Comparative analysis and epidemiological study of SARS-CoV-2 in first wave among different states of India

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Abstract

Severe Acute Respiratory Syndrome Corona Virus-2 (SARS-CoV-2) has now spread worldwide, and various governments are attempting to control the disease's spread before it becomes a global health crisis. Data from 28 Indian states and 8 Union Territories (UTs) provide a detailed look at the transmission pathways and case fatality rate (CFR) of the SARS-CoV-2. Among the global data, India was found to be the third country with the highest mortality cases of 157K, and Maharashtra was having the most higher number of mortality cases followed by Tamil Nadu and others. The percent distribution of CFR calculated in each geographical zone of India i.e. Central, Eastern, North Eastern and Northern, Southern and Western zone were 17%, 14%, 7%, 22%, 12%, and 28%, respectively. Furthermore, the CFR was calculated at different periods of the month using a standard formula. The CFR was significantly higher ($P<0.01$) in April to June of 2020. CFR was significantly different ($P<0.01$) depending on the month. Moreover, CFR was compared in different zones in India, western zone showed the highest CFR as compared to other zones. The effectiveness of SARS-CoV-2 was evaluated in patients of various ages and co-morbidities. Patients >21 years had the highest age-specific positivity rate. The prevalence of SARS-CoV-2 patients in acute and chronic disease was 12.87 and 87.13 percent, respectively. Thus, this analytical epidemiological study serves specifically in establishing a relationship between SARS-CoV-2 infection and other precipitating factors causing morbidity and mortality during the given time frame in the first wave, in the year 2020.

Introduction

In Wuhan (China 2019), a severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) infection caused by a virus, i.e. coronavirus, has completely spread all over the world, creating an emergency situation [1]. This pandemic disease has caused 3.2 million deaths and infected more than 158 million people worldwide by May 11, 2021 [2]. During the early stages of the pandemic, epidemiologic studies and disease surveillance were conducted in China [3-5], Europe [6, 7], and North America [8-10], to better understand the current SARS-CoV-2 pandemic. The majority of confirmed cases occurred in low and middle-income countries (LMICs), where a significant number of individuals were at increased risk of outcomes and faced barriers to access high-quality health care [11-13]. Although many more studies are needed to assess how SARS-CoV-2 affects individuals and communities [14-16], there is almost no fundamental approach available to inform intervention strategies of SARS-CoV-2 transmission dynamics and clinical outcomes [17].

At the end of the year 2019 and the beginning of the 2020 year, human infection with SARS-CoV-2 was first identified in Wuhan, Hubei Province, China. Coronavirus is a single-strand ribonucleic acid that is genotypically and phenotypically diverse. Globally, as of December 31, 2020, SARS-CoV-2 cases have been reported to the World Health Organization (WHO). Fever (99%), fatigue (70%), dry cough (60%), myalgia (44%), and dyspnea are the most common symptoms of SARS-CoV-2 [18-20]. Headache, dizziness, diarrhea, nausea, and vomiting are the additional symptoms of SARS-CoV-2 that are less common [21]. Symptoms of severe illness include pharyngeal pain, dyspnea, dizziness, abdominal pain,

and anorexia [19]. Elderly patients with co-morbidities such as hypertension, diabetes, cardiovascular disease, and cerebrovascular disease are experiencing negative outcomes. Lymphopenia, prolonged prothrombin time, elevated lactate dehydrogenase, and elevated D-dimer were found in SARS-CoV-2 patients who were hospitalized, which is similar to SARS-CoV that caused an outbreak in 2003 in China and MERS-CoV infections. Chest imaging reveals some bilateral patchy shadows and ground-glass opacities. Acute respiratory distress syndrome, acute cardiac injury, arrhythmias, acute kidney injury, and shock, are all SARS-CoV-2 complications [22-24]. The virus spreads at a rate of 40% in hospitals. In hospitalized patients, the mortality rate is around 4% [22-24]. In the published literature, there is insufficient graphic evidence to develop complete clinical pictures of the disease. As a result, the requirement to design a study to provide multidisciplinary care in an integrated, single service area, and these should be used for humane and beneficial aesthetics, and this can be an important step for the empowering health system to mount an adequate response to the surge in cases.

In India, the total cases were 10.3M, recovered 9.9M and 148.4K death. Non-pharmaceutical measures (traveling restrictions, public transport closure and workplace closing) taken for limiting the spread of this pandemic incur social and economic costs. Hence, vaccination is used as an alternative (after conducting clinical trials on the duration of infectivity, the safety of the vaccine, severity of resultant disease, and efficacy of infection reduction) to overcome the spread of infectious SARS-COV2 [25,26].

Therefore, the present study was designed to analyze the case fatality ratio (CFR) in different states as well as geographical zones of India. Moreover, the data of SARS-CoV-2 cases were compared in different age groups and several co-morbidities diseases.

Material And Methods

SARS-CoV-2 data was collected from online available sources (*https://api.covid19india.org)*, co-morbidities and age group of SARS-CoV-2 patients data were taken from the website of National Centre for Disease Control, New Delhi. SARS-CoV-2 data for twelve months of the first wave was collected from January to December 2020 and also, classified into four different periods. Period I contained January to March; period II contained April to June, period III contained July to September, while period IV contained October to December of the year 2020. Further, data of SARS-CoV-2 was analyzed in different geographical zones of India as well as information based on different states of India cutting across co-morbidities and different age groups. The geo-epidemiological analysis was done using open source software, QGIS (Quantum GISD development Team, 2021).

Statistical analysis

Case Fatality Ratio

The CFR of SARS-CoV-2 was calculated by given formula:

CFR%= number of deaths*100/ Confirmed cases

Percent of Distribution

Percent of distribution is a measure of how a variable (Such as total cases) is distributed among the component parts that make up the total. The calculation of percent distribution is relatively simple and is derived from division of each component part by total to get a percent of distribution.

Least Squares Means Analysis

Least squares means analysis was used to estimate the variance components and parameter (LSMLMW, version-2.0) [27]. The following model was used to analyze the effect of various SARS-CoV-2 factors.

Model 1:

$Yij = \mu + Period_i + month_j$

Where Yij is the observation of i^{th}period (Jan-March, April-June, July-September, October-December 2020, j^{th}month)

Eij = random residual error associated with observation with mean 0 and variance 1

μ= population of mean

$Period_i$= fixed effect of ith period (Jan-March, April-June, July-September, October-December 2020, i=1,2,3,4)

$Month_j$= fixed effect of jth period (Jan to Dec 2020, j=1 to 12)

Result

Epidemiology, different geographical zones of India

The data of case fatality ratio (CFR) was calculated in 36 Indian states/UTs. Punjab, Maharashtra, and Sikkim had highest 3.22, 2.44 and 2.20 case fatality percent in India as compared to other states of India (Fig.1). Similarly, the CFR in India's various zones were calculated in all the six geographical zones used in the current study viz., Central Zone, Eastern Zone, North Eastern Zone, Northern Zone, Southern Zone, and Western Zone. Western zone of India had highest CFR percentage as compared to other zones (Fig. 2). The CFR percent of the Central Zone, Eastern Zone, North Eastern Zone, Northern Zone, Southern Zone, and Western Zone were 1.42, 1.15, 0.60, 1.77, 0.94, and 2.33, respectively,

Case Fatality Ratio

Least squares means of case fatality ratio (CFR) rates were examined from January 2020 to December 31, 2020, spanning 337 days. Coefficient variation, R squared and average of CFR were 17.91, 0.884, and 1.908% respectively over the year. The CFR was calculated in different months of the year 2020. During the months of April, May, and June, CFR consistently increased (Fig. 3). ANOVA of month-wise data showed a significant effect ($p<0.01$) on CFR (Table 1). Furthermore, the least squares means were examined in different period of months and classified into 4 (four) distinct periods, namely period I (Jan to Mar 2020), period II (Apr to Jun 2020) period III (Jul to Sept 2020) and period IV (Oct to Dec 2020). CFR of the period was calculated as per decease so zero deceased or zero CFR data were removed from the data analysis for least squares means. Co efficient variation, R squared and average of CFR in different period were 27.97, 0.768 and 1.908%, respectively. The least squares mean of CFR of different periods were presented in Table 2. The CFR was significantly (P<0.01) higher in period II contained April to June of the year 2020. Also it was observed that there was significant difference in the CFRs while comparing month-wise data (Table 3). The CFR percentage was calculated for each state by period, as shown in Fig. 4. The CFR of Indian states was comparatively higher from April to June as compared to January to March, July to September, and October to December of the year 2020.

Percent of distribution of SARS-CoV-2 cases in India

In the current study, we estimated the case fatality ratio (CFR) percent in various geographical zones of the country. In India, the Percent distribution of CFR in Central, Eastern, North Eastern, Northern, Southern, and western were 17%, 14%, 7%, 22%, 12%, and 28%, respectively (Figure 5). Maharashtra had a significantly (P<0.01) higher percentage of SARS-CoV-2 positive cases than the other states. By December 2020, India had reported several million cases of SARS-CoV-2; with cases trending shows a percent of distribution of different zones of India. The percent of distribution of SARS-CoV-2 positive patients ware 7.0% in Central Zone, 8.0% in Eastern zone, 12.0% in North Eastern, 25.0% Northern, 24.0% in Southern zone and 24.0% in Western Zone, respectively (Fig. 6A). The highest positive SARS-CoV-2 cases were found in Northern zone (25%) followed by Western zone (24%) and the Southern zone (24%) of India. The percent of the distribution of mortality was highest in the Western zone (38%) followed by the Northern zone (29%) than others (Fig. 6B).

Effect of SARS-CoV-2 in various age groups

The trend of SARS-CoV-2 cases was estimated in a different age group based on the limited data available from online. Incidence rate of different age group was evaluated in the Indian population. Age-specific estimates ranged from 12.37% at ages <20 years to 0.09% at ages >81years. Age-specific SARS-CoV-2 incidence rate showed that the >21 years age group was most affected, while the old (>81 years) age group was least affected in India (Fig. 7). Similarly, age-specific data showed an almost similar trend on the statista website (• India: COVID-19 cases by age group 2021 | Statista).

Co-morbidities in SARS-CoV-2 patient in India

Co-morbidity data was classified into two different categories in the present analysis i.e. acute and chronic. The acute diseases included cardiac affections, Asthma, Bronchitis and Neuromuscular affections, while chronic disease included Hypertension, Diabetes, Liver disease, chronic renal diseases, Chronic obstructive pulmonary disease (COPD), Immuno-compromised conditions and Malignancy. The incidence percent of SARS-CoV-2 patient in acute disease and chronic disease exhibited 12.87 and 87.13 percentage, respectively (Fig. 8). The chronic patients were significantly affected by SARS-CoV-2. From the all co morbidities, hypertension was the most reported followed by diabetes and liver disease. CFR for SARS-CoV-2 was shown to be increased with presence of co-morbidities [28-30] such as hypertension (CFR=6.0%), diabetes (CFR=7.3%), cardiovascular disease (CFR=10.5%), chronic respiratory disease (CFR= 6.3%) and neoplasm (5.6%).

SARS-CoV-2 trend over the period

SARS-CoV-2 trend was analyzed during January, 2020 to December 2020. We plotted the trend of SARS-CoV-2 cases observe the impact during different months. However, the trend of SARS-CoV-2 confirmed cases were slightly higher after the month of May, 2020 than before. Similarly, SARS-CoV-2 patients had the same mortality trend as SARS-CoV-2 confirmed cases (Fig. 9 and Fig.10).

Discussion

Our findings are based on extensive surveillance and contact-tracing data collected from 36 Indian states/UTs. Present investigation was carried out in different states of India and moreover comparative study was conducted in different age groups and several co-morbidities in India. Similarly, the finding based on comprehensive surveillances from the Indian state of Tamil Nadu and Andhra Pradesh [1].

SARS-CoV-2 had been reported from 58 countries and territories around the world as of February 28, 2020, and one international conveyance, the Diamond Princess Cruise Ship [31]. As of December 29, 2020, there had been 4 million new SARS-CoV-2 cases and 72,000 new deaths were reported. This brings the cumulative numbers to over 79 million reported cases and over 1.7 million deaths globally since the start of the pandemic. [32]. This study shows that, in India a total number of 11.06 Million SARS-CoV-2 cases, total 0.16 Million death cases and 10.75 Million recovered cases have been reported. Out of the total cases, 2.13 Million cases mostly reported from Maharashtra, with 51,993 death cases. Similarly, the vast majority of cases (78,824 out of 83,704; 0.9416 - 95 percent CI 0.94 to 0.9433) and deaths (2,790 out of 2,859; 0.9758 95 percent CI 0.9696 to 0.9809) have been reported from mainland China [32]. The first U.S. cases of non-travel-related SARS-CoV-2 were confirmed on February 26 and 28, 2020, which clearly suggested the community transmission in U.S. by late February [33].

This study was compared, the CFR among states that reported a large number of SARS-CoV-2 cases at 12 months of the pandemic, namely Jan 2020 to December 2020 reported that Maharashtra (2.441%), Punjab (3.215 %) and Sikkim (2.201 %) had highest CFR than other states of India. Similarly,

the SARS-CoV-2 cases rate was calculated in two different states (Tamil Nadu and Andhra Pradesh) of India. However, the CFR was calculated in different countries at the two-time point of the pandemic namely 12 March 2020 to 23 March 2020 reported that Italy (6.22%), China (3.91%), Iran (3.62%), USA (3.07%) and Spain (2.12%) had highest CFR [34]. The case-fatality ratio was calculated in Turkey as well as European countries [35].

To begin, assume that the number of deaths reported is equal to or very close to the actual value in the investigation, which may not be the case in many countries. The CFR was calculated for each Interval class, namely January to March 2020, April to June 2020, July to September 2020, and October to December 2020. Our finding also proved that the CFR was significantly increased due to lack of facilities in the initial days and thereafter the CFR trend decreased as facilities were more. There at the time as well identified cancer as a co-morbidities disease. Ideally, the CFR should be low at first due to the incubation time and delay in developing complications from the infection, which was gradually increased until it reaches a plateau that will eventually become the ultimate CFR for the diseases.

In the present investigation, SARS-CoV-2 patients suffered with several co-morbidities which were further classified into two: Acute and Chronic. The incidence percent of acute and chronic were 12.87% and 87.13%, respectively. In India, it is important to know the mortality rates related to different age groups and underlying co-morbidities. So it could be implemented for high-risk populations and utilize the limited resources effectively.

Furthermore, elderly patients with underlying co-morbidities such as diabetes, hypertension, cerebrovascular disease and cardiovascular disease, are more likely to have negative outcomes [36]. People of any age who have underlying medical conditions such as hypertension or diabetes have a worse prognosis [37]. Diabetic patients have higher morbidity and mortality rates, as well as more hospitalizations and intensive care unit (ICU) admissions [37]. People with chronic obstructive pulmonary disease (COPD) or any other respiratory illness are more likely to develop severe SARS-CoV-2 illness [38]. SARS-CoV-2infection is four times more likely in patients with COPD than in patients without COPD [38]. The elderly, particularly those in long-term care facilities and people of any age with serious underlying medical conditions are at a higher risk of contracting SARS-CoV-2, according to current research and clinical expertise [39]. The population having chronic health conditions like cardiovascular, diabetes or lung disease is not only at a higher risk of developing severe illness, but also has higher chances of mortality if they become ill [40]. People with uncontrolled medical conditions such as hypertension, diabetes, lung, liver, and kidney disease, smokers, transplant recipients cancer patients on chemotherapy, and patients on long-term steroid therapy are more likely to contract SARS-CoV-2 [39]. Chronic obstructive pulmonary disease (COPD), among other co-morbidities, has been linked to poor disease progression. A four-fold increase in mortality in patients with pre-existing COPD who were diagnosed with SARS-CoV-2 has been found in a meta-analysis of multiple Chinese studies [38].

There are various reports published recently that clearly prove the decrease in CFR after vaccination. India has approved two vaccines for SARS-CoV-2 i.e. Covaxin (developed by Bharat Biotech) and Covishield

(Manufactured by Serum Institute of India), and Covaxin is reported to be 93.4% effective against severe SARS-CoV-2 (https://www.reuters.com/world/india/indias-bharat-biotech-says-vaccine-934-effective-against-severe-covid-19-2021-07-03/). In India, a total of 707 million population has the first dose, whereas, 291 million (30%) population were fully vaccinated by end of January 2021 (https://www.bbc.com/news/world-asia-india-56345591). A significant decrease in death rate by 72% and 84%, respectively, has been reported from 14 to 20 days and from 21 to 27 days, respectively, after mass vaccination of first dose [41]. Similarly, the fatality rate was decreased by 96.7% after the administration of the second dose [42]. In the United States, three vaccines have been recommended for SARS-CoV-2 prevention. SARS-CoV-2 mRNA vaccine mRNA-1273 (Moderna SARS-CoV-2 vaccine) and adenoviral vector vaccine Ad26.COV2.S (Janssen SARS-CoV-2 vaccine) has been approved by emergency use authorization (EUA) for the prevention of SARS-CoV-2. The other vaccine SARS-CoV-2 mRNA vaccine BNT 162b2 (Pfizer-BioNtech SARS-CoV-2vaccine) has been approved by Food and Drug Administration (FDA) [43,44].

A simulation study has proved the reduction of SARS-CoV-2 deaths by 69.3% after vaccination in the United States. In addition, studies on vaccination campaigns have also proved the reduction in the incidence of SARS-CoV 2 in Israel [45-48]. A recent study by Liang and coworkers has proved a large variation in health benefits for vaccination at the global scale. The vaccination rate is recorded to be more in seven countries including Chile, Israel, United Arab Emirates United Kingdom, Bahrain, Hungary, and the United States, where approximately one-third of the population is vaccinated [245].

In this particular study, age criteria were classified into 4 different class interval namely: <20 years, >21-50 years, >51-80 years and >80 years. Out of these, the incidence percentage was higher in >21-50 years class of interval followed by others. It is essential to know age groups which are affected most by the infection in a pandemic situation, so that the effective preventive measures can be under taken for the high risk group. It is shown that the CFR of SARS-CoV-2 increase with ages [39,49] across different countries. Italian population (23%) was either 65 years of age or older [50]. This would explain the higher mortality rates of Italy compared to other countries. A similar study has been reported by Russell and his coworkers, for the detection of infection and CFR for SARS-CoV-2 in February 2020 using age-adjusted data (0-9 years, 10-19 years, 20-29 years, 30-39 years, 40-49 years, 50-59 years, 60-69 years, 70-79 years, 80-89 years) from the outbreak on the Diamond Princess cruise ship. The highest CFR of 14.8% was detected in the age group between 80-89 years, and the potential bias in the age-specific severity level of SARS-CoV-2 was reported due to a lower level of detection in children if their symptoms are mild [51]. Similarly, the CFR rate of SARS-CoV-2 is reported to be higher in older adults than younger individuals i.e. 42% for those above 65 years and 65% below 65 years; and the association of chronic conditions and risk of dying across different age groups follows the same trend [52].This study shows that the globally mortality cases was 2.68M. The mortality cases were higher in United State (538K) followed by Brazil (282K) and India (157K). It represents that India was the third highest country in respect to mortality cases. In India, Maharashtra was having the most higher number of mortality cases followed by Tamil Nadu and others. And the overall percentage of mortality SARS-CoV-2 cases was significantly higher in Western zone as compared to other zones. Wuhan had a higher mortality rate of 4.9 percent, while its'

province Hubei had a lower mortality rate of 3.1%. In China, a significant proportion of deaths (26%) occurred in people over the age of 60. However, at this stage in the epidemic's evolution, temptations to make policy decisions based on mortality data should be avoided [53]. The age-specific SARS-CoV-2 death rate in Korea was higher among patients over 70 years of age with underlying diseases in their circulatory system such as arrhythmia, cerebral infarction, hypertension and myocardial infarction [54]. A recent study has proved the highest mortality rate per million inhabitants of SARS-CoV-2 cases in Belgium between April 11, 2020, and August 26, 2020 [55].

Similarly, two groups of countries emerged, one with a higher mortality rate (Spain, Italy, and the United Kingdom) and the other with a lower mortality rate (USA, Germany, China). This analysis showed that the mortality in Maharashtra was higher because of the poor adherence to the safety norms and due to the most visited, crowded place in India. Furthermore, Iran must have begun to report or test care only after seeing facilities due to the disease [56]. Higher CFR values have reported at the start of the pandemic.

There lies a relational trend between higher CFR rates and advancement of the pandemic in the first wave of 2020. This could be largely due to the temporal adaptation of the virus in the population. This explains why period II showed the peak CFR, followed by a decreasing trend in the CFR.

Similarly, the first wave in India has non-immunization control, where vaccination was not practiced widely in the population. The pandemic dynamics of the first wave actually represent the vanilla strain (un-mutated) that created the pathogenesis without any herd immunity. This data can further be compared with the second wave CFR and disease pattern caused by a novel strain (delta and delta plus variant) in the future. The comparison of these data on CFR vis-à-vis the immunization started at various stages of second wave could provide a meaningful conclusion on the pandemic dynamics and herd immunity.

Conclusion

SARS-CoV-2 is an infectious disease that poses a significant threat to global health and will most likely persist until an effective vaccine is developed or herd immunity is achieved. India was the third highest country in respect to mortality cases. The overall CFR rate was higher during April to June, 2020 period as compared to other periods. And the overall percentage of mortality due to SARS-CoV-2 cases was significantly higher in Western zone as compared to other zones. Many factors played a key role in the transmission dynamics, and one reason may be due to imposing lockdowns that led to large scale migration of peoples from western India to other parts, precipitating higher spread and mortality. Besides, the western zone (cities like Mumbai, Ahmedabad etc.) is an important business hub and international gateway for Indian sub-continent. Hypertension was the most commonly reported co-morbidity, followed by diabetes and liver disease. In India, it is important to know the mortality rates related to different age groups and underlying co-morbidities. As a result, this study could be implemented for high-risk populations which are predisposed toward viral pathogenesis and also effectively utilize the limited resources that our nation’s healthcare system possesses. This study may be validated using additional

data and associated with other factors. Also, this study can be useful in containing and effectively devising the strategies for future pandemics and outbreaks. This complete information will provide researchers, clinicians, and other health care professionals to think rationally in recognizing the gaps which can be fulfilled by proper management and effective use of the already existing system that we have till newer and effective medications are not available. Thus this study is a complete analytical protocol for cheaper and more effective SARS-CoV-2 containment and management in India.

Declarations

Conflict of interest

The authors declared no conflict of interest.

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Disclaimers

The views expressed in the submitted articles are own and not an official position of the Institution of Funder.

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Tables

Table 1. ANOVA of CFR in different months of the year 2020

Source	D.F	Sum of Squares	Mean Squares	F	P
Month	11	288.105	26.191	224.292	0.0000 **P<0.001**

Month, January to December 2020; D.F, degree of freedom; F, F value; P, probability

Table 2. Least Squares means (LSM) of CFR in different period

Period	Month	Year	Days	LSM
Period 1	Jan-March	2020	62	0.622±0.605
Period 2	April-June	2020	91	3.094±0.499
Period 3	July-September	2020	92	2.045±0.497
Period 4	October-December	2020	92	1.464±0.497

Table 3. ANOVA of Case Fatality Ratio (CFR) in different period

Source	D.F	Sum of Squares	Mean Squares	F	Prob
Period	3	250.421	83.473	367.509	0.0000 **P<0.001**

Period , January to December, April to June, July to September and October to December 2020; D.F, degree of freedom; F, F value; P, probability

Figures

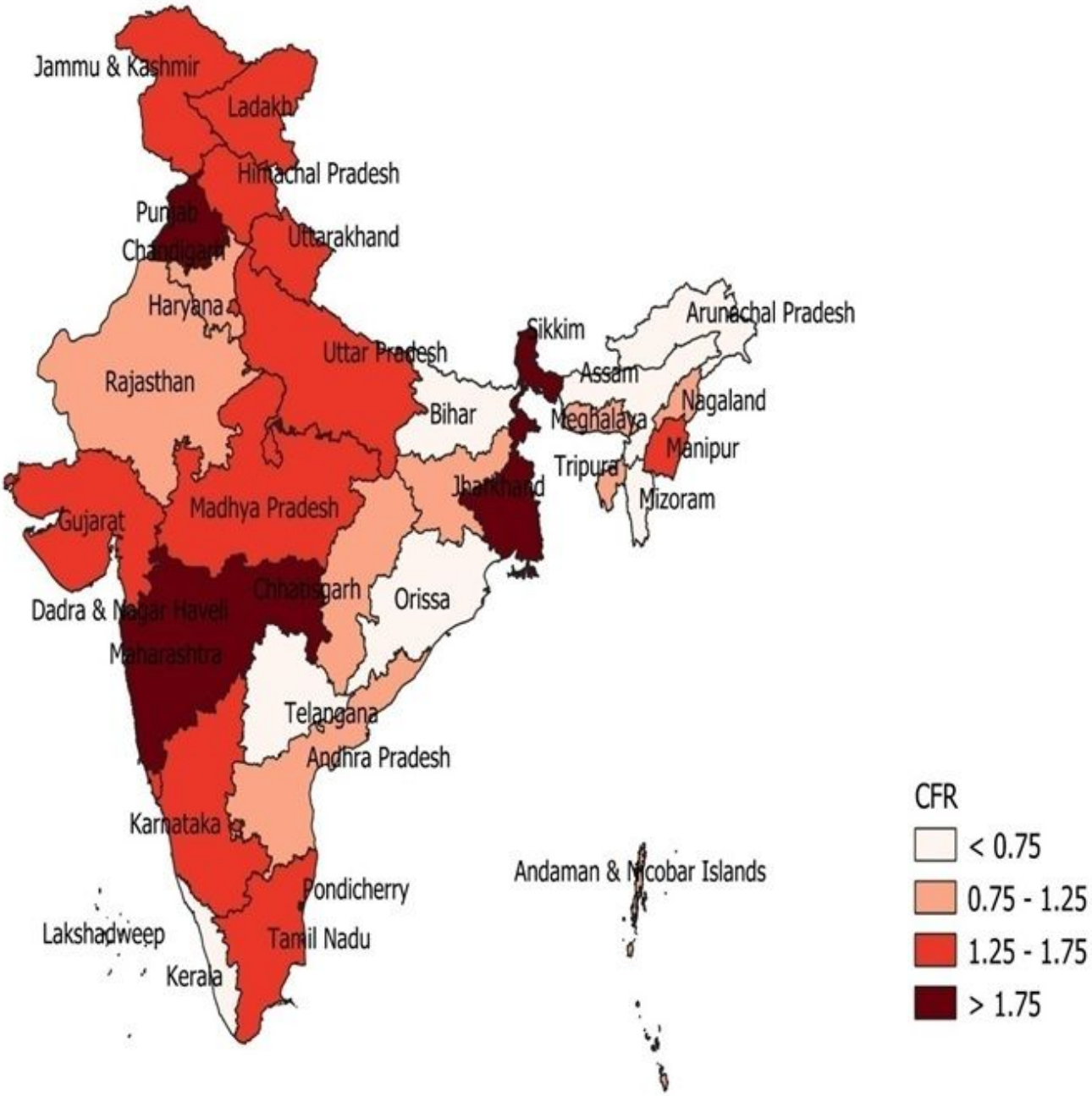

Figure 1

CFR percentage in different states of India

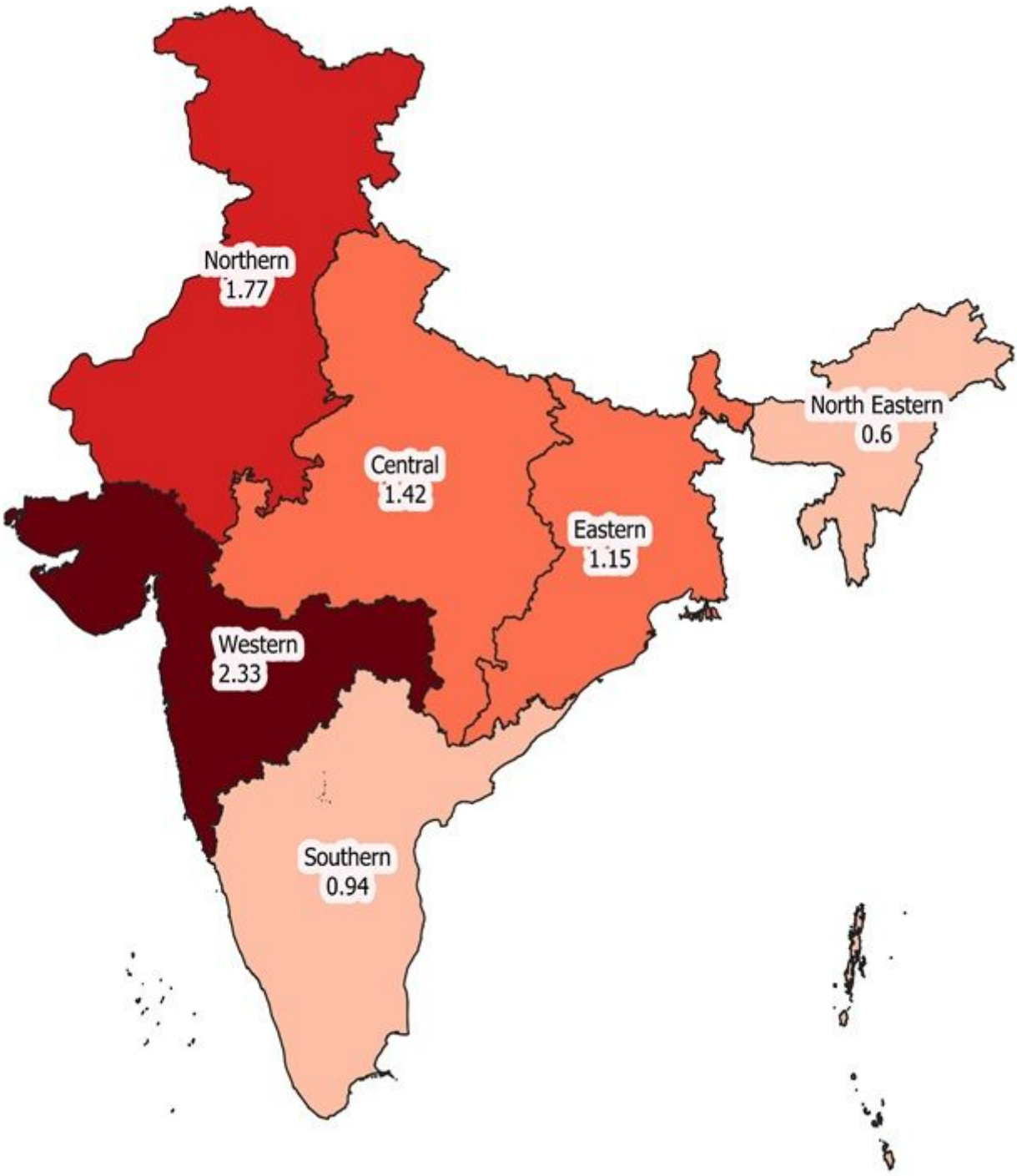

Figure 2

CFR percentage in different zones of India

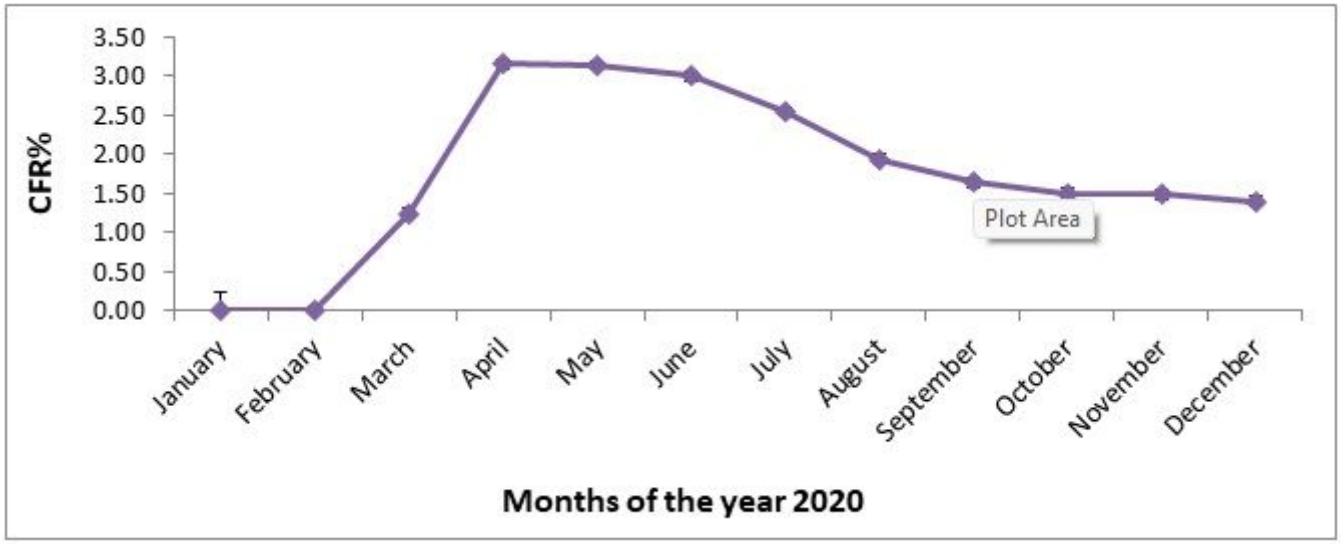

Figure 3

Least Squares Mean (LSM) of CFR% in various months of 2020.

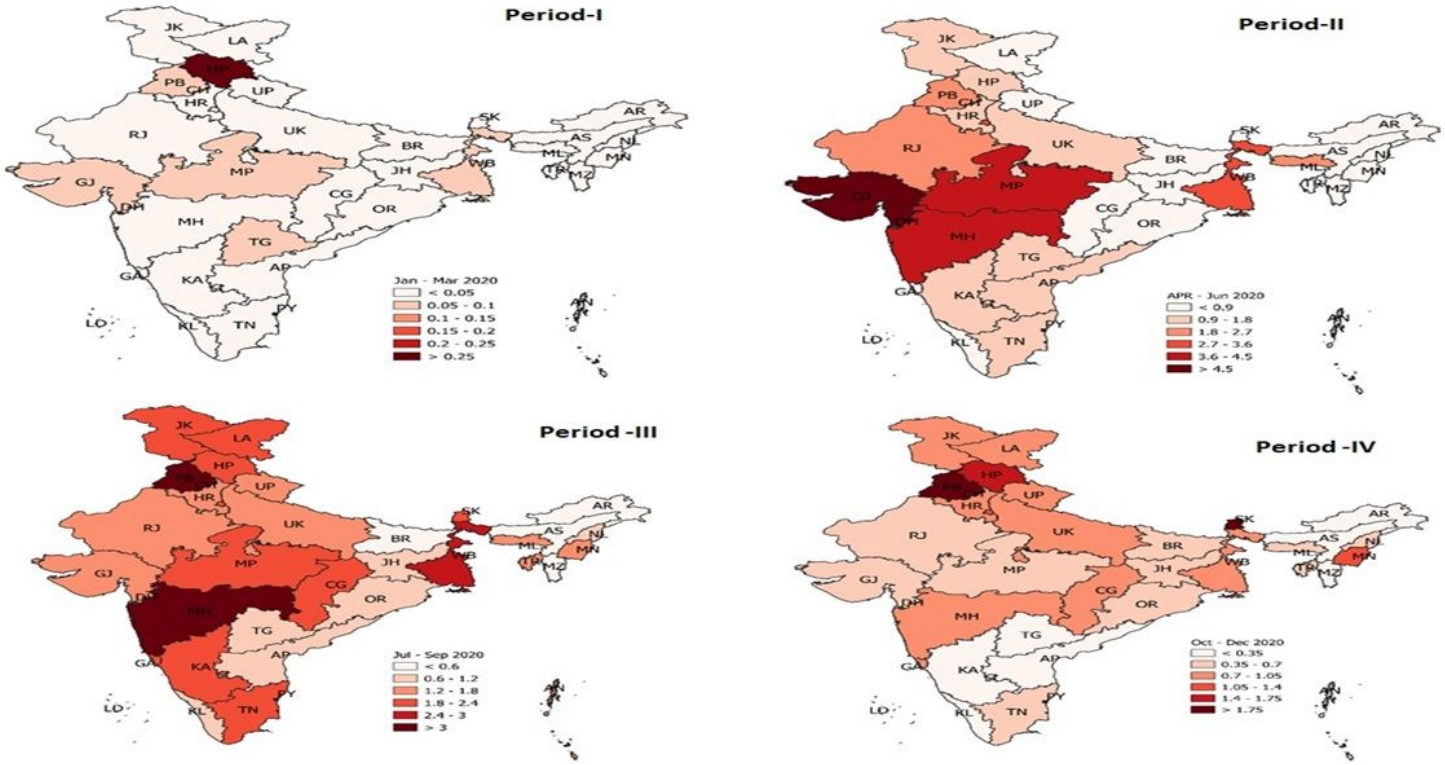

Figure 4

CFR percentage in Period v/s different zones of India

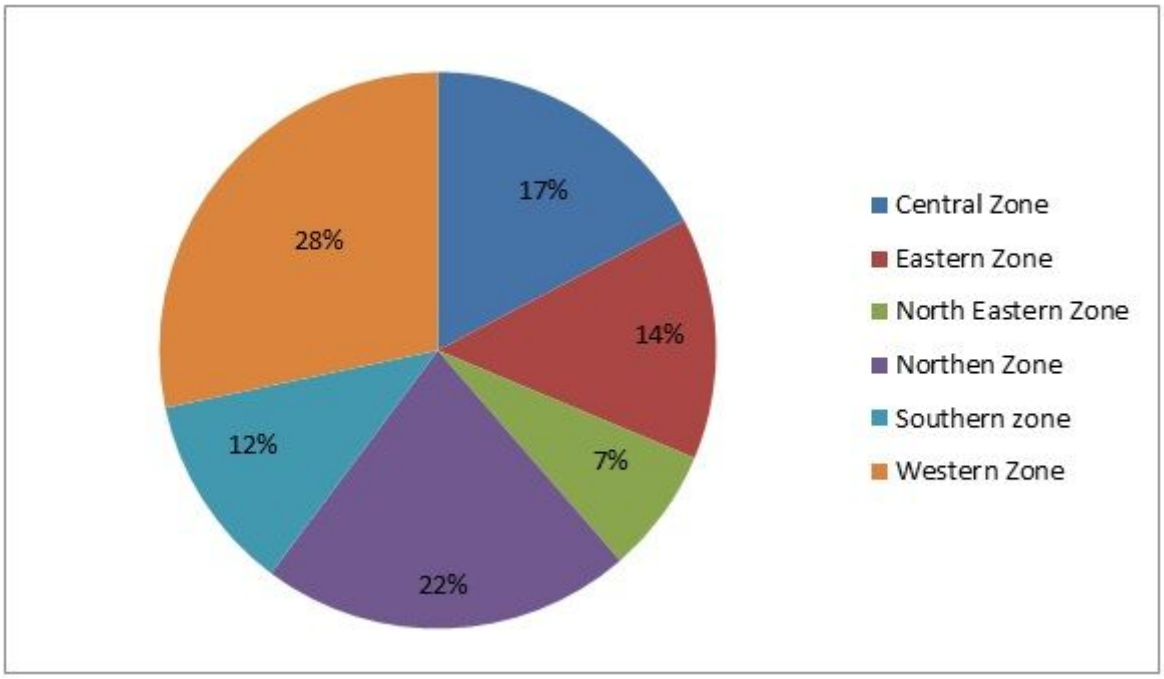

Figure 5

Percent of Distribution of Case Fatality Ratio of SARS-CoV-2 patients in different zones of India

Figure 6

a. Percent of distribution of SARS-CoV-2 cases in different zones in India

b. Percent of distribution of SARS-CoV-2 mortality % in different zones in India

Figure 7

Histogram of SARS-CoV-2 cases in different age group in India

Figure 8

Percentage of distribution of different co-morbidities in SARS-CoV-2 patients in India

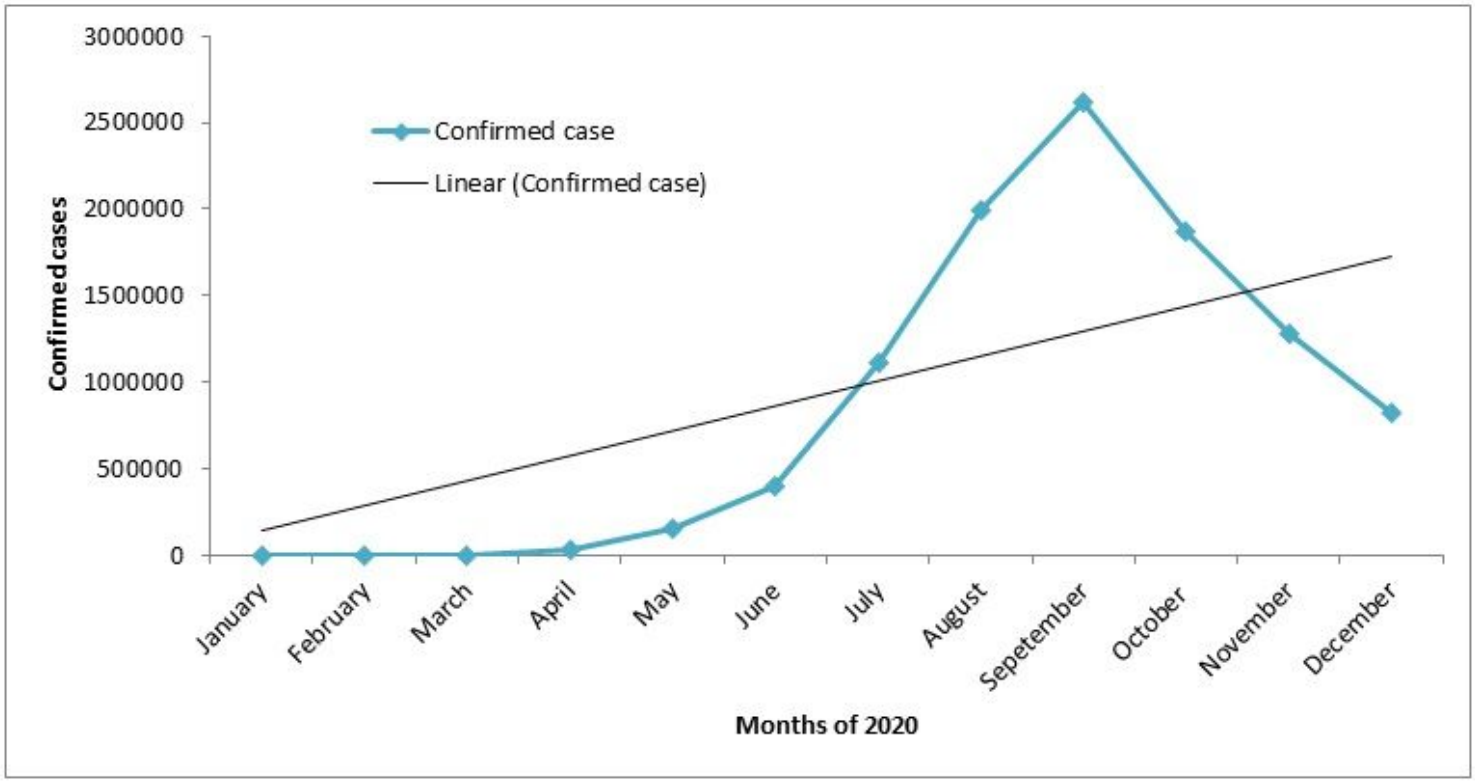

Figure 9

Trend of SARS-CoV-2 confirmed cases in different month of 2020

Figure 10

Trend of SARS-CoV-2 deceased in different month of 2020