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Assumptions for disparities in case-fatality rates of coronavirus disease (COVID-19) across the globe

K. UNDELA[1], S.K. GUDI[2]

[1]Department of Pharmacy Practice, JSS College of Pharmacy, JSS Academy of Higher Education & Research, Mysuru, Karnataka, India
[2]College of Pharmacy, Rady Faculty of Health Sciences, University of Manitoba, Winnipeg, Canada

Abstract. **In a short span, Coronavirus disease (COVID-19) has become the world pandemic by rapidly spreading almost to all the countries around the globe, irrespective of the continent, population size, economic status and healthcare system. Despite the number of cases increasing exponentially in most of the countries, there exist certain disparities in terms of case-fatality rates. As of April 24, 2020, the case-fatality rate of COVID-19 is about 7.0%, with 193,671 deaths and 2,761,121 confirmed cases around the world. Although the United States of America (USA), Spain, Italy, France, and Germany are the top-most affected counties in terms of confirmed cases; France, Italy and Spain are leading the list in terms of case-fatality rates. Therefore, through this mini-review, authors sought to brief on possible assumptions (five D's) that might contribute to the varying case-fatality rates among different countries across the globe.**

Key Words:
Novel coronavirus, COVID-19, SARS-CoV-2, Coronavirus disease, Pandemic, Case-fatality rate.

Introduction

Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) has initially originated from the province of Hubei, China, in late December 2019, and ever since then, it is being spread at a rapid pace and continues expanding almost to all the countries around the world. As of April 24, 2020, there are 2,761,121 confirmed cases of Coronavirus disease (COVID-19) and 193,671 deaths affecting 185 countries worldwide with a case-fatality rate of 7.0%[1]. Although the United States of America (USA) (880,112 cases), Spain (219,764 cases), Italy (192,994 cases), France (159,495 cases) and Germany (153,584 cases) are the top most-affected counties in terms of confirmed cases, France (21,889 deaths, 13.7%), Italy (25,969 deaths, 13.5%) and Spain (22,524 deaths, 10.2%) are leading the list in terms of case-fatality rates by leaving the USA behind at a 5.7% case fatality rate, despite its highest number of confirmed cases in the world[1].

In simpler terms, the case-fatality rate is the number of deaths divided by the number of infections for any given country. The impact of COVID-19 appears to be varying from one country to another, especially in terms of case-fatality rates, and yielding stark differences among numbers, although the actual situation seems similar. Thus, making fatality rates unreliable, both for the governments that are trying to calibrate their policy response and as well as for the citizens who are trying to keep themselves updated with the rapidly changing scenarios. As an illustration, France has a case-fatality rate of 13.7%, while Germany has close to 3.6%, despite having similar number of confirmed cases in both the countries. In this regard, presumptuously, these disparities could be justified by certain factors (five D's) such as Demographic characteristics of population, Definition of COVID-19 related deaths, Differences in testing strategies, Differences in healthcare systems and Dissimilarity in preventive strategies. Through this mini-review, authors sought to brief on these possible assumptions that might contribute to the varying case-fatality rates across different countries in the world.

Demographic Characteristics of Population

The first and foremost factor to be considered in affecting the fatality rates is the demographic characteristics of the population, such as age, sex, underlying risk factors like comorbid conditions and smoking. Any extent of variations in these factors among the specific population in each country would make an enormous difference in the case-fatality rates. Looking at the different age groups that are commonly being infected by the COVID-19, older people exhibit higher risk

Corresponding Author: Sai Krishna Gudi, B.Pharm., Pharm.D., M.Sc., (Ph.D); e-mail: sknanu06@gmail.com

as they often have underlying co-existing health conditions, which make them immune-compromised and eventually get affected[2].

Current data around the world indicate that older people are more prone to and experience higher deaths from COVID-19. In Italy, around 38% of the confirmed cases and 88% of deaths are attributed to 70 years or older individuals, whereas in China, it is 12% of cases and 51% of deaths[3]. In support of this point, the average age of patients that are infected from COVID-19 in Germany is 46, whereas it is 63 years in Italy, as it has one of the world's oldest populations, and thus highest mortality rate. Besides, available evidence[4] also suggests that men are more prone to and dying from this novel pandemic than women. Underlying comorbid conditions, such as cardiovascular diseases, diabetes, high blood pressure, chronic respiratory disease, and cancer could play a major role in mortality from COVID-19[5]. Alongside these characteristics, interestingly, recent investigations infer that individuals who smoke are also at higher risk of being affected by COVID-19[6].

Definition of COVID-19-Related Deaths

Currently, there are no standard criteria for defining COVID-19-related deaths. In Italy, the case-fatality rate is defined as the proportion of COVID-19 related deaths among patients who tested positive through reverse transcription-polymerase chain reaction (RT-PCR), independently from pre-existing diseases that may have caused death, which could be an over-estimation of the case-fatality rate[3]. In support to this, a detailed chart review of 355 Italian patients who died with COVID-19 revealed that 30%, 35.5%, 24.5%, 20.3%, 9.6% and 6.8% of them had ischemic heart disease, diabetes, atrial fibrillation, cancer, stroke, and dementia, respectively[7]. Similarly, the national government of Spain reports the number of people who died within those confirmed cases and would not provide any other information on other underlying medical conditions, which could incorporate differences in case-fatality rates.

Differences in Testing Strategies

Arguably, a considerable degree of uncertainty lies in adequate testing and in identifying the true number of infected individuals. Adequate testing is a crucial factor in determining an accurate case-fatality rate, as it captures broader cases, including those with mild or no symptoms, which eventually drive down the mortality rate. On this note, Germany has been tested around 120,000 people per week, which is the reason why it has one of the lowest case-fatality rates in the world[8]. Most of the cases, i.e., 85% that have been confirmed so far around the world, are mild to moderate, where people might not display any symptoms, and will remain absent from the data unless they are tested. With limited resources being available, different countries are testing their population to different extents, which plays a major role in disparities among death rates. During the early days of the outbreak, health authorities only knew about a few dozen cases, and thus, it seems to have a higher mortality rate. However, once testing was performed in a broader range, hundreds of thousands of people who have infected but never got sick were identified, which deflated the death rate remarkably. If testing has been limited to people who are sick, it means the only cases that were counted are the people who are most likely to die. Thus, the denominator is missing a huge number of infected people with mild or no symptoms.

To further exemplify this, on February 25, the Italian Ministry of Health recommended prioritized testing for patients with more severe clinical symptoms who were suspected of having COVID-19 and required hospitalization, and testing was relaxed for asymptomatic people or those who had limited, mild symptoms. Thus, this testing strategy resulted in a high proportion of positive cases and a drastic increase in the case-fatality rate from 3.1% on February 24 to 13.5% on April 24[3]. Similarly, with a slow initial response from the government, the UK has tested only the most serious cases giving a death rate of more than 6%, whereas, Germany has been testing both people who are ill and those with milder symptoms since from the beginning, which is the major reason to observe less case-fatality rate. Similar to Germany, governments and health authorities in South Korea have been performing massive testing since their initial days of disease detected might be one major reason for the case-fatality rate in South Korea has been observed around 2%. In the USA, testing has been included a younger and healthier population, which led the case-fatality rate in USA (5.7%) similar to Germany (3.6%) and South Korea (2.2%).

Differences in Healthcare Systems

The ability and preparedness of the respective country's healthcare system is the chief aspect in handling outbreaks like COVID-19, and whether or

not it can succeed in containment by flattening the curve. In certain countries, infected people are more likely to die due to a lack of facilities and an overburdened healthcare system[3], leaving critically ill patients without access to lifesaving care. Initial high case-fatality rates were probably due to the inability of hospitals to handle the huge number of patients who were infected by the SARS-CoV-2. Especially while experiencing high peaks of the outbreak, healthcare systems could be overwhelmed and, therefore, may not have enough beds or ventilators to provide critical care that is needed. This might be a possible reason for the high case-fatality rate in countries like Italy. Of that note, Italy has about 60 million people, but have only 5000 ICU beds[9]. While Germany has a population of about 80 million and 28,000 beds in ICUs. Furthermore, Germany has 29 beds per 100,000 people, the USA has 34 beds per 100,000 people, whereas Italy has just 12 and Spain has 10 ICU beds per 100,000 people[10].

Dissimilarity in Preventive Strategies

In Italy, there was a lot of spread before people realized the virus was present because people assumed the outbreak was a problem elsewhere. Italy implemented its first lockdown measures in late February in 11 municipalities in the northern part of the country, and only the nationwide lockdown came into action on March 9. China saw a higher level of compliance with the lockdown measures compared to Europe. Germany, like many other countries, enforced severe lockdown regulations, which might be one possible reason for experiencing the low number of cases of and deaths from COVID-19[11].

Conclusions

With regards to the disparities in case-fatality rates concerned with the COVID-19, numerous factors may impact a country's death rate, including demographic characteristics of the population, the definition of COVID-19 related deaths, differences in testing strategies, differences in healthcare systems and dissimilarity in preventive strategies. However, it is still uncertain how many of the individuals would have died of other underlying health reasons if this pandemic had not occurred. Among all the possible assumptions, testing capacity is considered crucial as missing the asymptomatic proportion might lead to a wide range of disparities in case-fatality rates. On those grounds, testing capacity could be used as a tool of surveillance. Therefore, efforts should be made in capturing the total infected individuals in order to measure the true case-fatality rate, without which fair comparisons cannot be made regarding the case-fatality rates among different countries across the world.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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References

1) Coronavirus resource centre. Johns Hopkins University. [cited 2020 Apr 04]. Available from: https://coronavirus.jhu.edu/map.html.
2) Wang L, He W, Yu X, Hu D, Bao M, Liu H, Zhou J, Jiang H. Coronavirus disease 2019 in elderly patients: characteristics and prognostic factors based on 4-week follow-up. J Infect 2020; pii: S0163-4453(20)30146-8.
3) Onder G, Rezza G, Brusaferro S. Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. JAMA 2020. Doi: 10.1001/jama.2020.4683.
4) Wenham C, Smith J, Morgan R. COVID-19: the gendered impacts of the outbreak. Lancet 2020; 14; 395: 846-848.
5) CDC COVID-19 Response Team. Preliminary estimates of the prevalence of selected underlying health conditions among patients with Coronavirus Disease 2019 - United States, February 12-March 28, 2020. Weekly 2020; 69: 382-386.
6) Cai H. Sex difference and smoking predisposition in patients with COVID-19. Lancet Respir Med 2020. 2020; 8: e20. Doi: 10.1016/S2213-2600(20)30117-X.
7) Livingston E, Bucher K. Coronavirus disease 2019 (COVID-19) in Italy. JAMA 2020. Doi: 10.1001/jama.2020.4344. [Epub ahead of print].
8) Konrad R, Eberle U, Dangel A, Treis B, Berger A, Bengs K, Fingerle V, Liebl B, Ackermann N, Sing A. Rapid establishment of laboratory diagnostics for the novel coronavirus SARS-CoV-2 in Bavaria, Germany. Euro Surveill 2020; 25. Pii: 2000173.
9) Society of Critical Care Medicine. United States Resource Availability for COVID-19. [cited 2020 Apr 04]. Available from: https://www.sccm.org/Blog/March-2020/United-States-Resource-Availability-for-COVID-19.
10) Rhodes A, Ferdinande P, Flaatten H, Guidet B, Metnitz PG, Moreno RP. The variability of critical care bed numbers in Europe. Intensive Care Med 2012; 38: 1647-1653.
11) Gudi SK, Tiwari KK. Preparedness and lessons learned from the novel coronavirus disease. Int J Occup Environ Med 2020; 11: 108-112.