Archives of Academic Emergency Medicine. 2024; 12(1): e66

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ORIGINAL RESEARCH

Basic Reproduction Number (R0), Doubling Time, and Daily Growth Rate of the COVID-19 Epidemic: An Echological Study

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Received: May 2024; Accepted: June 2024; Published online: 5 September 2024

Abstract: **Introduction:** In infectious diseases, there are essential indices used to describe the disease state. In this study, we estimated the basic reproduction number, R0, peak level, doubling time, and daily growth rate of COVID-19. **Methods:** This ecological study was conducted in 5 provinces of Iran. The daily numbers of new COVID-19 cases from January 17 to February 8, 2020 were used to determine the basic reproduction number (R0), peak date, doubling time, and daily growth rates in all five provinces. A sensitivity analysis was conducted to estimate epidemiological parameters. **Results:** The highest and lowest number of deaths were observed in Hamedan (657 deaths) and Chaharmahal and Bakhtiari (54 deaths) provinces, respectively. The doubling time of confirmed cases in Kermanshah and Hamedan ranged widely from 18.59 days (95% confidence interval (CI): 17.38, 20) to 76.66 days (95% CI: 56.36, 119.78). In addition, the highest daily growth rates of confirmed cases were observed in Kermanshah (0.037, 95% CI: 0.034, 0.039) and Sistan and Baluchestan (0.032, 95% CI: 0.030, 0.034) provinces. **Conclusions:** In light of our findings, it is imperative to tailor containment strategies to the unique epidemiological profiles of each region in order to effectively mitigate the spread and impact of COVID-19. The wide variation in doubling times underscores the importance of flexibility in public health responses. By adapting measures to local conditions, we can better address the evolving dynamics of the pandemic and safeguard the well-being of communities.

Keywords: Basic Reproduction Number; COVID-19; Disease Transmission, Infectious; Epidemics; Public Health Surveillance

Cite this article as: Karimi R, Farrokhi M, Izadi N, et al. Basic Reproduction Number (R0), Doubling Time, and Daily Growth Rate of the COVID-19 Epidemic: An Echological Study. Arch Acad Emerg Med. 2024; 12(1): e66. https://doi.org/10.22037/aaem.v12i1.2376.

1. Introduction

The novel coronavirus disease 2019 (COVID-19) began in China in December 2019. It spread worldwide and the World Health Organization (WHO) confirmed that it became a public health concern (1). For infectious diseases, there are key indices that are used to describe the disease state.

One of these indices is the basic reproduction number (R0), defined as the average number of new infections caused by an infected person in a susceptible population (2). In the spread of coronavirus infections, the reproduction number has been shown to vary, affecting the dynamics of coronavirus outbreak transmission and the reporting rate of cases (3). Reported estimates of COVID-19 R0 vary widely, ranging from 1.4 to 6.49 (4, 5). The influences of all other related factors are reflected in the change in case numbers over time, making an important contribution to the development of public health interventions (6).

Another important index is the point in time at which the number of cases doubles. In other words, the doubling time of the epidemic characterizes the sequence of intervals in which the cumulative incidence doubles (7). The doubling time measures the rate at which the epidemic is growing, and an increase in the doubling time indicates that transmission is decreasing (8). An increase in doubling time indicates a decrease in transmission if the underlying reporting rate remains unchanged (9). Understanding the rapid transmission or reducing trend within the country is crucial for designing interventions.

By analyzing these key epidemiological parameters, researchers and policymakers can gain insight into the transmission potential of the virus in specific regions, which is essential for the development of targeted intervention strategies. This analysis enables the identification of areas with higher transmission potential and helps to guide efforts to contain the spread of the virus in these regions. In addition, understanding the dynamics of COVID-19 transmission at the local level is crucial for adapting response strategies tailored to the specific needs and challenges of each province, ultimately contributing to a more effective containment of the epidemic. Furthermore, estimating these epidemiological parameters can help predict the future trajectory of the COVID-19 epidemic. This proactive approach enables the development of contingency plans and the implementation of measures to minimize the burden on healthcare systems.

Therefore, in this study we aimed to estimate the basic reproduction number, R0, peak date, doubling time, and daily growth rate using confirmed and death cases of COVID-19 in five provinces of Iran.

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2. Methods

2.1. Study design and setting

This ecological study was conducted in 5 provinces of Iran, including Kermanshah, Hamedan, Kurdistan, Chaharmahal and Bakhtiari, and Sistan and Baluchestan. We extracted the number of daily infections and symptom onset information for primary cases (infectors) and secondary cases (infectees) from the integrated healthcare system and calculated the duration of symptom onset from January 17 to February 8, 2020, to determine R0, peak date, doubling time, and daily growth rates in all five provinces.

We selected the five provinces to capture a diverse and representative sample of Iran's population. These provinces were chosen due to their geographical diversity, varying epidemiological profiles, differences in healthcare infrastructure and public health response, socioeconomic variability, and the availability of reliable data. This selection ensures that our study reflects a broad spectrum of conditions, providing comprehensive insights into the dynamics of the COVID-19 epidemic across different regions.

The ethical approval was granted by review board of the National Institutes for Medical Research Development (NIMAD), Tehran, Iran (IR.NIMAD.REC.1390.075). This study adhered to ethical recommendations and guidelines for research involving human subjects and data. All data were anonymized to protect the privacy and confidentiality of the included subjects.

2.2. Participants

All approved cases of COVID-19 from the aforementioned provinces, which were reported in the COVID-19 patient registry were included. Cases with incomplete data necessary to compute the main epidemiological parameters of our study were excluded.

2.3. Data gathering

After the confirmation of the epidemic of COVID-19 in Iran, data on patients with COVID-19 (confirmed, probable, and suspected cases), diagnosed baed on real-time polymerase chain reaction (RT-PCR) test or chest CT-scan or clinical symptoms were collected by the Disease Control Unit of the Health. This data includes all information on province, district, age, gender, date of onset of symptoms, hospitalization, bed confinement and discharge or death date, severity of infection, symptom (cough, fever, shortness of breath, headache, runny nose, etc.), history of chronic diseases, travel history, history of other treatments, close contacts with other people, and if they are confirmed cases of COVID-19.

In each province, the information about confirmed, probable, and suspected cases of coronavirus has been registered daily since February 22, 2020. The operators in each province were responsible for entering COVID-19 case data into the registry. Data collection from the registry for this study was conducted by one of the authors (SSHN).

2.4. Definitions

- Basic reproduction number (R0) was defined as the average number of new infections caused by an infected person in a susceptible population.
- The doubling time characterizes the sequence of intervals in which the cumulative incidence of the epidemic doubles. If an epidemic grows exponentially at a constant growth rate (r), the doubling time remains constant and is equal to (ln 2)/r.
- Daily growth rate was defined as the rate of daily increase in number of confirmed cases.

2.5. Statistical analysis

2.5.1 Serial interval

Since we did not have clear information on the full spectrum of serial interval distribution, we assumed that the serial interval at the beginning of the outbreak in Iran was similar to that in a study of 5405 confirmed cases with 139 transmission chains in China (3).The estimated serial intervals in this study had a mean of 4.27 days and a standard deviation (SD) of 3.44 days. Other studies have also reported a range of serial intervals with a mean of 4.7 to 7.5 and a standard deviation of 2.9 to 4.2 days (10-13), and the total sample size in these studies ranged from 28 to 425 confirmed cases. We used a gamma distribution with shape and scale parameters compatible with the mean and SD mentioned. All analyses were performed using R version 3.6.3. Parameters were estimated using the exponential growth rate method, maximum likelihood estimation, and the time-dependent Bayesian method explained in another paper (14), using the R0 package (15).

2.5.2 Exponential Growth Rate (EGR)

In the initial phase of an epidemic, the number of infected cases increases exponentially. The number of newly reported confirmed cases corresponds to the number of individuals infected on each day, and the corresponding serial interval approximates the generation time. Supposing the exponential growth rate of the epidemic is R, which can be determined by fitting a least squares line to the daily number of reported new confirmed cases on a logarithmic scale, namely log (Nt). Hence, the reproduction number can be calculated according to the Euler-Lotka equation in a moment-generating form (16). The parameter r indicates the rate of spread of the disease (17).

2.5.3 Time-dependent method

Wallinga and Teunis developed the time-dependent calculation of the reproduction number (R) in 2004 (17). In this method, the effective reproduction number (R) is calculated by taking the arithmetic mean of the effective reproduction number of the case (Rj) for all those who indicate the first symptoms of the disease on day t. The Epistemic R package software (version 2.2.3) was used to estimate the time-varying R0 using a Bayesian method.

2.6. Sensitivity analysis

A sensitivity analysis was conducted to assess the significance of generation time in evaluating the reproduction number. Indeed, the reproduction number is sensitive to the generation time distribution function. Different measures of R0 (95% confidence interval (CI)) estimates were computed in the sensitivity analysis by varying the mean serial interval between 4 and 8 and the mean standard deviation between 2 and 5.

3. Results

3.1. Baseline characteristics of studied cases

From February 22 to April 9, the confirmed COVID-19 cases were detected by PCR. The number of confirmed cases and deaths were 32122 and 1958 cases, respectively, in five provinces of Iran (Kermanshah, Kurdistan, Hamedan, Chaharmahal and Bakhtiari, and Sistan and Baluchestan).
The date of peak, doubling time (the time needed to double the number of cases), and daily increase in confirmed cases and deaths are shown in Table 1. Kermanshah with 13668 confirmed COVID-19 cases and Hamedan with 2064 COVID-19 cases had the highest and lowest number of cases, respectively. The highest and lowest number of deaths was observed in Hamedan (657 deaths) and Chaharmahal and Bakhtiari (54 deaths). The epidemic curve (basic reproduction number, peak date, doubling time, and daily growth rate) of the confirmed cases and deaths is shown in Figures 1-4.

3.2. Doubling time

During the study, the doubling time of confirmed cases in Kermanshah and Hamedan was 18.59 days (95% CI: 17.38, 20) and 76.66 days (95% CI: 56.36, 119.78), respectively. The minimum and maximum doubling time of deaths were observed in Kermanshah and Chaharmahal and Bakhtiari with 21.22 days (95% CI: 19.80, 22.86) and 334.20 days (95% CI: 162.09, 540.70), respectively.

3.3. Basic reproduction number (R0)

As shown in Figure 1, the estimated R-values of COVID-19 were high in all five provinces between February and March. From March to June, a gradual fluctuation was observed in four provinces, with the values of R0 fluctuating between 1 and 2; however, in Kermanshah, the fluctuation was more drastic. While the R0 value was 0.5 on March 23, it reached 2 on April 6.

3.4. Peak date and daily growth rate

The first peak was reached on June 13, 2022, in Kurdistan and on July 5, 2020, in Kermanshah. The doubling time and daily growth rate of COVID-19 in Kermanshah and Sistan and Baluchestan showed a similar pattern. The highest daily growth rate of confirmed cases was observed in Kermanshah and Sistan and Baluchestan with 0.037 (95% CI: 0.034, 0.039) and 0.032 (95% CI: 0.030, 0.034), respectively. This index was 0.028 (95% CI: 0.026, 0.031) and 0.022 (95% CI: 0.020, 0.025) for Kurdistan, and Chaharmahal and Bakhtiari, respectively. However, as the epidemic progressed, the time to doubling of cases was shorter in Kurdistan than in Chaharmahal and Bakhtiari (23.91 vs. 30.45 days). In Hamedan, a gradual increase in the daily growth rate (0.009) coincided with the increase in doubling time (76.66 days). The doubling time of deaths increased sharply in Hamedan compared to the other four provinces. While the daily growth rate was 0.012 in Kermanshah, it was 0.008 in Kurdistan, and Sistan and Baluchestan, 0.005 in Hamedan, and 0.002 in Chaharmahal and Bakhtiari.

4. Discussion

This study aimed to determine the basic reproduction number, peak date, doubling time, and daily growth rate of confirmed cases and deaths of COVID-19 in five provinces in Iran, including Kermanshah, Hamedan, Kurdistan, Chaharmahal and Bakhtiari, and Sistan and Baluchestan. The estimated R0 values indicate the potential for transmission intensity, guiding the urgency and scale of interventions such as testing, contact tracing, and social distancing measures. Shorter doubling times highlight rapid epidemic growth, necessitating immediate and aggressive control measures to mitigate spread. Conversely, longer doubling times suggest a slower pace of transmission, allowing for more targeted and adaptable public health strategies. These insights underscore the importance of context-specific approaches in pandemic response efforts. The basic reproduction number reflects the ability of an infection to spread uncontrollably (18). The results of the reproduction number are consistent with other studies.

Musa et al. rated the basic reproduction number, R0, as 2.37 (95% CI: 2.22, 2.51) (12). D'Arienzo reported R0 values ranging from 2.43 to 3.10 (10). According to Locatelli (11), the basic reproduction number in Western Europe is 2.2 (95% CI: 1.9, 2.6). Similar studies have also determined the R0 in various regions in Iran. In studies conducted by Rahimi et al. in Lorestan province, the number of R(t) was estimated to be 0.56-4.97 and 0.76-2.47 for periods of 7 and 14 days, respectively (13). Azimi et al. evaluated the value of R0 using three different methods in Tehran. The value of R0 from February 19 to 29 using the exponential growth method, maximum likelihood method, and Bayesian time-dependent method was 4.70 (95% CI: 4.23, 5.23), 3.90 (95% CI: 3.47, 4.36), and 3.23 (95% CI: 2.94, 3.51), respectively (14).

One item that can directly affect the increase or decrease of R0 is the intensity of the control measure. The simultaneous application of multiple restrictions decreases the value of R0 due to the reduction of close contact in the population; however, the elimination of or reduction in the number of control measures may lead to high susceptibility of individuals and families to this disease, which can be considered as a possible reason for an increase in the epidemic curve (13).

The doubling time indicates the rate of the spread of the disease and the extent of control measures required to contain the disease. Our estimates of the doubling time are longer than other estimates (1, 2). The doubling time of confirmed cases in Iran is 18.59 (95% CI: 17.38, 20.00) to 76.66 (95% CI: 56.36, 119.78) days. Rodriguez estimated the doubling time of COVID-19 by province in China. The doubling times estimated from cumulative incidence ranged from 1.4 (95% CI: 1.2, 2.0) days in Hunan province to 3.1 (95% CI: 2.1, 4.8) days in Xinjiang province from January 20 to February 9, 2020 (9). Shim et al. determined the doubling time over two waves of the COVID-19 pandemic in South Korea.

The time in which the cumulative incidence doubles was shorter in the first wave (between 2.8 and 4.6 days) than in the second wave (between 3.6 and 10.1 days) from February to July 2020 (19). In the Xu study, the doubling time was 5 days (95% CI: 4, 7 days) from March 13 to March 19, 2020 (20). The difference between our results and other studies lies in the extent of non-pharmaceutical interventions implemented by each country (21).

For example, strict social distancing, quarantine, and lockdown can extend the doubling time. Another important reason for this difference is the effectiveness of contact tracing, improving accurate case definition and strategic testing (21). Higher testing rates help to identify the hosts of the virus; therefore, countries with mass testing have lower doubling rates (22). In this context, different protocols are carried out in Iran depending on the epidemic conditions in each province. The doubling time may vary in 5 provinces due to the specific control strategy implemented by each province. The variation of the doubling time can also be observed in death rates. Kermanshah and Chaharmahal and Bakhtiari had the lowest and highest doubling times of 21.22 (95% CI: 19.80, 22.86) and 334.20 (95% CI: 162.09, 540.70) days, respectively. The accuracy of COVID-19 mortality registration and disease intensity are significant factors that directly affect the number of deaths in patients with COVID-19.

Similar to the doubling time result, the daily growth rate of both confirmed cases and deaths also has a wide range. The results show that the minimum and maximum growth rates were 0.009 and 0.037 for confirmed cases, and 0.005 and 0.012 for death cases in Hamedan and Kermanshah, respectively. For deaths, the minimum and maximum daily growth rates were 0.002 in Chaharmahal and Bakhtiari and 0.012 in Kermanshah, respectively. Numerous growth rates were reported in other studies. For example, in 2020, the growth rate from March 13 to 19 was 0.18 (95% CI: 0.11, 0.24) and reached a minimum of 0.19 (95% CI: 0.29, 0.10) in the study by Xu conducted in the USA. (20). An important factor that directly affects the growth rate is changes in testing rates, resulting from limited diagnostic testing capacity, ultimately masking the epidemic's growth rate (23).

The differences observed in the above-mentioned epidemiological indices between five provinces can be attributed to several key factors. Variability in public health interventions, such as the timing and stringency of measures like lockdowns, testing strategies, and contact tracing play a crucial role in shaping transmission dynamics. Additionally, differences in population density, healthcare infrastructure, socioeconomic status, and adherence to preventive measures may also influence the regional spread of COVID-19. Furthermore, local variations in virus strains, reporting practices, and the timing of epidemic peaks can contribute to the observed disparities.

We performed multiple analyses to ensure the robustness of our estimates. These included sensitivity analyses to account for variations in non-pharmaceutical interventions and testing rates. Our findings demonstrate significant regional variability in epidemic parameters, underscoring the need for tailored public health responses.

Given the limitations and variability in our estimates, a cautious interpretation is warranted. While our study provides valuable insights into the dynamics of the COVID-19 epidemic in Iran, the results should be interpreted in the context of the specific regional and temporal conditions. Policymakers should consider these factors when using our estimates to inform public health strategies.

4.1. Limitations

One of the main limitations of our study stems from potential biases in the data due to possible underreporting and incomplete data across the provinces studied. Variations in healthcare infrastructure and reporting practices could lead to discrepancies in the reported number of COVID-19 cases and deaths, affecting the accuracy of our estimates. Moreover, the reliance on mathematical models to estimate epidemiological parameters such as the basic reproduction number (R0), doubling time, and daily growth rate introduces inherent uncertainties. These models rely on assumptions about disease transmission dynamics and may be sensitive to variations in parameter inputs and model structure. Despite efforts to mitigate these limitations through sensitivity analyses and robust data validation, these inherent biases and uncertainties should be considered in the interpretation of our findings.

To estimate the actual value of R0, we need to identify all daily counts of COVID-19; however, due to the high number of asymptomatic patients and the limitations in detecting and identifying all patients, there is a major limitation in determining R0, but as far as the proportion of confirmed cases to all cases is constant, the estimated R0 will be valid. A key consideration is the relationship between R0, doubling time, and growth rate. Although the measurements in this paper were compared with results from other countries, the timing of the epidemic in different regions should be considered. It should also be noted that the estimated values of the indices used in this work depend on the model used and the values of other parameters, which may affect the value of the indices.

5. Conclusion

In light of our findings, it is imperative to tailor containment strategies to the unique epidemiological profiles of each region in order to effectively mitigate the spread and impact of COVID-19. The wide variation in doubling times underscores the importance of flexibility in public health responses. By adapting measures to local conditions, we can better address the evolving dynamics of the pandemic and safeguard the well-being of communities.

6. Declarations

6.1. Acknowledgments

The authors thank all those who contributed to this study.

6.2. Data Availability

Data is available upon request.

6.3. Funding/Support

The authors would like to thank the Ministry of Health and Medical Education of Iran and National Institutes for Medical Research Development (NIMAD), which supported us with their services (Grant number : 993716).

6.4. Conflict of interest

None.

6.5. Author contributions

All authors approved the final version of manuscript to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

RK: the conception and design of the study, analysis, and interpretation of data, and drafting the work

HG: analysis and interpretation of data, drafting the article, and revising it critically for important intellectual content

KS: acquisition of data and drafting the work

FN: acquisition of data and drafting the work

ES: acquisition of data and drafting the work

MK: acquisition of data and drafting the work

MS: acquisition of data and drafting the work

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AA: acquisition of data and drafting the work

AHM: acquisition of data and drafting the work

MS: acquisition of data and drafting the work

AZ: acquisition of data and drafting the work
AMB: acquisition of data and drafting the work
SSHN: the conception and design of the study, analysis, and interpretation of data, and drafting the work.
MF: Analysis and interpretation of data and revising it critically for important intellectual content.

6.6. Using artificial intelligence chatbots

None.

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Table 1: Estimation of the basic reproduction number, peak date, doubling time, and daily growth rate of confirmed cases based on the time-dependent method during the COVID-19 epidemic in 5 provinces of Iran

Province	Confirmed cases				Death cases			
	No.	**Peak date**	**Doubling time**	**Daily growth rate**	**No.**	**Peak date**	**Doubling time**	**Daily growth rate**
Kermanshah	13668	2020-07-05	18.59 (17.38, 20.00)	0.037 (0.034, 0.039)	522	2020-07-05	21.22 (19.80, 22.86)	0.012 (0.009 0.015)
Hamedan	2064	2020-07-03	76.66 (56.36, 119.78)	0.009 (0.005, 0.012)	657	2020-07-05	130.84 (85.05, 283.40)	0.005 (0.002 0.008)
Kurdistan	9758	2020-06-13	23.91 (21.69, 26.62)	0.028 (0.026, 0.031)	343	2020-06-17	80.27 (56.80, 136.81)	0.008 (0.005 0.012)
Chaharmahal o Bakhtiari	2089	2020-06-23	30.45 (27.17, 34.62)	0.022 (0.020, 0.025)	54	2020-06-20	334.20 (162.09,540.70)	0.002 (-0.000 0.004)
Sistan and Baluchestan	4543	2020-07-05	21.22 (19.80, 22.86)	0.032 (0.030 0.034)	381	7 2020-06-19	77.48 (60.34, 108.21)	0.008 (0.006 0.011)

Data are presented with 95% confidence interval. No.: number of cases.

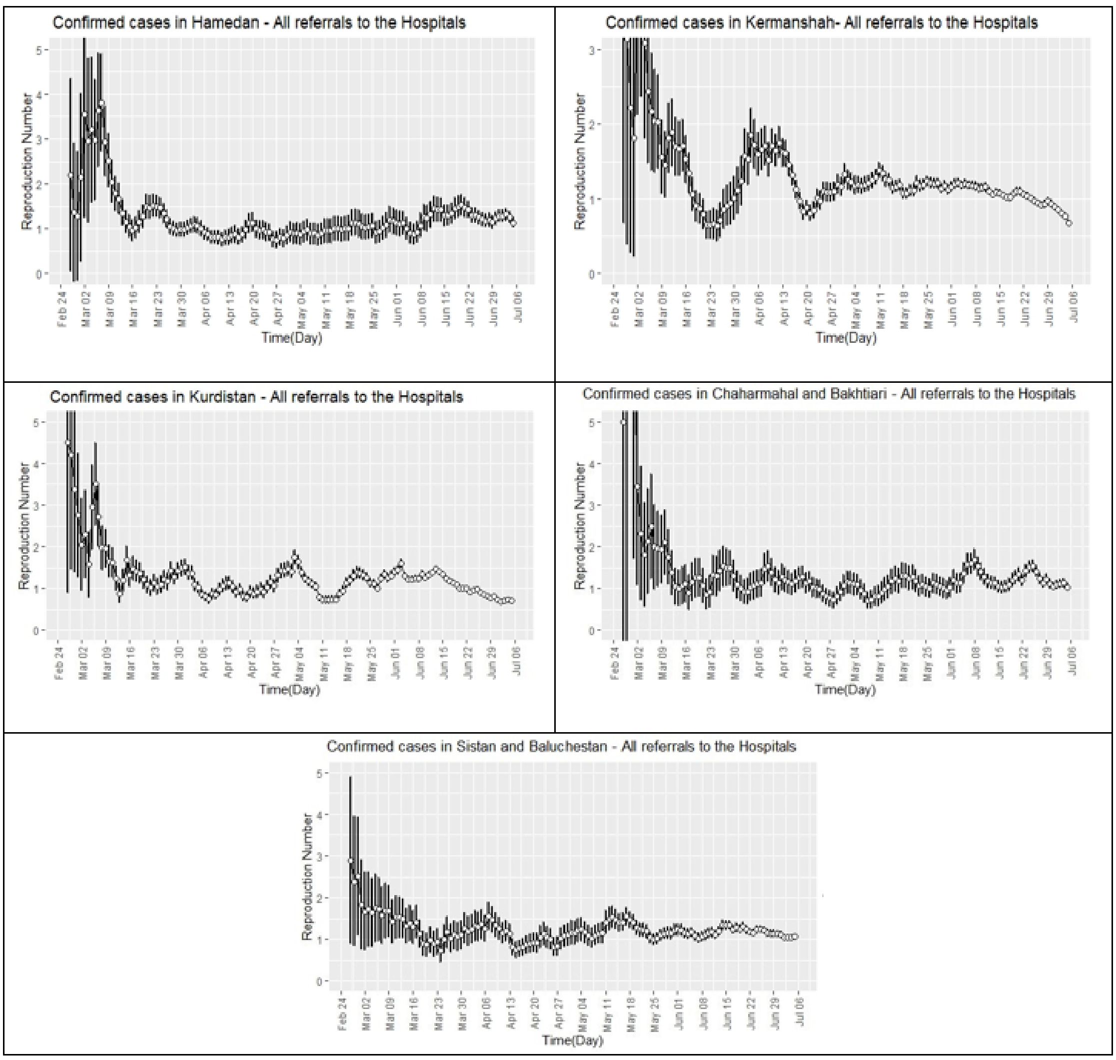

Figure 1: Estimation of the basic reproduction number (R0) of confirmed cases based on the time-dependent method during the COVID-19 epidemic in five provinces of Iran.

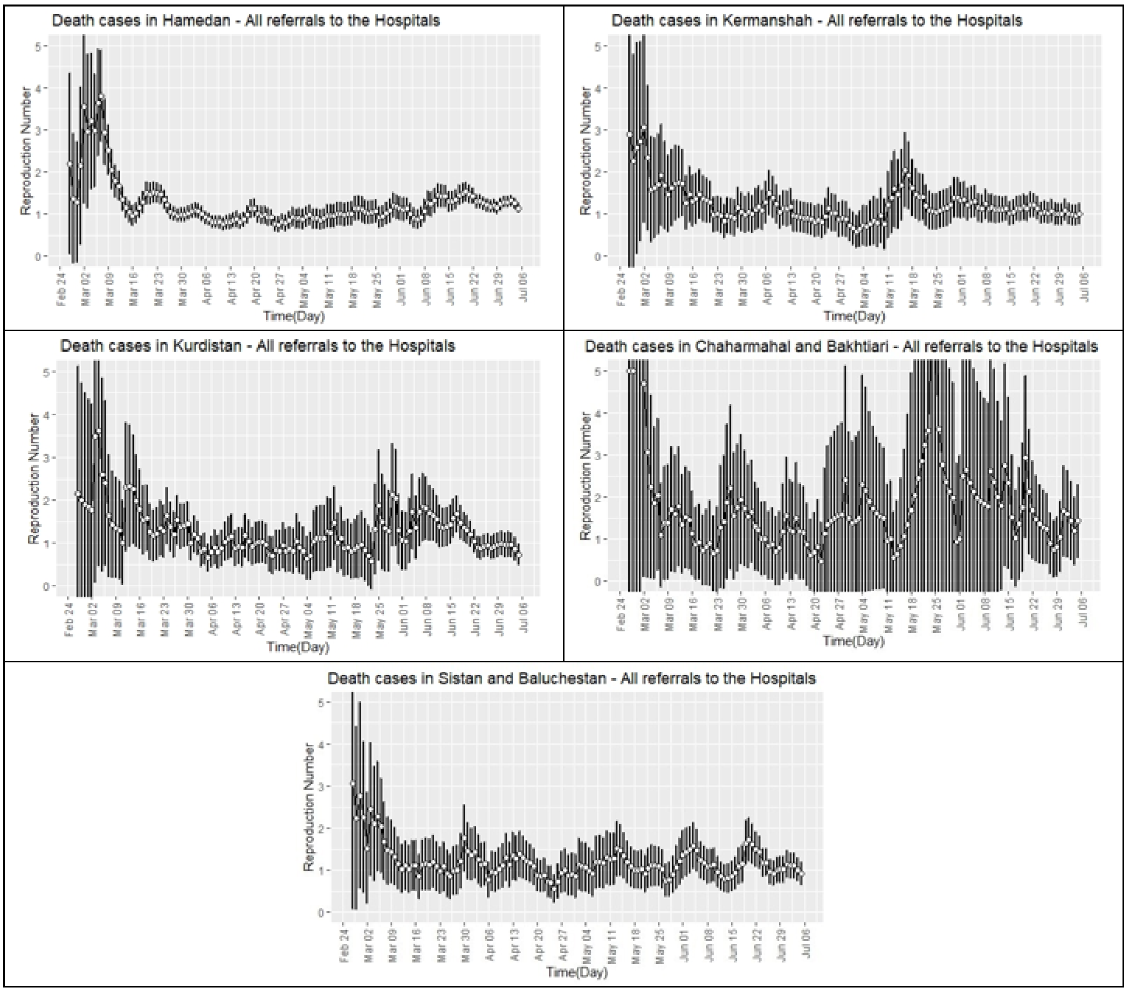

Figure 2: Estimation of the basic reproduction number of death cases based on the time-dependent method during the COVID-19 epidemic in five provinces of Iran.

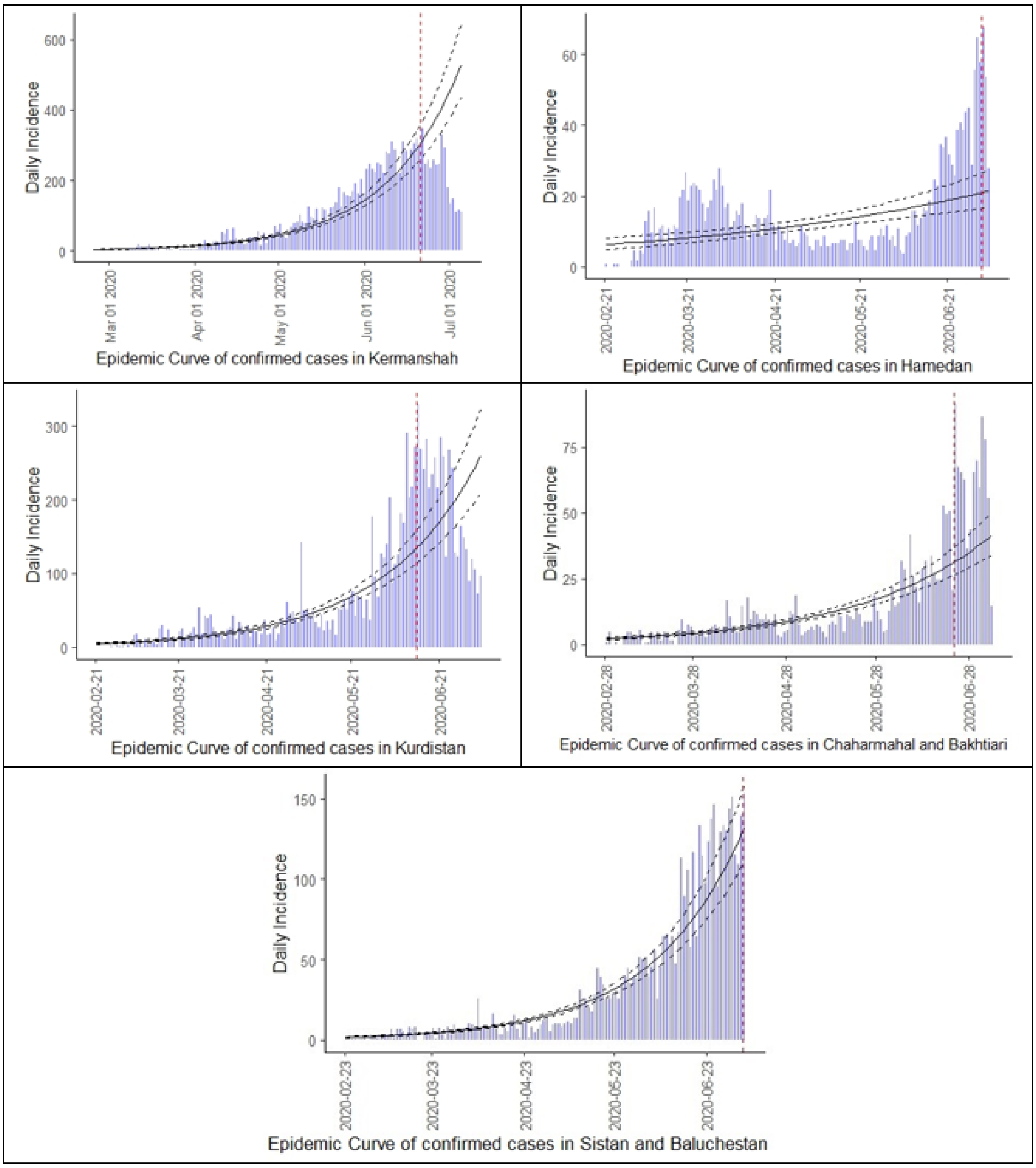

Figure 3: Estimation of the peak date, doubling time and daily growth rate of confirmed cases based on the time-dependent method during the COVID-19 epidemic in five provinces of Iran.

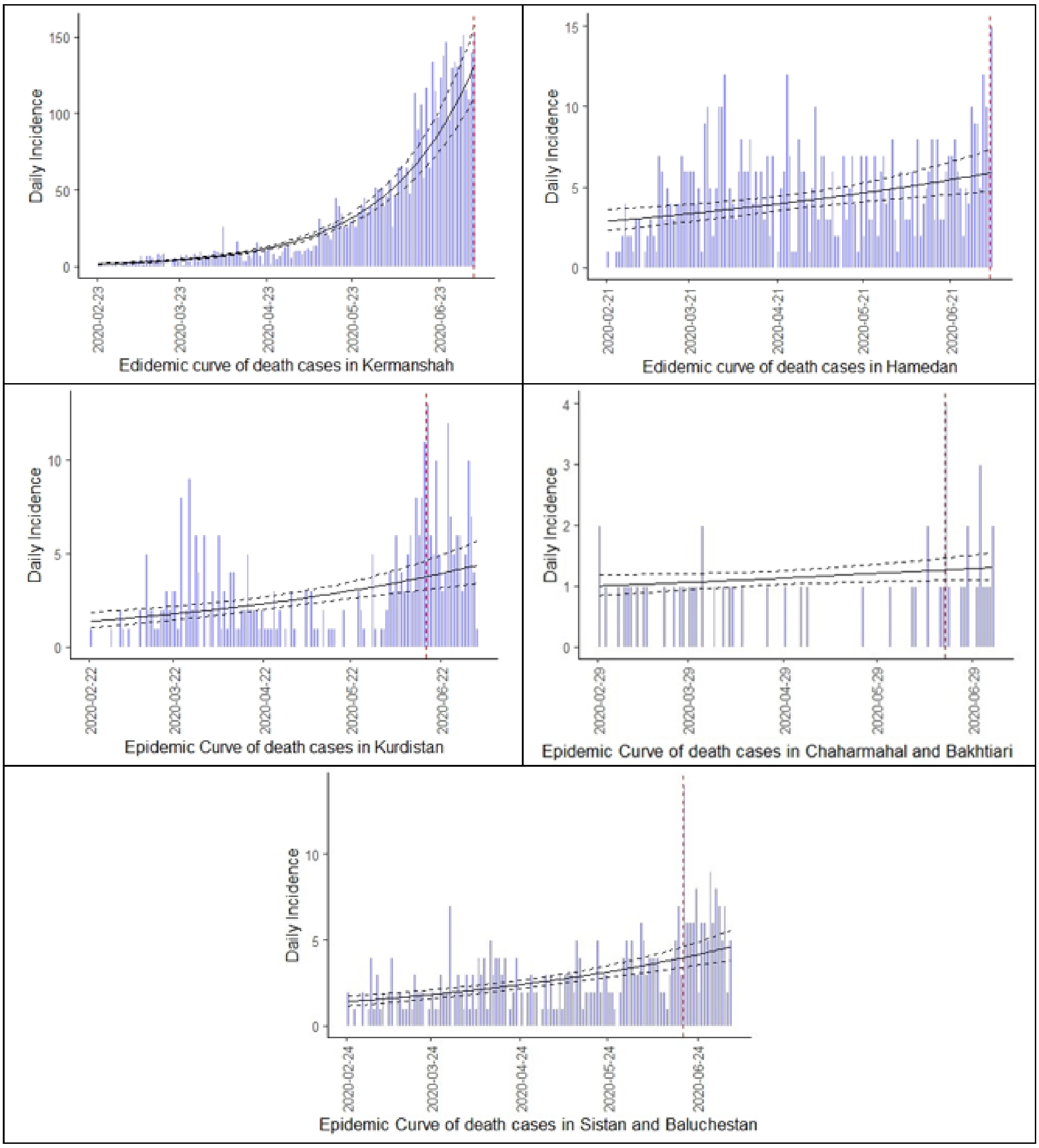

Figure 4: Estimation of the peak date, doubling time and daily growth rate of death cases based on the time-dependent method during the COVID-19 epidemic in five provinces of Iran.