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Trend of case fatality rate during first 30 days of COVID-19 epidemic; the example of Iran

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Abstract

Introduction: One of the unusual aspects in coronavirus disease 2019 (COVID-19) pandemic is changing case fatality rate (CFR) in different time series. Many researchers are trying to find the reasons of this variability.

Objectives: This study aimed to present a model for a 30-day trend of CFR in any infectious disease epidemic using the example of COVID-19 in Iran.

Patients and Methods: As a case study, we tried to use statistical mining of scientific databases. A descriptive approach with quantitative tools was conducted. The World Health Organization (WHO) database was used to access daily reports of CFR. Funnel plot and Z score were used to study and graph the trend.

Results: During this period of time, a total of 20610 cases were confirmed based on real-time polymerase chain reaction (PCR). Among them, 1556 individuals died. Therefore, CFR was calculated as 7.549% (95% confidence intervals 7.189%-7.910%). This frequency was considered as the pooled frequency. Daily CFR with 95% CI was compared with the pooled frequency.

Conclusion: In our case, the epidemic was started from high CFR due to low number of cases and testing only highly suspicious individuals. Then, the CFR was reduced due to increased number of patients and improvement in screening. Finally, CFR went back to its moderate rate due to the addition of the death numbers related to the cases of previous days.

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Introduction

Coronaviridae is a family of single-stranded RNA viruses that is one of the most common viruses, which are the cause of common cold syndrome. Many types of these viruses cause common cold syndromes (1). The first well-known mutation in this family happened in 2002 that ended to the severe acute respiratory syndrome (SARS) (2). The next prominent mutation which resulted in the Middle East respiratory syndrome (MERS) took place in the year 2012 (3). Finally, the recent mutation occurred in 2019 [severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)] that became the cause of coronavirus disease of year 2019 (COVID-19). This virus has a capsid and is medium size. Therefore, it has short range and is easily washed (4). Regarding its pathogenesis, it is noted that this virus causes complications of the disease by locating on angiotensin converting enzyme (ACE) II, although its main pathogenesis is yet to be examined (5).

Key point

In this study, we showed the trend of case fatality rate (CRF) changes. We discussed the reasons of this change in order to reach a general model for such epidemics in the future. We achieved the trend model in our study case as the high-low-moderate.

SARS infected 8096 people worldwide with a mortality rate of 9.6% in total (6). MERS globally infected 1789 cases with a total mortality rate of 31.1%, finally (7). One of the distinct characteristics of COVID-19 compared to the two previous mutations, is its high rate of transmission and contagion that despite the relatively low mortality rate of approximately 6% has up till now infected millions of people with hundreds of thousands of deaths. So far, more than 180 countries in the world have been involved, and therefore, the World Health Organization (WHO) confirmed its pandemic status. So far, in Iran more than 70 000 cases as morbidity and more than 4000 cases as mortality have been reported (7).

COVID-19 is associated with older age, high sequential organ failure assessment (SOFA) score and d-dimer >1 µg/mL (related to 28-day mortality in patients) which can help physicians screen patients with poor prognosis at initial phase. Long-term viral spreading offers a logical justification for the policy of isolating infected cases and optimal antiviral treatments in the future (8).

Objectives

One of the strange points in such pandemic status is changing case fatality rate (CRF). Many researchers are trying to find the reasons of this change. In order to present a model for a 30-day trend of CFR in any infectious disease epidemic, the present study used the example of Iran.

Patients and Methods

Study design

As an instrumental case study, we tried to use statistical mining of scientific databases. Descriptive approach with quantitative tools was conducted. The WHO database was used to access daily reports of CFR (7). The confirmed cases were based on real-time polymerase chain reaction (PCR).

Iran country was regarded as the case of study. February 19th of 2020 was day 1 of COVID-19 confirmation in Iran. We collected data from day 2 (February 20th) up to day 32 (March 21st) as a 31 day period of time. Raw data were collected from the database (the WHO report dates had one day delay which was regarded during data collection). Daily CFR was calculated through dividing daily number of fatalities by daily number of confirmed case.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. The present study does not contain human or animal subjects, and is a part of an ecological study approved by Lorestan University of Medical Sciences (# IR.LUMS.REC.1399.012).

Data analysis

For quantitative analysis graphing of the results, Excel 2013 (Microsoft, US) and Stata 14 (StataCorp LLC, USA) were used. CFR at day 32 (7.5%) was considered as the null hypothesis for evaluation of the trend using a funnel plot, calculation of Z score and 95% confidence intervals (CI) of the frequencies.

Results

During this time period, a total of 20610 cases were confirmed. Among them, 1556 individuals died. Thus, CFR was calculated as 7.549% (95% CI: 7.189%-7.910%). This frequency was considered as the pooled frequency. Daily CFR with 95% CI is shown in Table 1. The funnel plot of daily report showed that most daily CFRs were outside the funnel (outside the predicted frequency, based on the pooled frequency) (Figure 1). The Z score of deviation

Table 1. Daily CFR of COVID-19 from day 2 of epidemics to day 32

Day	Mortality	Lower limit	Upper limit	Z score*
2	0.4	-0.02941	0.829414	2.746524
3	0.222222	0.03016	0.414284	2.356243
4	0.214286	0.062299	0.366273	2.779792
5	0.186047	0.069732	0.302361	2.74391
6	0.196721	0.096963	0.29648	3.583716
7	0.168421	0.093165	0.243678	3.428219
8	0.136691	0.079582	0.193799	2.73081
9	0.106122	0.067555	0.144689	1.814433
10	0.087629	0.059494	0.115764	0.904507
11	0.072513	0.051639	0.093386	-0.27511
12	0.055215	0.0409	0.069529	-2.4009
13	0.043971	0.033598	0.054343	-4.62326
14	0.032962	0.025722	0.040203	-7.78149
15	0.031485	0.025154	0.037817	-9.00517
16	0.030458	0.024776	0.036141	-10.1043
17	0.026122	0.021584	0.030659	-12.8766
18	0.024901	0.020899	0.028904	-14.614
19	0.029546	0.02545	0.033642	-14.0938
20	0.033096	0.028953	0.037239	-13.5815
21	0.036185	0.032103	0.040267	-13.3441
22	0.039333	0.035317	0.043349	-12.9861
23	0.042581	0.038638	0.046523	-12.506
24	0.045231	0.04141	0.049051	-12.2127
25	0.048001	0.044287	0.051714	-11.7424
26	0.051944	0.04826	0.055629	-10.5251
27	0.056901	0.053192	0.060609	-8.61841
28	0.061105	0.057413	0.064797	-6.92732
29	0.065376	0.061699	0.069053	-5.04763
30	0.069756	0.066076	0.073436	-2.94835
31	0.072948	0.069312	0.076585	-1.35219
32	0.075497	0.07189	0.079104	0

* This Z score is based on the pooled frequency 7.549% calculated as "(CFR-pooled)/√(pooled(1-pooled)/case)" in each day.

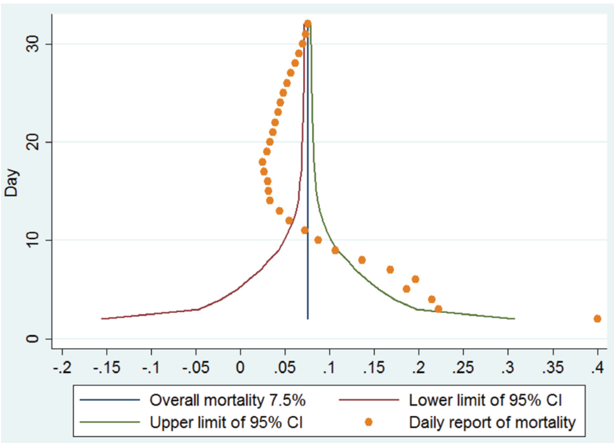

Figure 1. Funnel plot of case fatality rate.

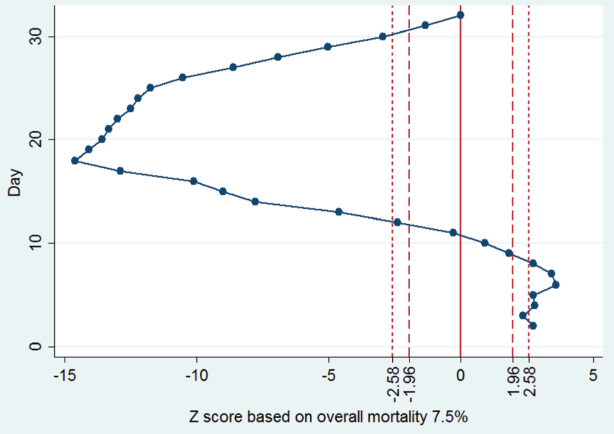

Figure 2. A plot showing Z score changing of daily report of case fatality rate

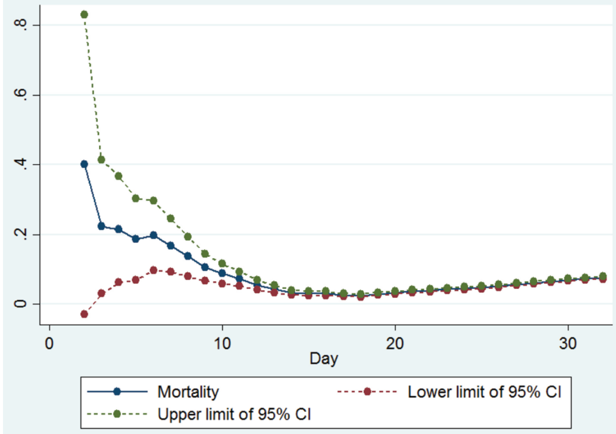

Figure 3. Trend of case fatality rate from day 2 to day 32. CI: confidence intervals.

of daily CFR from the pooled frequency is shown (Table 1 and Figure 2). The trend of CFR change in this 31-day period is also shown (Figure 3).

Discussion

The present study aimed to show the trend of CFR change and discuss the reasons for this change in order to reach a general model for such epidemics in the future. We achieved a trend model in our case study.

We started reading the plots from day 2. In the funnel plot, days 2-8 are outside the funnel (shift to right). It indicates that at the start of each epidemic, the CFR is significantly higher than the pooled CFR. The first reason is that the number of positive samples is low, and therefore each deceased case highly increases the proportion of CFR. The second reason is that at the beginning of each epidemic only highly suspicious cases are tested , although it may be different in other countries. Days 9-11 are inside the funnel. It indicates that some days after starting each epidemic, the CFR goes around the pooled CFR due to an increase in number of cases. Days 12-30 are outside the funnel (shift to left). The first reason is that the screening policies are improved and therefore a greater number of cases from different stages are diagnosed. The second reason is that these cases are newly diagnosed and therefore the number of deaths will increase cumulatively. Days 31 and 32 are inside the funnel; because we considered day 32 of the CFR as the pooled CFR. In our plot of Z score, days 2 and 4-8 are outside the 99% CI, days 9-11 are inside the 95% CI, day 12 is inside the 99% CI, days 13-30 are outside the 99% CI, and days 31 and 32 are inside the 95% CI of the pooled CFR. Its interpretation is similar to the funnel plot. The overall trend of CFR is achieved as high, low and moderate. Obviously, this trend is merely for the first month of epidemic. Different scenarios may occur in the next days, weeks and months. For instance, performing a new treatment strategy may reduce CFR again.

In the recent literature, there are some studies about trends of COVID-19 (9,10). However, there have been no studies on the causes of the observed variability of the CFR.

Conclusion

In our study, the epidemic started from high CFR due to low number of cases and testing only highly suspicious individuals. Then, the CFR decreased due to increased number of patients and improvements in screening. Finally, CFR went back to its moderate rate due to addition of the death numbers related to the cases of previous days.

Limitations

We did not perform inferential statistics, because they were not measurable to be used in statistical analyses.

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Authors' contribution

KA participated in design and conceptualization. SAYA prepared the primary draft. ME participated in final revision and critical approval.

Conflicts of interest

The authors declared no competing interests.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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