How Health Knowledge That Can Influence Patient Outcome

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Mestrado em Gestão

Orientador:
Prof. Doutor Carlos Miguel Correia Hernandez Jerónimo, Professor Auxiliar Convidado, ISCTE Business School

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Abstract

Since Covid-19 was declared a global pandemic, it has killed more than two million people worldwide. Some directly due to complications and symptoms of the virus others due to lack of resources to take care of all the patients affected by it. A proper triage can go a long way to an efficient resource allocation, which makes it extremely relevant to understand which factors can affect Covid-19 complications or mortality risk. With the input form front-line Portuguese doctors, it was possible to identify the main comorbidities and health issues that can influence patient outcome: age, cancer, immunosuppression, transplant, obesity, diabetes, hypertension, and kidney, respiratory and cardiovascular disease, body temperature, blood pressure, oxygen saturation, glucose, C-protein, D-dimer and PaO2/FiO2 levels.

Keywords: Covid-19; mortality risk; comorbidities; severity of symptoms.

JEL Classification System Code: I0 General, I1 Health

Resumo

Desde que a Covid-19 foi declarada como uma pandemia global, já matou mais de dois milhões de pessoas em todo o mundo. Algumas mortes diretamente devido a complicações e sintomas causados pelo vírus, outras devido à falta de recursos para cuidar de todos os pacientes afetados pelo mesmo. Uma triagem adequada pode contribuir muito para uma atribuição eficiente de recursos, o que torna extremamente relevante compreender quais os fatores que podem influenciar as complicações ou o risco de mortalidade pela Covid-19. Com o preenchimento de formulário de entrada realizado pelos médicos portugueses da linha da frente, foi possível identificar as principais comorbilidades e problemas de saúde que podem influenciar o efeito no paciente: idade, cancro, imunossupressão, transplante, obesidade, diabetes, hipertensão, doenças renais, respiratórias e cardiovasculares, temperatura corporal, pressão sanguínea, saturação de oxigénio, glicose, proteína C, D-dímero e níveis de PaO2/FiO2.

Palavras-chave: Covid-19; risco de mortalidade; comorbilidades; gravidade de sintomas.

Classificação JEL: I0 Geral, I1 Saúde

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1. Introduction

Since World Health Organization declared coronavirus disease 2019 (Covid-19) a global pandemic on March 11th 2020, 2 876 691 people worldwide have died from it (Anon., n.d.) by early April 2021. Portugal had already 824 368 cases and 15 026 deaths, leading to shortage of capacity of intensity care units, especially during the third wave that started after Christmas. There have been serious efforts to implement control measures to prevent spreading and to mitigate Covid-19 effects globally (EURO WHO, 2020). Knowing which factors can have associations with Covid-19 evolution allows for a more efficient triage of patients, not only saving precious time, but also identifying the most vulnerable patients that may need extra resources (Nogueira et al., 2020).

This study aimed to find which factors are associated with Covid-19 mortality risk or the level of severity of symptoms developed. It is the first step of a larger project that will develop predictive models to assist in hospital screening by providing most likely scenarios based on demographics, comorbidities and indicators. The factors collected in this study will be used as input for the models to develop.

The present paper is structured as follows. Existing papers on the subject were reviewed to gather a starting point of which factors could be relevant. Then, the methodology used is detailed and the results described. On the following section the findings are compared to those discovered by others in the Discussion. Finally, they are summarized and the limitations identified.

2. Literature Review

Demographic factors have been analyzed by several authors (Götzinger et al., 2020; Goujon et al., 2020; Harapan et al., 2020; Lapostolle et al., 2020; Meena et al., 2020; Nogueira et al., 2020b; Rivera-Izquierdo et al., 2020; Shahid et al., 2020). Rivera-Izquierdo et al. (2020) found that starting from 50 years old the mortality probability increases exponentially – 5,8% for patients between 50 and 59, 12,8% between 60 and 60, 28,6% between 70 and 79 and 79,2% for patients over 80 years old. Nogueira et al. (2020) found mortality rates of 9,5% for patients between 75 and 85 and 12,61 for people over 85 years old in Portugal, which are considerably lower than those previously reported. Data from China reported 3% to 11% of mortality rate for patients between 65 and 84 and 27% over 80 years old (Shahid et al., 2020). On the other hand, Meena et al. (2020) and Götzinger et al. (2020) found that children are less likely to have Covid, are usually asymptomatic or have lighter symptoms than adults and are less likely to die from it.

In the European Union mortality rates are higher for men than for women – 24,1 % versus 14,4% (Goujon et al., 2020; Harapan et al., 2020; Nogueira et al., 2020b). Men are also more likely to develop serious symptoms than women (Lapostolle et al., 2020).

Associated comorbidities have also been highly studied for Covid, in order to understand which diseases or conditions can affect Covid incidence of mortality probabilities. While studying mortality by Covid-19, Shahid et al. (2020) found that 86% of deceased patients had associated comorbidities, and among them identified chronic kidney disease. Patients doing hemodialysis treatment or that have had transplants are more likely to needed mechanical ventilation or have higher mortality rates (Arenas et al., 2020; Pei et al., 2020).

Cancer patients were also found to have higher mortality rates or be more likely to develop serious complications (Liang et al., 2020), especially if considering cancer in the respiratory systems (Gallo, 2020). This risk is caused by a compromised immune systems, which has a crucial role stopping major symptoms to develop (Paces et al., 2020).

Diabetes also plays a major role in Covid incidence; it was the comorbidity associated with more patients needing to be admitted and to have mortality rates that can be up to three times higher than patients without (Erener, 2020). Lampasona et al. (2020) confirmed these findings, also identifying patients with diabetes to be more likely to develop serious symptoms or dying, and this probability is even higher for patients going through intensive treatment (insulin injections). Obesity can be also linked with higher mortality rates or more serious symptoms, it is an independent factor but can also be related to several other comorbidities such as cardiovascular diseases (Erener, 2020; Kassir, 2020; Korakas et al., 2020).

Cardiovascular diseases have been extensively studied and identified as a main comorbidity associated with Covid deaths (Bansal et al., 2021; Cheng et al., 2021). Su et al. (2020) found that arterial pressure is a crucial factor while assessing the severity of Covid infection, especially the case of hypotension should be monitored closely at the time of admittance (Lee & An, 2016). Hypertension was also found to increase mortality rates and the development of more serious symptoms including the need for mechanic ventilators. Nevertheless, European Society of Cardiology was not able to isolate the effects of hypertension since they were always associated with older patients (European Society of cardiology, 2020). Covid-19 was also found to cause lesions in the myocardium and cardiac arrhythmia and increases the probability for heart attacks. Once again, transplanted patients were found to have higher risks to develop serious symptoms (European Society of cardiology, 2020).

Covid affects the respiratory system and, therefore, patients with previous respiratory fragilities are more likely to develop serious symptoms or have higher mortality rates than those who do

not (Olloquequi, 2020; Rivera-Izquierdo et al., 2020; Xiao et al., 2020; Yang et al., 2020). Smokers were also found to have higher risks of developing serious symptoms (Çakır Edis, 2020). Patients with arterial oxygen saturation levels below 93%, less than 30 respiratory cycles per minute and PaO2/FiO2 lower than 300 mmHg were also found to be more likely to develop severe symptoms (Duan et al., 2020; Ferrando et al., 2020; Fuentes & Chowdhury, 2020).

Some authors were also able to identify relationships between indicators such as body temperature or glucose levels and the probability either of developing serious symptoms or of dying from Covid. Levenfus et al. (2020) found that Covid patients usually have a body temperature between 38ºC and 41ºC, although the author could not relate higher temperatures with higher mortality rates, they tend to be admitted for longer periods.

Glucose levels were found to have a linear relationship with the probability of being admitted, and patients with levels higher than 7mmol have critical high risk of being admitted (Alahmad et al., 2020). These higher probabilities are true even for patients without diabetes, and Covid-19 can change the way metabolisms process sugar (Wang et al., 2020).

Wang (2020) found that protein reactive C levels are positively correlated to the size of pulmonary lesion, which can be an indicator of severity of Covid infection. High levels of this protein can also indicate inflammation, cell destruction or muscular tissue lesions, and are usually higher in deceased patients or patients with serious symptoms (Levenfus et al., 2020; Luo et al., 2020; Nehring et al., 2021).

Some authors found that while blood groups B, AB or RH+ are more likely to test positive for Covid, blood type O is less likely to do so (Ellinghaus et al., 2020). Furthermore, blood type A was considered a risk factor to develop more serious symptoms, to be admitted or even for death (Latz et al., 2020; Li et al., 2020). Regarding D-Dimers high levels ($\geq$2.0µg/ml) were found to be related with higher mortality rates and increases the probability of pulmonary embolism (Y. Li et al., 2020; Sakka et al., 2020; Schutgens, 2020). Naymagon et al. (2020) found that each increase of 1 µg/m in D-dimer level, the death ratio increased 1.06, the intubation increased to 1.08 as well as the ratio for the need of mechanic ventilation, for 6 different hospitals.

Finally, there are evidences that Covid-19 has higher incidence and higher mortality rates in people with lower education levels, lower income and without easy access to health care (Sesé et al., 2020; Strang et al., 2020). Living conditions were also found to influence the decision of admitting the patient to hospital care or monitor the situation at home (Hawkins et al., 2020), since usually have more difficulty in maintaining social distancing (Truong & Asare, 2021).

3. Methodology

In order to understand which factors influence Covid diagnosis and mortality probability a survey was design. The survey includes all the factors encountered by previous authors and was reviewed by an expert in order to confirm its adequacy. It was divided in two parts, one that assessed the severity of Covid incidence dividing it into four risk levels: low, moderate, severe and critical; and the second that aimed to evaluate the probability of mortality categorized into three levels: low, moderate and severe. The survey was then distributed among Portuguese doctors that have been on the front-line of Covid for the past year. Between 25th of February and 19th of March it was possible to collect the opinions of 23 experts on which factors are indicators of each severity level of disease and mortality probability.

Once all the data was collected, it was divided into contingency tables and the different proportions were evaluated with Chi^2 analysis to detect the significant ones. Since there are more than two risk levels and some factors are also categorized into more than two options, the analysis was also performed isolating two levels at a time or combining different levels together. The tests performed allowed to not only identify the factors that can influence the severity of Covid incidence, but also were these can be divided and which levels can lead to worse scenarios.

4. Data Analysis

The 18 factors retrieved from the literature were evaluated separately in order to assess their impact either on the severity of symptoms developed or the mortality rates. Although gender, blood type and respiratory frequency were identified as factors, these two fields of the survey were not properly answered and no conclusions could be drawn from them.

4.1 Living Conditions

According to the experts, there is an association between the living conditions, the admittance to the hospital and the severity of the disease (p-value: 0.033). For lower or moderate severity, the living conditions can influence the decision to admit the patient, while for serious or critical severity levels it is no longer a factor (p-value: 0.018).

4.2 Age

It was possible to find a significant association between age and the severity of the disease (p-value: 0.000) and the mortality risk (p-value: 0.000). Older patients are more likely to develop

more serious symptoms (p-value: 0.000) and have higher mortality risks (p-value: 0.000), there are no significant differences between patients younger than 49.

4.3 Kidney disease

Although it was not possible to find significant differences between the severity of disease for patients with kidney disease (p-value: 0.053), it was possible to find it for patients in dialyses (p-value: 0.002). Being on dialysis and the severity of the disease are related and the low risk level has lower proportions of patients in dialysis than other risk levels (p-value: 0.014), as well as low and moderate have lower proportions than the higher levels (p-value: 0.000). Regarding mortality risk it was possible to associate the different levels with renal patients, kidney patients (p-value: 0.004) as well as those on dialysis (p-value: 0.000) have higher mortality risk.

4.4 Cancer

Cancer patients show no association with different severity risks, with the exception of those doing chemotherapy treatments (p-value: 0.002). These have more serious than low severity cases (p-value: 0.003), more critical than low (p-value: 0.021) and more serious than moderate (p-value: 0.032). On the other hand, all cancer patients are associated with higher mortality risk (p-values: 0.006 and 0.000).

4.5 Immunosuppression

It was possible to find significant association between immunossupression and the severity of Covid-19 (p-value: 0.007) and mortality risk (p-value: 0.000). These patients are more likely to develop serious than light (p-value: 0.011) or moderate symptoms (p-value: 0.043). The differences between low and high mortality risk (p-value: 0.003) are also significant.

4.6 Transplants

The opinion of the experts shows that there is an association between having received a transplant and the severity of Covid-19 (p-value: 0.007) and mortality risk (p-value: 0.000). Transplanted patients are more likely to develop serious symptoms than light ones (p-value: 0.010) or moderate (p-value: 0.044). There are also significant differences between low and high (p-value: 0.001) or moderate and high (p-value: 0.014) risk of mortality.

4.7 Respiratory disease

It was possible to find a significant association between chronic respiratory disease, the severity of Covid-19 incident (p-value: 0.015) and mortality risk (p-value: 0.000). The differences between low and moderate (p-value: 0.043) and low and high (p-value: 0.000) mortality risks are significant. Furthermore, these patients are more likely to develop more serious (p-value: 0.007) or critical (p-value: 0.014) cases than light ones.

4.8 Cardiovascular disease

For chronic cardiovascular disease it was only possible to find association with the severity of the disease if only two levels – low and high, are considered (p-value: 0.049). On the other hand, it was possible to find significant association with all mortality risk levels (p-value: 0.003). There are significant differences between low and moderate (p-value: 0.005) or high (p-value: 0.002) risk of mortality between patients with cardiovascular disease and those without.

4.9 Hypertension

Once again, for patients with hypertension it was only possible to find association with the severity of the disease if only two levels – low and high are considered (p-value: 0.023). Nevertheless, it was possible to find an association with mortality risk (p-value: 0.029). There are significant differences between low and moderate (p-value: 0.025) or high (p-value: 0.013) risk of mortality.

4.10 Diabetes

Diabetes are associated with the severity of Covid-19 incidence (p-value: 0.036) and mortality risk (p-value: 0.000). Patients with diabetes, regardless of the type (p-value: 0.002 – type I, p-value: 0.003 – type II), show higher mortality risk. When considering the development of symptoms, it is only possible to find significant differences between patients with and without diabetes, between light and higher severity symptoms (p-value: 0.030).

4.11 Obesity

The experts' opinion shows association between obesity and the severity of Covid-19 (p-value: 0.000) and mortality risk (p-value: 0.000). Not only was it possible to distinguish between obese and non-obese patients (p-value: 0.005), but also class 3 obese are more likely to develop serious symptoms and have higher mortality risk than class 1 obese (p-value: 0.002).

4.12   Body temperature

It was possible to find significant associations between body temperature and severity of Covid-incidence (p-value: 0.000) and mortality risk (p-value: 0.000). As body temperature increases, the probability of developing more serious symptoms (p-value: 0.000) and mortality risk (p-value: 0.015) increase as well.

4.13   Glucose

Glucose levels are associated with the severity of the disease (p-value: 0.047) and its mortality risks (p-value: 0.016). Patients with glucose levels higher than 126 are less likely to develop light symptoms than serious (p-value: 0.023) or critical (p-value: 0.024). These patients are also likely to have high mortality risks (p-value: 0.020).

4.14   Blood pressure

It was possible to find significant associations between blood pressure (systolic and diastolic) and the severity of the disease (p-values: 0.000) and mortality risk (p-value: 0.000). It was possible to separate systolic pressure in <60, 60-90 and >90 and find significant differences between all severity levels (p-values: 0.000) and for all mortality risks (p-values: 0.000). Diastolic pressure was divided between <90, 90-140 and >140 and there are also significant differences between all severity levels (p-values: 0.000) and for all mortality risks (p-value: 0.000).

4.15   C-protein

There is an association between C-protein levels and the severity of Covid-19 (p-value: 0.000) and mortality risk (p-value: 0.000). It was possible to find associations between low and higher mortality risk for patients with C-protein levels lower or higher than 10 (p-value: 0.000), lower or higher than 20 (p-value: 0.000) and lower and higher than 30 (p-value: 0.004). The same groups of patients have different proportions of light more serious symptoms (p-values: 0.006, 0.000, 0.000), and the last two between moderate and critical symptoms (p-values: 0.023 and 0.010).

4.16   D-dimer

It was possible to find significant association between D-dimer levels and severity of the disease (p-value: 0.000) and its mortality risk (p-value: 0.000). It was possible to separate between patients with <1, 1-2 and >2 µg/ml and associate them with the different levels of disease

severity (p-values: 0.003 and 0.000). Furthermore, there are significant differences for these patients between moderate and high mortality risk (p-values: 0.034 and 0.000).

4.17 Oxygen saturation

Oxygen saturation levels show association with the severity of the disease (p-value: 0.000) and its mortality risk (p-value: 0.000). The mortality risks show significant differences between all levels (low, moderate, high) for patients with saturation levels lower and higher than 85 (p-value: 0.003), 90 (p-value: 0.000) and 94 (p-value: 0.000). These same groups of patients show significant differences between low and serious symptoms (p-value: 0.000), and critical and lower symptoms (p-value: 0.002).

4.18 PaO2/FiO2

It was possible to find significant association between PaO2/FiO2 levels and the severity of Covid-19 incidence (p-value: 0.000) and mortality risk (p-value: 0.000). There are significant differences between the different levels considered (<100, 100-200, 200-300 and >300) in developing light or moderate and serious or critical symptoms (p-value: 0.000) and low and high mortality risk (0.026).

5. Discussion

The experts that answered the survey agree with previous studies that age is a relevant demographic factor while predicting mortality risk or the severity of Covid-19 incidence. On the other hand, it was not possible to evaluate their opinion on gender.

Regarding the different comorbidities detailed in the literature, the experts did not find them all relevant to predict either mortality risk or the severity of symptoms developed. They agree with Shahid et al. (2020) that chronic kidney disease increases mortality risk, even though does not influence the severity of the disease. Furthermore, there is a consensus that patients on dialysis treatment can develop more serious symptoms and have higher mortality risks (Arenas et al., 2020; Pei et al., 2020). While it was possible to validate Liang et al. (2020) finding regarding the elevated risk of mortality for cancer patients, these were not found to develop more serious symptoms unless they were doing chemotherapy treatments. Immuno-compromised patients are more likely to develop major symptoms and die from Covid-19 (Paces et al., 2020). It was also possible to validate Erener's (2020) findings regarding the influence of diabetes and obesity on Covid-19 complications and mortality rates. Cardiovascular diseases and hypertension were associated with mortality risk (Bansal et al., 2021; Cheng et al., 2021), but

the consensus regarding their impact on the development of more serious symptoms was weaker. As expected and stated by several authors (Olloquequi, 2020; Rivera-Izquierdo et al., 2020; Xiao et al., 2020; Yang et al., 2020), respiratory diseases influence mortality risk and severity of symptoms developed.

There were also previous studies performed on the influence or predictive value of certain indicators and, therefore, these were also included in the present study. With the exception of respiratory cycles, which information was not properly answered, it was possible to find association between all the considered indicators and mortality risk and severity of symptoms developed. It was possible to validate the findings of Duan et al. (2020) regarding oxygen saturation and PaO2/FiO2 and add that these indicators can also predict mortality risk. The same happened with Levenfus et al. (2020) on body temperature, Alahmad et al. (2020) on glucose levels and Su et al. (2020) on arterial pressure.

Finally, it was possible to find some association between the housing situation and hospital admittance raised by Hawkins et al. (2020) and Truong and Asare (2021), these can also probably be associated with less healthy nutrition leading to higher BMI and consequent effects. For patients in serious or critical state only their health conditions dictate the need for admittance; however, patients that are not able to maintain social distancing at home may be admitted even in less serious conditions.

6. Conclusion

It was possible to use the experience of Portuguese doctors on the front line to identify which factors are associated with mortality risk and severity of symptoms developed from Covid-19. Mortality risk was associated with age, cancer, immunosuppression, transplant, obesity, diabetes, hypertension, and kidney, respiratory and cardiovascular disease. Body temperature, blood pressure, oxygen saturation, glucose, C-protein, D-dimer and PaO2/FiO2 levels are also associated with mortality risk and severity of symptoms. Different symptoms development was also associated with age, immunosuppression, transplants, patients doing chemotherapy or dialysis treatments, diabetes and obesity.

7. Limitations and future lines of research

The associations identified depend on the opinion and experience of a small sample of front line doctors. Nevertheless, this study was a first approach to understand which data could be collected to develop models that will help predict mortality risk and what symptoms could be expected at first screening at the hospital.

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