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Original Article:

Estimating Effective Reproductive Number of COVID-19 in Shiraz, Iran, from April to October in 2021

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Abstract

Introduction: COVID-19 is an infectious disease that was first reported in Wuhan, China, on 31st of December, 2019. After about three years, it is still one of the main health problems all over the world. Interventions to control COVID-19 should be based on epidemiological parameters which describe the dynamics of the disease. The goal of this study is to estimate the reproductive number parameter to understand the speed and dynamics of COVID-19 in Shiraz, Fars province of Iran.

Materials and Methods: 479 cases of COVID-19 were sampled in Shiraz, Iran. Case-pairs of infector-infectees were obtained by brief phone interviews with the patients. Considering time between symptom onsets of the infectors and their infectees as serial interval, best possible distribution was fitted to the serial interval data. To estimate reproductive number, it is assumed that reproductive number is linked to daily incidence and serial interval distribution.

Results: Gamma distribution with mean of 4.610 and standard deviation of 5.746 was fitted on serial interval data. Using this distribution and daily incidence, reproductive number was estimated. The reproductive number values ranged from 0.730 (95% CI: 0.713, 0.747) to 2.181 (95% CI: 2.183, 2.224). These values indicated that there were two peaks in April and May; following the interventions after those peaks, reproductive number values reduced to below 1. Hence, the interventions were effective and successfully managed the outbreak in both waves.

Conclusion: low reproductive number values in some periods of time indicates that preventive measures were effective in Shiraz, Fars province of Iran. In order to control the disease, reproductive number should decrease to below 1 which is happening at the end of the study.

Keywords: COVID-19, Infectious disease, Iran, Machine learning, Reproductive number, Serial interval.

1. Introduction

Coronavirus disease 2019 (COVID-19) is a respiratory infectious disease that was first reported in Wuhan city, Hubei province of China on December 31st in 2019. COVID-19 is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1, 2]. Early studies of COVID-19 have confirmed the human-to-human transmission [3]. The most common symptoms of COVID-19 are fever, cough, fatigue, dyspnea, and sputum [4]. Due to the rapid spread of the disease worldwide, World Health

Organization (WHO) declared COVID-19 situation as a pandemic on March 11th, 2020 [5]. Since the first report of COVID-19 cases in Iran on February 19th, 2020, the number of confirmed cases and deaths due to COVID-19 have also increased [6]. So far, 604,306,622 individuals have been infected and 6,495,135 have died throughout the world [7].

Many interventions and restrictions were established around the world to control the disease. Thus, specific indicators or parameters are needed to assess the effectiveness of interventions [8]. Reproductive number (R) is an important infectious disease parameter for managing outbreaks and understanding the dynamics of the disease. R definition can be divided into two parts including basic reproductive number (R_0) and effective reproductive number (R_t). R_0 is defined as the expected number of cases caused by an individual in an entirely susceptible population. In practice, the entire population is not always susceptible to the disease. Therefor, R_t can be used instead of R_0 estimating the average number of cases caused by an individual in a population including both susceptible and immune individuals [9, 10]. If R exceeds 1, each individual infects more than one person on average and, as a result, the number of cases increases and the epidemic becomes more widespread. In order to control the epidemic, the R value should decrease to below 1 [11]. The value of R_t varies over time, so this study was conducted to estimate R_t from April 4th to October 7th, 2021, in Shiraz, Fars province of Iran. Using these values, we can assess the speed and dynamics of the disease and examine whether the interventions were effective or not.

2. Materials and Methods

There were 169,227 confirmed COVID-19 patients over the six-month period of conducting this study, from April 4th to October 7th, 2021, in Shiraz located in Fars province of Iran. A confirmed COVID-19 patient is a person with a positive result for SARS-CoV-2 virus by real-time reverse transcriptase-polymerase chain reaction (RT-PCR) test. From April 4th, the researchers collected information about patients on a monthly basis from Shiraz Medical University of Sciences. A total number of 479 patients were randomly selected according to the monthly incidence. Then, pairs of primary and secondary cases were found via brief phone interviews with the patients.

In order to estimate R_t, the distribution of generation interval (GI) is needed [9, 11]. GI is defined as the time between infection of primary case (infector) and infection of secondary case (infectee). In practice, however, the exact time of infection is usually unknown. Thus, the serial interval (SI) is used as a proxy for the GI. SI is defined as the time between symptom onset of the infector and symptom onset of Infectee [12]. The best-fitting distribution for SI was extracted from the data using "est.GT" function in "R0" package from R (4.2.1) software. To estimate R_t, it is assumed that R_t is linked to daily incidence I_t and SI:

$$I_t = R_t \sum_{s=1}^{t} I_{t-s} w_s,$$

in which w_s is infectivity profile approximated by SI distribution. R_t can be estimated at time t using past incidence values I_{t-s}:

$$R_t = \frac{I_t}{\sum_{s=1}^{t} I_{t-s} w_s}.$$

"EpiEstim" package from R (4.2.1) software was used to estimate R_t and 95% bootstrap confidence intervals were obtained by 5000 simulations [13].

3. Results

From April 4th, after Iranian new year holiday, to October 7th, 169,227 confirmed cases of COVID-19 were reported in Shiraz based on RT-PCR tests. The plot of daily incidence is shown in Figure 1. The epidemic curve shows two peaks in the study period; the first one after the holidays and the second in the middle of summer.

172 case-pairs of infector-infectees were found to estimate SI distribution. For each pair, the time between system onset of infector and infectee was calculated. Many statistical distributions have been tested (e.g., weibull, log-normal, etc.) and the best fitting distribution on SI data was Gamma with mean of 4.610±5.746 days (See Figure 2).

Figure 3 shows estimated R_t values with 95% confidence intervals. The R_t values range from 0.730 (95% CI: 0.713, 0.747) to 2.181 (95% CI: 2.138, 2.224). The R_t starts with a high number, then becomes stable and fluctuates around 1 toward the end of the study period.

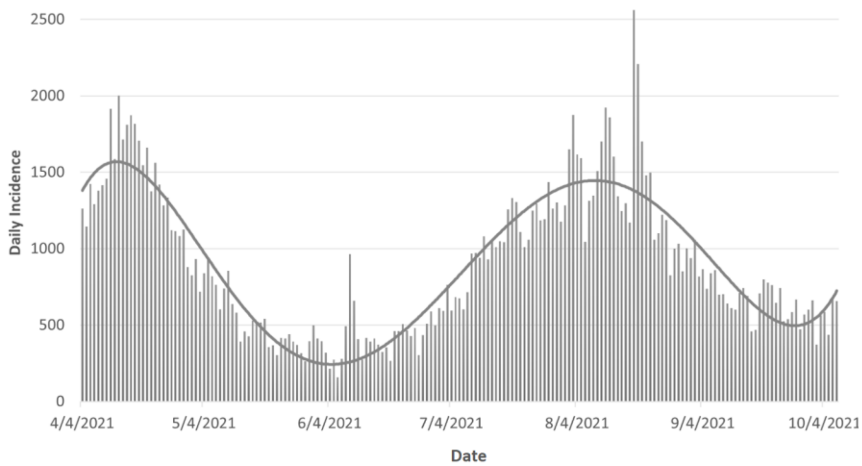

Figure 1. Epidemic curve of COVID-19 from 4th of April to 7th of October in Shiraz, Fars province.

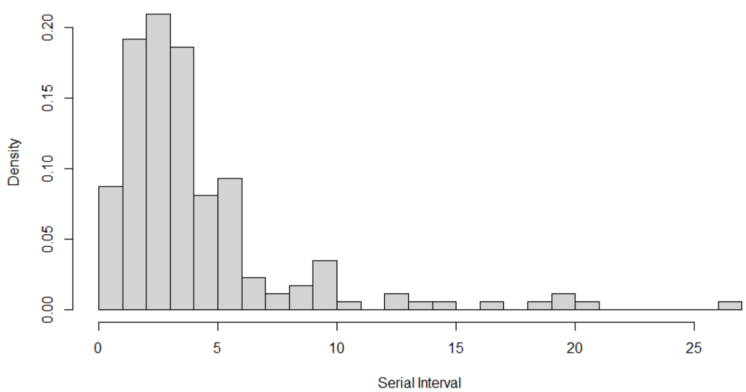

Figure 2. Distribution of serial interval in Shiraz, Fars province.

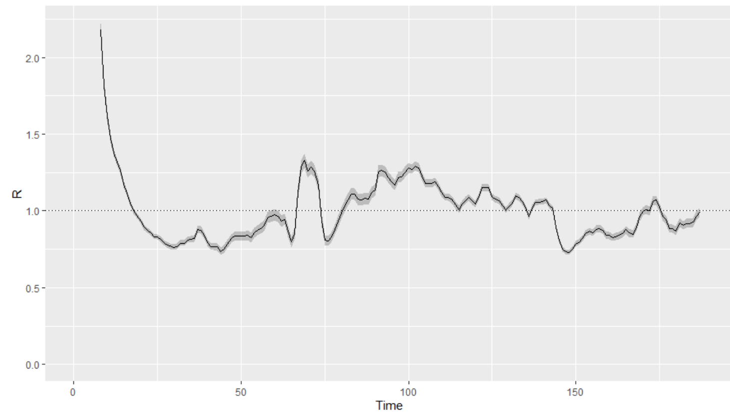

Figure 3. Effective reproductive number (95% confidence interval) of COVID-19 in Shiraz, Fars province.

4. Discussion

It was in late March 2021 (at the end of 1399, based on the Persian Calendar) that COVID-19 in Iran became almost stable. Most of the cities including Shiraz were in “low-risk” and “moderate-risk”, and most of the restrictions were lifted. Hence, many trips were taken during the new year holidays and several businesses were allowed to resume their activity. After that, the number of cases increased rapidly leading to the 4th wave of COVID-19 in April. Hence, the previous restrictions and some new ones were set to control the disease on April 5th. A few months later, the 5th wave of COVID-19 occurred in the middle of the summer. During this time, the restrictions were back again and administration of vaccines became more widespread and faster. Following these interventions, the number of cases decreased gradually after both waves.

From 172 case-pairs of COVID-19 patients, SI distribution was extracted. The best fitting distribution was Gamma distribution with the mean and standard deviation of 4.610 and 5.746 days, respectively. This finding is in agreement with that of other studies that have been conducted in Iran [14-16]. Also, it is in line with two systematic review studies by Ali et al. (2021) and Alene et al. (2021) where they indicated that the SI Mean for COVID-19 to be 1-9.9 and 4.2-7.5 days [17-19]. Differences in estimates of SI for COVID-19 could have many reasons like incompleteness of data or recall bias [19, 20]. Using this distribution, we estimated weekly R_t. R_t started at the high the value of 2.181 at the beginning of the study. After a while, R_t became more stable, but it varied around 1 over the study period. In Figure 3, two peaks in the number of cases can be seen in April and August, as mentioned before. Low R_t values in some period of the study may be an indication of the effectiveness of interventions, e.g., restrictions and vaccination, applied in Shiraz.

5. Conclusion

It can be concluded that preventive measures for COVID-19 in Shiraz, Fars province, were effective because after both peaks, interventions like quarantine, social distancing, and vaccination led to the reduction of R_t to below 1. At the end of the study, R_t values got smaller; this could indicate that COVID-19 was about to be brought under control.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Shahid Beheshti University of Medical Sciences Ethics Committee (IR.SBMU.RETECH.REC.1400.704). We confirm that informed consent was obtained from all patients or their parents (for children under 18 years old). In addition, we confirm that there is no intervention in this study. Also, we can confirm that all the methods used in this study is in accordance with relevant guidelines and regulations of the AAB journal.

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Author's contributions

The roles of the authors are as followed: Soheila Khodakarim and Reza Taherian presented the ideas of the paper, collected and processed the data, supervised the interviews, statistical analysis, interpretation of results. Hamid Alavi Majd and Abbas Alipour revised the manuscript after a thorough examination. All authors have read and approved the final manuscript.

Conflict of interest

There is no conflict of interest in this Paper.

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