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Finding the real COVID-19 case-fatality rates for SAARC countries

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Abstract

The crude case fatality rate (CFR), because of the calculation method, is the most accurate when the pandemic is over since there is a possibility of the delay between disease onset and outcome. Adjusted crude CFR measures can better explain the pandemic situation by improving the CFR estimation. However, no study has thoroughly investigated the COVID-19 adjusted CFR of the SAARC countries. This study estimated both survival interval and underreporting adjusted CFR of COVID-19 for these countries. Moreover, we assessed the crude CFR between genders and across age groups and observed the CFR changes due to the imposition of fees on COVID-19 tests in Bangladesh. Using the daily records up to October 9, we implemented a statistical method to remove the delay between disease onset and outcome bias, and due to asymptomatic or mild symptomatic cases, reporting rates lower than 50% (95% CI: 10%-50%) bias in crude CFR. We found that Afghanistan had the highest CFR, followed by Pakistan, India, Bangladesh, Nepal, Maldives, and Sri Lanka. Our estimated crude CFR varied from 3.708% to 0.290%, survival interval adjusted CFR varied from 3.767% to 0.296% and further underreporting adjusted CFR varied from 1.096% to 0.083%. Furthermore, the crude CFRs for men were significantly higher than that of women in Afghanistan (4.034% vs. 2.992%) and Bangladesh (1.739% vs. 1.337%) whereas the opposite was observed in Maldives (0.284% vs. 0.390%), Nepal (0.006% vs. 0.007%), and Pakistan (2.057% vs. 2.080%). Besides, older age groups had higher risks of death.

Moreover, crude CFR increased from 1.261% to 1.572% after imposing the COVID-19 test fees in Bangladesh. Therefore, the authorities of countries with higher CFR should be looking for strategic counsel from the countries with lower CFR to equip themselves with the necessary knowledge to combat the pandemic. Moreover, caution is needed to report the CFR.

Keywords: COVID-19; SARS-CoV-2; Case Fatality Rates; SAARC; Southeast Asia

1. Introduction

COVID-19 is a highly contagious disease, and the outbreak went global within three months of being first discovered. The disease kept spreading so uncontrollably that even the most adequate healthcare systems worldwide were overwhelmed by it. Developing countries are struggling even more [1]. The nature of the disease forced the world to ask questions about the Case Fatality Rate (CFR) of this disease [2]. CFR is an important readout to understand the pandemic severity, and, in the media, CFR is often used to describe the situation regarding COVID-19 and any other pandemic. However, during a pandemic, CFR can be misleading [3]. The CFR of a disease is the total number of deaths divided by the total number of cases, i.e., the ratio of fatal cases of a specified condition within a specified time [4]. In CFR calculation during a pandemic, patients might be defined as the total number of confirmed cases, which does not account for the delay between onset of the disease symptoms and outcome, i.e., recovery or death. Therefore, the CFR calculation becomes an underestimate of the actual CFR. By contrast, if we only consider the closed cases where patients have either recovered or died, the real-time CFR estimate remains consistently high throughout [5]. While the crude CFR can give us an approximate idea about the risk of death during the pandemic, it is the most accurate after the pandemic is over [6]. An adjustment to the crude CFR measure can significantly improve the CFR estimates and give us a better idea about the pandemic situation [7].
The Chinese Center for Disease Control and Prevention (China CDC) (2.3%) [8], Lim et al. (approximately 1%-2%) [9] and He et al. (2.72% with 95% CI:1.29%-4.16%) [10] estimated the CFR of COVID-19. However, different geographical areas, such as East Asian and Central European countries, differ in the CFR of COVID-19 [11,12]. A study from April 2020 found that the CFR of COVID-19 in Italy was 10.8%, while in Germany, it was just 0.7% [13]. The variation in preventive measures and government policies can be responsible for this CFR difference [9,14]. For example, about three months into the COVID-19 outbreak, the Bangladesh government inflicted fees on COVID-19 tests on all government labs and hospitals from June 30. Before that, all government-run facilities offered COVID-19 tests for free, and 90% of the whole country's tests were being conducted on government-controlled sites [15]. The imposition of fees on COVID-19 testing made Bangladesh the only country to do so among all South Asian countries. The Bangladesh government's official stance was that fees were inflicted to ensure better management and discourage unnecessary tests. Health Experts in Bangladesh believed the imposition of any fee on Covid-19 tests might increase the outbreak size [16–18]. Furthermore, COVID-19 mortality differences have been observed across age [19–21] and between genders, with female gender associated with better outcomes [22–24]. Comorbidities, obesity, lifestyle, immune system, genetic and hormonal differences between genders can be responsible for the COVID-19 outcomes [25,26].

The CFR difference for different countries, genders, and age groups can provide much-needed information to combatting the pandemic, such as what factors are responsible for speeding up or slowing the outbreak's progression. Moreover, it will give us a better idea about the fatality rate of COVID-19 of the countries of interest. Therefore, it is of the utmost importance to calculate the CFR of a country with a high degree of representativeness, highlighting the importance of calculating adjusted CFR. However, no study has thoroughly investigated the COVID-19 adjusted CFR of SAARC countries, a regional union of eight nations—Afghanistan, Bangladesh, Bhutan, India, Maldives, Nepal, Pakistan, and Sri Lanka. Therefore, this study's objective was to calculate and compare the COVID-19 CFR for SAARC countries adjusted by the disease's

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survival interval and reporting rates. Moreover, we estimated the crude CFR between genders and across age groups for the selected SAARC countries and explored the COVID-19 CFR of Bangladesh before and after the test fees imposition.

2. Material and methods

We collected the daily record of confirmed cases and deaths attributed to COVID-19 of all member countries of SAARC up to October 9, 2020 [27]. Bhutan was not considered in this study since, curiously, no death has been recorded there at all due to COVID-19. We also collected sex and age-specific data from the publicly available source for Afghanistan (up to 9th October) [28], Bangladesh (up to 6th October) [29], Maldives (up to 9th October) [30], Nepal (up to 8th October) [31,32], and Pakistan (up to 9th October) [33]. Unfortunately, publicly available reliable demographic data could not be found for India & Sri Lanka to conduct the sex and age-specific CFR analysis.

Then crude CFR, based on confirmed cases at the time point [t], was calculated as

$$crude\ CFR = \frac{Total\ Number\ of\ Deaths\ [t]}{Total\ Number\ of\ Cases\ [t]} \times 100$$

Then we adjusted the crude CFR value by considering the survival interval of COVID-19. As during any point of an ongoing epidemic, the crude CFR denominator contains the total number of patients, some of whom may fall to their demise due to the disease. The deaths that eventually happen cannot possibly be considered in the calculation of CFR. Therefore, we applied a statistical technique to reduce the bias in the crude CFR calculation. The method thought the uncertainty related to the variability of the interval between disease emergence and death by enabling the survival interval's probabilistic distribution to vary within a wide range.

Initially, given that our observations of the cumulative cases were $\mathrm{C}(0), \mathrm{C}(1), \mathrm{C}(2), \dots, \mathrm{C}(\mathrm{t})$, we maximized the following likelihood function to estimate the growth rate (r) of the COVID-19 outbreak in the selected SAARC countries [34].

$$L(r) \propto \exp\left(-r\sum_{i=0}^{t-1} C(i)\right)\left(1 - exp(-r)\right)^{C(t)-C(0)}$$

Further details regarding the estimation of the growth rate (r) are given in the Supporting Information.

In Monte-Carlo simulations (with 1000 independent replications), Gamma distribution’s moment generating function was used to calculate the correction factor

$$M(-r) = (1 + \frac{r}{b})^{-a}$$

For the adjusted CFR on each calendar day [7,34], the simulation follows the standard procedure presented in the literature. The model parameters are random variables, and in each simulation run, the parameters can take different values according to their distribution functions [7]. Briefly,

the Gamma distribution's mean was 13.59 days, and the standard deviation was 7.85 days (shape parameter: a=2.99, rate parameter: b=0.22) [7,35]. To allow the mean survival interval to vary between 2 to 6 weeks [36,37], the Gamma distribution was sampled from a normal distribution with a mean of 13.59 days and a standard deviation of 2 days. Likewise, the standard deviation was sampled from a normal distribution with a mean and a standard deviation of 7.85 days and one day. Finally, we calculated the adjusted CFR using the following formula:

$$adjusted\ CFR = \frac{crude\ CFR}{M(-r)}$$

Furthermore, assuming 50% lower reporting rates (95% CI: 10%– 50%) of COVID-19 [3,38] due to the asymptomatic cases or exhibition of mild symptoms, we again adjusted the calculated adjusted CFR. The probability of underreporting (u) was sampled from a Beta distribution with the shape parameter a = 10 and scale parameter b = 4 as,

$$u \sim Beta\ (10, 4)$$

for each Monte-Carlo replication. The distribution parameters were selected as such that the daily reporting rates may vary from 10% to 50%. The 95% confidence interval for u was 0.5 - 0.9, while u was drawn in the range 0 - 1. The true incidence (t) was then estimated by:

$$Incidence\ [t] = \frac{Confirmed\ Cases\ [t]}{1 - u}$$

Using the sampled incidence modified for a given probability of low reporting rates, we again estimated the adjusted CFR by fitting a log-normal distribution to the simulated data points [7].

3. Results

Table 1 shows the total number of tests, confirmed cases and deaths, and the confirmation date of the first case of the COVID-19 in the selected SAARC countries. As of October 9, 2020, a total of 7,751,878 confirmed cases of COVID-19, and 120,611 deaths were recorded. India had the highest number of confirmed cases (6,906,151) and deaths (106,490) whereas, Sri Lanka had the lowest numbers (4,488 confirmed cases and 13 deaths) among these countries.

Table 2 and Supplementary Figure S1 show the crude CFR, adjusted CFR (accounted for the survival interval), and further adjusted CFR (also considering reporting rates of less than 50%) of the selected South Asian countries on October 9, 2020. In all three scenarios, Afghanistan had the highest CFR, and Sri Lanka had the lowest. The crude CFR varied from 3.708% (Afghanistan) to 0.290% (Sri Lanka), while adjusted CFR varied from 3.767% (95% CI: 3.714%-3.845%) to 0.296% (95% CI: 0.290%-0.304%). When we further adjusted the CFR considering the underreported cases, the CFR varied from 1.096% (95% CI: 1.068%-1.123%) to 0.083% (95% CI: 0.081%-0.085%). Figure 1 and figure 2 indicate that the CFR’s of Maldives, Nepal, and Sri Lanka were relatively low throughout. For Maldives and Nepal, the CFRs were

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consistent throughout the pandemic period, whereas, for Sri Lanka, CFR considerably decreased over time. In Bangladesh, there was a sharp spike in CFR, which became stable over time.

Table 3 shows the total number of COVID-19 confirmed cases, total deaths, and crude CFR of COVID-19 according to gender. The total number of cases and deaths were significantly higher for the male gender in these countries. Similarly, the crude CFRs for male patients were significantly higher than that of females in Afghanistan (4.034% vs. 2.992%) and Bangladesh (1.739% vs. 1.337%). However, the differences were very narrow in Maldives (0.284% vs. 0.390%), Nepal (0.006% vs. 0.007%), and Pakistan (2.057% vs. 2.080%), where the crude CFRs for females were just slightly higher.

Figure 3 represents the age-specific crude CFR for Afghanistan, Bangladesh, Maldives, Nepal, and Pakistan. A similarity was observed among the different countries when it comes to the CFR across age groups. The older age groups had higher risks of death due to COVID-19. The crude CFR begins to rise significantly around age 40 and upwards. About 13.261% of all infected people aged 60 and above had died in Afghanistan, which was the highest for any age group among SAARC countries. The overall CFR has been very low in the Maldives. Nevertheless, it had a higher CFR (4.835%) for the 60+ age group. Moreover, we found that crude CFR increased from 1.261% to 1.572% after imposing the COVID-19 test fees in Bangladesh (Figure 4).

4. Discussion

Understanding the case fatality rate of the COVID-19 allows policymakers to mitigate the outbreak impact by implementing efficient and effective interventions for disease control. Therefore, in this study, we estimated the adjusted CFR of the COVID-19 outbreak for the selected SAARC countries, i.e., Afghanistan, Bangladesh, India, Maldives, Nepal, Pakistan, and Sri Lanka. To our knowledge, this is by far the most comprehensive estimation for the COVID-19 CFR for these selected countries.

There was a difference in estimated CFRs of SAARC countries. Ranking the nations, we observed the highest CFR in Afghanistan, followed by Pakistan, India, Bangladesh, Nepal, Maldives, and Sri Lanka. The variation can be attributed to the public health system, preparedness, and effective interventions of each country. For example, Sri Lanka has a free public health system and has been ranked 10th on Global Response to Infectious Disease, while Bangladesh is 80th [39].

According to our findings, the survival interval adjusted CFR values were slightly more significant than that of the respective countries' crude CFR. The reason is that during an epidemic, crude CFR estimation becomes an underestimate of the actual CFR [5]. However, there are unreported cases because of both limited tests and asymptomatic or mild patients [40–43]. Therefore, after further adjustment for reporting rates lower than 50%, estimated CFRs became less than one-third compared to crude CFR, and survival interval adjusted CFR.

In agreement with previous studies [44,45], our estimated CFRs for selected countries were lower than most developed countries' CFR. For example, adjusted CFRs in Canada and the

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United States were 1.6% and 1.78%, respectively [7]. The numbers mentioned above are maybe puzzling as South Asia mainly consists of densely populated developing countries. Most of these countries lacked proper preparedness or infrastructure, or medical facilities to fight the COVID-19 pandemic [46]. Moreover, South Asia's COVID-19 testing rate is still meager [47], contributing to the high CFR [14]. Therefore, higher CFR values were expected in these regions.

Several factors, such as temperature and humidity, genetic factors, can be responsible for this CFR variation [12,14,19,48–50]. However, none of these results are confirmed based on appropriate studies, while other studies have contradicted these factors [51,52]. The age structure of a country, an influential factor for the COVID-19 fatality rate [53], can be considered as an explanation of this puzzle. Older people are far more likely to die from COVID-19 [19–21]. On that note, South Asian countries have a higher proportion of younger people than European countries [44] and a lower median age than America and Canada [54,55] and, therefore, results in a lower CFR. Another plausible explanation for lower adjusted CFR can be the lack of valid, reliable, accurate, and complete data surrounding COVID-19 reporting in South Asia. Significant COVID-19 deaths were not recorded in parts of the region, which lowers fatality rates [56,57]. In contrast, developed countries are doing a better job in this regard [58].

According to previous studies, the male gender was a risk factor for more severe COVID-19 outcomes [22–24]. Similarly, we found higher crude CFR values for men relative to women in Afghanistan and Bangladesh. Several reasons have been suggested to explain the sex-differential risk in COVID-19 death, such as better immunological response against viral infections and higher levels of antibodies in women relative to men, and sex-related differences in lifestyle factors (e.g., alcohol, smoking) [25,26]. However, although fewer women have been infected, our estimated crude CFRs for females were slightly higher in Maldives, Nepal, and Pakistan. While the lower case fatality rates in men were undoubtedly unique, a study using Indian patients' data until May 20 estimated CFR among men and women was 2.9% and 3.3%, respectively [59]. Women's median age is significantly greater in these countries, and women outlive men [54]. As older people are more vulnerable to COVID-19 death [12,19,20], this may lead to higher CFR among women.

Moreover, women in this region are more likely to delay seeking appropriate and early care [60]. A higher percentage of women are becoming inactive and have low physical fitness as they age [61]. Furthermore, in contrast with the findings from the early stage of this pandemic, data from the later stages suggests that men and women may equally be developing severe outcomes [62]. Therefore, better gender data is needed for certainty and to support policy decisions. At the same time, medical care should be unbiased towards women.

Consistent with the previous studies [19–21], we observed a typical pattern in these countries, higher CFRs in older age groups. Older patients have a probably weaker immune response [63]. Moreover, the average number of pre-existing conditions (e.g., hypertension, coronary heart disease, diabetes) and body mass index steadily increase as people age [64,65], which makes age a contributing factor to COVID-19 death. We also found that the CFR of the COVID-19 pandemic is less than SARS, MERS, Bird flu, and Ebola [66,67]. However, as it is highly infectious, and there are many mild or asymptomatic cases, public health concerns must be addressed.

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In our estimation, the crude CFR of Bangladesh increased after the COVID-19 test fees imposition to discourage unnecessary tests; therefore, ensure better management. As a result, in the first ten days since the imposition of test fees, there had been a decrease of 8,736 tests in total from the previous 10-day period. More tests can detect more asymptomatic or mild cases, which reduced the mortality rate [12,14]. However, as the decision affected the poor citizen's ability or willingness to test [18], the Bangladesh government decided to cut the test fees by almost half on August 20 [68]. Since the government-imposed price for COVID-19 increases the country's CFR, immediate steps should be taken to remove the fees so that the tests are affordable to everybody.

This study has some limitations too. The first limitation is that the calculated case-fatality rates refer to the countries' entire population. Patients with critical health conditions, populations with a higher proportion of older adults, inadequate resources, and unorganized health care systems can have a higher CFR. [12,69–71]**.** Second, we could not use the country-wise mean survival time of COVID-19 patients for the adjusted CFR estimation. Third, we assumed that there were no age-specific or country-specific differences in under-reporting. The children and youths with mild symptoms are tested less often.

Moreover, factors such as testing capacity, awareness about the importance of reporting symptoms, etc., directly affect the disease's reporting rates [72]. Fourth, we used publicly available data with considerable gaps in reporting sex and age-specific information of all the COVID-19 patients. For example, no publicly available reliable demographic data of COVID-19 patients were found for India and Sri Lanka. So, we were unable to conduct the sex and age-specific CFR analysis for these two countries. Authority should collect, report, and share detailed data to overcome this problem. It is recommended that future research on similar issues should consider improving on these limitations.

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5. Conclusion

Survival intervals, gender, and ages of the patients and many underreported cases affect the CFR estimation, therefore affecting the countries' policies. In this regard, the gender and age-specific bias-adjusted CFR measure can provide better information to health professionals and policymakers. Therefore, age, gender, survival interval, and underreported cases should be considered while calculating COVID-19 CFR. All these findings will equip us with a much better knowledge of the COVID-19 scenario worldwide.

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Conflict of interest statement

The authors declare that there are no conflicts of interest.

Author contributions

Md. Rafil Tazir Shah: Data curation, Formal analysis, Software, Visualization, Writing - original draft. **Tanvir Ahammed**: Conceptualization, Methodology, Data curation, Visualization, Supervision, Visualization, Writing- Original draft, Writing - review & editing. **Aniqua Anjum**: Writing- Data curation, Original draft. **Anisa Ahmed Chowdhury**: Writing- Original draft. **Afroza Jannat Suchana**: Writing- Original draft.

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Table 1

Overview of the COVID-19 (up to 9 October 2020) situation in the selected SAARC countries.

Country	First Confirmed Case	Total Tests	Confirmed Cases	Deaths	Population
Sri Lanka	28 January 2020	313813	4,488	13	21,413,250
Maldives	08 March 2020	164326	10,742	34	540,542
Afghanistan	25 February 2020	134258	39,693	1,472	38,928,341
Nepal	25 January 2020	1131958	98,617	590	29,136,808
Pakistan	27 February 2020	3795287	317,595	6,552	220,892,331
Bangladesh	09 March 2020	2042376	374,592	5,460	164,689,383
India	30 January 2020	84634680	6,906,151	106,490	1,380,004,385
Total			7,751,878	120,611	1,855,605,040

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Table 2

Crude CFR, Adjusted CFR, and Adjusted CFR considering underreporting for selected SAARC countries.

Country	Crude CFR	Adjusted CFR (95% CI)	Adjusted CFR considering reporting rates of less than 50% (95% CI)
Sri Lanka	0.290%	0.296% (0.290, 0.304)	0.083% (0.081, 0.085)
Maldives	0.316%	0.325% (0.317, 0.337)	0.093% (0.090, 0.095)
Nepal	0.598%	0.626% (0.601, 0.664)	0.182% (0.178, 0.187)
Bangladesh	1.458%	1.492% (1.462, 1.540)	0.422% (0.411, 0.432)
India	1.542%	1.601% (1.548, 1.684)	0.455% (0.444, 0.467)
Pakistan	2.063%	2.100% (2.068, 2.152)	0.586% (0.571, 0.602)
Afghanistan	3.708%	3.767% (3.714, 3.845)	1.096% (1.068, 1.123)

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Table 3

Total Cases, total deaths, and crude case fatality rates of COVID-19 by gender in Afghanistan, Bangladesh, Maldives, Nepal, and Pakistan.

nder	Country														
	Afghanistan			Bangladesh			Maldives			Nepal			Pakistan		
	Total Cases	Total Deaths	Crude CFR	Total Cases	Total Deaths	Crude CFR	Total Cases	Total Deaths	Crude CFR	Total Cases	Total Deaths	Crude CFR	Total Cases	Total Deaths	Cru CF
ale	27295	1101	4.034%	266495	4635	1.739%	7392	21	0.284%	64784	394	0.006%	235211	4838	2.05
male	12398	371	2.992%	103637	1386	1.337%	3334	13	0.390%	2[illegible]029	168	0.007%	82384	1714	2.08

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HIGHLIGHTS

Scientific question

Survival interval and reporting rates adjusted CFR measure can give us a better idea about the COVID-19 severity. However, adjusted, age and sex specific CFRs for SAARC countries have not been thoroughly investigated.

Evidence before this study

Adjustments to the crude CFR measure can better explain the pandemic situation by improving the CFR estimation. Therefore, several studies evaluated adjusted CFRs for developed countries. As different geographical areas differ in the COVID-19 CFR, broader studies are warranted to estimate CFRs for SAARC countries.

New findings

We found that CFRs for selected SAARC countries were lower than most developed countries' CFR. Among these SAARC countries, Afghanistan had the highest CFR, followed by Pakistan, India, Bangladesh, Nepal, Maldives, and Sri Lanka. Moreover, we found higher crude CFR for men relative to women in Afghanistan and Bangladesh. However, CFRs for females were slightly higher in Maldives, Nepal, and Pakistan.

Significance of the study

Our estimates provide a more accurate picture of the COVID-19 mortality in SAARC countries and suggest that age, gender, survival interval, and underreported cases should be considered while measuring virulence and disease burden of COVID-19.

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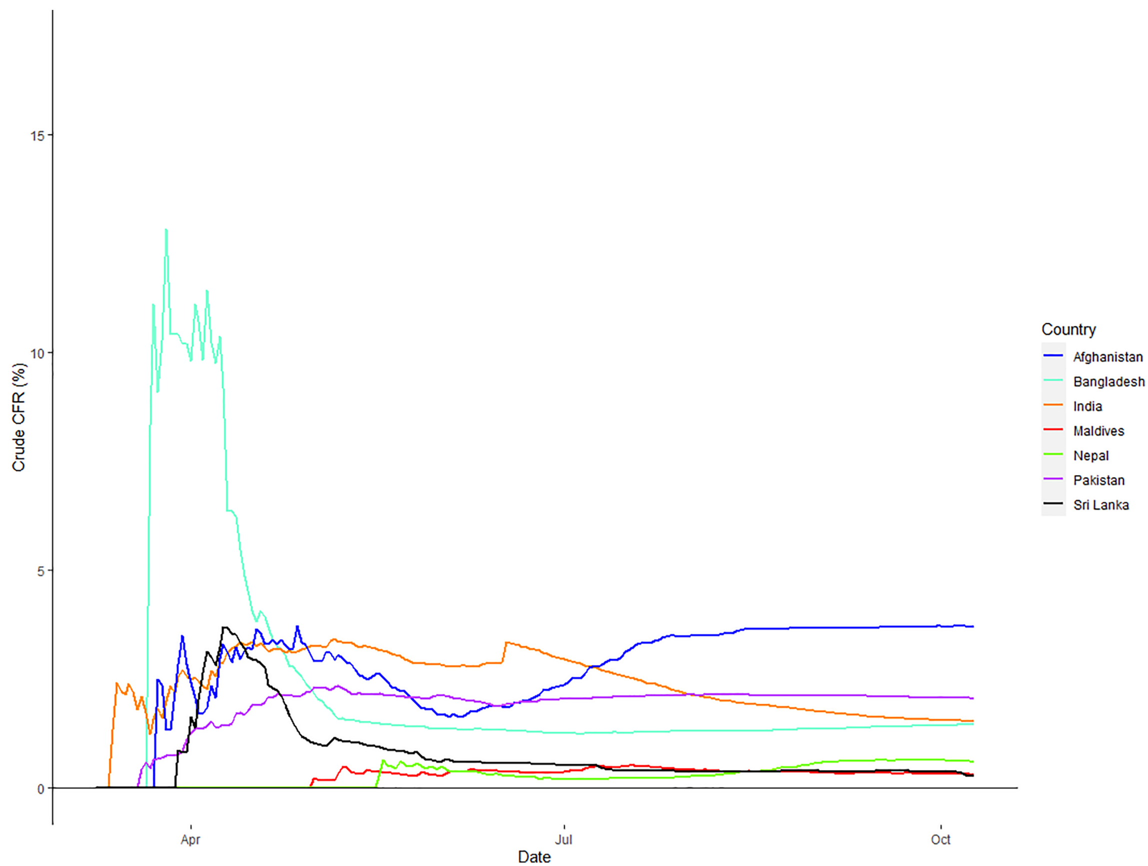


Figure 1

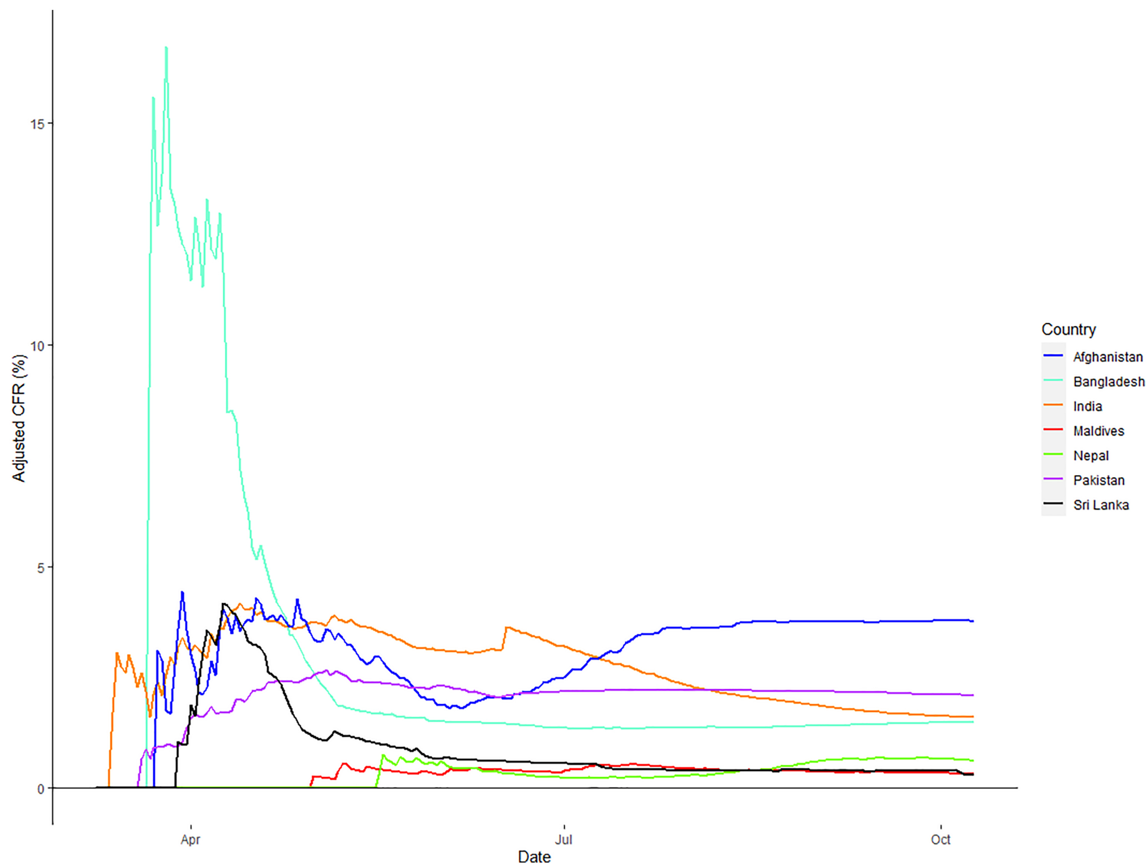
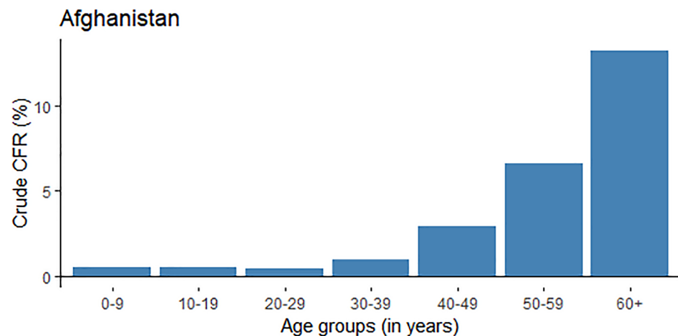
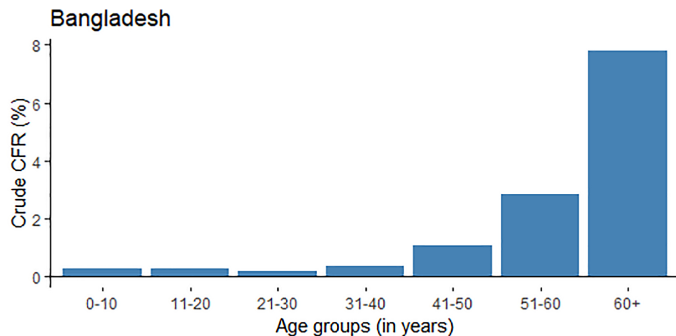
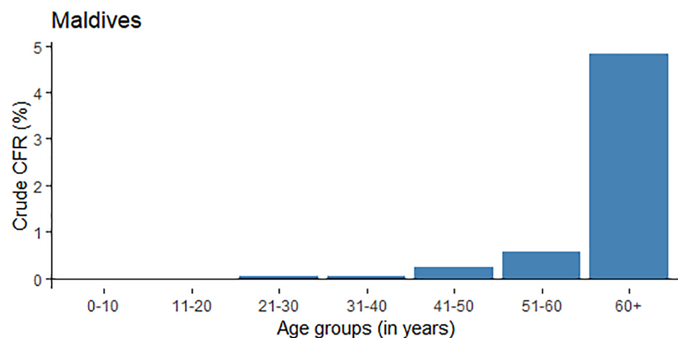
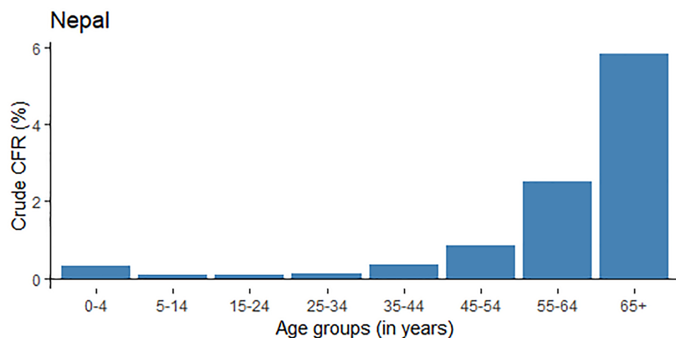


Figure 2









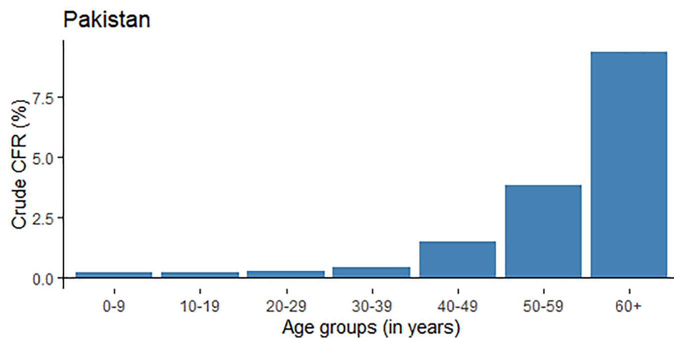


Figure 3

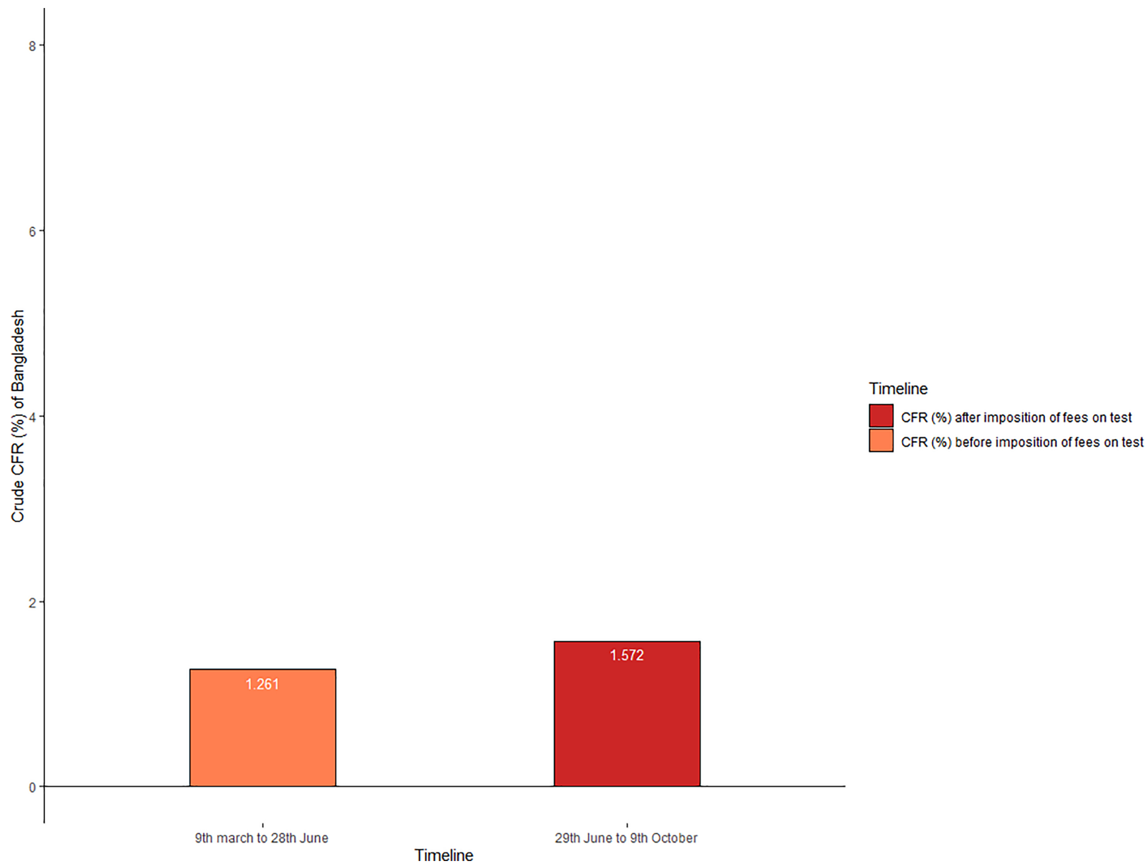


Figure 4