Surging COVID-19 in Bangladesh driven by B.1.351 variant

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Abstract
A dramatic resurgence of COVID-19 cases and deaths in Bangladesh in March 2021 occurred together with a sharp rise in frequency of the SARS-CoV-2 B.1.351 (501Y.V2) variant of concern. Concurrent increases in detected COVID-19 reinfections and the effective Reproductive number, R_t, despite reported high levels of prior infection in Dhaka city, suggest that resurgence was driven by the B.1.351 variant. These data support the prediction that protection from past infection is lower for re-infection with the B.1.351 variant, and highlight the major public health concern posed by immune escape variants, especially in populations where vaccination coverage remains very low.

Main

In recent weeks Bangladesh has experienced a rapid and unprecedented increase in reported COVID-19 cases and deaths (Figure 1). Most cases in March 2021 were reported from Dhaka and Chattogram (70% and 10% of 65,000 total), where >13% of the population resides, but 56/64 districts are now showing exponential growth.[1] On the current trajectory, COVID-19 deaths in April 2021 will far exceed the 2020 peak.

Sequenced viruses from Bangladesh in 2021 have been dominated by variants of concern that are associated with higher transmissibility and disease severity and potential for immune evasion.[2] The variant B.1.1.7 (20I/501Y.V1) that emerged in the UK was first detected in Bangladesh on 31 December 2020. The variant B.1.351 (20H/501Y.V2) that emerged in South Africa was first detected in Dhaka on 24 January 2021, followed by two more cases of B.1.351 collected from distant geographic locations in Bangladesh in late February.[3] By the end of March the frequency of B.1.351 reached 73% (95%CI: 52-87%, 16/22 sequences)[4] contemporaneous with the increased cases and deaths.

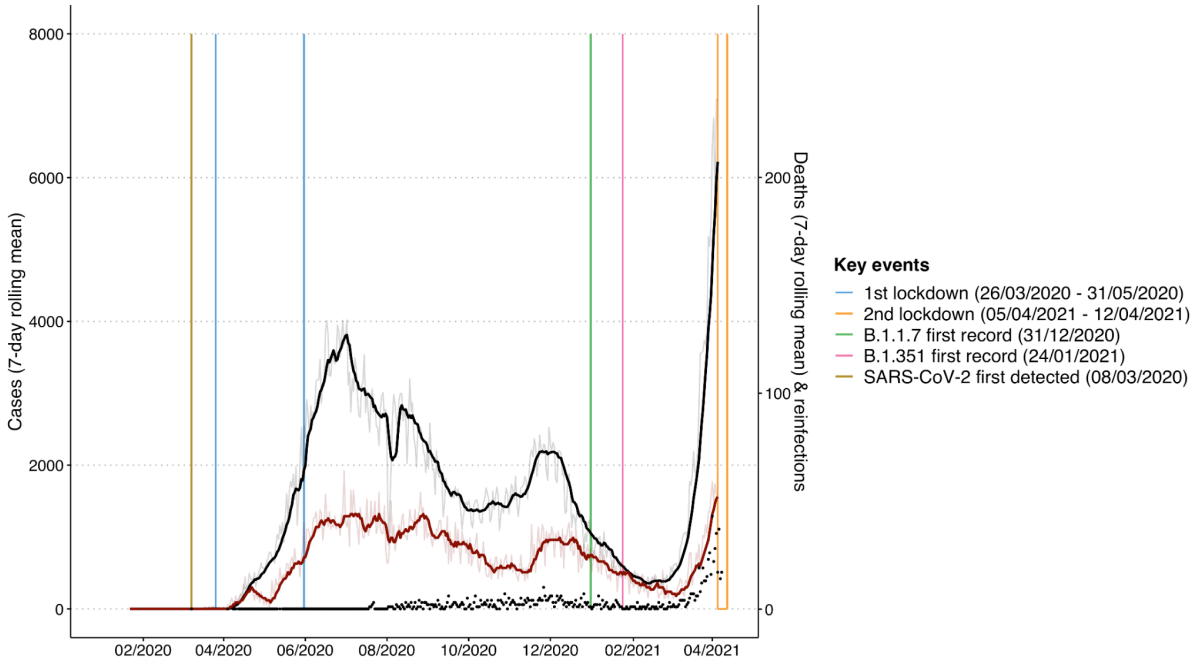

Figure 1. Time series of recorded cases, deaths, and identified reinfections in Bangladesh and first detection of variants of concern. Case numbers are presented on the left y-axis and deaths and identified reinfections (black dots) on the right. Both cases and deaths are summarised as a 7-day rolling mean, with daily raw values shown with reduced transparency. Key points annotated include the first detection of SARS-CoV-2, the two periods of lockdown and first detection of variants of concern B.1.1.7 and B.1.351. Data from John Hopkins University (coronavirus.jhu.edu/map.html), nextstrain[4], the MIS, DGS Covid-19 dashboard[1] and the a2i data warehouse.

The B.1.351 variant is notable for multiple substitutions in the receptor-binding area of the spike protein.[5] B.1.351 is considered an escape variant from neutralizing antibody immunity developed through natural infection.[6] The B.1.351 variant is reportedly less sensitive or even insensitive to sera from convalescent individuals and recent vaccine recipients.[7–9] These laboratory studies suggest that the B.1.351 variant will cause reinfections in individuals who

have recovered from infections with previously circulating lineages. Critically, these findings may explain the escalating numbers of reinfections identified in Bangladesh (Figure 1) and their correspondence to the rise of B.1.351 detection, warranting genomic follow-up to ascertain the variants responsible, their distribution and prevalence.

The Astra-Zeneca vaccine appears efficacious in protecting against severe infection from the B.1.351 variant, but does not confer protection against mild and moderate infection.[10] Limited data are currently available on clinical characteristics of this variant. Several reports raise concerns about the degree to which vaccines may block transmission of B.1.351.[6,8] Six million Astra-Zeneca vaccine doses have been administered in Bangladesh since early February,[11] almost all as first doses, covering just 3.5% of the population. Irrespective of vaccine impacts on transmission, these vaccinations, at current coverage levels, are expected to have only minimal impact on reducing severe disease and deaths during the current wave.

A critical question is what properties of B.1.351, if any, underlie Bangladesh's resurgence. Several lines of evidence suggest that a large proportion of the Dhaka population were infected by COVID-19 in 2020. Bangladesh's 513,510 recorded cases in 2020 underestimates total cases, as testing was initially restricted to the national laboratory, and like most countries, focused on symptomatic testing. Additionally, surveys in Dhaka city from April-June 2020 (prior to the peak) found point prevalence of almost 10% and seroprevalence of 45%, reaching 74% in slums.[12] For reasons that remain unclear, case fatality rates in 2020 were fortuitously low, but healthcare capacity was still stretched at the peak. The age patterns of deaths and hospitalizations in 2021 need comparing to 2020 to assess whether B.1.351 causes more or less severe disease, particularly in lower age groups.

A combination of non-pharmaceutical interventions (NPIs) and naturally-acquired immunity likely contributed to prior declines in cases (Figure 1). The basic reproduction number (R_0) for SARS-CoV-2 in Bangladesh was estimated at 3.4 prior to lockdown measures which were initiated 18 days after the country's first confirmed case.[13] In that period masks were mandated[14] and community-level NPIs began. By early 2021 overall test positivity reached a low of <4% (27 January 2021, Figure 2C).[1] However, by late January 2021 mobility levels within the general population were higher than pre-pandemic levels[15] and a decrease in mask-wearing was observed coinciding with vaccination announcements.

The reproduction number (R_t) in Bangladesh remained near 1 throughout 2020 but rose to almost 2 in March. Although relaxation of NPIs may have facilitated this growth, the introduction and rapid growth of B.1.351 raises the worrying possibility that immune escape has played a role. Resurgence of previously dominant variants is not evident, presumably limited by herd immunity of around 65-75%. In contrast, we found more support for lower protection against B.1.351 (~25%), more in line with laboratory studies. From calibrating an SEIR model to 2021 COVID-19 death data we estimated R_0 of 3.5 for B.1.351[13], explaining the increased R_t. However, the precision and range of our R_0 estimate for B.1.351 (2.3 to 6.5) is subject to uncertainties in the extent of prior infection and degree of protection conferred.

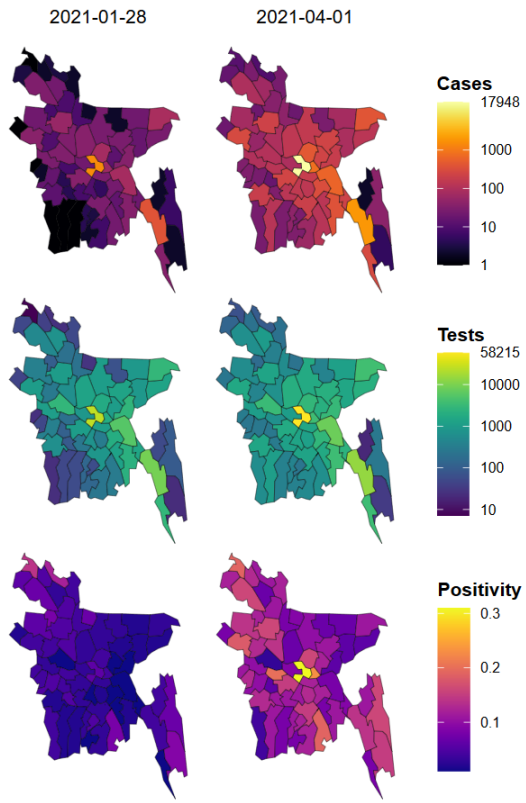

Figure 2. The spatial distribution of weekly cases, testing and test positivity across Bangladesh districts when B.1.351 was first detected on 27 January and by 1 April 2021. Cases and test numbers represent the cumulative count for that given week. Positivity was calculated as the ratio between the weekly cases and tests.

In the absence of immunity from mass vaccination and with the next tranche of vaccines possibly delayed,[16] urgent measures are needed to minimize the potentially devastating impacts of the current surge. The Bangladesh government recently announced a more strictly enforced second lockdown offering a window for strengthening the response.[17] To limit transmission national and social media communications amplified by community-level advocacy for staying home and wearing masks should be linked with mass mask distribution beginning in the most densely populated areas. Oxygen supplies need reassessing and triage practices need review to ensure prioritization of hospital resources that are already approaching capacity.[1] Personnel, transport, and procurement need reinforcement to secure diagnostic and surveillance capacity as daily tests are saturating at >30,000/day, sample-to-reporting delays are increasing with test volumes and overall test positivity now exceeds 30% (Figure 2).[1] Vaccine import needs expediting.

Genomic and epidemiological evidence from Bangladesh highlights the threat from immune escape in populations where vaccination coverage remains negligible and serves as forewarning for other densely populated countries. We emphasize the importance of genomic surveillance and timely sharing of information for effective response to the changing epidemiological situation around the world.[18]

Methods

Data on SAR-CoV-2 variants were downloaded from the Bangladesh-build[3] from nextstrain[19] and on COVID-19 cases, deaths and vaccinations using the coronavirus[20] and tidycovid19[21]

packages in R.[22] Data on reinfections, defined as confirmed rt-PCR positive tests collected from the same individual more than 90 days apart, were extracted from the a2i data warehouse. R*t* and 95% confidence intervals were estimated over the course of the epidemic and for the B.1.351 variant using the EpiEstim function[23]. We estimated R*t* for the B.1.351 variant in two ways: 1) assuming that B.1.351 infections matched the variant's daily interpolated frequency, accounting for the small numbers of sequenced cases, and 2) by assuming recorded reinfections were due solely to B.1.351 since first detection. We recalibrated an SEIR model to the daily confirmed COVID-19 deaths in Bangladesh, tuning to starting numbers of cases in January 2021 and examining across a range of levels of prior immunity. Full details on https://github.com/boydorr/BGD_Covid-19.

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