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Short Communication

Estimation of the true infection rate and infection fatality rate of coronavirus disease 2019 in each country

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ABSTRACT

The True Infection Rate (TIR) in the whole population of each country and the Infection Fatality Rate (IFR) for coronavirus disease 2019 (COVID-19) are unknown although they are important parameters. We devised a simple method to infer TIR and IFR based on the open data. The prevalence rate of the Polymerase Chain Reaction (PCR) tests among the population (Examination Rate; ER) and the positive rate of PCR tests (Infection Rate; IR) for 66 countries were picked up at a website 5 times from April 10th to June 13th, 2020, and the trajectory of each country was drawn over the IR vs. ER plot. IR and ER showed a strong negative correlation for some countries, and TIR was estimated by extrapolating the regression line when the correlation coefficient was between -0.99 and -1. True/Identified Case Ratio (TIR) and IFR were also calculated using the estimated TIR. The estimated TIR well coincided with local antibody surveys. Estimated IFR took on a wide range of values up to 10%; generally high in the Western countries. The estimated IFR of Singapore was very low (0.018%), which may be related to the reported gene mutation causing the attenuation of the viral virulence.

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Coronavirus disease 2019 (COVID-19) pandemic is a worldwide peril. The True Infection Rate (TIR) in the whole population of each country would be an important parameter for guiding the strategy of public health. However, this has only been inferred from local surveys using Polymerase Chain Reaction (PCR) tests or antibody tests [1–4]. The Infection Fatality Rate (IFR) is another important parameter to evaluate the disease severity. However, this is also unknown since TIR is not known. The mortality rate per population has been frequently used instead [5], although this is a product of TIR and IFR and is dependent on TIR. Another similar index, case fatality rate would be greatly influenced by the way of selecting cases [6]. We devised a simple method to infer TIR and IFR based on the open data.

We picked up the data at a website 5 times from April 10th to June 13th, 2020, approximately every 2 weeks [7]. Countries or regions (hereafter called just countries) having more than 1000 cases on April 10th were included. The prevalence rate of PCR tests among the population (Examination Rate; ER) and the positive rate of PCR tests (Infection Rate; IR) were calculated. The trajectory of each country was drawn over the IR vs. ER plot (logarithmic scales for both). We hypothesized that IR and ER are negatively correlated for a specific country because PCR examinations will be restricted to cases with strong suspicion while ER is low, whereas it will be expanded to general population as ER increases. Then, the TIR of a country can be estimated as the IR value at 100% ER by extrapolating the regression line. The ratio of the infected persons in the population to the already identified cases was calculated and named True/Identified Case Ratio (TICR). IFR was estimated using the num-

Abbreviations: COVID-19, coronavirus disease 2019; TIR, True Infection Rate; IFR, Infection Fatality Rate; ER, Examination Rate; IR, Infection Rate; PCR, Polymerase Chain Reaction; TICR, True/Identified Case Ratio; CI, confidence interval; CR, Containment Ratio.

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ber of total deaths on June 13th at the same website [7]. For each parameter, 95% confidence interval (CI) was calculated. All statistical calculation was done using Microsoft Excel for Mac (version 2019; Microsoft Corp, Redmond, WA).

Included were 64 countries. Trajectories of representative countries are shown in Fig. 1. Many countries presented with downward-sloping straight lines, while others show upward-sloping or fluctuating lines. An upward line indicates that IR increases despite expansion of the PCR tests, i.e. the infection has been still spreading during the investigation period. Our estimate would not be applicable to these countries. In contrast, a downward straight line indicates that our hypothesis on the IR-ER relationship is valid for such a country. Close inspection of individual countries reveals that the first point (April 10th) is shifted downward from the line extended from the latter 4 points in several countries (Belgium, USA, UK and Japan). This is probably due to insufficient containment in these countries until middle of April. Because of this, we decided to calculate the regression line from the later 4 points.

The correlation coefficients and the slope values of the regression line for representative countries are listed in Table 1, together with estimated TIR, TICR, and IFR values. Those for all investigated countries are presented in the supplementary table. The correlations were often very high, and we confined the estimation to countries having a correlation coefficient between −0.99 and −1 because the extrapolation would cause a great error unless the correlation is very high. Countries having a slope value close to −1, such as New Zealand, Iceland, or Thailand, are especially noticeable. The slope value of −1 indicates that the number of infected persons remained the same despite expansion of the PCR tests and therefore no patients probably exist in the unexamined population, i.e. the containment has been completely successful. In our preceding study, we defined the Containment Ratio (CR) as the latest value of the new cases during 7 days divided by its highest value, representing the success of containment [8,9]. CR showed a good correlation ($r = 0.784$) with the slope value (Table 1).

The present method has several limitations. First, we cannot estimate TIR or IFR for countries in which the infection is still spreading. Therefore, this method was applicable only when the first wave once subsided in some countries before this article was first submitted (1 July 2020). The infection flamed up again in all countries and the estimation is no more applicable now. Second, the theoretical ground for our key hypothesis (negative correlation between ER and IR) may be obscure. However, the extremely high correlation found in the countries where the pandemic is relatively well controlled supports the validity of our estimate. Many parallel downward-sloping lines in Fig. 1 reflect the wide variety of TIR among countries achieving relatively good containment. TIR is generally higher in European countries than in East/Southeast Asian and Oceanian countries.

Comparing the present results with local surveys at similar periods is interesting. Reported IRs in USA using antibody tests were 1.5–13.9% [1,2], and our estimate of TIR in the whole USA was 2.6%. Regarding Japan, reported IRs using antibody tests were 0.03% to 0.43% [3,4]. Our estimate of TIR was 0.10% although the CI was wide (0.04–0.30) because of the inaccurate extrapolation due to the low ER. The reliability of the antibody test may not be always guaranteed [10], and therefore our methods would have a certain role.

Estimated IFR also took on a wide range of values, generally high in the Western countries, and extremely low in Singapore (0.018%). In Singapore, a gene mutation causing the attenuation of the viral virulence has been discovered [11]. Pandemic might be ended by complete containment or herd immunity. The former, however, has not been successful at present in most countries. Herd immunity
by natural infection would be a long way but that by vaccination is a promising goal. Besides these, attenuation of the viral virulence is another promising way to make the pandemic less damaging [12]. This is achieved in animals by natural selection, but in humans the prevention of in-hospital infection, especially from severe cases, would be the key.

Authors’ contribution

MS and HH designed the whole study. TK, TS, and HH made literature search and review. MS and MI analyzed the data. MK and MS made statistical analyses. MS wrote the first draft and finalized the manuscript, and all co-authors made significant comments and corrections on the draft.

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Conflicting interests

None declared.

Ethical approval

Not required.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.jiph.2021.12.010.

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Table 1

Parameters of the COVID-19 pandemic in representative countries.

| Country or region | Slope | r   | CR | TIR (%) (95% CI) | TICR (95% CI) | IFR (%) (95% CI) |
|-------------------|-------|-----|----|-----------------|---------------|------------------|
| New Zealand       | −1.01 | −0.999 | 0.000 | 0.029 (0.020–0.042) | 0.97 (0.68–1.39) | 1.503 (1.049–2.155) |
| Iceland           | −0.97 | −1.000 | 0.004 | 0.560 (0.553–0.567) | 1.06 (1.04–1.07) | 0.523 (0.517–0.530) |
| Thailand          | −0.94 | −1.000 | 0.030 | 0.006 (0.006–0.007) | 1.36 (1.25–1.48) | 1.360 (1.254–1.476) |
| Australia         | −0.93 | −1.000 | 0.025 | 0.034 (0.034–0.035) | 1.19 (1.17–1.21) | 1.168 (1.147–1.189) |
| Hong Kong         | −0.87 | −1.000 | 0.039 | 0.023 (0.021–0.026) | 1.58 (1.41–1.77) | 0.228 (0.204–0.256) |
| Belgium           | −0.83 | −1.000 | 0.159 | 0.770 (0.702–0.844) | 1.49 (1.36–1.63) | 10.821 (9.870–11.862) |
| Spain             | −0.83 | −1.000 | 0.056 | 0.944 (0.838–1.063) | 1.52 (1.35–1.71) | 6.147 (5.458–6.924) |
| S. Korea          | −0.81 | −0.999 | 0.061 | 0.048 (0.033–0.075) | 2.10 (1.38–3.18) | 1.093 (0.720–1.160) |
| Italy             | −0.80 | −0.999 | 0.094 | 0.667 (0.471–0.944) | 1.70 (1.20–2.41) | 8.506 (6.008–12.044) |
| Germany           | −0.78 | −0.999 | 0.083 | 0.431 (0.301–0.617) | 1.93 (1.35–2.76) | 2.456 (1.717–3.515) |
| UK                | −0.70 | −0.998 | 0.472 | 0.917 (0.602–1.395) | 2.11 (1.39–2.32) | 6.697 (4.400–10.193) |
| Japan             | −0.66 | −0.996 | 0.046 | 0.103 (0.035–0.302) | 7.52 (2.58–21.97) | 0.706 (0.242–2.063) |
| USA*              | −0.47 | −0.999 | 0.646 | 2.599 (2.200–3.070) | 4.01 (3.46–4.74) | 1.367 (1.157–1.614) |
| Iran              | −0.33 | −0.989 | 0.689 |                             |               |                  |
| Canada            | −0.29 | −0.913 | 0.571 |                             |               |                  |
| Indonesia*        | −0.26 | −0.995 | 0.920 | 1.395 (0.783–2.487) | 99.66 (55.90–177.68) | 0.056 (0.031–0.100) |
| Sweden            | −0.18 | −0.918 | 0.816 |                             |               |                  |
| Singapore         | −0.16 | −0.620 | 0.488 |                             |               |                  |
| India             | 0.09  | 0.690 | 1.000 |                             |               |                  |
| Mexico            | 0.13  | 0.935 | 1.000 |                             |               |                  |
| Russia            | 0.17  | 0.999 | 0.800 |                             |               |                  |
| Saudi Arabia      | 0.19  | 0.964 | 0.815 |                             |               |                  |
| Peru              | 0.20  | 0.996 | 1.000 |                             |               |                  |
| Bahrain           | 0.45  | 0.972 | 0.861 |                             |               |                  |
| UAE               | 0.55  | 0.930 | 0.920 |                             |               |                  |
| Brazil            | 0.66  | 0.963 | 1.000 |                             |               |                  |
| Qatar             | 0.67  | 0.984 | 1.000 |                             |               |                  |
| Singapore*        | −0.49 | −1.000 | 0.488 | 2.452 (1.405–4.279) | 3.53 (2.02–6.16) | 0.018 (0.010–0.032) |

Parameters for 27 countries depicted in Fig. 1 are presented. The countries are sorted by the ascending order of the slope value. TIR, TICR, or IFR are not estimated when the correlation coefficient (r) between IR and ER was outside of −0.99 and −0.1. CR was calculated on May 29th, 2020.

CI confidence interval; COVID-19, Coronavirus disease 2019; CR, containment ratio; ER, examination ratio; IFR, infection fatality rate; IR, infection ratio; r, correlation coefficient; TICR, true/identified case ratio; TIR, true infection ratio.

* Estimated parameters may not be reliable because containment is insufficient (CR > 0.5).

* For Singapore, parameters were estimated from the regression analysis of the later 3 points.
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