Covid-19: Comorbidities, Symptoms, and Hospitalization – a Review

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***Abstract*—The increased number of daily Covid-19 infections in several countries around the world has proven to be a public health concern. To verify the association between comorbidities, hospitalizations, deaths, recoveries, symptoms, age and gender, this article investigates related studies in the databases "Medrxiv", "Google Scholar" and "Science Direct", with the following search terms "Covid-19 ", "Models", "Comorbidities", "Infection", "Hospitalization" and "Recovered". Thus, it was possible to verify that the most verified comorbidity is cardiovascular disease and that comorbidities together with Covid-19 infection are the main cause of hospitalization worldwide, prolonging the infection status that can lead to death. The analysis of the results allowed showing the indicators and trends, as well as the relationship between the variables that can assist in future decision making.**

Keywords- Covid-19; Comorbidity; Symptoms; Hospitalization; Age.

I. INTRODUCTION

Covid-19, also known coronavirus, emerged in December 2019 in the Chinese city of Wuhan. According to [1], everything indicates that the epicentre of the virus happened in a Wild Animal Market where there are birds, snakes, bats, and other animals. Coronavirus is a virus that causes respiratory infections in humans and animals whose name Covid-19 was reported by the "World Health Organization" (WHO) [2] and is the result of the fusion of the words "corona" and "virus", with the year it emerged, 2019 [3]. After exposure to the virus, infected humans begin to have the first symptoms in the first 2 to 14 days. The symptoms include dry and persistent cough, fever above 38ºC, excessive tiredness, generalized muscle pain, headache, sore throat, runny nose, or stuffy nose, diarrhea, loss of taste and smell [4]. There were also infected individuals who did not reveal symptoms, being asymptomatic. So far, the only way to know the presence of Covid-19 is by testing. Currently, there are 4 types of tests: molecular Nucleic Acid Amplification Tests (TAAN), also called Polymerase Chain Reaction (PCR), Rapid Antigen Tests (TRAg), Self-Testing and Serological Tests [5]. The most reliable and required by the authorities to travel are mainly PCR tests.

The first 14 days in which the human being was exposed to the virus are the days when contagion is greatest, isolation being therefore mandatory, since it is at this stage that the chains of contagion are created. After 14 days, the virus ceases to be transmitted and the human in question can end the isolation [6].

To prevent the spread of the virus, the National Health System (SNS) recommends specific prevention measures such as social distancing, the use of masks, frequent hand washing, disinfection, cleaning, and disinfection of spaces and recommends citizens to be aware of symptoms [7]. As there is still no direct treatment for Covid-19, the infected are medicated according to the symptoms presented with existing medications to reduce the fever and difficulty breathing. However, comorbidities may influence the severity of symptoms and infection [8]. Over months, it has also been verified that people with comorbidities are more prone to contracting the virus. This fact is reflected in regular hospitalizations and in intensive care units, where the number of deaths in these circumstances has increased.

Thus, a systematic study was carried out to identify associations between people infected with Covid-19 in ages, gender, symptoms, hospitalization, recoveries, and deaths, focusing on the associated comorbidities. This study corresponds to the first part of a more wide-ranging project to identify, in future work, the respective correlations and specific values for the measures/tests.

This article is divided into four sections. In Section I, we explain the methodology used and the article selection process. Section II contains the analysis of results and Section III the discussion of the results. Finally, in Section IV, the conclusions and further work are presented.

II. METHODOLOGY

Based on the PRISMA systematic review methodology [9] this article investigates related studies in the “Medrxiv”, “Google Scholar” and “Science Direct” databases with the following search terms "Covid-19", "Models", "Comorbidities ", "Infection", "Inpatient" and "Recovered".

Three reviewers independently assessed each study. The compliance was determined unanimously by all parties involved. The aim of this study was to verify the different methods of data analysis and models applied to the study and evolution of the mentioned terms. The search for articles was carried out between February and May 2021.

A. Research questions

The main research questions about this review were:

(Q1) Association between comorbidities and hospitalizations/deaths.
(Q2) Association between comorbidities and recoveries.
(Q3) Association between symptoms and hospitalization.
(Q4) Association between age, death, and gender.

B. Inclusion criteria

The inclusion criteria of studies and evaluation methods for this review were:

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- Studies that aim to analyze pandemic data in various vacancies and in multiple countries of the world.
- Studies using machine learning and data processing to make predictions of the evolution of the pandemic.
- Studies that relate the numbers of Covid-19 infected people with hospitalizations and deaths.
- Studies that relate the numbers of Covid-19 infected people with comorbidities and recovered.
- Studies published between 2019 and 2021.

After the search using the referred terms, 263 articles were found, of which 42 were considered by application of the inclusion criteria. Figure 1 illustrates the resulting flowchart of feature extraction. During the study selection process, 11 repeated articles and 2 studies that were not in article format were initially removed. Then, 10 articles were removed because they did not fit the Covid-19 theme and finally 199 articles because they did not fit the research objective, although they addressed the Covid-19 theme. Of these 199 articles, 6 addressed climatic conditions and Covid-19, 2 the presence of Covid-19 in migrants, 141 study of the behaviour of other specific diseases in the presence of covid-19, 12 transmissibility factors, 23 socioeconomic factors and 15 hospital logistics. The remaining 42 studies were presented in the qualitative and quantitative synthesis. Data were extracted from all identified studies using a predefined format. Data extracted included: Study; Publication Year; Data Range Study; Methods; Comorbidity. Three reviewers extracted the information, and any disagreements were resolved via discussion. Table I identifies the extracted data and the characteristics of the included studies.

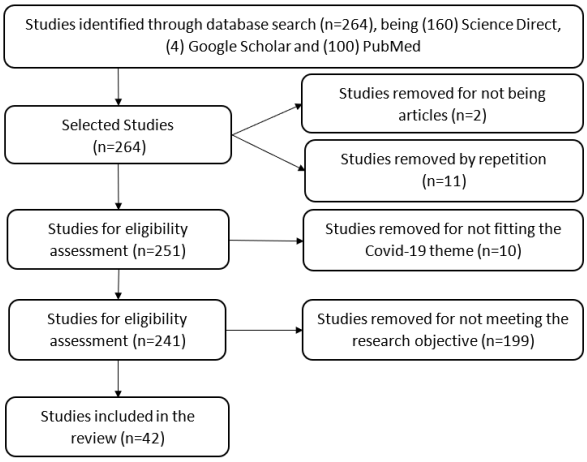

Figure 1 - Flow diagram for new systematic reviews (adapted from [9])

TABLE I . EXTRACTED DATA.

Study	*Data Range Study*	*Methods*	*Comorbidity*
[10]	February to June 2020	Machine Learning and Cox Regression Model	Neoplasm, diabetes, asthma, pulmonary, hepatic, hematological, renal, neurological, neuromuscular and immunodeficiency conditions
[11]	June 2020	Seaborn and SciPy	Asthma, malignancy, chronic hematological disorder, diabetes, HIV/other immunodeficiency, renal disease, liver disease, chronic lung disease, and neuromuscular disorder.
[12]	April 2020	Cohort and Poisson Regression	Comorbidities in general
[13]	February 2021	Developed a simple model	Type II diabetes, hypertension, cardiovascular disease, chronic kidney disease etc
[14]	April 2020	Empirical observation	Obesity in males, lung cancer death rates
[15]	November 2020	Review of literature published	HIV
[16]	NA	Methodology Mantegna	–
[17]	November 2020	Machine Learning	Medical condition
[18]	NA	Data-driven modelling MFTG	–
[19]	May 2020	Applied meta-analysis and meta-regression	–
[20]	June 2020	Spearman	Advanced age, obesity, cardiovascular disease, diabetes, and cancer
[21]	June 2020	Machine Learning algorithms	Comorbidities in general
[22]	May 2020	Developed the "Covid-19 trajectory viewer"	Comorbidities in general
[23]	March 2020	Meta-Analyses	Comorbidities in general
[24]	April 2020	Linear models regression	Comorbidities in general
[25]	First 14-16 weeks	Data extraction and analysis	–
[26]	February 2020	Monte Carlo simulation	Hypertension, diabetes, cardiovascular disease, chronic respiratory disease, and cancer
[27]	December 2019	Machine Learning	Comorbidities in general
[28]	May 2020	Developed a script program	Comorbidities in general
[29]	April 2020	Data processed with MS Excel	Comorbidities in general
[30]	NA	CFR	Comorbidities in general
[31]	April 2020	Random-effects and meta-analysis	Comorbidities in general
[32]	March to June 2020	Statistical analysis	Comorbidities in general
[33]	February to March 2020	Data processed with MS Excel	Comorbidities in general
[34]	December 2019 to October 2020	Aggregation data	Chronic respiratory illnesses, cardiovascular disease, hypertension, or diabetes mellitus

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Study	*Data Range Study*	*Methods*	*Comorbidity*
[35]	January 2020	Random effects model	Cardiac, pulmonary, renal functions, and immunosuppressive states
[36]	NA	Mathematical model	–
[37]	NA	Meta-analysis	Hypertension, cardiovascular and cerebrovascular disease, and diabetes were
[38]	NA	Aggregation data	Comorbidities in general
[39]	14-16 weeks since the first death	Aggregation data	Pneumonia, cardiovascular disease combining ischaemic heart disease and stroke, chronic obstructive pulmonary disease, cancer, road traffic accidents and dementia
[40]	December 2020 and 24 April 2020	Statistical software package	Comorbidities in general
[41]	April 2020	Aggregation data	Comorbidities in general
[42]	December 2019 to April 2020	Stepwise forward regression	Diabetes, hypertension, chronic respiratory diseases, cancer, and cardiovascular disorders,
[43]	May 2020	Aggregation data	Comorbidities in general
[44]	May 2020	Aggregation data	Comorbidities in general
[45]	March 2020 until April 2020	Machine learning models	Comorbidities in general
[46]	NA	Aggregation data	Hypertension, type 2 diabetes, ischaemic heart disease, chronic obstructive pulmonary disease, cancer and overweight or obesity
[47]	March 2020	Exponential growth	Comorbidities in general
[48]	April 2020	Cohort	Chronic kidney disease
[49]	April 2020	Meta-analysis	Hypertension, diabetes, cardiovascular disease, lung disease, renal disease, cancer, and immunosuppression
[50]	June 2020	Meta-analysis	High blood pressure, diabetes mellitus, ischemic heart disease, and chronic obstructive pulmonary disease

III. DISCUSSION / RESULTS ANALYSIS

This work shows how the collection of daily data of people infected by Covid-19 is important, because it allows contributing to the knowledge and evolution of the pandemic and to understand how the new virus acts and propagates.

The research of the articles was conducted between February and May of 2021 in the databases "Medrxiv", "Google Scholar" and "Science Direct" and of which resulted 42 articles, 27 addressed data analysis, 7 article research, 5 " Machine Learning", 2 CFR Method and 1 Mathematical Model "Data-Driven MFTG", as illustrated in the graph in Figure 2.

Throughout the study, several data collection dates were verified, but still the data from the first wave were the ones that prevailed in most articles, even though some did not read this same information, as illustrated in the graph in Figure 3. In the articles studied, some methods of data analysis and tools were used, such as "Machine Learning" methods or a simple spreadsheet for statistical analysis. With these methods and tools, it is possible to draw several conclusions.

(**Q1**) Association between Comorbidities and Hospitalizations/Deaths: Comorbidities in conjunction with Covid-19 infection have been shown to be the leading cause of hospitalization, both in wards and in ICU's [10][40]. These hospitalizations by Covid-19, where comorbidities are present were not only in Portugal [11], but in several countries of the world as referenced in [20]. As for the most frequently verified comorbidities, cardiovascular diseases [34][37][49] diabetes, hypertension, respiratory diseases, among others. Figure 4 shows comorbidities most frequently reported in the studies analyzed. It is [14] also evidenced that pre-existing diseases prolong the state of Covid-19 infection and that it can lead to death mainly in the older population. Age together with comorbidities showed an increase in the number of hospitalizations and the risk of death as reported in [25] where the most affected ages were between 80 and 89 years of age [12]**.** Similarly, in [29], it is reported that age was the main risk factor and that the virus mainly affected the elderly population, reinforced by [33]**,** however [23] reported that the median of the ages of the infected varied between 28 and 70 years.

(**Q2**) Association between Comorbidities and Recoveries: Recovery time was also shown to be influenced by comorbidities, because the more severe the comorbidity, the longer the recovery time [22]. Also, the data analysis [48] showed that the mean follow-up time of a patient infected by Covid-19 was 27 days and that the median age was 50 years, with the male gender being the most affected. However, many studies have not been found, which at this stage, addressed those recovered and their post-infection health status.

(**Q3**) Association between symptoms and hospitalization: Many Covid-19 infected patients were considered asymptomatic due to the absence of symptoms, however, many of the symptomatic patients had to be hospitalized due to their severity. In [15]**,** it was found that the diagnosis rate of Covid-19 was directly linked to the presence of symptoms and consequent hospitalization in the most severe cases, thus increasing the risk of mortality. Applications of data analysis and creation of illustrative graphs were also developed to assist in the treatment of Covid-19. The 'Covid-19 trajectory viewer' [22] generates graphs with data of recovered and dead as well as of the spread of the epidemic in the population through hospitalized versus not hospitalized, symptomatic versus asymptomatic, highly exposed versus less exposed professions.

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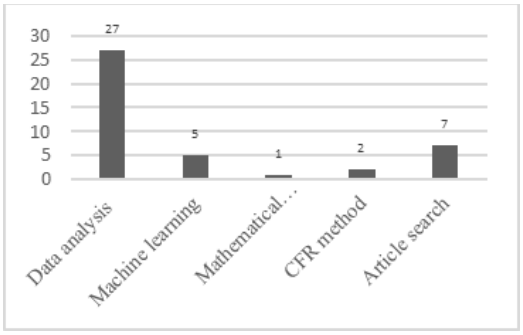


Figure 2 - Type of methods

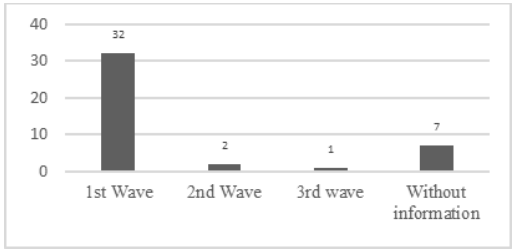


Figure 3 - Distribution of data by vacancy

(**Q4**) Association between age, death, and gender: As mentioned in Q1, the age and gender of the infected may vary considerably, but in [19], the authors found that men were more susceptible to death than women. Also in [26] [31] and [36], it is shown that patients over 60 and 70 years of age had a higher risk of contracting Covid-19, which was even higher than any comorbidity. The genus masculine was the one with the highest rate of infection referred to in [35] [39] [43]. In [41], it was found that individuals aged 80 years or older were responsible for most deaths in Europe. As for patients between 30 and 39 years of age, they had some immunity or resistance to the disease. In [34] and [51], it was found that patients with cardiac complications associated with SARS-CoV-2 were, on average, 10 years older than those who did not. The graph in Figure 5 was presented in [10] and is similar to the conclusions presented in [13], clearly showing that death from Covid-19 occurs in the older age groups and that in the younger age groups the number of deaths is practically nil.

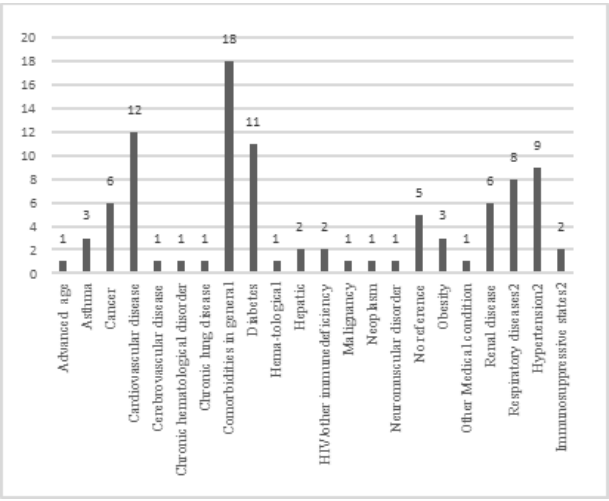
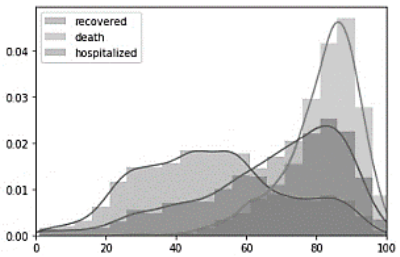


Figure 4 - Frequency of comorbidies



(a) age distribution

Figure 5 - Curve of ages most affected in the Covid infection-19 (adapted from [12])

IV. CONCLUSIONS

In December 2019, little was known about the virus called Covid-19 by the WHO, nor how to combat it. To avoid the rapid contagion seen in China, many countries have chosen to implement mandatory containment measures, mandatory use of masks on public roads and social distancing measures that later proved to have a major impact on transmission chains [16]. The way the virus operated by different infected patients was also a major object of study [18] [21], where not all infected had symptoms and others were so severely attacked that they had to be admitted to intensive care units and breath with the help of ventilators. As for symptoms, they varied from patient to patient depending on both the presence and the type of comorbidities. However, the comorbidity that stood out was cardiovascular disease followed by diabetes, hypertension, respiratory diseases, cancer, kidney diseases, asthma, obesity, immunosuppressive diseases, liver diseases, HIV, neuromuscular and cerebrovascular diseases, advanced age and other unspecified or unreported [34][37][49]. Comorbidities in conjunction with Covid-19 infection have also been found to be the leading cause of hospitalization worldwide [11] [20], prolonging the state of the infection that can lead to death. Recovery time was also shown to be influenced by comorbidities, where the more severe the comorbidity, the longer the recovery time [22], compared to the mean time of infection and recovery of 27 days [15][22][48]. Age, together with comorbidities, increased the number of hospitalizations and the risk of death, where the most affected ages were between 70 and 89 years [12] [25]. Still, in addition to comorbidities, the age group between 60 and 70 years of age also has a very high risk of contracting covid-19 infection [26] [31]. The number of deaths is strongly observed in males [19] and occurs in the older age groups [13]. In the younger age groups, the mean age of the infected varied between 28 and 70 years [41] and the number of associated deaths is very close to zero. Covid-19 has been shown to be present in virtually all age groups, but it is in the population over 60 years of age that infections are more severe. This population over 60 years of age revealed a higher presence of comorbidities, mainly cardiac and respiratory, which hinders recovery and, consequently, can lead to death.

In future work, in the next phase of this study, the available data sets will be combined with the statistical measures to quantify the respective values/metrics of correlations between the identified associations.

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