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Mortality among the early cases of COVID-19 and its association with key comorbidities in a large state in South India

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ABSTRACT

Background: The mortality associated with the pandemic COVID-19 is a subject of intense scrutiny as COVID-19 can cause severe disease leading to hospitalization in ICU and potentially death, especially in the elderly with comorbidities. A statistical analysis is carried out to study the impact of age, gender and comorbidities on deaths among early one lakh infected population of Karnataka, a large state in south India.

Methods: Daily case fatality rate and adjusted case fatality rate (CFR) (adjusted to median death time) are estimated. The impacts of age, gender and comorbidities on mortality outcomes of COVID patients are studied.

Results: The daily CFR on 27th July for Karnataka is estimated from the dataset to be 1.93%. However, the adjusted CFR based on the median number of days from diagnosis to death was found to be 2.15% (95% confidence interval 2%-2.3%) on that day. The deaths among male patients outnumber those in females. As far as age of the patients is concerned, more than 50% of the deaths occurred in the age group 50-60 and 60-70 years. Majority of deaths reported in the state were associated with at least one of the comorbidity. Diabetes mellitus and hypertension were the most significant comorbidities.

Conclusions: The daily adjusted CFR for the study region is found to be lower than the CFR of the whole nation. Also the age, gender and comorbidities were found to be associated with the deaths as opposed to the infection alone. It was also deduced that, patients with a history of diabetes or hypertension or ischemic heart disease or a combination of any of these were most likely to experience severe outcomes of the infection.

Keywords: COVID-19, Case fatality rate, Comorbidities, Diabetes mellitus, Hypertension, Ischemic heart disease

INTRODUCTION

Infectious diseases that affect a significant proportion of the world population have been the bane of the civilised world since written history has been recorded. Malaria, cholera, bubonic plague, pox, tuberculosis, Spanish flu are all historical pandemics and are embedded in our collective psyche as grave threats to humanity. Since December 2019, the world has faced one of the most serious public health emergencies in the recent times. Starting from the city of Wuhan, Hubei province of China, COVID-19 has rapidly spread across the world and has now been detected in almost all the countries. The world health organisation (WHO) declared the infection as a 'pandemic of global importance on 11th March 2020.¹ By the end of the first week of September 2020, there are about 26 million confirmed cases of COVID-19 in the world with United States, Brazil, India and Russia contributing the most number of cases. In addition to confirmed number of cases, most countries are reporting the mortality data and the trends in mortality have followed different trajectories in different regions.

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The global death toll attributed to the virus is nearly 0.9 million and the major contributors to the death statistics of COVID-19 pandemic are USA, Brazil, India, Mexico, Spain, UK, Italy and France. The countries which have reported the most number of deaths per million populations are Peru, Spain, UK and Belgium.²

It has also come to the attention of the scientific community that there is a correlation between severity of the disease and comorbidities such as cardiovascular disease, diabetes mellitus, chronic respiratory disease, hypertension and cancer. There is also evidence of association of age with severity of the infection and consequently the symptoms.

One of the stark differences from the previous pandemics and the COVID-19 scourge that we are facing is the environment of information explosion and seamless real time availability of the data related to the spread of the disease. This treasure trove of epidemiological data can be analysed to derive meaningful inferences and usable data which can help in our collective fight against the epidemic. Karnataka, a large state in south India, has been publishing daily updates on the number of cases detected, the deaths as well as other data such as morbidities, age and presenting symptoms. The first COVID-19 case was reported on 9th March, 2020 and it took about 140 days to cross the one lakh threshold. In stark contrast it took only 16 and 14 days to cross the subsequent one lakh marks respectively. Currently (1st week of September) the total number reported by the government of Karnataka stands at about 3.7 lakhs. This paper aims to analyse the mortalities reported among the early one lakh COVID-19 patients of Karnataka, and try to find associations with comorbidities.

METHODS

Sources of data

Epidemiological data was collected from publicly available sources including the COVID-19 information portal of the Directorate of the health and family welfare services of the Government of Karnataka.³ Data collected includes the daily number and details of the laboratory confirmed COVID-19 positive cases, daily number of deaths and the comorbidities among the deceased for first one lakh infected population of Karnataka from 9th March 2020 to 27th July 2020.

Case fatality rates

Daily case fatality rates (CFR) were calculated as cumulative number of deaths divided by cumulative number of confirmed infected cases. During an on-going epidemic, number of deaths from infection (numerator) will not represent the total number of deaths among infected cases in the denominator. The denominator includes infected population, some of whom will succumb to the disease in near future. Hence, the CFR

thus calculated will be an underestimation and an attempt is made by us to correct this. To calculate the adjusted CFR, we used the cumulative number of cases reported X days ago where X denotes the median number of days from diagnosis to death.⁴

We calculated the median days from diagnosis to death by conducting survival analysis using the Kaplan-Meier estimate.⁵ The cases which were reported as brought dead or dead at residence were not taken into consideration for this analysis.

Comorbidities, age and gender

The comorbidities were analysed and descriptive statistics was applied. There was a lot of variation in the descriptive medical terminology of the comorbidities and we have made an effort to rationalise and club the comorbidities into coherent groups. The leading comorbidities among the deaths are reported. The age groups with the most number of deaths are also reported.

RESULTS

As of 27th July, there were a total of 1941 deaths in Karnataka against a total of 101465 cases reported. The daily number of confirmed cases and the number of deaths reported are depicted in (Figure 1). The CFR for Karnataka was estimated to be 1.93% on 27th July. When the correction using the method described above was applied the adjusted CFR was found to be 2.15 % (95% confidence interval 2%-2.3%) on that day. The median number of days from diagnosis to death calculated by using K-M estimate was 2 days (95% confidence interval 1-2).

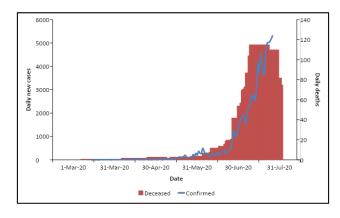


Figure 1: Daily incidence of COVID-19 cases and associated deaths.

The age and gender distribution of the mortalities is depicted in (Figure 3). The deaths reported among male patients (67.95 %) outnumber those in females (32.05 %) by a ratio of 2:1. For both the genders, more than 50% of the deaths occurred in the age group 50-60 and 60-70 years. Three quarters of deaths occurred in ages above 50 years making advanced age a predictor of severe disease

and mortality. The frequencies of comorbidities were estimated and the results are presented in (Table 1).

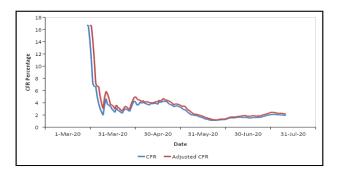


Figure 2: CFR and adjusted CFR of Karnataka till July 27 2020.

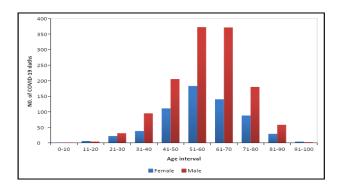


Figure 3: Age and gender wise distribution of COVID-19 deaths.

Table 1: Comorbidities among COVID-19 deaths.

Comorbidity	Frequency	Percentage
Ischaemic heart disease	280	14.42555
Diabetes mellitus	919	47.34673
Hypertension	845	43.53426
Chronic respiratory disease	46	2.369912
Liver disease	37	1.906234
Renal failure	141	7.264297
Others	93	4.791345
No comorbidities reported	574	29.57239

Majority of deaths reported in the state were associated with at least one comorbidity. However, many of the reported deaths had multiple comorbidities listed. Diabetes mellitus and hypertension were the most common comorbidities reported with 47.3% and 43.5% respectively. Ischaemic heart disease (14%), renal failure (7.2%), chronic respiratory disease (2.3%) and liver disease (2%) constitute the other common comorbidities. Another significant observation is that 29.6 % of the deaths did not have any comorbidity reported.

DISCUSSION

Comparison of CFR reported in other states and countries

The upsurge in the CFR values during early days of pandemic is attributed to less number of cases as well as still less number of deaths. On 27th July, 2020 the CFR for India was 2.28% which is higher than the CFR of Karnataka on that day. When compared with the CFR reported in several other countries, the CFR in Karnataka as well as India was much lower. Some of the countries that reported higher CFR include Italy (14.3%, highest), Mexico (11.2%), Indonesia (4.8%), Germany (4.4%), Brazil (3.6%), United States of America (USA) (3.5%) and Norway with 2.8%. South Korea (1.7%) and New Zealand (1.6%) had lower daily CFR than India.⁶

There are several methods to adjust the CFR to account the underestimation during an on-going epidemic. We chose to do it by calculating the median time from detection to death. For count data, KM analysis is most suitable statistical tool to study the event of interest. Median time from detection to death for COVID-19 patients varies for different countries. Compared to other populations, the data under study has very low median number of days from diagnosis to death. This difference may be explained by considering the time gap between getting the infection and hospitalization. Another factor for variation could be the difference in detection, reporting and follow up strategies.

Researchers from around the world have reported associations between comorbidities and outcome of the infection since the beginning. One of the prominent works by Guan et al. considers a sample of 1590 patients from China out of which 399 (25.1%) had at least one comorbidity. Like our analysis, hypertension (16.9%), diabetes (8.2%) and cardiovascular diseases (3.7%) were the most common comorbidities reported. Out of the sampled patients, 131 (8.3%) reached a more complex status during the study period. It was to be noted that, among the patients having reached these complex end points, 77 (19.3%) had at least one comorbidity.

Another study by Singh et al have reported and compared comorbidities among the patients of COVID-19 in China, USA, Italy, United Kingdom (UK), Spain, Mexico, Kuwait and India across different time periods. According to the data collected and analysed by the authors, presence of cardiovascular disease (CVD), diabetes, chronic obstructive pulmonary disease (COPD), hypertension and cancer in patients from China pulled the CFR up to 10.5%, 7.3%, 6.3%, 6.0% and 5.6% from 2.3% for overall population. Among the patients of USA, CVD (including hypertension, coronary heart disease, stroke, heart failure and other cardiovascular diseases) accounted for 60.9% of the total deaths in the study period. For Mexico, the major comorbidities among the deaths were obesity, diabetes, chronic kidney disease (CKD), COPD,

and hypertension. In case of Kuwait, presence of Asthma was the only major comorbidity associated with high risk of mortality. In UK, chronic cardiac disease, COPD, CKD, obesity and liver diseases were associated with the mortality. The meta-analysis by the authors concluded that across these regions, hypertension or diabetes or CVD or CKD or COPD and or cancer were associated with at least 1.5 to 3 fold increase in the risk due to COVID-19. Similar results have been reported by studies conducted in different regions and populations since the start of the pandemic. 11-15

Limitation of the study

One of the limitations of our study is that the analysis described herein and the results reported are very much dependent on the state of health care affairs in the system. The robustness of the health care system and the data collecting machinery in the state are a major influence. Since this is an evolving epidemic, there may be temporal changes in reporting of cases, deaths, morbidities and presenting symptoms either due to human factors as well as changes in policies by the local administration. An ideal way to calculate the data reported here would be to conduct a longitudinal study in controlled conditions. Some authors have also tried to account this limitation by assuming decreased reporting rates while calculating the CFR. ¹⁶

CONCLUSION

In conclusion, the deaths due to COVID-19 were mostly associated with age, gender and comorbidities. It was found that, a patient to be most likely to succumb to the infection whenever the person is an elderly male with at least one of the comorbidities. However, one should note the limitations of the study while arriving at any conclusions.

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