros, com média e desvio-padrão de (35.099,5±49.151,4). Dentre as comorbidades e fatores de riscos identificados, as cardiopatias contabilizaram a maior preponderância com 39,2% (n=151.358) e a Síndrome de Down (SD) a menor com 0,4% (n=1.384). **Conclusão**: Foi possível identificar a relação existente entre as várias comorbidades e fatores de risco identificados, no que se refere a SRAG por COVID-19 no recorte geográfico e histórico analisados.

Descritores: Comorbidade; Fatores de Risco; Síndrome Respiratória Aguda Grave; COVID-19; Brasil.

ABSTRACT

Objective: To analyze the frequency of records of cases of comorbidities and risk factors related to deaths from Severe Acute Respiratory Syndrome (SRAG) by Covid-19 until the Epidemiological Week (SE) 40, in the geographic cut formed by "Brazil", in the clipping history formed by the year "2021". **Method:** Exploratory, descriptive and quantitative approach study. Data were acquired from the Influenza Epidemiological Surveillance Information System (SIVEP-Influenza) of the Ministry of Health (MS). **Results:** The universe of 386,094 records was identified, with a mean and standard deviation of (35099.5±49151.4). Among the comorbidities and risk factors identified, heart disease accounted for the greatest preponderance with 39.2% (n=151,358) and Down Syndrome (DS) the smallest with 0.4% (n=1,384). **Conclusion**: It was possible to identify the existing relationship between the various comorbidities and risk factors identified, with regard to SRAG by COVID-19 in the geographic and historical context analyzed.

Descriptors: Comorbidity; Risk factors; Severe Acute Respiratory Syndrome; COVID-19; Brazil.

RESUMEN

Objetivo: Analizar la frecuencia de registros de casos de comorbilidades y factores de riesgo relacionados con muertes por Síndrome Respiratorio Agudo Severo (SRAG) por Covid-19 hasta la Semana Epidemiológica (SE) 40, en el corte geográfico formado por "Brasil", en el historial de recortes formado por el año "2021". **Método:** Estudio exploratorio, descriptivo y de abordaje cuantitativo. Los datos se obtuvieron del Sistema de Información de Vigilancia Epidemiológica de Influenza (SIVEP-Influenza) del Ministerio de Salud (MS). **Resultados:** Se identificó el universo de 386,094 registros, con una media y desviación estándar de (35099.5±49151.4). Entre las comorbilidades y factores de riesgo identificados, la cardiopatía representó la mayor preponderancia con el 39,2% (n=151.358) y el Síndrome de Down (SD) el menor con el 0,4% (n=1.384). **Conclusión:** Se pudo identificar la relación existente entre las distintas comorbilidades y factores de riesgo identificados, respecto al SRAG por COVID-**19** en el contexto geográfico e histórico analizado.

Descritores: Comorbilidad; Factores de riesgo; Síndrome respiratorio agudo severo; COVID-19; Brasil.

ORIGINAL

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Introduction

The term epidemic is etymologically natural from the greek "ἐπιδημία", of the adjective "ἐπιδήμιος", meaning what is in the people, composed of "ἐπί", that is, which lies over or above, beyond "δῆμος" which means people, constituting as a collective phenomenon of a disease, which is quickly transmitted, directly or indirectly, reaching a high number of people present or belonging to a geographical territory, which may become extinct after a period of time.[1-2] The word pandemic, on the other hand, originated from the greek "πανδήμιος", is formed by the neutral prefix "pan" and the expression "demos" means "of all the people", was first used by the greek philosopher Platão (348/347 a.C.), in his work entitled "Of the laws".[1-3]

Platão used in his writings the term pandemic in the generic sense, referring to any event that occurred, capable of reaching an entire population, and it is also important to mention that one of his main students, the philosopher Aristoteles (384/322 a.C.) also used this term.[2] Historically, they can be cited as examples of complex epidemic events that came to decimate populations and entire cities, the Plague of Egypt (430 a.C.), the Antonine Plague (165–180 d.C.), the Plague of Cyprian (250–271 d.C.), Justinian's Plague (541-544 d.C.) and the Black Plague (1346-1352 d.C.).[4-14]

As species of pandemics that triggered alarming levels of transmissibility and mortality in numerous international nations, we can mention Cholera (1817), Spanish flu (1918-1920), Swine flu caused by the H1N1 virus (2009) and currently Covid- 19.[15-25] In 1966, coronaviruses were first described by Tyrell and Bynoe, who cultivated the aforementioned species of virus, from patients who had common colds.[26-27]

In its morphology, the coronaviruses are constituted as microorganisms of great size and their RNA is constituted by having its single strand, being able to infect humans and also a great variety of non-human animals.[26-27] Covid-19 can be understood as an expression, formed by the junction of the acronym "CO" understood as corona, "VI" which means virus and also the letter "D" related to the disease in question and, in this sense, the term corona comes from Latin and has as a meaning "crown", because the virus is in the form of circles, being visualized in the form of drops by means of electron microscopy, as a crown.[28-29]

Covid-19 virus classified as zoonotic, of the order *Nidovirales* on account of your RNA and family *Coronaviridae*, had its distribution in humans, other mammals, birds and, while hosts were identified in human animals and bats.[30-32] In the year 2019, in December, an outbreak of pneumonia (PNM) was identified in the city of *Wuhan*, province of *Hubei* in the People's Republic of China, rapidly spreading to approximately twenty-four (24) other nations, believed to have been caused by a new strain of coronavirus.[32-33]

As presented by Coronavirus Resource Center of Johns Hopkins University, were identified worldwide on 10/21/2021 at 18:00 hours, the universe of 242,403,265 registered cases of Covid-19, which generated 4,927,975 deaths and also 6,732,461,811 doses of applied vaccines.[34] Thus, the ten (10) international nations are presented, with the highest frequencies of numbers of registered cases of Covid-19, number of deaths and doses of vaccines applied[35]:

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Table 1 – Frequency of registered cases, deaths and doses of vaccines applied in relation to Covid-19 in the ten (10) nations with their respective highest preponderance[*],[**],[***]

Nations	Registered Cases	Deaths	Applied Doses
U.S	45.301.092	733.218	409.314.310
England	8.681.795	139.562	95.824.552
Turkey	7.772.574	68.472	114.807.774
Rússia	8.005.376	223.331	99.965.267
Índia	34.143.236	453.042	1.009.945.663
Brazil	21.697.341	604.679	261.002.038
Ukraine	2.851.173	67.061	15.386.831
Romania	1.519.532	43.487	11.485.084
Iran	5.833.525	124.763	74.113.680
Phelippines	2.740.111	41.237	53.838.248
Other nations	**242.403.265**	**4.927.975**	**6.732.461.811**

Source: Johns Hopkins University Coronavirus Resource Center, 2021.
* Data extracted on 10/22/2021, at 12:00 pm
** Data may vary as updates to this database are daily.
*** The authors of this research are faithful to the database consulted.

In Brazil, according to the Ministry of Health (MH), the most identified qualities of coronavirus to date are the "alpha coronavirus HCoV-NL63", the "alpha coronavírus HCoV-229E", the "beta coronavirus HCoV-HKU1", the "beta coronavírus HCoV-OC43", the "SARS-CoV", which is the cause of severe acute respiratory syndrome (SARS), the "MERS-CoV", which is the cause of Middle East respiratory syndrome (MERS) and the SARSCoV-2.[36] As defended by the scientific literature, there are several comorbidities with regard to Severe Acute Respiratory Syndrome (SARS) by Covid-19, such as diabetes mellitus (DM), cardiovascular diseases, chronic kidney disease (CKD) and chronic lung diseases.[15,36,37]

In this sense, the objective of the present study was to analyze the frequency of records of cases of comorbidities and risk factors related to deaths from Severe Acute Respiratory Syndrome (SARS) by Covid-19, in the geographical area formed by "Brazil", in the historical cut formed by the year of "2021".

Method

This is an exploratory, descriptive study with a quantitative approach, which acquired data for its construction from the Information System for the Epidemiological Surveillance of Influenza (SIVEP-Influenza) of the MS. For organizational purposes, the data acquired are related to Epidemiological Week number 40 (SE 40), extracted in the first half of October of the year 2021.

SIVEP-Gripe/MS has been in operation since 2000, aiming to develop the efficient monitoring of the influenza virus in Brazil, proceeding from a sentinel-type surveillance network with regard to the flu syndrome (SG). [38] With the identification of the pandemic generated by the Influenza Virus A(H1N1) pdm09 in 2009, it was necessary to carry out the implementation process of the Severe Acute Respiratory Syndrome (SRAG) surveillance and, in this process, the MH has been strengthening the surveillance of different types of respiratory viruses.[38]

Currently, the official system for recording SARS cases and deaths is the Influenza Epidemiological Surveillance Information System (SIVEP-Gripe).[38] In

this research, the data from SIVEP-Gripe/MS are updated on 10/11/2021 at 12:00 pm, and they are subject to constant revisions. Electronic bibliographic surveys in digital databases were also developed, making it possible to acquire articles from scientific journals, official documents, and technical documents and positions and professional associations.

After acquiring the necessary subsidies for the construction of this study, they were organized using for this activity the software Microsoft Excel 2016®, belonging to the package Microsoft Office 2016®, for Windows®. Descriptive statistical analysis was implemented with percentage calculations (%), mean ( ) and standard deviation (σ) and, the results were presented using four (04) explanatory tables and one (01) table. The authors declare no conflicts of interest.

Results

In the process of organizing and analyzing the data, it was possible to identify the universe of 386,094 records of comorbidities and risk factors related to deaths from SRAG and Covid-19 in Brazil in the year 2021 to SE 40, in addition to the mean and standard deviation of (35,099.5±49,151.4). It was also possible to verify that heart diseases were the most prevalent comorbidities among those analyzed, accounting for 39.2% (n=151,358) records and Down Syndrome (DS) added the lowest preponderance with 0.4% (n=1,384), as shown in Table 2.

Table 2 – Frequency of comorbidities and risk factors related to SARS deaths by Covid-19, Brazil, 2021 to SE 40 (n=386.094):*,**,***

Comorbidities and risk factors	f	%
Heart Disease	151.358	39,2
Diabetes	107.644	27,9
Obesity	44.951	11,6
Neurological Disease	18.598	4,8
Kidney Disease	18.360	4,8
Lung Disease	16.786	4,3
Immunosuppression	11.418	3
Asthma	8.267	2,1
Liver Disease	4.369	1,1
Hematologic Disease	2.959	0,8
Down's Syndrome	1.384	0,4
Total	**386.094**	**100**

Source: SIVEP-Gripe/MS, 2021.

* Data extracted on 10/22/2021, at 12:00 pm

** Data may vary as updates to this database are daily.

*** The authors of this research are faithful to the database consulted.

In Table 3, it was possible to identify the universe of 114,950 records of people under the age of sixty (60) years, who had comorbidities and risk factors related to deaths from SARS by Covid-19, in addition to mean and standard deviation (10450±13275.3). In this sense, heart diseases registered the greatest preponderance among those analyzed, totaling 32.3% (n=37,176) and DS the smallest with 0.8% (n=936) records of SARS by Covid-19 in people under the age of 60 years in Brazil in 2021.

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Table 3 – Frequency of comorbidities and risk factors related to deaths of people under the age of 60 years, from SRAG by Covid-19, Brazil, 2021 to SE 40 (n=114.950):*,**,***

Comorbidities and risk factors	f	%
Heart Disease	37.176	32,3
Diabetes	28.437	24,7
Obesity	26.248	22,8
Neurological Disease	5.026	4,4
Kidney Disease	4.690	4,1
Lung Disease	3.555	3,1
Immunosuppression	3.411	3
Asthma	2.708	2,4
Liver Disease	1.785	1,6
Hematologic Disease	978	0,9
Down's Syndrome	936	0,8
Total	**114.950**	**100**

Source: SIVEP-Gripe/MS, 2021.
* Data extracted on 10/22/2021, at 12:00 pm
** Data may vary as updates to this database are daily.
*** The authors of this research are faithful to the database consulted

In Table 4, it was possible to identify the universe of 271,144 registered cases of people aged over sixty (60) years, who had comorbidities and risk factors related to deaths from SARS by Covid-19, in addition to mean and standard deviation (24,649.5±36,962.7). Thus, heart diseases registered the highest preponderance with 42.1% (n=114,182) and DS the lowest with 0,2% (n=448).

Table 4 – Frequency of comorbidities and risk factors related to deaths of people aged over 60 years, from SRAG by Covid-19, Brazil, 2021 to SE 40 (n=271.144):*,**,***

Comorbidities and risk factors	f	%
Heart Disease	114.182	42,1
Diabetes	79.207	29,2
Obesity	18.703	6,9
Neurological Disease	15.187	5,6
Kidney Disease	14.078	5,2
Lung Disease	13.334	4,9
Immunosuppression	6.728	2,5
Asthma	4.712	1,7
Liver Disease	2.584	1
Hematologic Disease	1.981	0,7
Down's Syndrome	448	0,2
Total	**271.144**	**100**

Source: SIVEP-Gripe/MS, 2021.
* Data extracted on 10/22/2021, at 12:00 pm
** Data may vary as updates to this database are daily.
*** The authors of this research are faithful to the database consulted

Discussion

With regard to the issue of people aged sixty (60) years old or older registering a greater preponderance with comorbidities and risk factors for SRAG by Covid-19, a correlation was identified with the scientific literature, when it is argued that this pandemic presents its greatest impacts on the population formed by the elderly.[39,40] This condition of greatest impact and fragility identified in elderly people due to Covid-19, is identified mainly among its most clinically vulnerable subgroups, such as those with dementia syndromes, chronic diseases and residents of long-stay institutions for the elderly (ILPI).[39,40,41]

For some researchers, the highest mortality rate in the elderly by Covid-19 is found among those who are 80 years old or more, with a mortality rate of approximately 14.8% of those infected and 8% of those aged between 70 and 79 years.[42] For the Brazilian Society of Geriatrics and Gerontology (SBGG), another issue that hinders greater understanding regarding the aforementioned frailty, transmissibility and mortality of the elderly by Covid-19, is related to their underrepresentation in clinical studies , and also in immunization/vaccination tests for other illnesses, for example, for influenza type H1N1.[39]

Regarding cardiac comorbidities related to Covid-19, a correlation with the scientific literature was also identified when it is argued that cardiovascular diseases induced by the generated effects are myocarditis, increased inflammatory cytokines, rupture of atheromas, microvascular disease, o infarction, and stress cardiomyopathy.[43] As for other researchers, in a study that surveyed 138 patients, 16.7% had arrhythmia and 7.2% had acute cardiac injury, among the identified cardiac complications.[44]

The complexity and magnitude verified with regard to cardiac comorbidities and Covid-19 are such that there are several positions presented by the Brazilian Society of Cardiology (BSC) for better processing of this issue, such as guidelines for resuscitation cardiopulmonary assessment of patients diagnosed or suspected of this disease, on the use of antiplatelet agents and anticoagulants in patients infected with the new coronavirus, and also for cardiovascular rehabilitation on medical performance in their areas during the pandemic.[45,46,47]

Other positions presented by the BSC were the protocol for reconnecting cardiology services with patients during the Covid-19 pandemic, the one indicated for pregnancy in women with heart disease, the one related to pre-participation cardiology evaluation after the pandemic in the guidelines for returning to practice of physical exercises and sports, as well as the indications and reintroduction of safe cardiovascular imaging methods.[48,49,50,51] Regarding DM, as a comorbidity and risk factor with regard to SARS by Covid-19, correction was found with what is exposed in the scientific literature, when the increase in severity is defended, for example, predisposing infected people to hyperglycemia and, the interaction with other risk factors, can modulate the emergence of inflammatory and immunological responses with death effect.[52]

As advocated by some researchers, the greater preponderance of available scientific evidence did not develop a distinction in relation to the different types of DM, with a greater preponderance of DM2 being verified, due to its high prevalence, when compared to the other types.[52] In an important study developed , using transgenic mice as a model for analysis, it was possible to express the DPP-IV receptor with pulmonary alveolar cells, thus allowing to identify the worsening of the severity of DM in relation to Covid-19, also realizing an association between the greater loss of weight and greater pulmonary inflammatory process, in addition to macrophage infiltrate similar to those clinically identified.[53,54]

In other studies, advanced age, DM and other comorbidities are reported as significant predictors of morbidity and mortality in relation to Covid-19,[54,55] In the same way as the expansion of the coagulation activity, the chronic inflammation process, the involvement together the immune response and the potential damage to the pancreatic gland due to SARS-CoV-2 may be directly related to the different underlying mechanisms of association between DM and Covid-19.[54,55]

Regarding obesity as a comorbidity and a risk factor related to deaths from SRAG/Covid-19, it is in common agreement with what is exposed in the scientific literature, when it is argued that it constitutes a chronic, multifactorial, underreported disease , with changes related to the continuous inflammatory process, reduced capacity to develop an immune response to infectious and viral processes.[56,57] In this analytical context, obesity as a comorbidity of Covid-19 results in a greater risk of triggering thromboembolic phenomena, as it has a direct relationship with other diseases such as arterial hypertension (AH), DM among many others, weakening the development of care and assistance to patients who are in serious conditions.[56,57,58]

Thus, the possibility of the emergence of respiratory difficulties and, by extension, pulmonary diseases, difficulty in acquiring venous access, transport and limitation in performing computed tomography (CT) and procedures such as orotracheal intubation (OTI), can also be mentioned, facilitating the prognosis of death.[56,57,58] According to the Brazilian Association for the Study of Obesity and Metabolic Syndrome (ABESO) and the Brazilian Society of Endocrinology and Metabolism (SBEM), the problem of obesity increases the various risks of outcomes negatives related to Covid-19, as from the body mass index (BMI) of 30 kg/m², that is, grade 1, and this risk increases even more when compared to people who have their BMI ≥ 35 kg/m², that is, grade 2 and, in those with BMI ≥ 40 kg/m² by extension, grade 3.[57,58,59]

Regarding kidney diseases as comorbidities and risk factors for death from **SRAG**/Covid-19, a correlation was identified with what is exposed in the scientific literature, when it is argued that there is the emergence of renal impairment in patients who are under treatment in a hospital environment, due to an infectious process caused by SARS-CoV-2. [60,61] In this way, it is also possible to carry out a direct association due to the increase in the frequency of mortality and even a worse degree of evolution of the clinical type, doubling the concerns of those with chronic kidney disease (CKD).[60,61,62,63]

According to the latest data generated in July 2018, approximately 133.5 thousand Brazilians have diagnoses as chronic kidney patients, and of these 92% are undergoing dialysis treatments and, in this sense, this population is classified as while high risk for complications resulting from Covid-19.[63,64] According to the Brazilian Society of Nephrology (SBN), the risk of being infected is increased by comorbidities related to kidney disease, added to the need to acquire treatment in environments classified as collective , for the development of interpersonal contact while traveling between home and clinics for dialysis procedures and their care.[65]

In an important research, which had a universe of 37,852 people who were on hemodialysis, it was possible to verify that there were 1,291 cases of infection by Covid-19 and of these, 357 deaths were registered, and the registered incidence rate was 341/ 10,000 people, the mortality rate was 94.3/10,000 and the lethality 27.2%.[66] In relation to immunosuppressive conditions and diseases, while comorbidities and risk factors related to Covid-19, a correlation was identified in what is presented in the scientific literature, when it is defended that people who are carriers of SIDA/AIDS are more vulnerable to the pandemic disease today.[67,68]

Studies carried out in England and also in South Africa, it was possible to verify that, in people living with HIV, the possibility of dying as a result of Covid-19 and its complications is double (2x), when compared to the general population.[67] As for other authors, patients who have one or more types of cancer (CA) tend to have a greater risk of contracting or worsening Covid-19, in addition to having a worse prognosis than those without.[68,69] A The issue of immunosuppression, as comorbidities and risk factors related to deaths from **SRAG**/Covid-19, is so broad that numerous diseases, in addition to SIDA/AIDS and various types of CAs are cited as examples of chronic diseases and situations of immunosuppression, such as chronic respiratory disease (CKD), severe asthma in use of systemic corticosteroids, chronic obstructive pulmonary disease (COPD), bronchiectasis, cystic fibrosis (CF) among many others.[70] As a way to

better understand nt of such a complex issue, a table of diseases listed by the Federal Senate (SF) was adapted, which presents other chronic diseases and situations related to immunodepression:

Table 1 – Examples of chronic illnesses and immunosuppression situations:

* Chronic Respiratory Disease (CRD)	* Nephrotic syndrome (SN)
* Severe asthma in use of systemic corticosteroids	* Dialysis patient
* Chronic obstructive pulmonary disease (COPD)	* Chronic liver disease (DHC)
* Bronchiectasis	* chronic hepatitis
* Cystic Fibrosis (CF)	* Cirrhosis
* Hereditary and degenerative diseases of the nervous or muscular system	* Interstitial lung diseases
* Bronchopulmonary Dysplasia (DBP)	* Diabetes mellitus (DM)
* Type I and type II diabetes mellitus under medication	* Pulmonary hypertension
* Chronic heart disease	* Immunosuppression
* Congenital or acquired immunodeficiency	* Congenital heart disease
* Cardiac Insufficiency (CI)	* Systemic heart disease
* Immunosuppression by diseases or medications	* Chronic kidney disease (CKD)
* Kidney disease in stages 3, 4 and 5	* Transplanted

Source:
Adapted from the Federal Senate (SF), 2021.
* Available in: [https://www12.senado.leg.br/institucional/covid/area-de-saude/doencas-cronicas-e-situacoes-de-imunodepressao].

Regarding asthma as a comorbidity and a risk factor related to Covid-19, it was found that, despite the recognized Centers for Disease Control and Prevention (CDC) in the United States of America (USA), they list this respiratory disease as a risk factor , Chinese studies indicate that asthma and respiratory allergy were not identified as significant risk factors for this pandemic disease in analyzed case series.[71,72] The issue of asthma not being identified as a significant risk factor related to Covid -19, it is possibly related to its reduced expression, with regard to angiotensin converting enzyme (ACE) receptors in atopic asthma.[72,73]

For other researchers, the issue of susceptibility and also the risk related to severe Covid-19 among patients diagnosed with asthma may be different depending on some situations, such as age, the complexity of the disease, their endotype and its phenotype, in addition to the type of treatment chosen for its implementation.[74] Therefore, it is argued that the relationship between asthma and Covid-19 is not yet well understood, requiring further studies and research to be carried out to a better elucidation of this question.[72,73,74]

With regard to neurological diseases as comorbidities and risk factors related to deaths from SRAG/Covid-19, a correlation was identified with what is exposed in the scientific literature, when it is argued that currently, there is a high quantity of publications which has strongly defended the involvement of the Central Nervous System (CNS) with the issue of Covid-19, however, there are still numerous questions regarding its pathophysiology to be answered.[75,76] In this sense, they can be cited as pathophysiological conditions related to

neurological impairments and risk factors, the indirect consequences with regard to biochemical and multiorgan dysfunction, and also, in its medium and long-term impact, due to the neuroinvasive properties of the virus.[75,76]

For some researchers, SARS-CoV has a high homology when compared to SARS-CoV-2, which is demonstrably classified as a neurotropic, as they use surface-related proteins, aiming to bind with the angiotensin-2 converting enzyme receptor (ECA2).[75,76,77] Thus, the location of that receptor, possibly, determines the cellular tropism process of the virus structure, with the central nervous system (CNS), that is, with the astrocytes, neurons, microglia and oligodendrocytes.[75,76,77]

As identified in the scientific literature, the signs of neurological symptoms observed in patients with SARS-CoV-2 are ageusia, anosmia and headache.[75,76,77,78] Other neurological manifestations, epileptic seizures, acute cerebrovascular disease, encephalopathy, CNS infections and neuromuscular manifestations were also identified in the consulted research.[75,76,77,78]

With regard to pneumopathies as comorbidities and risk factors related to deaths from SRAG/Covid-19, a scientific correlation was identified when it is argued that SARS-CoV-2 is a virus that has a high potential to cause pulmonary thromboembolism , in addition to acute respiratory distress syndrome (ARDS), respiratory and systemic symptoms classified as mild, as well as severe cases with sepsis, and multiple organ dysfunction.[79,80] For some researchers, the Middle East Respiratory Syndrome Coronavirus (MERS- CoV) and Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) are strains related to diseases classified as potentially fatal, being correlated to etiological agents of severe acute respiratory syndrome (SRAG) in 2002 and 2012.[29,80,81]

When genetically analyzed, the genome belonging to SARS-CoV-2 is able to encode four (04) main structural proteins, namely the E protein (envelope), the M protein (membrane), the N protein (nucleocapsid), and the S protein (spike).[80,81] In this sense, it is verified that the S protein has the possibility of binding to the ACE2, which constitutes itself as the receptor for the entry of the virus into the cell and, after these phenomena, it occurs the phenomenon known as tropism type II alveolar epithelial cytological structures, which represent pulmonary-type surfactant-secretors and, possibly, resident alveolar macrophages that will express this receptor.[80,81,82,83]

With regard to liver diseases, as comorbidities and risk factors related to deaths from SRAG/Covid-19, a correlation was identified with what is exposed in the scientific literature, when the need for care, treatment and immunization of these patients, with chronic liver disease (CHD) and liver cirrhosis, as a risk group related to one or more pathologies and who need immunization in Phase 2 of the Vaccination Plan in Portugal.[84] Among the known liver diseases, they can cirrhosis, non-alcoholic fatty liver disease (NAFLD), hepatitis A, hepatitis B, hepatitis C, hereditary hemochromatosis type 1 and alcoholic hepatitis.[84,85,86]

Even with the existence of a clinical diagnosis of liver cirrhosis, the onset of liver failure is not assumed at that exact moment, being possible the presence of an increased risk of death, in cases related to infection by Covid-19, with a mortality rate of approximately 30%.[85,86,87] According to American Association for the Study Liver Diseases – AASLD, people with advanced age, with the presence of comorbidities such as, for example, cirrhosis, heart disease, CA,

obesity, immunodeficiencies and solid organ transplants, are at greater risk for the development of death due to Covid-19.[88]

On the other hand, because people diagnosed with cirrhosis, liver transplants and other immunosuppressed patients were not included in initial research, there is a lack of evidence related to the effects generated, due to the immunization and vaccination process.[88,89] With regard to hematological diseases, as comorbidity and risk factors related to deaths from SRAG/Covid-19, a correlation was identified with what is exposed in the scientific literature, when it is argued that this pandemic disease causes laboratory changes, clinical and hematological, such as thrombocytopenia and lymphopenia.[90,91]

For some researchers, a person infected with Covid-19 ends up developing hypercoagulability due to microthrombosis, in addition to the occlusion process of small pulmonary vessels, expanding the existing state of decreased oxygenation (hypoxia) and, subsequently, an association occurs with regard to intravascular forms of coagulation having dissemination and also systemic reverberation.[92,93] In this sense, it is essential to pay attention to the complications related to the issue of delay in the hospitalization process and bed restriction, in patients diagnosed with Covid-19 and with hematological complications, allowing the emergence of risks of deep vein thrombosis (TVP).[92,93]

In another study, a significant risk of death was found in patients diagnosed with Covid-19 admitted to the intensive care unit (ICU), in those who presented high values of total leukocytes and neutrophils, in addition to reduced hemoglobin values.[94] With regard to Down Syndrome (DS), as a comorbidity and risk factor related to Covid-19, a correlation was identified, when it is argued that it is verified in these people, prevalence between 40 to 50% of cardiovascular diseases, in addition to a greater possibility of developing overweight, obesity, high blood pressure and also, because they have changes in the airways, there is greater ease of infection by the Covid-19 virus, increasing complications with the patient.[95,96,97,98]

For some researchers, people diagnosed with DS are at greater risk of contracting this pandemic disease, due to their immune dysfunction, greater propensity to need hospitalization and even greater possibility of mortality due to Covid-19.[98,99,100] The complexity and The emergence of the issue is such that the Brazilian Society of Pediatrics (SBP) has come forward, developing a warning note regarding the issue of care for children with DS, suggesting actions for attention in cases of suspected Covid-19.[101]

In the document cited by the SBP, an important warning is also identified regarding the pediatric age group, being the one affected in a reduced way by the impacts of Covid-19, children with DS are vulnerable and much more susceptible to infectious processes of the respiratory type, due to including known comorbidities such as heart disease, DM, immunodeficiencies, obesity, added to the predictive factors of increased severity.[102]

Conclusion

Through the present study, it was possible to verify the considerable quantity of comorbidities and risk factors related to deaths from SARS by Covid-19, in the analyzed geographic and historical context. Among the comorbidities

and risk factors identified, heart disease, DM, obesity, kidney disease, immunosuppression, asthma, neurological diseases, lung diseases, liver diseases, hematological diseases and DS can be mentioned.

Although the present study has limitations, it managed to meet the proposed objectives, allowing for a better elucidation of the relationship between comorbidities and risk factors, with regard to recorded deaths from SRAG by Covid-19 in Brazil in the time period in question. On the other hand, there are still several doubts regarding Covid-19 and its comorbidities and risk factors, which need to be encouraged to carry out more robust studies and research, aiming to better elucidate this very complex and violent disease .

Another doubt that exists in this complex international and national public health problem is in relation to the direct and indirect impacts generated, on victims and victims of the Covid-19 pandemic, constituting an issue that will reverberate with future generations. In this sense, it is up to all people, society and international nations, to redouble their efforts in order not to allow the progress and expansion of Covid-19, as well as its variants, in order to mitigate its devastating effects.

Measures such as the use of masks, hand hygiene, social distance and the immunization process are powerful strategies for combating and controlling Covid-19 and its variants. Other strategies for health education, health communication, prevention, combat and control of Covid-19 and its different variants need to be redoubled, aiming to encourage better awareness of all members of societies and mitigating its devastating and incalculable effects on contemporaneity and in future generations.

Acknowledgment

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