The second wave of COVID-19 in South and Southeast Asia and vaccination effects

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Research Article

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Abstract

**Background** By February 2021, the overall impact of the coronavirus disease 2019 (COVID-19) in South and Southeast Asia had been relatively mild. Surprisingly, the second wave in early April 2021 in this region becomes devastating and attracts worldwide attention.

**Methods** We focus on the nine countries with the highest accumulative deaths due to the disease by July 30, 2021. We study the transmission dynamics of the COVID-19 in South and Southeast Asia using the reported death data and fit into a mathematical model with time varying transmission rate.

**Results** We estimated the transmission rate, the infection fatality rate, and the infection attack rate, the effects of vaccination in the nine countries in South and Southeast Asia. Our study suggests that the infection attack rate is still low in most of the countries and vaccination is needed to prevent further waves.

**Conclusion** The implementation of the non-pharmacological interventions (NPIs) could have helped South and Southeast Asia to keep the COVID-19 under control in 2020 as reflected in our estimated low transmission rate. Factors like the emergence of the new Delta variant, social unrest, and migrant workers could have been the trigger of the second wave of COVID-19.

**Trial registration.** NA

Introduction

The Coronavirus Disease 2019 (caused by SARS-CoV-2) attacked the world with an unexpected way in 2019 and changed human life tremendously [1]. The SARS-CoV-2 virus is transmitted via respiratory droplets with an incubation 2–14 days [2]. Symptoms includes light infection of fever, cough, and shortness of breath, to severe infections that patients may require intensive care or the support of ventilators [2]. Ever since the world Organization (WHO) declared the disease a pandemic on March 11, 2020 [3], there are 199.67 million confirmed cases worldwide and more than 4 million deaths reported [4] by August 4, 2021.

The pandemic of COVID-19 in South and Southeast Asia has been mild in 2020 compared to other hot spots of the world like Europe or North America. However, the appearance of the new variants of concern (VOC), changes the pandemic dramatically in South and Southeast Asia with a sudden increase of cases in many countries in this region [5]. For instance, the COVID-19 in Singapore, Vietnam, and Malaysia had been well controlled at the earlier stage of the pandemic with the usage of non-pharmacological interventions (NPI) [5] and later the vaccination champion. But the emergence of the new VOC has reversed the trend and caused a new wave of infection. Since April 2021, South and Southeast Asia have been plagued by a new, more contagious Delta variant of COVID-19, which was first reported in India in October 2020 [6]. According to [6], the new variant was one of the main factors accounts for the ongoing wave of COVID-19 in South and Southeast Asia.
The Delta variant causes an increasing crisis in Indonesia as well as other countries in the nearby region [7–8] (see Fig. 1). By August 18, 2021, Southeast Asia has been fighting with the world’s highest COVID-19 death toll which is caused by VOC but enhanced by the relative low coverage of vaccines [9]. Based on the survey [10] by the Indian Council of Medical Research (ICMR), around 21.4% of 28,589 adolescents participants had been infected by February 4, 2021. Another serological study [11] found that the prevalence of IgG antibody (indication of past infection) to SARS-CoV-2 was 11.4% in East Java, Indonesia. A serological study [12] among healthcare workers, in the Kathmandu valley, Nepal, showed a 23% positivity for PCR (polymerase chain reaction) testing. SARS-CoV-2 seroprevalence study [13] indicated that a symptom-based PCR-testing strategy missed 62% COVID-19 diagnoses, and approximately 36% of individuals with SARS-CoV-2 infection were asymptomatic. These serological studies found a much higher infection attack rate (IAR, proportion of the population being infected) than the estimated IAR based on reported cases. Therefore, these serological studies should be considered in modelling if a reasonable IAR estimation and useful forecast for the pandemic is expected.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Reported the third COVID-19 serum survey conducted by the Ministry of Home Affairs and Government of India at the end of 2020 and January 2021.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time</td>
<td>Place</td>
</tr>
<tr>
<td>2020/12-2021/01</td>
<td>India</td>
</tr>
</tbody>
</table>

In Table 1, the survey involved 70 districts in India. Each district recruited 400 members of the general population (over 10 years old) and 100 healthcare workers. After adjustment for weighting and assay characteristics, for 28,598 serum samples, the sero-positive rate of antibodies against either N protein or S1-RBD protein was 24.1% [20]

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Reported overall prevalence of IgG antibodies against SARS-COV-2 in 1819 subjects between June and December 2020 (see [11]).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time</td>
<td>Place</td>
</tr>
<tr>
<td>2020/06-2020/12</td>
<td>East Java, Indonesia</td>
</tr>
</tbody>
</table>

Due to the limited data on COVID-19 prevalence in Indonesia, there is an investigation into SARS-COV-2 which caused the COVID-19 disease. From June to December 2020, 1,819 participants aged 16 years or older were recruited from Surabaya city. An overall 11.4% prevalence of IgG antibodies against SARS-COV-2 was observed in the subjects. By chi-square test of categorical variables, there is a significant difference in the prevalence of SARS-COV-2 antibodies between working and occupational groups. A
higher prevalence of IgG was detected in laboratory technicians (22.2%) compared with health care workers (6.0%) directly treating COVID-19 patients and other health care workers (2.9%)[21].

Table 3
Reported PCR or serological test results for migrant workers residing in all dedicated hostels in Singapore between 25 March and 25 July 2020.

<table>
<thead>
<tr>
<th>Time</th>
<th>Place</th>
<th>People</th>
<th>Blood serum</th>
</tr>
</thead>
<tbody>
<tr>
<td>2020/03/25-2020/07/25</td>
<td>Singapore</td>
<td>198,320</td>
<td>111,280 residents with a positive PCR or serology result, for an overall infection prevalence of 56.1% with 55.9–56.3% (95%CI).</td>
</tr>
<tr>
<td></td>
<td>Migrant workers</td>
<td></td>
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</tbody>
</table>

As part of the national public health response to COVID-19, PCR and serum tests were conducted on migrant workers residing in all dedicated hostels in Singapore between 25 March and 25 July 2020. This included 43 dormitories with a total population of 198,320 (63.6% underwent PCR testing and 68.4% underwent serological testing). PCR or serological results were positive in 111,280 inhabitants, with an overall infection rate of 56.1% (and 55.9–56.3% of 95% confidence interval) [22].

Method

Mathematical modelling has been successfully used to forecast the trend of COVID-19 and assisted the public health in policy making. This paper uses a simple compartment epidemic model. Our model considers a time-dependent transmission rate since both human behaviors change and the use of control measures can alter the transmission rate of the disease. Other epidemic parameters, like the latent periods and the infection fatality rate, may vary as well. But for simplicity of the model, we choose to focus only on time-varying transmission rate and assume other parameters to be constant.

We choose the model and parameters value from [14] and [15], with the addition of vaccination.

\[
\begin{align*}
\dot{S} &= -\beta SI - vS \\
\dot{E} &= \beta SI - \sigma E \\
\dot{I} &= \sigma E - \gamma I \\
\dot{T} &= \varphi \gamma I - \kappa T \\
\dot{D} &= \theta \kappa T \\
\dot{R} &= (1 - \theta) \gamma I + (1 - \pi) \kappa T + vS
\end{align*}
\]

Here $S$, $E$, $I$, $R$, and $D$ are susceptible, exposed, infectious and recovered/immunized classes, $T$ denotes a delay class between infectious and death classes, $D$ denotes death class. $\beta$ denotes a time-varying
transmission rate which is modelled via an exponential cubic spline. $\sigma$, $\gamma$ and $\kappa$ are rates at which individual loses exposed status and infectious status, $\sigma=0.5$ days, $\gamma = \frac{1}{3}$ days, and $\kappa = \frac{1}{12}$ days. Thus, we have a mean generation time $\left(\sigma^{-1} + \gamma^{-1}\right)$ of five days which is well line with estimates of generation time in all previous studies. The infection fatality rate is $\phi \theta$, which cannot be estimates simultaneously with only death data. We fix $\phi$ and estimates $\theta$. $\nu$ is effective vaccination rate per capita, when we incorporated this effective vaccination rate, we take into account of a 14-day delay for vaccine to take effect and a uniform vaccine efficacy 85%. We note that our model is the simplest form one can come up for this situation. Given that 7 of the 9 countries have a vaccination coverage (fully vaccinated) less than 20%, thus the effect of the vaccination in these 7 countries would be mild. In Malaysia and Singapore, and especially in Singapore, the vaccination coverage is high, we first fit the model with the vaccination, the we simulate our fitted model without vaccination; thus, we showed the effects of the vaccination campaign. We fixed the number of nodes at 9 for this work. We used the famous R package POMP. The step-by-step description of the usage of this package on epidemiology models can be found here https://kingaa.github.io/clim-dis/parest/odes.html.

We fit a unified model to reported COVID-19 deaths in nine countries in this region. Our study period is from March 12, 2020, to July 30, 2021. We assume the transmission rate to be an exponential cubic spline function spanning for the whole time series. This semi-mechanistic approach of modelling multiple waves of infections has been successfully used in previous epidemic and pandemic.

Results

Using the data from WHO dashboard, Fig. 1 shows the trends of the confirmed COVID-19 deaths and vaccination coverage (including one plus dose and two-dose) of the nine countries (India, Indonesia, Malaysia, Myanmar, Nepal, Singapore, Sri Lanka, Thailand and Viet Nam). These nine countries account for most deaths in South and Southeast Asia [16]. The time range of Fig. 1 is March 12, 2020, to July 30, 2021. Figure 1 shows that the first wave remains at a relatively low level of COVID-19 epidemic when there is no vaccine coverage, while the second wave causes a much higher level of COVID-19 pandemic when certain vaccine coverage is achieved.

In Fig. 2, the SEIHDR (Susceptible-Exposed-Infectious-Hospitalized-Dead-Recovery) model was used to simulated the reported death of COVID-19 for the nine countries in South and Southeast Asia to investigated the dynamics of COVID-19 in this region. The fitting results are used to evaluate the time-varying effective reproduction number $R_0(t)$ and the time varying transmission rate for each country. From Fig. 2, except for Singapore, all other eight countries share a similar pattern: a lower level of first wave and a higher level of second wave of COVID-19 infection. The red circles are the daily reported deaths; the black curve denotes the median of 1000 model simulations; the shaded region denotes the 95% confidence interval (CI) of the 1000 simulations. The green curve shows the simulation median without vaccination. The blue dashed curve denotes the reconstructed time varying transmission rate. The deviation of the green and the black curves illustrates the effects of the vaccination. Sensitivity analysis is provided in supplementary Figure S1-3.
Discussion And Conclusion

Ever since the emergence of COVID-19 in 2019, it occupied the world rapidly (more than 200 countries and territories). South and Southeast Asia countries have implemented the prevention and mitigation strategies to combat COVID-19 pandemic, which includes testing, contact tracing, and the border control [5].

Table 1 shows that the Indian government-initiated serum surveys indicate a 24.1% positivity of serum antibody [20]. In Table2 shows an overall 11.4% prevalence of IgG antibody but the prevalence of IgG in laboratory technicians was much higher than other professions in East Java, Indonesia [21]. The Singapore government tested all migrant workers in dedicated hostels through PCR and serological methods within four months, and obtained an overall infection rate of 56.1% [22].

Figure 1 gives the trends of COVID-19 deaths and vaccination coverage in South and Southeast Asia, and shows that the first wave remains at a relatively low level of COVID-19 epidemic without vaccination coverage, while the second wave attained a much higher level of COVID-19 epidemic with certain vaccination coverage having been done. This counterintuitive observation motivates us to do further investigation by a simple compartment epidemic model to forecast the COVID-19 epidemic in South and Southeast Asia and seek for the potential reasons for this phenomenon.

As it is well noticed that due to the implementation of NPIs, the COVID-19 in South and Southeast Asia had been under control in 2020 [5]. Subsequently, a new wave of COVID-19 pandemic appears in 2021 in this region. The emergence of VOC was believed to be one of the key driving factors for the second wave of COVID-19 in South and Southeast Asia [6]. Except for this common factor, the second wave of COVID-19 also demonstrates some special features varying among countries. For example, multiple factors (a lack of preparations exists national wide, and health and safety precautions poorly implemented or enforced during festivals, sporting events, and state/local elections) could have caused the rapid expansion of the epidemic in India and caused a large number of deaths, and the test positivity has increased dramatically from 2% on March 1 to 22% on May 1 during the period of the second wave in India. In Myanmar, the military coup of February 1st, 2021 brought a threat to the national health and caused healthcare workers and other civil servants to stop working [17]. The second wave in Nepal is worse since it is bordered by India and it has many migrant workers from neighboring countries [18]. In Thailand, a group of young urban upper middleclass people who got infected after visiting night clubs and restaurants at Bangkok during the long weekend. And then the disease spreads to their families and relative and across the whole country quickly [19]. All these particular reasons could have caused the second wave of COVID-19 further worse in South and Southeast Asia. The low infection fatality rate estimated here is due that first we assume that COVID-19 death data are accurate, while in reality deaths are under reported; second the serological studies in these countries suggest a large proportion of the population has been infected. Thus, the infection fatality rate in this work may be regarded as a ratio of infection to reported death, rather than the intrinsic IFR in these countries.
The limitation of this work includes: we assume all parameters are constant except for the transmission rate; the model is for the whole country while we ignore the heterogeneity across age groups and regions. We only relied on the reported death data and adopted a non-mechanistic cubic spline type of transmission rate. Alternatively, one could consider explicitly incorporate all kinds of control measures (e.g., google mobility matrix) into their model and may expect to get more insightful observations on the transmission status of COVID-19 in South and Southeast Asia. This work should be treated as a conceptual simple modelling attempt to estimate the size of the epidemic in this region and the large-scale trend. Our estimated infection attack rate is largely in line with serological studies and we illustrate the effects of vaccination via very simple approach. The real situation of infection fatality rate and vaccination is much more complicated than what we modelled here. Nevertheless, we laid a ground work for further improvement.

**Declarations**

**Consent for publication**

Not applicable

**Availability of data and materials**

All data used in this work were publicly available. We used open source R package, for which detailed instruction is available online.

**Competing interests**

None.

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**Authors' contributions**

DH, HS, and GF conceived the study, carried out the analysis, and wrote the draft. DH, HS, YL and GF discussed the results, revised the manuscript critically, and approved it for publishing.

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None
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References


Figures
Figure 1

Reported confirmed COVID-19 deaths (black curve) in nine countries in SEA and SA, with vaccination coverage all vaccinated proportion (red, partly vaccinated/one plus dose) and fully vaccinated proportion of the population (blue, fully vaccinated/two-dose).
Figure 2

Fitting an SEIHDR model to the reported death in India, Indonesia, Malaysia, Myanmar, Nepal, Singapore, Sri Lanka, Thailand and Vietnam with a time varying transmission rate. The red circles denote daily reported COVID-19 deaths. The black curve denotes the median of 1000 model simulations with vaccination. The green curve shows the simulation median without vaccination. The shaded region denotes the 95% confidence interval of the 1000 model simulations. The blue dashed curve denotes the reconstructed transmission rate. $\Phi = 0.01$ for India; $\Phi = 0.03$ for other countries.

Supplementary Files

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- SupplementalFigures.docx