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 belonging to Coronaviridae family of RNA viruses caused an epidemic in China, which led to a global 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 about the disease including the daily figures of confirmed cases and mortalities related to the pandemic. At this early stage of this outbreak, healthcare officials and public, require the epidemiological patterns to understand the situation. Case fatality rate is one of the key parameter for epidemiology of an outbreak of this kind. Here, we aimed to compute the CFR for European countries and Turkey until 31st March 2020.

Methods: We used linear regression analysis on cumulative number of cases and deaths for constructing a slope for estimating CFR values of COVID-19 in selected countries. We compared the computed 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, UK, France, Germany, Switzerland, Belgium, Austria, Netherlands and Portugal. Later, we computed CFR values for these countries from their cumulative confirmed cases and cumulative deaths until 31st March.

Results: This data driven analysis showed that CFR for Turkey was 1.85 (95% CI: 1.513-2.181) with R2 value of 0.92 which was comparable to fifteen day analysis of France as 1.979 (95% CI: 1.798-2.159) and 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 linear trend in 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 belongs to Coronaviridae family of betacoronaviruses and is an RNA virus containing plus sense single stranded RNA genome with helical symmetry confined in an envelope having overall spherical shape.[9] The term “corona” comes from the glycoprotein peplomers that are present over the envelop of the virus making a “crown” like shape with spikes formed by the proteins that can bind to receptors of the host cells in case of infection.
The use of cryo-electron microscopy and transmission electron microscopy identified the “spike” like glycoproteins in SARS-CoV-2 that bind to the receptors on the surface of the host cell.[1, 2] This pneumonia-causing virus was named by ICTV as SARS-CoV-2 due to similarities with SARS-CoV of 2002-2003. Overall, there are seven viruses in Coronaviridae family that can infect humans including three that cause severe illnesses; MERS, SARS-CoV-1 and SARS-CoV-2 (COVID-19) leading to epidemics around the world.[3] Genomic sequence analysis indicated that SARS-CoV-2 originated or evolved from SARS-CoV as there are only a few nucleotide sequence difference was spotted.[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 by transmission from animal to human and from human to human through airborne particles or droplets.[6, 7] An early review on the clinical features of COVID-19 reported the main clinical manifestations to be fever in 90%, cough in 75% and dyspnea in approximately 50% of the cases of the disease, while other symptoms were gastrointestinal in nature. The overall fatality of the disease has been linked to 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) greater than 13 percent in polymorbid and hospitalized COVID-19 cases with 20% of those cases requiring intensive care unit (ICU) for monitoring.[9] Previously, two types of human coronaviruses were involved in global epidemics; Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) and Middle East Respiratory Syndrome Coronavirus (MERS), leading to number of cases more than 10.000.[16, 11] According to World Health Organization (WHO) data, globally 750.890 confirmed cases and 36.405 deaths from CO-VID-19 were reported as of 31st March 2020, making SARS-Cov-2 a cause of deadly global pandemic.[12] There are two key parameters that are usually utilized to better understand the outbreaks and their epidemiological features; the estimates of the case fatality rates (CFR) and the basic reproduction number ($R_0$).[13, 14] There are many studies that reported the estimation and predictions for basic reproduction number for the COVID-19 outbreaks, since this is a global pandemic and there is a need for reliable and efficient estimates for case fatality rates of the disease that are based on statistical models.[15, 16] SARS outbreak of 2002-2003 globally had an estimated 9.6% CFR, while CFR for MERS outbreak at global scale was 34.5%. Interestingly, CFR of SARS for China (6.4) was less than global CFR while for MERS, CFR in Saudi Arabia (37.1) was higher than global CFR.[17–20] In this study, we compared the current scenario of Turkey until 31st March with other European countries with number of COVID-19 cases more than 5000. We summarized the timeline of increment in number of cases in the countries selected for the study for the month of March. 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 for estimation of CFR with previous outbreaks in different parts of the world.[21–24] 

### Methods

#### Data Sources

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

#### Statistical Model of the Study

For estimation of Case Fatality Rate of SARS-CoV-2 in different countries in a certain period of time, linear regression statistical analysis was performed on the number of
confirmed cases and number of deaths using GraphPad Prism5 and Microsoft Excel. For each country, the starting point for regression model was first death reported by the relevant authorities in order to avoid the influence of initial number of cases with no death or lack of testing on CFR statistics. The predictor variable for calculating CFR by regression modeling was cumulative number of confirmed cases, while cumulative number of deaths was termed as the outcome variable for CFR estimation. The confidence interval (95%) was calculated by the standard error of the slope, while slope of the fitted line generated by using statistical analysis was termed as the CFR estimate. R² value of 0.91-0.99 for the analysis usually show 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 as comparison for modelling the epidemic curve was also used in the study. We compared the linear model with the exponential model for comparison of 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 10th of March, and the first death due to coronavirus infection was reported on 17th of March. The statistics for March 2020 is given as; 92,403 tests performed, 13,531 reported positive, 214 deaths and 243 recoveries were reported. The highest number of cases and the highest number of deaths were reported on 31st of March (2,704 and 46 respectively). Figure 1 summarizes the situation of Turkey in March 2020 in the aspects of number of cases and number of deaths. Figure 2 shows the overall March timeline for the COVID-19 spread in the countries that were selected for this study, indicating the early spread of the virus in Italy, Spain, Germany, France and UK before others. This data could be skewed due to lack of testing in other countries. However, Turkey showed a steep rise from mid of March until 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 on the epidemiological data of Co-Vid19 disease was performed for different countries. The purpose of this study was to determine and estimate the case fatality rate of COVID-19 in Turkey for the first fifteen days since first fatality (March 16th to March 31st) and compare it with CFR estimated for European countries (with >5000 confirmed cases of COVID-19 since March 31st) in their initial stage of the outbreak. This data driven analysis showed that CFR for Turkey was 1.85 (95% CI: 1.513-2.181) with R² value of 0.92 was comparable with France having CFR of 1.979 (95% CI: 1.798-2.159) and R² value of 0.98 for the first fifteen days since the report of first death from COVID-19 in both countries. However, the number of cases for Turkey were 13,531 and number of deaths were 314, while for France, number of cases were 22,811 and number of deaths were 48. Therefore, this comparison of CFR however statistically comparable, showed us that COVID-19 had spread more quickly in Turkey as compared to France. In Germany, the number of confirmed cases rose to 29,056 with 123 deaths from COVID-19 in fifteen days since the report of first death and CFR value turned out to be the lowest in the analysis, as 0.41 (95% CI: 0.3696-0.4528) with R² value of 0.97. This data showed us that Germany inspite of having more than twice the patient load as compared to Turkey during its early stages of COVID-19 epidemic had lower than one fourth of the CFR as compared to Turkey. UK was reported to be hit worstly in terms of initial epidemic if 15 day cut-
The CFR estimation is applied. CFR for UK in that period was 4.40 (95% CI: 3.893-4.915) with R² value of 0.96 with 3269 cases and 144 reported deaths from COVID-19 outbreak. This data showed us that in UK virus was not as much widely spread as in Turkey during early days of the outbreak, however, CFR for UK was more than twice as compared to Turkey (with statistics taken for fifteen days since the report of first death in both countries). COVID-19 epidemiological data from Italy and Spain for the first fifteen days since the report of first death in both countries, 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 R² value of 0.96, respectively (Fig. 3). Interestingly, for the duration under consideration for this study, Spain had comparable number of cases (11826) as compared to Turkey, with more than twice the CFR value. This data indicated the high fatality rate of COVID-19 in Spain as compared to Turkey in initial phase of the outbreak. Initial data suggests that Turkey had compa-
rable number of cases to Spain, but the number of deaths in Turkey were in between Italy and Spain in total, as the number of cases in Italy were more than half the number of cases in Turkey, while number of deaths in Turkey (314) were 1.5X the number of deaths 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 Belgium, which obeyed exponential growth curve, for which goodness of fitting for the duration (first fifteen days of the outbreak since the report of first death) $R^2$ value improved from 0.92 to 0.94 (Fig. 5). The CFR calculation data for other countries included in the statistical analysis is listed in Table 1.

**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

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

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

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

When the cumulative number of cases and cumulative number of deaths by COVID-19 until 31st March 2020 were used for linear regression analysis to determine the slope of the fitted line, estimated values of CFR increased for the European countries under analysis (Table 2). $R^2$ 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 worsened the most having 105792 cases and 12428 deaths, and reached 10.94 (95% CI: 10.52-11.37) with $R^2$ value of 0.98. CFR value for Spain also doubled and approximated to 8.595 (95% CI: 8.196-8.995) with $R^2$ 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 day cut off to March 31st cut off by linear regression. UK’s CFR reached 6.5 (95% CI: 6.151-6.868) with $R^2$ value of 0.98 due to 25150 confirmed cases and 1789 deaths. The situation of Germany also worsened as CFR value more than doubled from initial 15 day after report if first death to 31st March and reached to 0.93 (95% CI: 0.8077-1.064) with $R^2$ value of 0.92 on cumulative analysis up to 71808 cases and 775 deaths until 31st March cut off duration. France, for which initial 15 day CFR was comparative to Turkey, also reached to a high CFR value of 6.482 (95% CI: 6.109-6.856) 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 $R^2$ value of 0.97 by 16605 number of cases and 433 deaths in the duration under statistical analysis (Fig. 4). Portugal reported the first death from COVID-19 one day before Turkey and CFR value for Portugal is 2.297 (95% CI: 2.147-2.448). The epidemic curve modeling for Austria obeyed the exponential growth until 31st March cut-off date with $R^2$ value of 0.93 for exponential model (as compared to 0.89 for linear fit model). However, for Belgium, linear model gave $R^2$ value of 0.958 as compared to 0.819 for exponential curve. Until 31st March. It can deduced that in Belgium, COVID-19 outbreak followed exponential curve in the very initial stage and progressed to a more linear trend until the cut-off date of the study (Fig. 5).

**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)

<table>
<thead>
<tr>
<th>Country</th>
<th>CFR</th>
<th>95% CI</th>
<th>$R^2$</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Italy</td>
<td>10.94</td>
<td>10.52-11.37</td>
<td>0.986</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Spain</td>
<td>8.595</td>
<td>8.196-8.995</td>
<td>0.986</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>UK</td>
<td>6.509</td>
<td>6.151-6.686</td>
<td>0.982</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Germany</td>
<td>0.9367</td>
<td>0.8077-1.064</td>
<td>0.917</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>France</td>
<td>6.482</td>
<td>6.109-6.856</td>
<td>0.974</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Switzerland</td>
<td>2.092</td>
<td>1.839-2.346</td>
<td>0.920</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Belgium</td>
<td>4.887</td>
<td>4.399-5.374</td>
<td>0.959</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Netherlands</td>
<td>7.538</td>
<td>6.945-8.132</td>
<td>0.966</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Austria</td>
<td>1.106</td>
<td>0.9210-1.291</td>
<td>0.898</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Portugal</td>
<td>2.297</td>
<td>2.147-2.448</td>
<td>0.987</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>*Norway</td>
<td>0.8224</td>
<td>0.6888-0.9560</td>
<td>0.903</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*<5000 number of COVID-19 confirmed cases.*

**Discussion**

Previously, COVID-19 CFR for Italy was compared with China and early report (28th February 2020) showed that...
CFR for China and Italy were quite similar at 2.3. In our study, CFR for Italy after 15 days of 1st death report was 3.95, which increased to 10.94 by 31st March. Therefore, the situation in Italy is quite alarming in terms of mortality rate of the COVID-19. This is the first report of COVID-19 CFR estimation on data of Turkey and its comparison of current situation with other countries. All the countries selected for the study showed a more linear trend of outbreak in the initial phase based on linear regression analysis, except for Belgium in the first fifteen days after the report of first death and Austria overall until 31st March, showed a more exponential growth. As of March 31st, CFR estimation indicates that within fifteen days of first death report, Turkey’s situation is similar to France.
However, in terms of spread of the virus, the numbers are quite alarming for Turkey. The tight linear trend of CFR estimation in this study from cumulative number of cases and cumulative number of deaths actually comes from outbreak being in initial phase. Therefore, these CFR estimates are likely to change. However, the model can be used in a cumulative manner in future.

Conclusion
COVID-19 outbreak since its initiation in China has caused a public health nightmare globally. As of today, Italy has lost more lives than any other country to this new viral infection. Europe has been hit more adversely as compared to other continents. Turkey, with its geographical position and importance is also at the center of this pandemic. Since the first COVID-19 death in Turkey reported on 17th March, we collected recent 15 day data and computed CFR through linear regression statistical analysis. However, this data in itself has not much importance, therefore, we estimated CFRs for European countries selected in this study to correlate a pattern of CFR for first fifteen days of data since first death was reported in these countries for a comparable estimate of Turkey’s scenario in a regional outbreak. Later, we calculated the overall CFRs of these countries and tabulated the data for real time analysis of any variance. CFRs of all countries under investigation showed rapid increase. Therefore, it can be estimated that COVID-19 CFR will more likely to be increased in future. This study is an attempt to record the statistical data on COVID-19 epidemiological data for Turkey and European countries selected for the study.

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.


References


