



Research Article

Case Fatality Rate estimation of COVID-19 for European Countries: Turkey's Current Scenario Amidst a Global Pandemic; Comparison of Outbreaks with European Countries

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Abstract

Objectives: SARS-CoV-2, which belongs to the Coronaviridae family of RNA viruses, caused an epidemic in China, leading to the pandemic of COVID-19. Various international and national authorities around the world have been attempting to halt the spread of the deadly virus by providing awareness of the disease including daily confirmed cases and deaths related to the pandemic. At this early stage of the outbreak, epidemiological patterns are required for healthcare officials and public, to understand the ongoing situation. The case fatality rate is one of the key parameters for the epidemiology of this type of epidemic. In this study, we aimed to compute the CFR for European countries and Turkey until 31st March 2020.

Methods: We used linear regression analysis on the cumulative number of cases and deaths to generate a slope to estimate CFR values of COVID-19 in selected countries. We compared the calculated CFR values of Turkey until 31st March (15 days since first COVID-19 death) with similar first fifteen days' data since the report of first death from Italy, Spain, the UK, France, Germany, Switzerland, Belgium, Austria, the Netherlands and Portugal. We then calculated CFR values for these countries from their cumulative confirmed cases and cumulative deaths up to March 31st.

Results: Based on This data-driven analysis showed that CFR for Turkey was 1.85 (95% CI: 1.513-2.181) with an R² value of 0.92 which was comparable to fa ifteen day analysis of France as 1.979 (95% CI: 1.798-2.159) and an R² value of 0.98. However, CFRs for selected countries increased in subsequent analysis when the threshold of fifteen days was released until March 31, 2020. However, the CFR estimates are time-dependent and show a linear trend in the initial stages of the outbreak.

Conclusions: Our findings suggest that the CFR of COVID-19 in Turkey at initial stages of the outbreak was similar to France. However, SARS-CoV-2 seemed to have spread quicker in Turkey since the report of first death, as compared to other countries based on the number of confirmed cases. This study was aimed at recording an update on the current epidemiological situation of COVID-19 for Turkey in comparison to European countries during a global pandemic.

Keywords: COVID-19, epidemiology, public health, SARS-CoV-2, Turkey, virology

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SARS-CoV-2 is an RNA virus that belongs to the Coronaviridae family of beta-coronaviruses and contains a plus-sense single-stranded RNA genome with helical symmetry confined in an envelope of overall spherical shape.^[1]

The term "corona" comes from the glycoprotein peplomers that form a "crown" like shape with spikes formed by the proteins on the virus that can bind to the receptors of host cells in case of infection.^[1,2] Using cryo-electron microscopy

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and transmission electron microscopy, the “spike” are identified similar glycoproteins in SARS-CoV-2 that bind to the receptors on the surface of the host cell.^[3, 4] This pneumonia-causing virus was named by ICTV as SARS-Cov-2 due to its similarities with SARS-Cov in 2002-2003. Generally, seven viruses in the Coronaviridae family that can infect humans, three of which, MERS, SARS-CoV-1 and SARS-CoV-2 (COVID-19) cause severe diseases and epidemics worldwide.^[5] Genomic sequence analysis showed that SARS-CoV-2 originated or evolved from SARS-CoV as only a few nucleotide sequence differences were detected.^[6] Recent reports have suggested that the virus usually infects bronchial-ciliated epithelial cells and pneumocytes through binding with angiotensin-converting enzyme 2 (ACE2) receptors on the cell surface, usually transmitted from animal to human and from human to human via airborne particles or droplets.^[6, 7] An early review of the clinical features of COVID-19 reported that the main clinical manifestations of the disease have been fever in 90%, cough in 75% and dyspnea in approximately 50% of the cases of the disease, while other symptoms had gastrointestinal character. The overall fatality of the disease has been associated with subsequent or eventual acute respiratory distress syndrome (ARDS), myocardial injury or acute kidney injury.^[8] An early meta-analysis performed on case reports and publications related to COVID-19 reported that the case fatality rate (CFR) was greater than 13 percent in polymorbid and hospitalized COVID-19 cases, 20% of which required intensive care unit (ICU) monitoring.^[9]

Previously, two types of human coronaviruses were involved in global epidemics; the Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) and the Middle East Respiratory Syndrome Coronavirus (MERS) that led to several cases of more than 10.000.^[10, 11] According to World Health Organization (WHO) data, globally 750.890 confirmed cases and 36.405 deaths from CO-VID19 were reported as of 31st March 2020, making SARS-Cov-2 a cause of the deadly global pandemic.^[12] There are two basic parameters commonly used to better understand outbreaks and their epidemiological features; the case fatality rates (CFR) and the basic reproduction number (R0) estimates.^[13, 14] Many studies are reporting basic reproduction number estimates and predictions for COVID-19 outbreaks as this is a global pandemic and reliable and efficient estimates of disease case fatality rates based on statistical models.^[15, 16] The 2002-2003 SARS outbreak had an estimated 9.6% CFR globally, compared with 34.5% for the MERS outbreak. Interestingly, for China, while the SARS CFR (6.4) was lower than the global CFR, while for MERS, the CFR in Saudi Arabia (37.1) was higher than the global CFR.^[17-20]

In this study, we compared Turkey's current scenario for

the period until March 31 with the other European countries having than 5000 COVID-19 cases more. We summarized the timeline for the increase in the number of cases for March in the countries selected for the study. Moreover, we applied linear regression analysis to estimate the CFRs for each country based on the incidence and mortality data provided by their national authorities. Similar statistical approaches have been used to estimate CFR with previous outbreaks in different parts of the world.^[21-24]

Methods

Data Sources

Epidemiological data for COVID-19 cases in Turkey were retrieved from the database created by the Republic of Turkey Ministry of Health (<https://www.saglik.gov.tr>). The data for Italy was retrieved from the repository of the Presidency of the Council of Ministers- Department of Civil Protection (available online at <https://www.protezionecivile.gov.it/>). For Spain, data generated by the Ministry of Health (Ministerio de Sanidad) (<https://www.mscbs.gob.es>) was used. Data from Germany was taken from the Robert Koch Institute (https://www.rki.de/EN/Home/homepage_node.html). COVID-19 cases data for France was retrieved from the French Public Health Agency (<https://www.santepubliquefrance.fr/>). Data from the UK was taken from the Department of Health and Social Care and Public Health, England (<https://www.gov.uk/>). The number of confirmed cases and deaths from COVID-19 in Switzerland were collected from the Swiss Federal Office of Public Health. (<https://www.bag.admin.ch/bag/en/home.html>). Data from Belgium was available on Sciensano at the Belgian national public health institute (<https://www.sciensano.be/en>). The data for the Netherlands were from the Dutch National Institute for Public Health and the Environment (<https://www.rivm.nl/en>). Data from Austria was available on the website of the Austrian Federal Ministry for Social Affairs, Health, Nursing and Consumer Protection. (<https://info.gesundheitsministerium.at/>). COVID-19 epidemic data from Portugal was taken from information released by the Portuguese General Directorate for Health (<https://covid19.min-saude.pt/>). Data provided by the Norwegian Institute of Public Health was used to evaluate Norway's COVID-19 cases (<https://helsenorge.no/koronavirus>).

Statistical Model of the Study

For the estimation of SARS-CoV-2 Case Fatality Rate in different countries over a given time period, linear regression statistical analysis was performed on the number of confirmed cases and deaths using GraphPad Prism5 and Microsoft Excel. For each country, the starting point for the

regression model was the first death reported by the relevant authorities to avoid the impact of the initial number of cases without any death or test on the CFR statistics. The predictive variable to calculate CFR by regression modeling was the cumulative number of confirmed cases, while the cumulative number of deaths was named as the outcome variable for the CFR estimation. The confidence interval (95%) was calculated by the standard error of the slope, while the slope of the fitted line generated by using statistical analysis was named as the CFR estimate. The R^2 value of 0.91-0.99 for the analysis usually shows a tight linear trend, therefore, this co-efficient of determination could be an effective parameter in estimating a good fit for the model. Exponential growth was also used as a comparison to model the epidemic curve in the study. We compared the linear model with the exponential model to compare the best fit to understand the trend of the COVID-19 outbreak in the countries selected for the study.

Results

Initial Report on Epidemiological data of COVID-19 in Turkey (March 2020)

The first case of COVID-19 in Turkey was reported on March 10, and the first death due to coronavirus infection on March 17. The statistics for March 2020 were given as follows: 92,403 tests performed, 13,531 reported positive cases, 214 deaths and 243 recoveries. The highest number of cases and the highest number of deaths were reported on 31 of March (2704 and 46, respectively). Figure 1 summarizes the situation in Turkey in March 2020 in terms of the number of cases and number of deaths. Figure 2 shows the March overall timeline for the spread of COVID-19 in the countries selected for this study, indicating the early spread of the virus than the other countries in Italy, Spain,

Germany, France and the UK. This data could be skewed due to a lack of testing in other countries. However, Turkey showed a sharp rise from mid-March to the end of the month. *Case Fatality Rate estimation (First 15 days after 1st death report) of COVID-19.*

In this study, linear regression analysis was performed for different countries on the epidemiological data of COVID-19 disease.

This study aimed to determine and to estimate the case fatality rate of COVID-19 in Turkey for the first fifteen days after the first death reported due to the disease from (March 16 to March 31) and to compare this with the CFR estimated for the European countries (with >5000 confirmed cases of COVID-19 since March 31) at the initial phase of the outbreak. This data-driven analysis showed that CFR for Turkey was 1.85 (95% CI: 1.513-2.181) with an R^2 value of 0.92 was comparable with France having CFR of 1.979 (95% CI: 1.798-2.159) and R^2 value of 0.98 that was for the first fifteen days after the report of first death from COVID-19 in both countries. However, the number of cases for Turkey was 13531 and the number of deaths was 314, while for France, the number of cases was 2281 and the number of deaths was 48. Therefore, even if it was statistically comparable, this CFR comparison showed us that COVID-19 had spread more quickly in Turkey than France. The number of confirmed cases in Germany rose to 29056, with 123 deaths due to COVID-19 within fifteen days on the day the first death was reported, with a CFR of 0.41 (95% CI: 0.3696-0.4528) as the lowest value in the analysis with an R^2 value of 0.97. These data showed us that although Germany had the patient load more than twice that of Turkey in the early stages of the outbreak, its CFR was a quarter lower than Turkey. The UK was reported to be the worst hit in terms of the initial stage of the epidemic applying the 15 day cut-off value for the CFR estimation. At

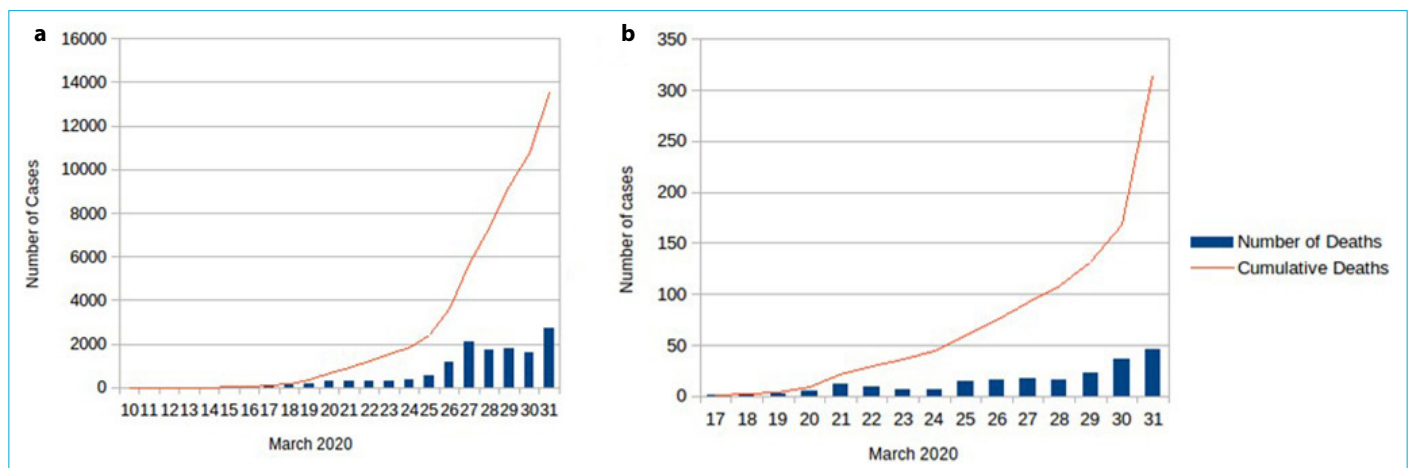


Figure 1. COVID-19 epidemiological data of Turkey (until March 31 2020). (a) Number of confirmed COVID-19 cases reported in the month of March. (b) Number of deaths caused by COVID-19 in Turkey during March 2020.

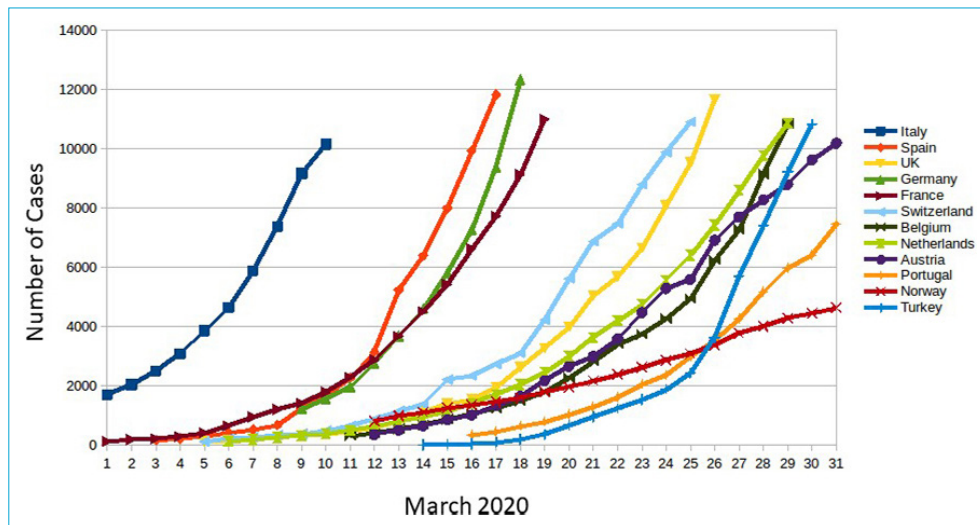


Figure 2. Trajectory of COVID-19 confirmed cases for the month of March for the countries selected in the study showing the timeline of viral spread in the region based on the reports of number of cases.

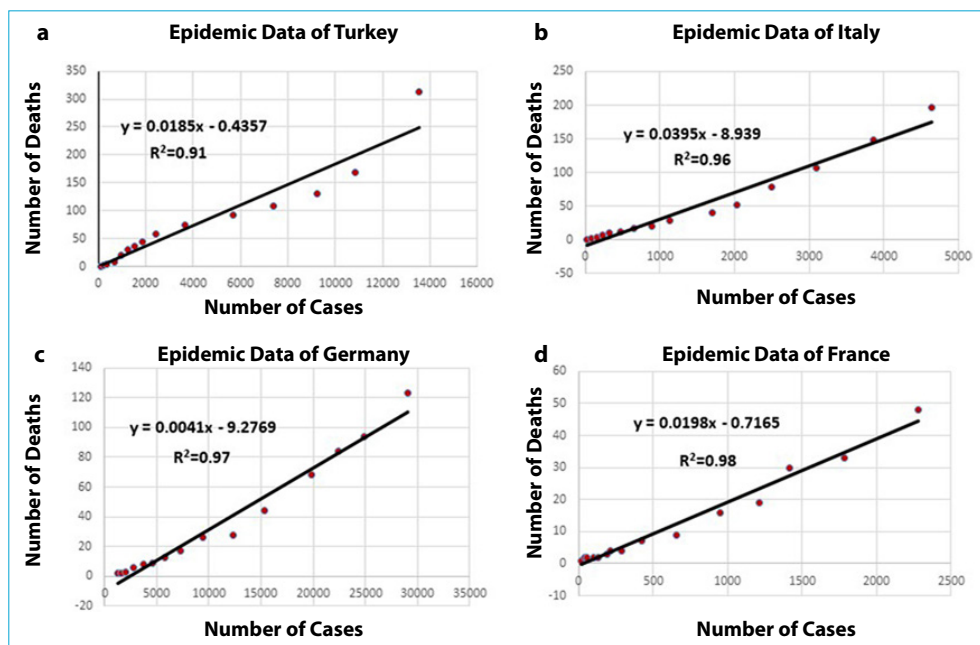


Figure 3. The linear regression model fitting for different datasets from represented countries for the first fifteen days since the report of first death from COVID-19. **(a)** Data from Turkey (March 17th to March 31st, 2020), **(b)** Data from Italy (February 21st to March 6th, 2020), **(c)** Germany (March 9th to March 23rd, 2020) and **(d)** France (February 26th to March 11th, 2020). Statistical analysis performed on the data depicted in this figure showed p-value <0.001***.

that time, CFR for the UK was 4.40 (95% CI: 3.893-4.915) with an R² value of 0.96, with 3269 cases and 144 deaths reports due to COVID-19. These data suggest, us that in the UK virus was not as much widely spread as in Turkey during the early days of the outbreak, however, CFR for the UK was more than twice as compared to Turkey (with statistics taken for fifteen days since the report of the first death in both countries). COVID-19 epidemiological data from Italy and Spain for the first fifteen days since the report of the first death in both coun-

tries showed comparable CFR values of 3.95 (95% CI: 3.504-4.405) with R² value of 0.96 and 4.01 (95% CI: 3.524-4.499) with an R² value of 0.96, respectively (Fig. 3). Interestingly, for the period considered in this study, Spain had a similar number of cases (11826) compared to Turkey, having more than twice the CFR value. This data indicated that the high COVID-19 fatality rate in Spain compared to Turkey in the first stage of the outbreak. According to initial data the number of cases in Turkey is close to Spain but the total number

Table 1. Case Fatality Rate estimation for Turkey and other European countries (First fifteen days after first death report). The data included in the linear regression analysis was taken for first fifteen days since the report of first death from Co-Vid19 in each country listed

Country	CFR	95% CI	R ²	p
Turkey	1.85	1.513-2.181	0.917	<0.001
Italy	3.95	3.504-4.405	0.965	<0.001
Spain	4.01	3.524-4.499	0.960	<0.001
UK	4.40	3.893-4.915	0.964	<0.001
Germany	0.411	0.3696-0.4528	0.972	<0.001
France	1.979	1.798-2.159	0.977	<0.001
Switzerland	1.019	0.9099-1.129	0.969	<0.001
Belgium	3.393	2.816-3.971	0.925	<0.001
Netherlands	3.496	2.998-3.995	0.946	<0.001
Austria	0.6607	0.5476-0.7737	0.925	<0.001
Portugal	2.249	2.073-2.425	0.983	<0.001
*Norway	0.5309	0.4608-0.6009	0.954	<0.001

*<5000 number of Co-Vid19 confirmed cases by 31st March 2020.

of deaths in Turkey was between Italy and Spain; as the number of cases in Italy was more than half of that in Turkey while the number of deaths in Turkey (314) was 1.5 times higher than that in Italy (197). All the countries selected for analysis showed a linear trend of the outbreak in terms of best fit for the data statistically, except for Belgium which followed an exponential growth curve in the goodness of fitting test for the duration (the first fifteen days of the outbreak after the report of the first death) R² value improved from 0.92 to 0.94 (Fig. 5). The CFR calculation data for other countries included in the statistical analysis are listed in Table 1.

Table 2. Case Fatality Rate estimation for European countries with more than 5000 COVID-19 confirmed cases until March 31st 2020. (The starting point for data in this linear regression analysis was first reported death and final cutoff date was 31st March 2020)

Country	CFR	95% CI	R ²	p
Italy	10.94	10.52-11.37	0.986	<0.001
Spain	8.595	8.196-8.995	0.986	<0.001
UK	6.509	6.151-6.868	0.982	<0.001
Germany	0.9357	0.8077-1.064	0.917	<0.001
France	6.482	6.109-6.856	0.974	<0.001
Switzerland	2.092	1.839-2.346	0.920	<0.001
Belgium	4.887	4.399-5.374	0.959	<0.001
Netherlands	7.538	6.945-8.132	0.966	<0.001
Austria	1.106	0.9210-1.291	0.898	<0.001
Portugal	2.297	2.147-2.448	0.987	<0.001
*Norway	0.8224	0.6888-0.9560	0.903	<0.001

*<5000 number of COVID-19 confirmed cases.

Case Fatality Rate estimation of COVID-19 for European Countries until March 31, 2020

When the cumulative number of cases and deaths due to COVID-19 till March 31, 2020, was used for linear regression analysis to determine the slope of the fitted line, estimated values of CFR increased for the analyzed European countries (Table 2). R² values also showed a variable trend as compared to the analysis performed under the fifteen-day initial cut-off. For instance, Italy's case fatality rate of COVID-19 was the most worsened having 105792 cases and 12428 deaths, and reached 10.94 (95% CI: 10.52-11.37) with an R² value of 0.98. CFR value for Spain also doubled and approaching to 8.595 (95% CI: 8.196-8.995) with an R² value of 0.98 due to 95923 cases and 8464 deaths by 31 March 2020. CFR values for each country under analysis increased from 15 days cut off to March 31st cut off by linear regression. UK's CFR reached 6.5 (95% CI: 6.151-6.868) with an R² value of 0.98 due to 25150 confirmed cases and 1789 deaths. The situation in Germany also worsened since the CFR value more than doubled from the initial 15 days after the report of the first death to 31st March and reached 0.93 (95% CI: 0.8077-1.064) with an R² value of 0.92 on cumulative analysis, reaching up to 71808 cases and 775 deaths until the cut off date. France, where the CFR for the initial 15 days was similar to Turkey, also reached a high CFR value of 6.482 (95% CI: 6.109-6.856) with R² value of 0.97 by 52128 number of confirmed cases and 3523 deaths until the cut-off date. For Switzerland, CFR increased to 2.09 (95% CI: 1.839-2.346) with an R² value of 0.92 by 16605 number of cases and 433 deaths in the period for statistical analysis (Fig. 4). Reported the first death from COVID-19 one day before Turkey, Portugal's CFR value was 2.297 (95% CI: 2.147-2.448). The epidemic curve modeling for Austria followed the exponential growth until 31st March cut-off date with an R² value of 0.93 for exponential model (as compared to 0.89 for linear fit model). However, for Belgium, the linear model gave R² 0.958 as compared to 0.819 for the exponential curve until 31st March. It can be concluded that in Belgium, the COVID-19 outbreak followed an exponential curve in the very initial stage and progressed to a more linear trend until the cut-off date of the study (Fig. 5). However, Portugal had reported fewer cases (7443) and deaths (160) as compared to Turkey who had 13531 cases and 314 deaths by 31st March. Table 2 summarizes the CFR estimates of European countries.

Discussion

Previously, COVID-19 CFR for Italy was compared with China and an early report (28th February 2020) showed that CFR for China and Italy were quite similar at 2.3.^[25] In

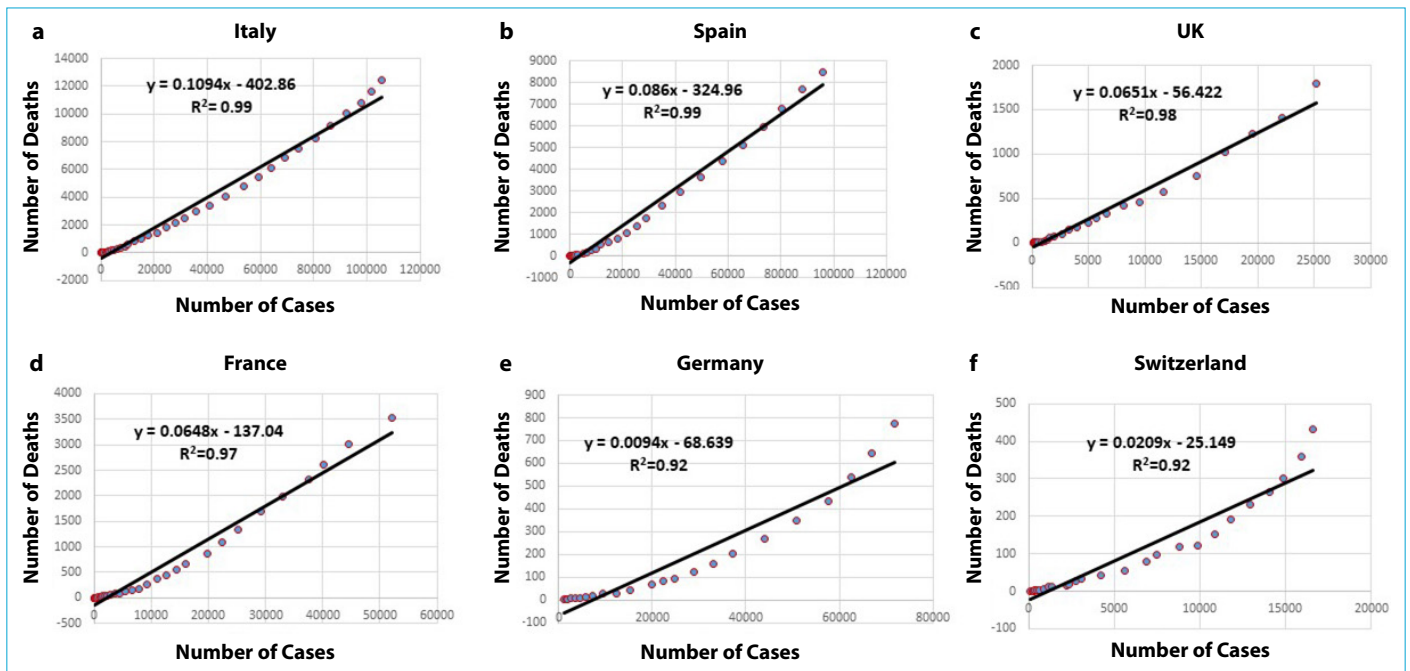


Figure 4. The linear regression model fitting for COVID-19 CFR estimation for different European countries. The statistical data for which are shown in Table no. 2. Epidemiological data on (a) Italy, (b) Spain, (c) UK, (d) France, (e) Germany and (f) Switzerland is represented in the form of graphs with the date of first death as initial point and 31st March as the cut-off date for statistical analysis. Statistical analysis performed on the data depicted in this figure showed p-value <0.001***.

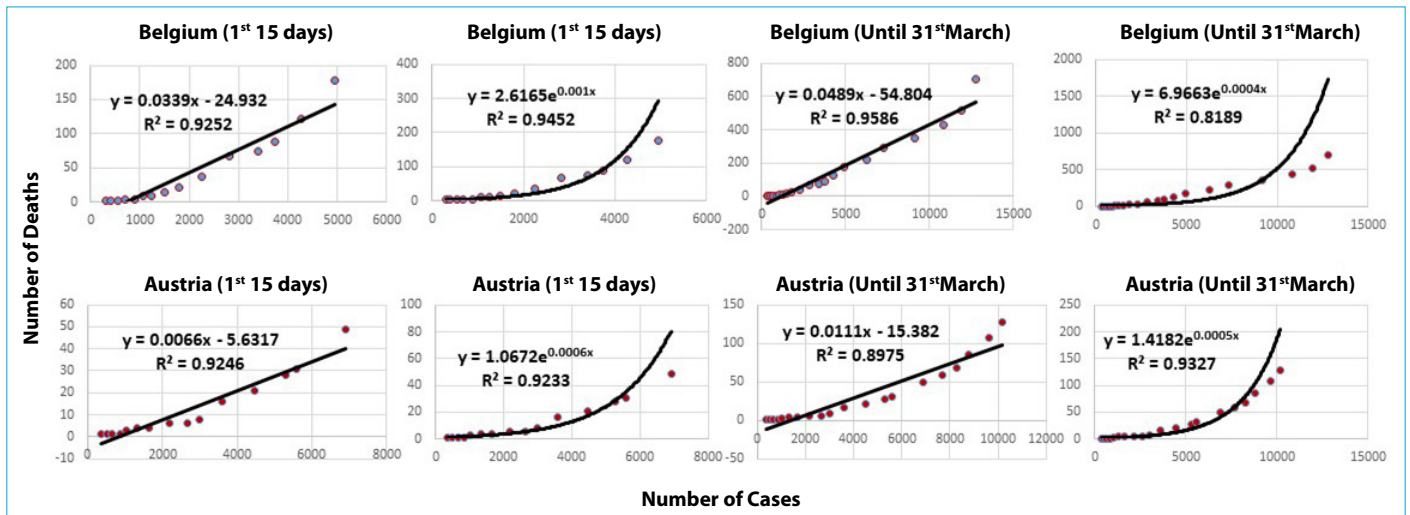


Figure 5. Comparison of Linear vs Exponential model for the goodness of the fit based on squared-R values. Data for 1st fifteen days for Belgium include COVID-19 cases and deaths reported from March 11 to March 25, 2020, and starting point of analysis for the cut-off date (March 31st) is March 11, 2020. For Austria, data for COVID-19 cases and deaths for 1st 15 days include data from March 12 to March 26, 2020. Statistical analysis performed on the data depicted in this figure showed p-value <0.001***.

our study, while CFR was 3.95 for Italy 15 days after the first death report, it increased to 10.94 as of 31st March. Therefore, the situation in Italy is quite alarming in terms of the mortality rate of the COVID-19. This is the first report of COVID-19 CFR estimation on data of Turkey and its comparison of the current situation with other countries. All countries selected for the study showed a more linear

trend of the outbreak in the initial phase based on linear regression analysis showed more exponential growth except for Belgium in the first fifteen days after the report of the first death and Austria overall until 31st March As of March 31st, CFR estimation indicates that within fifteen days after the first death report, Turkey's situation is similar to France. However, in terms of the spread of the virus, the figures

are quite alarming for Turkey. The tight linear trend of the CFR estimation in this study is derived from the cumulative number of cases and the cumulative number of deaths is actually due to the initial stage of the outbreak. Therefore, these CFR estimates are likely to change. However, the model can be used cumulatively in the future.

Conclusion

COVID-19 outbreak since its inception in China has caused a global public health nightmare. As of today, Italy has lost more lives than any other country due to this new viral infection. Europe has been affected more adversely by the epidemic than other continents. Turkey, with its geographical location and importance is also at the center of this pandemic. Since the first reported COVID-19 deaths in Turkey on March 17, we have collected the last 15-day data and calculated CFR through linear regression statistical analysis. However, these data are not significant on their own therefore, we estimated CFRs for European countries selected in this study to correlate a CFR pattern for the first fifteen day data obtained since the first death was reported from these countries to provide a comparable estimate for Turkey's scenario in a regional outbreak. Then, we calculated the overall CFRs of these countries and tabulated the data for real-time analysis of any variance. CFRs of all countries investigated showed a rapid increase. Therefore, it can be estimated that COVID-19 CFR will more likely to be increased in the future. This study is an attempt to record the statistical data on COVID-19 epidemiological data for Turkey and the selected European countries.

Disclosures

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Ethics Committee Approval: There was no ethics committee approval required for the study. The study was conducted by already disseminated information by national authorities of the selected countries.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – F.O., A.J.; Design – F.O., A.J.; Supervision – F.O., A.J.; Materials – F.O., A.J.; Data collection &/or processing – F.O., A.J.; Analysis and/or interpretation – F.O., A.J.; Literature search – F.O., A.J.; Writing – F.O., A.J.; Critical review – F.O., A.J.

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