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RAPID REPORTS

Is Coronavirus disease (COVID-19) case fatality ratio underestimated?

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Abstract

The number of cases of coronavirus disease (COVID-19) is increasing rapidly and case fatality ratio (CFR) is estimated to be around 2 to 3%. However, the epidemic is still ongoing and the outcome of many sick cases of COVID-19, particularly the outcome of severe cases, is not yet available, which may lead to underestimation of CFR. This was observed during the initial phase of severe acute respiratory syndrome coronavirus (SARS-CoV) outbreak as well, where CFR increased with the passage of time. We estimated the CFR of COVID-19 by extrapolating the data using SARS as an analogy. According to our estimates, the actual CFR of COVID-19 may be around 4.4 to 4.8%. However, these results should be interpreted with cautions as we did not adjust for many confounding factors. Various epidemiological and modelling techniques can be used to estimate CFR of COVID-19 during the epidemic. Precise estimates of CFR will be available after the end of the epidemic when the outcome of all cases will be available.

Introduction

A novel coronavirus (SARS-CoV2) emerged in Hubei province in China in December 2019 and as of 3rd March 2020, more than 90,000 cases and 3100 deaths have been reported from 72 countries (1). Most of the cases and deaths are reported from China; however, the number of cases and deaths are rapidly increasing in South Korea, Italy and Iran. More new cases are now being reported outside of China compared to inside China. More than 80% of cases are mild and aged between 30 to 79 years (2). Around 15% of cases are categorised as severely ill and 5% are categorised as critically ill. Case fatality ratio (CFR) is estimated to be 2.3% (3)- around 2.8% for males and 1.7% for females (2, 3). However precise estimates are not available due to presence of asymptomatic cases and unavailability of the outcome of existing severe cases with long duration of hospitalisation. Mortality is reported to be higher among older people and very low in young children. CFR is higher in critically ill people (~50%) and also in people with pre-existing medical conditions (3).

Many epidemiological and clinical characteristics of novel coronavirus (SARS-Cov2) are similar to the SARS-CoV virus (4) which emerged in 2002 from Guangdong province of China and caused more than 8000 cases and 800 deaths (5). Both are of zoonotic origin (likely bats) and spread via droplet and direct contact modes. However, CFR of SARS was much higher compared to the reported CFR of COVID-19 (6). This study aimed to estimate the CFR of COVID-19 by extrapolating the data using SARS as an analogy.

Methods

We collected data of COVID-19 and SARS from situation reports of the World Health Organisation (WHO) (1, 7). Daily data (wherever possible) on the number of cases were extracted from the individual reported and entered in an excel sheet. Data was plotted from the day (1st day of the epidemic) when WHO reported the epidemic and released the first situation report. The CFR was calculated by dividing the total number of deaths with the total number of cases. The CFR of COVID-19 was estimated by extrapolating the data, using SARS as an analogy. A graph was prepared using an excel tool and projection line was drawn using linear functions.

Results

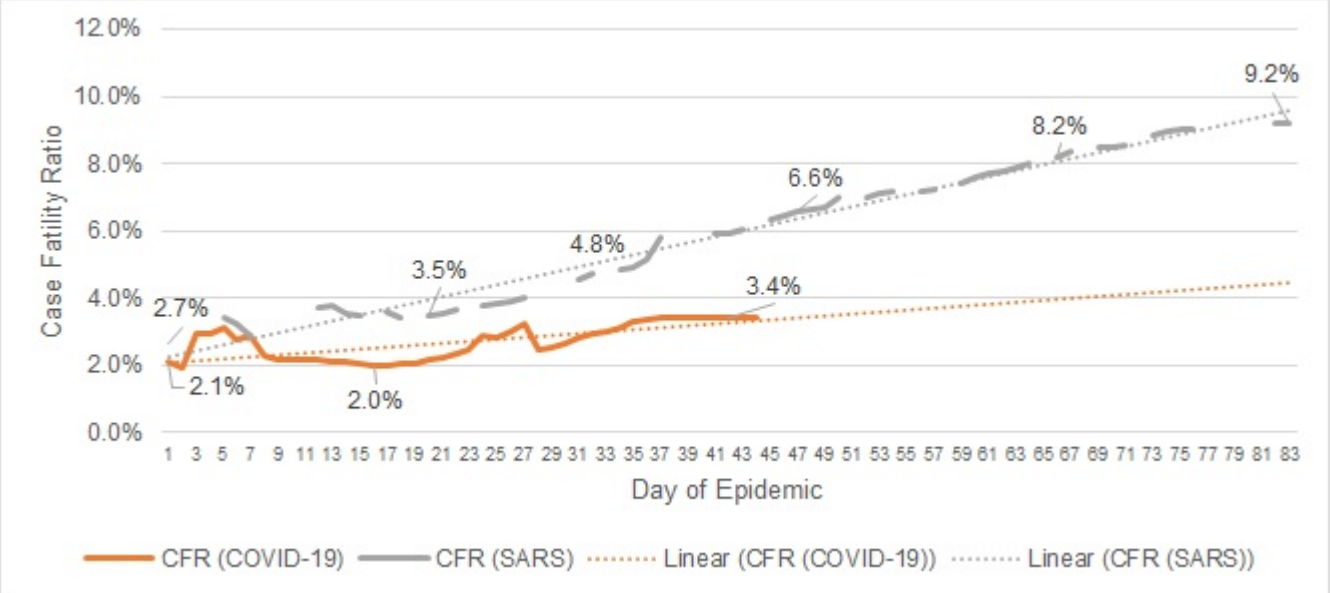
The first situation report on SARS on 15 March 2003 reported 150 cases and 4 deaths (CFR 2.7%). The CFR increased from 2.7% in March 2003 to 6.6% by the end of April 2003 to 9.2% by the end of the epidemic in June 2003. Most cases of SARS were reported from mainland China where CFR increased from 1.6% in March 2003 to more than 6% in June 2003 (Figure 1). In Hong Kong, the initial CFR reported in March 2003 was 3.8%, which increased to 5% in April 11% in May and around 17% in June 2003.

According to the first situation report by the WHO, 282 cases and 6 deaths (CFR 2.1%) were reported due to COVID-19 on 21 January 2020. CFR gradually increased to 3.2% on 16 February and then decreased to 2.5% on 17 February when the WHO changed the case definition and started reporting all confirmed cases, including both laboratory confirmed as previously reported, and those reported as clinically

diagnosed (currently only applicable to Hubei province, China). However, CFR again started climbing and by 1 March 2020 reached 3.4% (Figure 1). Most cases of COVID-19 are reported from China where initial CFR was reported to be 2.2%. As global CFR of COVID-19 is influenced by the China data, the same trends were observed in the CFR in China. At the start of the epidemic, CFR in China was around 2% and current CFR (as of 5th March 2020) is 3.7%. CFR in South Korea was 0% till 19th February 2020 and increased to 0.6% by 5th March 2020. Similarly the CFR was 0% in Australia till 1st March (25 cases, no death) and increased to 3.8% by 5th March (52 cases and 2 deaths (8).

Based on current projections, the actual CFR of COVID-19 may be from 4.4% (overall projection) to 4.8% (projection after changing case definition). The WHO situation reports presented data of severe cases from 21 January to 12 February 2020 and according to this data, the proportion of severe cases among the total cases was from 13% to 18% (1). The number of severe cases (including critical cases) under treatment is not known.

Figure 1. Case fatality rates of SARS and COVID-19 over the epidemic period



Discussion

We showed that the current definition of CFR may be underestimating the CFR of COVID-19 and magnitude of the epidemic when the number of cases are still being reported and the epidemic is ongoing. The outcome of sick cases, particularly the outcome of severe cases is not available, which may lead to underestimation of the CFR. According to our calculations, given that the duration of COVID-19 epidemic is the same as SARS, the CFR of COVID-19 will be around 4.4 to 4.8% . However, these results should be interpreted with cautions as we did not adjust for many factors such as the number of cases under treatment, existing proportion of severe cases, mortality rate among the severe cases and under-reporting due to asymptomatic infections. Precise estimates of CFR will be available after the end of epidemic once the outcome of all cases will be available.

This problem was faced during the SARS epidemics as well when initial CFR was low (2.7%) compared to the final CFR (9.6%) (1, 6). The WHO proposed a method to calculate the CFR using only those cases whose final outcome (i.e. died or recovered) is known (9). According to this method revised estimates of CFR in Hong Kong, Singapore, Canada, and China were quite close to what was finally reported by the end of the epidemic. Therefore, we propose that during the epidemic, CFR should also be calculated using only those cases whose outcome is known. This will give a higher value of CFR but will give a true estimate of CFR to plan for the surge capacity.

This analysis also explains why current CFR in China (3.7%) is higher compared to outside China (1.7%) (1). The epidemic started in China and the outcomes of some of the severe (including critical cases) are available now. Large epidemics in other countries have recently started and the outcomes of most of the severe cases are not yet available. Once the outcomes of all severe and critical cases in China and other countries become available, the overall CFR may also increase. Current estimates show that the proportion of severe case is around 15% and the proportion of critically ill cases is around 5% (3, 10). For example, as of 5th March 2020, out of a total of 52 reported cases in Australia, 22 have been recovered and 2 died (8)- the outcome of 28 cases is yet not available. Current CFR is 3.8% (2/52), which is expected to increase once the outcome of the remaining 28 cases become available.

Current CFR of COVID-19 would be much higher if COVID-19 case definition had not been changed

during the mid of epidemic. The initial case definition of COVID-19 included pneumonia but later mild cases were also included which resulted in a decrease in overall CFR. Precise estimates of CFR will be available after the end of the epidemic when the outcome of all cases will be available. However, even those estimates may not be correct, as in contrast to SARS-CoV, the new SARS-CoV2 replicates efficiently in both upper and lower respiratory tract (4). Due to many cases with an upper respiratory infection, many cases are mild and asymptomatic (3, 10), resulting in low overall CFR (2, 11). Large scale epidemiological and modelling studies should be conducted to estimate actual CFR during the epidemic.

There are limitations of this study. First, we did not adjust for many confounding factors, for example, the number of cases undergoing treatment, the existing proportion of severe and critical cases among those who are not yet recovered, the mortality rate among the severe cases and under-reporting due to asymptomatic infections. Second, we used publicly available data from the WHO situation reports (1, 7), which may change the proportion, due to the availability of new information. For example, we used data from the SARS epidemic until 5th June 2000 (WHO situation update 74), which reported 8403 cases and 775 deaths (CFR 9.2) (12). A few more cases were reported, confirmed or verified later, resulting in the final number of 8437 cases and 813 deaths (CFR 9.7%) (5). Third, the case definition was changed during the epidemic which may affect these results. To overcome this, we estimated the overall CFR and then CFR after the change in the case definition. Moreover, we also need to examine testing strategies used in various countries during SARS and COVID-19 epidemics. For example, South Korea is testing widely to diagnose mild cases of COVID-19 as well, which may explain low CFR South Korea. In contrast, the US and some other countries are not conducting widespread testing. Finally, in Figure 1 we plotted data from the day (1st day of the epidemic) when WHO reported the epidemic and released the first situation report. So, there is data from 83 days of the SARS epidemic, while in fact the epidemic was much longer than that. We included the period where most of the cases (around >99%) were reported. While extrapolating the data, we used SARS as an analogy and estimated COVID-19 CFR based on 83 days of the epidemic. In reality, the COVID-19 epidemic is expected to last longer than SARS. Precise estimates of CFR will only be available once the epidemic is over and the outcome of all cases is available.

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