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Research Article

Predictors of COVID-19 Case Fatality Rate in Highly Populated Developed Countries During the Emergence of the Delta Variant

Golan Benisti[1, †], Avi Magid[2, *, †]

[1]Department of Health System Management, Peres Academic Center, Rehovot, Israel

[2]Department of Health System Management, Emek Yezreel Valley College, Jezreel Valley, Israel

Email address:

magid.avi@gmail.com (A. Magid)

[*]Corresponding author

† Golan Benisti and Avi Magid are co-first authors.

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Abstract: By September 2021 the outbreak of the COVID-19 caused 228.19 million confirmed cases and 4.7 million deaths globally. Mortality measures are frequently used to estimate the severity of a pandemic. Among them is the Case Fatality Rate (CFR). Some mathematical models were developed to estimate the impact of specific factors on the disease's mortality. These models were developed before the COVID-19 vaccines were administrated, and therefore did not consider the vaccines influence on COVID-19 fatality. Moreover, some other factors associated with COVID-19 mortality such as diabetes and cardiovascular mortality were not included in these models. This study offers a mathematical model with some potential predictors of COVID-19 CFR during the fourth pandemic wave caused by the Delta variant. To evaluate these predictors, demographic and clinical information for 10 highly populated developed countries was retrieved from a real-time available website. Demographic data included population density, percent of population above age 65, GDP per capita, and percent of smoking. Clinical data included diabetes prevalence, cardiovascular death rate, percent of fully vaccinated population, and CFR. Single linear regressions were conducted to assess the association of each potential predictor with CFR. A backward multiple linear regression was conducted to identify the most parsimonious combination of the independent variables of this study predicting CFR. The model developed in this study suggests that percent of population above age 65, and cardiovascular death rate have a positive effect on CFR, i.e., they are associated with increased COVID-19 fatality rate during the fourth wave. In addition, GDP per capita has a negative effect on CFR, i.e. – higher GDP per capita is associated with lower fatality rate during COVID-19 fourth wave. Moreover, single linear regressions show a strong negative association between percent of fully vaccinated people in each country and CFR. This model sheds light on several potential demographic and clinical factors which may predict CFR in highly populated developed countries during the emergence of the Delta variant. Vaccination in accordance with the recommendations is recommended to reduce COVID-19 mortality.

Keywords: Pandemic, Linear Regression Model, Vaccine, Case Fatality Rate, Diabetes, Cardiovascular Mortality

1. Introduction

On March 11, 2020, the World Health Organization (WHO) declared the coronavirus disease (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) a global pandemic [1].

By September 2021 the outbreak of the COVID-19 caused 228.19 million confirmed cases and 4.7 million deaths globally [2].

Mortality measures are frequently used to estimate the severity of a pandemic. Among them is the Case Fatality Rate (CFR), which is defined as the number of deaths to date

divided by the number of all confirmed cases to date. CFR measures how severe or fatal is the disease [3].

In mid-2020, the Food and Drug Administration (FDA) approved three COVID-19 vaccines for emergency use in the U.S.: SARS-CoV-2-BNT162b2 mRNA (Pfizer-BioNTech), mRNA-1273 (Moderna), and Ad26.COV2.S (Janssen) [4]. Since the approval of the vaccines, approximately 3.4 billion doses of COVID-19 vaccine have been administrated worldwide [5]. Updated to September 2021, 2.7 billion people globally are fully vaccinated against COVID-19 disease, as prescribed by the vaccination protocol, [6]. As a result of the mass vaccination, a decrease in COVID-19 morbidity and mortality was observed worldwide [5].

From mid-November 2020 there has been a spread of several variants of the SARS-CoV-2 virus. Most recently, the Delta variant (B. 1.617.2) has become the dominant cause of COVID-19 in several highly populated countries [7]. As a result, and due to the Delta variant high transmissibility, many countries are witnessing an increase of COVID-19 incidence and hospitalizations [4]. Looking at trends of daily new cases, one can identify a fourth epidemic wave of the COVID-19 pandemic occurring recently in several countries [8].

Over the years, many models have been developed to predict mortality from infectious diseases. Some of them are based on the classical epidemiological approach known as the acronym SEIR models [9]. Other models are based on the virological and serological datasets collected intensively during previous pandemics [9, 10]. Some mathematical models were developed to estimate the impact of specific factors on the disease's spread. A study which examined risk factors associated with mortality from COVID-19 in highly populated European countries found that the percentage of population above age 65, the population's density, and the number of days of exposure to COVID-19 are potential risk factors for dying from the pandemic [9]. These models were developed before the COVID-19 vaccines were administrated, and therefore did not consider the vaccines influence on COVID-19 fatality. Moreover, some other factors associated with COVID-19 mortality such as diabetes and cardiovascular mortality were not included in these models [11, 12].

This study offers a mathematical model with some potential predictors of COVID-19 CFR during the fourth pandemic wave caused by the Delta variant.

2. Materials and Methods

2.1. Demographic and Clinical Data

Demographic and clinical information for 10 countries was retrieved from "Our world in data", a real-time available website [13]. Highly populated OECD countries with 8.5 million people and above, in which a fourth pandemic COVID-19 wave was observed (a continuous increase in daily new confirmed cases starting from June 2021 or later until September 14 2021) were selected. Demographic data included population density, percent of population above age 65, GDP per capita, and percent of smoking. Clinical data included diabetes prevalence, cardiovascular death rate, percent of fully vaccinated, and CFR. CFR was calculated as the number of deaths attributed to COVID-19 occurred during the fourth wave identified for each country, divided by the accumulated new COVID-19 cases during this period.

2.2. Statistical Analysis

IBM SPSS software version 20 was used to assess the bivariate associations, and to develop a linear regression model to predict the CFR for the COVID-19 fourth wave. First, the bivariate associations between the study variables were examined. Next, single linear regressions were conducted to assess the association of each potential predictor with CFR. Finally, a backward multiple linear regression was conducted to identify the most parsimonious combination of the independent variables of this study predicting CFR [14]. The explanatory variables were those found to be statistically significant ($P < 0.05$).

3. Results

3.1. Demographic Information

The demographic and clinical data are summarized in table 1:

Table 1. *Demographic information (percentage of population above age 65 years, population density, GDP per capita, and % smoking) and clinical data regarding COVID-19 pandemic (diabetes prevalence, cardiovascular death rate, % fully vaccinated, Case fatality Rate) of 10 European countries (data updated for September 14, 2021).*

Country	Population density (People/km^2)	% Of population above age 65	GDP per capita	% Smoking	Diabetes prevalence	Cardiovascular death rate	% Fully vaccinated	CFR per 100,000
Austria	107	19	45,436	30	6.4	145.2	58.7	227.0
Belgium	376	19	42,659	28	4.3	115.0	71.0	257.4
France	123	20	38,606	33	4.8	86.1	63.0	439.3
Germany	237	21	45,229	31	8.3	156.1	61.6	538.1
Israel	403	12	33,132	25	6.7	93.3	63.2	284.0
Italy	206	23	35,220	24	4.8	113.2	64.2	735.8
Romania	85	18	23,313	30	9.8	371.0	27.2	1,978.6
Spain	93	19	34,272	29	7.2	99.4	75.5	415.5
Sweden	25	20	46,949	17	4.8	134.0	60.4	159.5
United Kingdom	273	19	39,753	22	4.3	122.1	64.6	235.3

3.2. Examination of Demographic and Clinical Data from Table 1

A wide variation in population density (Mean=192.62; SD=128.27), percent of fully vaccinated (Mean=60.94; SD=12.87), cardiovascular death rate (Mean=143.52; SD=82.96) rate and CFR (Mean=527.04; SD=538.82) between the studied countries is observed. Bivariate correlations show that countries with lower GDP per capita, higher diabetes prevalence, higher cardiovascular death rate, and lower percent of fully vaccinated people have higher COVID-19 CFR (Pearson coefficient=-0.785, 0.694, 0.902, -0.85, respectively; $P < 0.05$).

3.3. Linear Model for Predicting Case Fatality Rate from COVID-19

Based on the data presented in table 1, a backward multiple linear regression was conducted for predicting CFR, using demographic as well as clinical information. The model that included percent of population above age 65, GDP per capita, and cardiovascular death rate was the most parsimonious model ($F(3, 6)=73.94$, $P < 0.0001$; adjusted $R^2=0.960$).

Table 2. *Linear regression model for predicting case fatality rate from COVID-19 in 10 European countries using backward step algorithm.*

Variables entered	Unstandardized coefficients		t	Sig.	Adjusted R^2	F value (df) (Sig.)
	B	Standard Error				
Constant	632.04	309.96				
% of population above age 65	42.74	13.20	3.24	0.018	0.960	F(3, 6)=73.94
GDP per capita	-0.04	0.01	-5.95	0.001		P < 0.0001
Cardiovascular death rate	3.99	0.53	7.48	< 0.0001		

3.4. Examination of the Suggested Linear Model from Table 2

As depicted in table 2, the model suggests that two variables: percent of population above age 65, and cardiovascular death rate have a positive effect on CFR, i.e., they are associated with increased COVID-19 fatality rate during the fourth wave. In addition, GDP per capita has a negative effect on CFR, i.e. – higher GDP per capita is associated with lower fatality rate during COVID-19 fourth wave.

Moreover, single linear regression shows a strong negative association between percent of fully vaccinated people and CFR ($B=-35.91$, $P < 0.002$), i.e., in countries where a higher percentage of fully vaccinated people was observed, CFR was lower. Percent of smoking was not associated with CFR.

4. Discussion

This study suggests a model for predicting COVID-19 CFR during the fourth pandemic wave attributed to the Delta variant in 10 developed countries (with population size of 8.5 million people and more). The model developed in this study indicates that in countries where the percentage of population above age 65 years is higher, the predicted CFR is higher. This finding is consistent with previous model developed for earlier COVID-19 pandemic waves [9]. Another demographic variable negatively associated with COVID-19 CFR is GDP per capita. Some previous studies assessing the relationship between GDP per capita and CFR few months after the pandemic outbreak pointed out that the overall relationship between investment, health care system and CFR might be more complex than one might expect [15, 16]. Nevertheless, this relationship was demonstrated in a statistically significant manner in this study. The differences might be due to the time passed from the pandemic outbreak: at the beginning of the pandemic, no country was prepared to deal with it, and the health services in many countries weighed down by the burden, regardless the GDP per capita and the country's investment in health. Nowadays, 18 months after the outbreak, countries around the globe managed to deal with the pandemic. At this point, differences in country's GDP per capita may affect its capability to deal with the pandemic. This may be a possible explanation to the association between GDP and CFR demonstrated in this study.

This study results demonstrate a strong positive association between cardiovascular mortality rate and CFR. This finding is consistent with previous studies [15]. Although the exact biological mechanism of how cardiovascular disease increases the severity and mortality of COVID-19 patients is still unclear, some previous studies pointed out several possible mechanisms, among them is that patients with cardiovascular disease are more likely to develop myocardial injury during the course of COVID-19, by a possible damage to cardiomyocytes caused by the SAR-CoV-2 virus, leading to systemic inflammatory responses [17]. Another possible explanation may be that countries with higher cardiovascular mortality rate may have worse health systems and therefore higher CFR. The model proposed in this study does not include the percent of fully vaccinated population in each country. However, the single linear regression shows a strong statistically significant association between the percentage of fully vaccinated population and CFR. This finding is consistent with recent studies [18], as well as the FDA latest recommendations to vaccinate with a booster individuals aged 65 years and older dose, and individuals of high risk of severe COVID-19 [19].

This study has some limitations: the proposed model assumes highly populated developed countries, and therefore may not be valid for smaller (less than 8.5 million people) and/or developing countries. Further research is required to validate this model to countries with different characteristics.

Another limitation is that the model proposed in this study did not consider the measures taken by the different countries during

the emergence of the Delta variant. These measures may also affect the COVID-19 morbidity and thereby the CFR [9].

The model also did not consider the quality of health system in each selected country, which may also be a factor affecting CFR [9]. Hence, this model may not provide with exact prediction of CFR during the Delta variant emergence, but it points out important associations between demographic and clinical factors and CFR.

5. Conclusion

The fourth COVID-19 pandemic wave caused by the Delta variant emphasizes the importance of developing models for predicting the disease case fatality rate. The model suggested in this study sheds light on several potential demographic and clinical factors which may predict CFR in highly populated developed countries during the emergence of the Delta variant. These factors may be considered by decision makers when deciding on measures during the fourth pandemic wave. Further research is required to establish this model for more countries with various characteristics. Vaccination in accordance with the recommendations is recommended to reduce COVID-19 mortality.

References

[1] Gulati A, Pomeranz C, Qamar Z, Thomas S, Frisch D, George G, Summer R, DeSimone J, Sundaram B. A comprehensive review of manifestations of novel coronaviruses in the context of deadly COVID-19 global pandemic. The American journal of the medical sciences. 2020 Jul 1; 360 (1): 5-34.

[2] Hannah Ritchie, Edouard Mathieu, Lucas Rodés-Guirao, Cameron Appel, Charlie Giattino, Esteban Ortiz-Ospina, Joe Hasell, Bobbie Macdonald, Diana Beltekian and Max Roser (2020) - "Coronavirus Pandemic (COVID-19) (Cases and deaths)". *Published online at OurWorldInData.org*. Retrieved 6 October 2021, from: 'https://ourworldindata.org/coronavirus' [Online Resource].

[3] Böttcher, Lucas, Mingtao Xia, and Tom Chou. "Why case fatality ratios can be misleading: individual-and population-based mortality estimates and factors influencing them." Physical biology 17, no. 6 (2020): 065003.

[4] Chhatwal J, Mueller PC, Ayer T, Adee MG, Dalgic O, Ladd MA, Linas B. Changing Dynamics of COVID-19 in the US with the Emergence of the Delta Variant: Projections of the COVID-19 Simulator. medRxiv. 2021 Jan 1.

[5] Barda N, Dagan N, Ben-Shlomo Y, Kepten E, Waxman J, Ohana R, Hernán MA, Lipsitch M, Kohane I, Netzer D, Reis BY. Safety of the BNT162b2 mRNA COVID-19 vaccine in a nationwide setting. New England Journal of Medicine. 2021 Aug 25.

[6] Hannah Ritchie, Edouard Mathieu, Lucas Rodés-Guirao, Cameron Appel, Charlie Giattino, Esteban Ortiz-Ospina, Joe Hasell, Bobbie Macdonald, Diana Beltekian and Max Roser (2020) - "Coronavirus Pandemic (COVID-19) (Vaccination)". *Published online at OurWorldInData.org*. Retrieved 6 October 2021, from: 'https://ourworldindata.org/coronavirus' [Online Resource]

[7] Alexandar S, Ravisankar M, Kumar RS, Jakkan K. A Comprehensive Review on COVID-19 Delta variant. International Journal of Pharmacology and Clinical Research (IJPCR). 2021, 5, 83-5.

[8] Shah SA, Moore E, Robertson C, McMenamin J, Katikireddi SV, Simpson CR, Shi T, Agrawal U, McCowan C, Stock S, Ritchie LD. Predicted COVID-19 positive cases, hospitalisations, and deaths associated with the Delta variant of concern, June–July, 2021. The Lancet Digital Health. 2021 Sep 1; 3 (9): e539-41.

[9] Eliyahu U, Magid A. Estimation of Risk Factor's Contribution to mortality from COVID-19 in Highly Populated European Countries. Biomedical Statistics and Informatics. 2021 Jan 22; 6 (1): 1.

[10] Yaari R, Katriel G, Stone L, Mendelson E, Mandelboim M, Huppert A. Model-based reconstruction of an epidemic using multiple datasets: understanding influenza A/H1N1 pandemic dynamics in Israel. Journal of The Royal Society Interface. 2016 Mar 31; 13 (116): 20160099.

[11] Kumar A, Arora A, Sharma P, Anikhindi SA, Bansal N, Singla V, Khare S, Srivastava A. Is diabetes mellitus associated with mortality and severity of COVID-19? A meta-analysis. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2020 Jul 1; 14 (4): 535-45.

[12] Pranata R, Huang I, Lim MA, Wahjoepramono EJ, July J. Impact of cerebrovascular and cardiovascular diseases on mortality and severity of COVID-19–systematic review, meta-analysis, and meta-regression. Journal of Stroke and Cerebrovascular Diseases. 2020 Aug 1; 29 (8): 104949.

[13] Mathieu E, Ritchie H, Ortiz-Ospina E, Roser M, Hasell J, Appel C, Giattino C, Rodés-Guirao L. A global database of COVID-19 vaccinations. Nature human behaviour. 2021 May 10: 1-7.

[14] Feinhandler I, Cilento B, Beauvais B, Harrop J, Fulton L. Predictors of death rate during the COVID-19 pandemic. InHealthcare 2020 Sep (Vol. 8, No. 3, p. 339). Multidisciplinary Digital Publishing Institute.

[15] Sorci G, Faivre B, Morand S. Explaining among-country variation in COVID-19 case fatality rate. Scientific reports. 2020 Nov 3; 10 (1): 1-1.

[16] Hashim MJ, Alsuwaidi AR, Khan G. Population risk factors for COVID-19 mortality in 93 countries. Journal of epidemiology and global health. 2020 Sep; 10 (3): 204.

[17] Yu JN, Wu BB, Yang J, Lei XL, Shen WQ. Cardio-cerebrovascular disease is associated with severity and mortality of COVID-19: a systematic review and meta-analysis. Biological Research for Nursing. 2021 Apr; 23 (2): 258-69.

[18] Haghpanah F, Lin G, Levin SA, Klein E. Analysis of the potential impact of durability, timing, and transmission blocking of COVID-19 vaccine on morbidity and mortality. EClinicalMedicine. 2021 May 1; 35: 100863.

[19] Vaccines and Related Biological Products Advisory Committee, September 17, 2021 meeting announcement, WHO https://www.fda.gov/advisory-committees/advisory-committe e-calendar/vaccines-and-related-biological-products-advisory-committee-september-17-2021-meeting-announcement.