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## Commentary

## COVID-19 case fatality rates can be highly misleading in resource-poor and fragile nations: the case of Yemen

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During a disease outbreak, estimation of the case fatality rate (CFR) is used as an indication of its severity, and as a guide to plan public health strategies. According to the Dictionary of Epidemiology, CFR is “the proportion of cases of a specified condition which are fatal within a specified time”. To calculate the CFR, the number of deaths from a given disease (the numerator) is divided by the number of diagnosed cases of that disease (the denominator), multiplied by 100 [1]. Underestimation of the CFR may lead to the disease threat not being taken seriously, while overestimation may lead to unnecessary panic. Governments of certain nations with low CFRs often boast about it as a sign of efficient management of the pandemic. However, apart from patient-related factors—such as the presence of comorbidities, age distribution of the population, ethnicity, etc.—several other factors affect the CFR of coronavirus disease 2019 (COVID-19), leading to false disparities between nations, especially resource-poor and fragile nations. These include disparities in resources (shortage of healthcare professionals,

testing capacities, etc.) and social and logistic problems associated with the ongoing conflict.

Although CFR may be a useful measure to assess the magnitude of a disease outbreak, it could be highly inaccurate and misleading in certain resource-poor and fragile nations, necessitating careful investigation and interpretation. For example, intentional or unintentional underreporting and lack of coordination between ministries and governorates can lead to wide inaccuracies in both the numerator and the denominator. This is especially true in war-torn nations that may be divided on the basis of different ruling factions. While a low case reporting will lead to an overestimation of the CFR, a low death registration will lead to its underestimation.

Testing capacity, which is associated with the availability of resources and manpower, is the single most important factor that can tremendously affect the CFR, as more asymptomatic and mildly symptomatic cases who are not likely to die are identified with increased testing. News media and scientific journal publications reporting on the CFR of fragile nations like Yemen have not considered this important parameter, thereby raising a false alarm and misleading readers. For example, the title of an article in a mainstream journal reads that “Covid-19: Deaths in Yemen are five times global average” [2]. It should be noted that the same publication reports a case count of only 1600 in Yemen (one of the lowest in the world, which is understandably an underestimation), after about 3 months from the first confirmed case. It is true that the reported CFR from COVID-19 in Yemen is several times the global average, but it does not necessarily represent the actual CFR, primarily due to the severe shortage in testing capacity. If the actual CFR in Yemen was 29%, as reported, we would be witnessing another humanitarian catastrophe with hundreds of thousands of fatalities.

Although the crude mortality rate in Yemen stands at about six per 1000 people from 2013 (just before the beginning of the conflict) through 2018 [3], the 6-year-long conflict has killed more than 100 000 people so far and displaced 3.6 million people internally [4]. With a population of about 29 million people, the population density of Yemen is only 54 people/km<sup>2</sup> [5], and more than 95% of the population is under the age of 60 years. Although large-scale studies on COVID-19 CFR in Yemen are scarce, it has been shown

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that surveillance strategies in Yemen have detected mainly severe cases, with mortality occurring in those reaching health facilities in critical condition. This has been confirmed by a study that indicated that, of the 268 individuals hospitalized with confirmed infection, 95 died in the hospital, 63% of these being under the age of 60 years [6]. Until the actual, or at least approximate, CFRs are available by improvement in testing strategies and increasing testing capacity, mainstream media should refrain from publishing them. False reporting can lead to creation of unnecessary panic in an already panic-stricken society, with drastic consequences.

Attempts should not be made to compare CFRs of nations, at least until testing capacities are comparable. They are bound to be skewed. For example, Yemen, with a shortage of healthcare professionals, and with one of the lowest testing capacities in the world, is currently reported to have a CFR of about 29%, the highest in the world. At a time when several countries are reporting second and third waves of the pandemic, even 9 months after the diagnosis of the first case of COVID-19 (9th December 2020) Yemen officially has only 2083 infections and 607 deaths [7]. On the other hand, Saudi Arabia, which shares borders with Yemen and has a population similar to that of Yemen, has a CFR of only about 1.6, even though the reported mortality is almost ten times higher. This is understandably due to its large-scale testing capacity leading to the identification of more than 359 000 infections (a high denominator) [8]. Saudi Arabia is reported to have carried out at least 4 000 000 tests by the middle of August 2020, whereas Yemen is capable of testing only highly suspected cases, or patients with severe symptoms who are likely to die, thereby increasing the CFR [9]. Considering the brief and slack lockdown, and non-adherence to preventive measures like social distancing and donning of mouth masks, there is good reason to believe that infections in Yemen may have been widespread but remain undetected due to the shortage of testing kits and facilities. In such a case scenario, the CFR in Yemen would be vastly lower than the reported 29%. Detecting fatality from COVID-19 may be subject to less bias than case detection, and since the probability of reporting to hospitals with severe symptoms is high, the probability of recording fatality also becomes higher, unless left out intentionally. A CFR close to the actual value in Yemen will only become apparent when more testing kits are supplied and the testing capacity is increased.

Even in the presence of testing facilities, fragile nations can pose additional impediments to the public in accessing testing and healthcare facilities due to the ongoing conflict. This could lead to only patients with severe symptoms seeking medical care. Difficulties in implementation of strict and coordinated lockdowns and contact tracing, and the lack of quarantine and isolation facilities, can lead to unchecked spread of the virus. Difficulties in spreading awareness of the symptoms of COVID-19, the importance of testing, self-isolation and quarantine, and the spread of false rumours can further result in cases going undetected.

A more reliable method of estimating the magnitude of a disease outbreak would be an assessment of the infection fatality rate (IFR) [10]. This, however, would require additional studies like seroprevalence tests that detect the presence of antibodies in the body. Seroprevalence studies for COVID-19 have suggested that the number of reported infections at a given time is far lower than the actual, thereby suggesting a significant variation between the IFR and CFR. For example, a seroprevalence study in India suggested that the number of infections on 3rd May 2020 was 6.4 million against the reported number of infections of only 49 720, a 130-fold difference [11]. Unfortunately, due to reasons mentioned earlier,

seroprevalence studies are difficult to carry out in war-torn nations. So far, there have not been any seroprevalence studies for COVID-19 in Yemen.

Healthcare systems of fragile nations are already overburdened by other disease outbreaks (cholera, diphtheria, etc.), famine, malnutrition, injuries from the ongoing conflict, etc., and depend largely on humanitarian assistance from donor nations and non-governmental organizations for resources [12]. Therefore, CFRs of resource-poor and fragile nations should be carefully interpreted considering all associated parameters, to identify deficiencies. This will serve as a guide in planning public health strategies, and channelling the limited resources and donations appropriately, taking into consideration other equally important healthcare needs in a crumbling healthcare system.

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