Original Research Paper

Epidemiological Insights and Case Fatality Analysis of SARS-CoV-2 in Indian States During the First Wave

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Abstract: Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) has globally spread, causing a significant health crisis. India, with over 157,000 fatalities, ranks third globally in mortality cases. While vaccine development has played a pivotal role in decelerating the virus's spread, understanding the specific factors influencing morbidity and mortality during the first wave remains essential. This retrospective study analyzes data from 28 Indian states and 8 Union Territories (UTs) to examine transmission pathways and Case Fatality Rate (CFR) associated with SARS-CoV-2. Data sources include national health records and government databases, encompassing all confirmed cases reported during the study period. The CFR was calculated using standard epidemiological formulas, with statistical analyses performed using least squares means analysis (Harvey Software). The study reveals significant variations in CFR across different geographical zones in India: Central (17%), Eastern (14%), North Eastern (7%), Northern (22%), Southern (12%) and Western (28%). Period II (April to June 2020) showed significantly higher CFR ($p<0.01$). Monthly CFR calculations revealed noteworthy variations throughout the year ($p<0.01$). The Western zone had the highest CFR compared to other zones. The analysis also highlights the impact of age and comorbidities, with individuals over 21 years exhibiting the highest age-specific positivity rate and patients with chronic diseases representing 87.13% of cases. This study provides novel insights into the epidemiological landscape of COVID-19 during India's initial wave, offering significant implications for public health strategies and contributing new dimensions to existing literature.

Keywords: Epidemiology, SARS-CoV-2, CFR, Indian States, Co-Morbidities, Mortality

Introduction

Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) infection, that arose in Wuhan, China in late 2019, completely spread all over the world, creating an emergency situation and the worst-ever pandemic of modern times (Laxminarayan *et al*., 2020). This pandemic caused 3.2 million deaths and infected more than 158 million people worldwide by May 11, 2021 (Liang *et al*., 2021). During the early stages of the pandemic, epidemiologic studies and disease surveillance were conducted in China (Li *et al*., 2020; Zhou *et al*., 2020; Guan *et al*., 2020b), Europe (Grasselli *et al*., 2020; Docherty *et al*., 2020) and North America (Richardson *et al*., 2020; Petrilli *et al*., 2020; Lewnard *et al*., 2020) 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 accessing high-quality health care (Dong *et al*., 2020; Clark *et al*., 2020; Coronavirus Disease (COVID-19) Situation Report 209, 2020). Although many more studies are needed to assess how SARS-CoV-2 affects individuals and communities (Walker *et al*., 2020;

Gilbert *et al*., 2020; Davies *et al*., 2020), there is almost no fundamental approach available to explore strategies for SARS-CoV-2 transmission dynamics and clinical outcomes (Gupta *et al*., 2020).

In the initial spells, the clinical diagnosis of SARS-CoV-2 was based on clinical symptoms, fundamentally, fever (99%), fatigue (70%), dry cough (60%), myalgia (44%) and dyspnea were identified as the most common symptoms of SARS-CoV-2 (Wang *et al*., 2020; Chen *et al*., 2020; World Health Organization, 2020). Headache, dizziness, diarrhea, nausea, and vomiting are the additional symptoms of SARS-CoV-2 were less common (Huang *et al*., 2020). Symptoms of severe illness include pharyngeal pain, dyspnea, dizziness, abdominal pain, and anorexia (Chen *et al*., 2020). Elderly patients with co-morbidities such as hypertension, diabetes, cardiovascular disease, and cerebrovascular disease experienced 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-1 that caused an outbreak in 2003 in China and MERS-CoV infections. Chest imaging showed some bilateral patchy shadows and ground-glass opacities. Acute respiratory distress syndrome, acute cardiac injury, arrhythmias, acute kidney injury, and shock, were among additional SARS-CoV-2 complications (Duan and Qin, 2020; Guan *et al*., 2020a; Cori *et al*., 2013). The virus reportedly spread at a rate of 40% in hospitals. In hospitalized patients, the mortality rate was around 4% (Duan and Qin, 2020; Guan *et al*., 2020a; Cori *et al*., 2013). During that period in India (the first wave of COVID-19), there was a dearth of holistic data to associate with the various clinical pictures manifested by patients affected by the disease. Eventually, it becomes necessary to make a holistic analysis based on the existing health system vis-à-vis the clinical picture, co-morbidities, and other vital parameters during the first wave, where the clinical infrastructure was unprepared for such an emergency.

In India, the total number of cases was 10.3 million, 9.9 million, and 148.4 thousand deaths (until the development of this manuscript). Non-pharmaceutical measures (traveling restrictions, public transport closure, and workplace closing) taken to limit the spread of this pandemic incur social and economic costs. Hence, vaccination was used as an alternative (after conducting clinical trials on the duration of infectivity, the safety of the vaccine, the severity of resultant disease, and the efficacy of infection reduction) to overcome the spread of infectious SARS-CoV-2 (Polack *et al*., 2020; Hodgson *et al*., 2021). However, the haste in limiting the pandemic left us with many questions and a lack of detailed epidemiological and spatiotemporal analysis of the data, which could refine and evaluate the strategies as well as enhance the preparedness for the future. Therefore, this study retrospectively analyzes mortality and morbidity data in India for 2020, integrating spatio-temporal dynamics, age-specific trends, and co-morbidity profiles. It aims to provide essential insights into COVID-19's impact in India, informing future public health strategies. The study's significance lies in its comprehensive data analysis approach, encompassing clinical manifestations, demographics, and co-morbidity factors. It offers a holistic view of the pandemic in India. The novelty lies in integrating spatio-temporal dynamics with age-specific and co-morbidity profiles, uncovering previously unexplored patterns and correlations to enhance public health interventions.

Materials 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 the 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, and period IV contained October to December of the year 2020. Further, data on 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 the given formula:

$$CFR\ \% = number\ of\ deaths \times 100/\ Confirmed\ cases$$

Percent of Distribution

Percentage 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 the division of each part by total to get a percent of the distribution.

Least Squares Means Analysis

Least squares mean analysis was used to estimate the variance components and parameters (LSMLMW, version 2.0) (Koonce, 1990). The following model was used to analyze the effect of various SARS-CoV-2 factors. Model 1:

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$$Yij = \mu + Period\ i + month\ j$$

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 *the* i^{th} period (Jan-March, April-June, July-September, October-December 2020, *i* = 1,2,3,4).

Month j = fixed effect of *the* j^{th} period (Jan to Dec 2020, *j* = 1 to 12).

"$Period_i$" represents the fixed effect of the four distinct periods of the year 2020: January-March, April-June, July-September, and October-December. "$Month_j$" represents the fixed effect of each month from January to December 2020. It aims to reveal how different times of the year affected the Case Fatality Ratio (CFR), providing insights into temporal trends and helping to identify critical periods for targeted public health interventions.

Calculate the Average CFR Across All Periods

Results

Epidemiology, Different Geographical Zones of India

The data of the Case Fatality Ratio (CFR) was calculated in 36 Indian states/UTs. Punjab, Maharashtra, and Sikkim had the 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. The western zone of India had the 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.

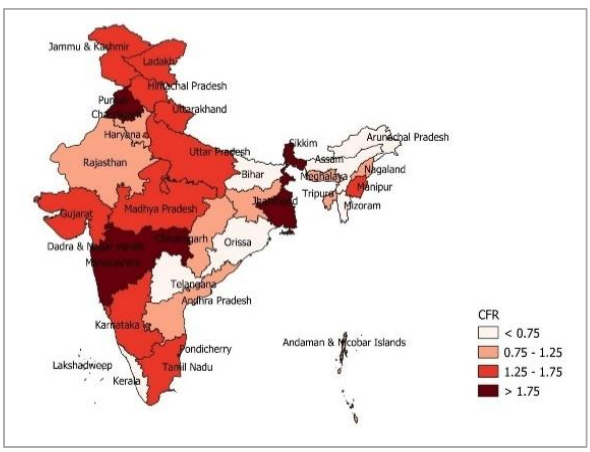

Fig. 1: CFR percentage in different states of India

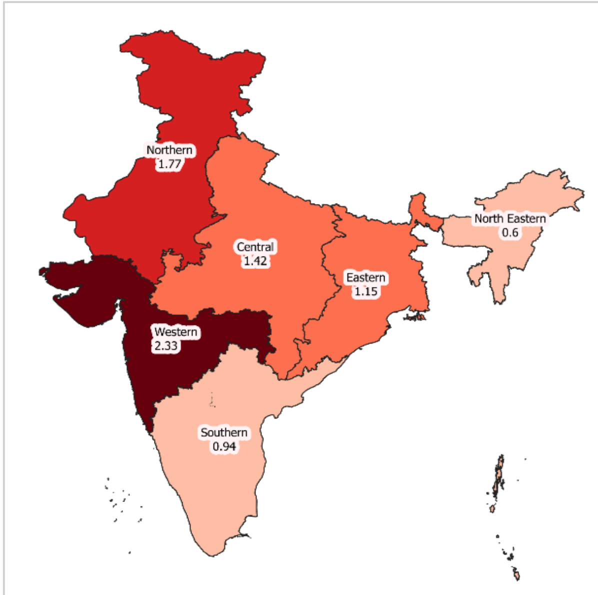

Fig. 2: CFR percentage in different zones of India

Case Fatality Ratio

The least squares mean of Case Fatality Ratio (CFR) rates were examined from January 2020 to December 31, 2020, spanning 337 days. Coefficient variation, R squared, and an average of CFR were 17.91, 0.884, and 1.908% respectively over the year. The CFR was calculated for every month of the year 2020. CRF% was at its highest between April and June 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 periods 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 the data of deceased, eventually 'zero' deceased or 'zero' CFR data were removed from the data analysis for least squares means. Coefficient variation, R squared and average of CFR in the different periods 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 comprising April to June of the year 2020. Also, it was observed that there was a 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.

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	P<0.01

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 periods

Source	D.F	Sum of Squares	Mean Squares	F	P
Period	3	250.421	83.473	367.509	P<0.01

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

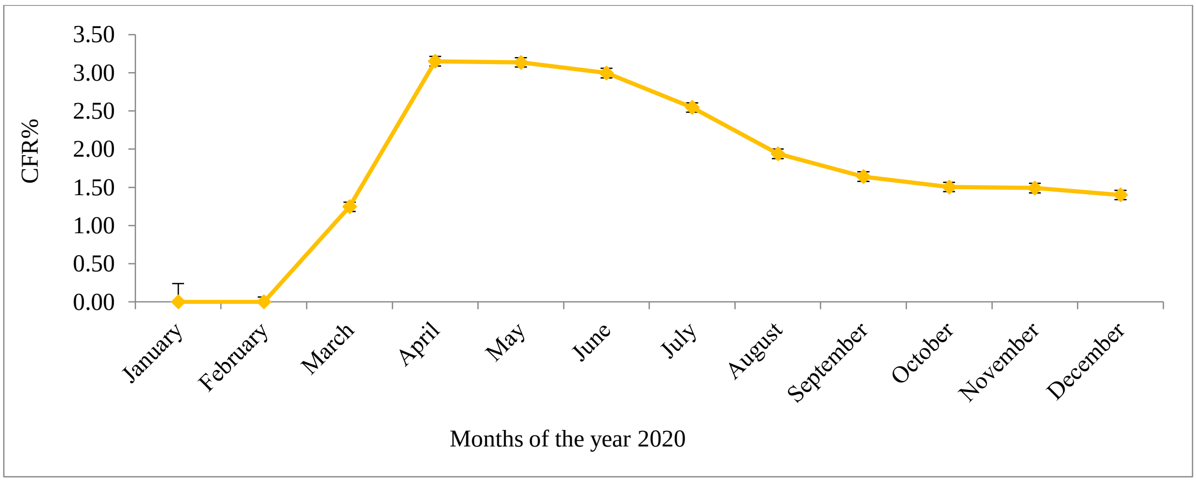

Fig. 3: Least Squares Mean (LSM) of CFR% in various months of 2020

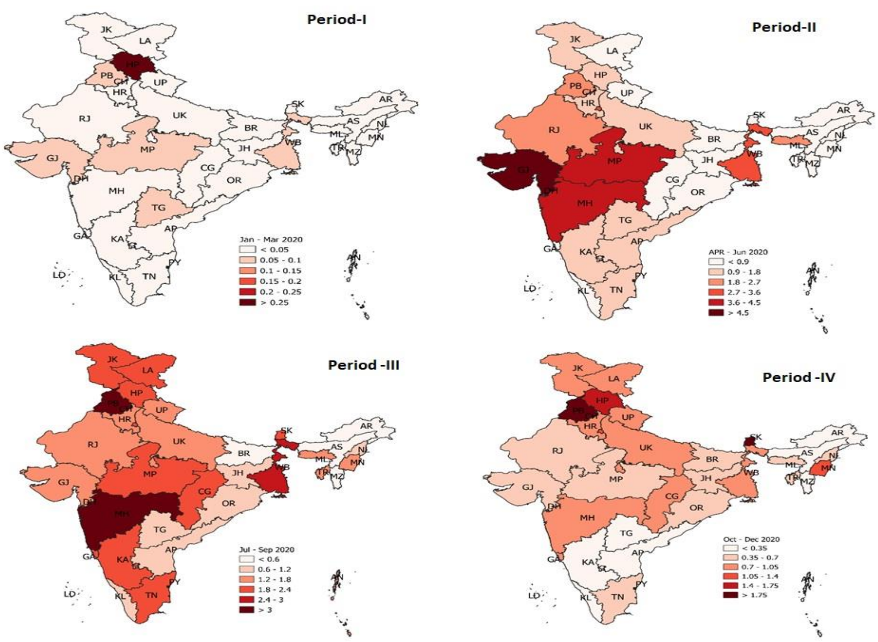

Fig. 4: CFR percentage in Period v/s different zones of India

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 (Fig. 5). Maharashtra had a significant ($p<0.01$) 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 showed their percent distribution among different zones of India. The percent of the distribution of SARS-CoV-2 positive patients was 7.0% in the Central Zone, 8.0% in the Eastern zone, 12.0% in North Eastern, 25.0% Northern, 24.0% in the Southern zone and 24.0% in Western Zone (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 different age groups based on the limited data available online. There were four age groups identified: <20 years (including those aged below 20 years), >21 years (including those aged 21-50 years), >51 years (including aged 51-80 years), and >81 years (including aged 81-90 years). The incidence rate among different age groups was evaluated in the Indian population. Age-specific estimates ranged from 12.37% at ages <20 years to 0.09% at ages > 81 years. 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 the 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).

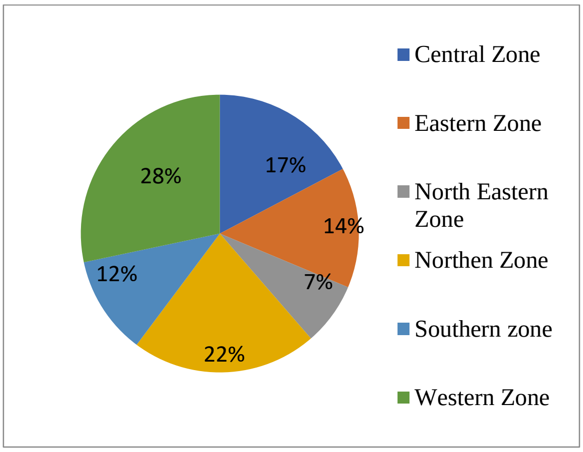

Fig. 5: Percent of Distribution of Case Fatality Ratio of SARS-CoV-2 patients in different zones of India

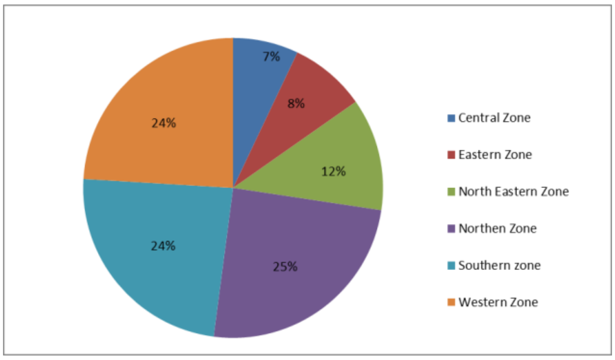

Fig. 6A: Percent of distribution of SARS-CoV-2 cases in different zones in India

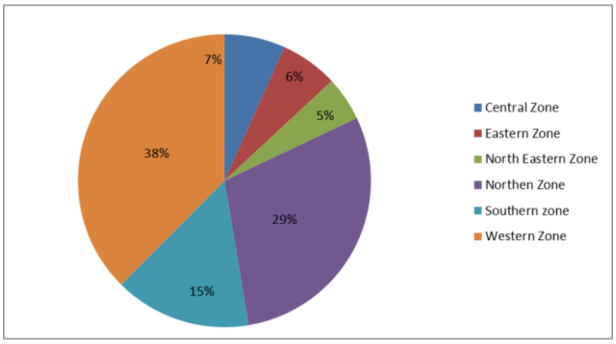

Fig. 6B: Percent of distribution of SARS-CoV-2 mortality % in different zones in India

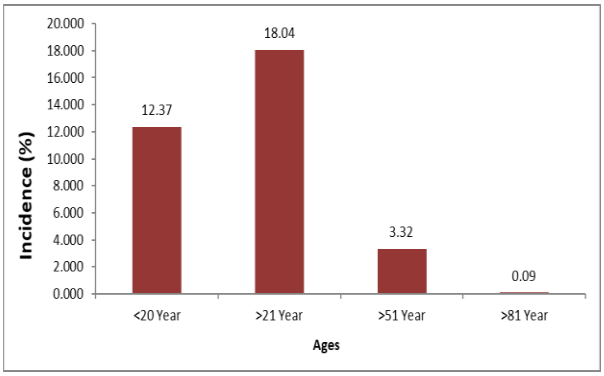

Fig. 7: Histogram of SARS-CoV-2 cases in different age groups in India (age groups: <20 years (including aged below 20 years), >21 years (including aged 21-50 years), >51 years (including aged 51-80 years) and >81 years (including aged 81-90 years)

Co-Morbidities in Sars-Cov-2 Patients in India

Co-morbidity data were 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 diseases 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 patients in acute and chronic disease exhibited 12.87 and 87.13 percent, respectively (Fig. 8). The chronic patients were significantly affected by SARS-CoV-2. Of 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 the presence of co-morbidities (Wu and McGoogan, 2020; Patel and Verma, 2020; Tiganelli *et al*., 2020) 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%) (Wu and McGoogan, 2020).

Sars-Cov-2 Trend Over the Period

The SARS-CoV-2 trend was analyzed from January 2020 to December 2020. We plotted the trend of SARS-CoV-2 cases and analyzed its impact across the timeline of 2020. However, the trend of SARS-CoV-2 confirmed cases was slightly elevated after the month of May 2020 than earlier. Similarly, SARS-CoV-2 patients had the same mortality trend as SARS-CoV-2 confirmed cases (Figs. 9-10).

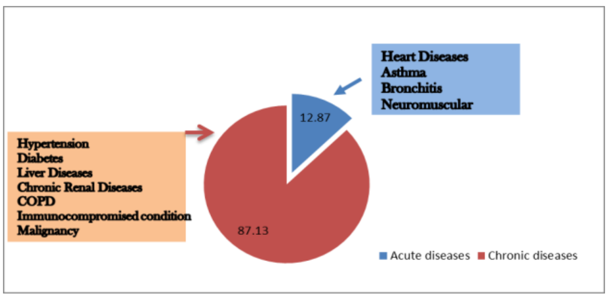

Fig. 8: Percentage of distribution of different co-morbidities in SARS-CoV-2 patients in India

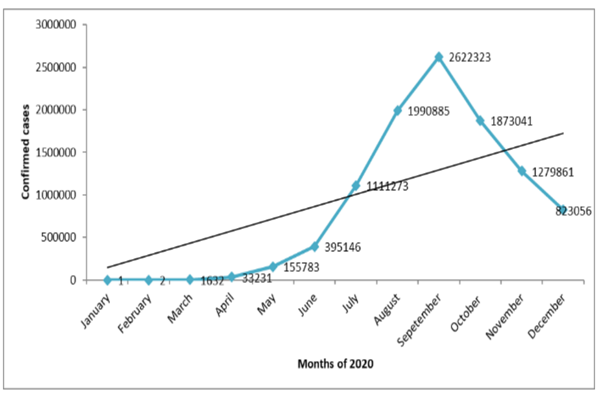

Fig. 9: Trend of SARS-CoV-2 confirmed cases in different months of 2020

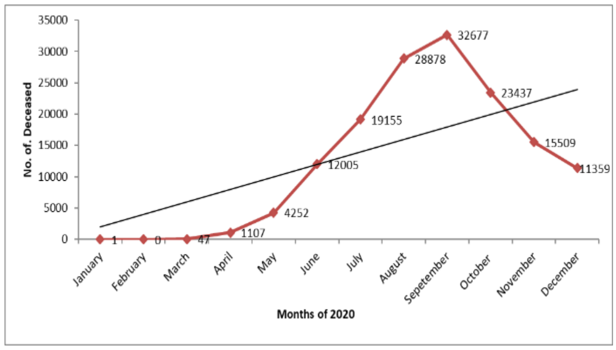

Fig. 10: Trend of SARS-CoV-2 deceased in different months of 2020

Discussion

Our findings are based on extensive surveillance and contact-tracing data collected from 36 Indian states/UTs. The present investigation was carried out in different states of India and comparative analysis was conducted cutting across various age groups and co-morbidities with comparisons drawn from a previous study which conducted a similar analysis but only in two states viz. Andhra Pradesh and Tamil Nadu (Laxminarayan *et al*., 2020).

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 (Countries where Coronavirus has Spread - Worldometer, 2020). 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 (Organization, 2020). This study shows that in India, a total number of 11.06 Million SARS-CoV-2 cases, a total of 0.16 Million death cases and 10.75 Million recovered cases have been reported. Out of the total cases, 2.13 Million cases were 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 ((World Health, 2020). The first U.S. cases of non-travel-related SARS-CoV-2 were confirmed on February 26 and 28, 2020, which clearly suggested community transmission in the U.S. by late February (COVID-19 *et al*., 2020). The aforesaid data is very important to elucidate the severity of the first pandemic wave of COVID-19 in states majorly affected. Hence, in the current study to get a clear picture, we analyzed all the 36 Indian states/UTs of the country for a comprehensive analysis of various parameters vis-à-vis SARS-CoV-2 infection.

Further, this study compared the CFR among the states that reported a large number of SARS-CoV-2 cases at 12 months of the pandemic, namely Jan 2020 to December 2020. As per our current analysis, it is reported that Maharashtra (2.441%), Punjab (3.215%), and Sikkim (2.201%) had the highest CFR than other states of India. In a previous study, a similar analysis has been conducted for the southern states viz., Tamil Nadu and Andhra Pradesh. The findings showed that CFR in all ages was 2.06 (1.98-2.14%) and CFR in various ages was also examined (Laxminarayan *et al*., 2020). However, the global picture for CFR as far as the first wave of COVID-19 was also studied in a specified period (12^{th}-23^{rd} of March 2020) of the pandemic which showed higher CFR rates in Italy (6.22%), China (3.91%), Iran (3.62%), USA (3.07%) and Spain (2.12%) (Khafaie and Rahim, 2020). The case-fatality ratio was calculated in Turkey as well as European countries including the findings in Turkey, Italy, Spain, the UK, Germany, France, Switzerland, Belgium, Netherlands, Austria, Portugal, and Norway were 1.85, 3.95, 4.01, 4.40, 0.41, 1.979, 1.019, 3.393, 3.496, 0.660, 2.249 and 0.531 percent, respectively (Javed, 2020).

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 period, namely period I (January to March 2020), period II (April to June 2020), period III (July to September 2020) and period IV (October to December 2020). Our finding also proved that the CFR was significantly increased due to a lack of facilities in the initial days and thereafter the CFR trend decreased as facilities were improved. Ideally, the CFR should be low at first due to the incubation time and delay in developing complications from the infection, which gradually increases until it reaches a plateau that will eventually become the ultimate CFR for the diseases. Although the number of cases started increasing in periods II and III, it is also to be noted that the number of samples tested was also proportionally higher during that period. From the first case reported in India in January 2020 to the start of the first wave, the number of labs equipped to test the samples was very less in number, but eventually, the testing centers increased in India (Jain *et al*., 2021; Sarkar *et al*., 2021). The first wave in India occurred relatively for an extended period of time and the reasons may be due to multiple lockdowns and restrictions. The nationwide lockdowns during the second quarter of the year 2020 and further lockdowns throughout the year have slowed down the spread of SARS-CoV-2, which has contributed to the extended period of the first wave.

In the present investigation, SARS-CoV-2 patients suffered from several co-morbidities which were further classified into two: Acute and Chronic. The incidence percentages 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. Further, the first wave saw a high risk for co-morbid patients affected with SARS-CoV-2, which is due to the dearth of Knowledge Attitudes, and Practices (KAP) for a relatively new disease with less proven treatment protocols. Hence, it is important to analyze the data on COVID-19 in co-morbid patients, so that it could be a model for implementation in high-risk populations (Jain *et al*., 2021). Also, the lessons learned from the first wave of COVID-19 are altogether different compared to the second wave, with the first wave having the unmutated strain of SARS-CoV-2 that showed fewer positive cases but more CFR. The Omicron BA.1 strain thus exacerbated the condition in patients with co-morbidities due to a lack of KAP and clinical infrastructure.

Furthermore, elderly patients with underlying co-morbidities such as diabetes, hypertension, cerebrovascular disease, and cardiovascular disease, are more likely to have negative outcomes (Chatterjee *et al*., 2020). People of any age who have underlying medical conditions such as hypertension or diabetes have a worse prognosis (Singh *et al*., 2020). Diabetic patients have higher morbidity and mortality rates, as well as more hospitalizations and Intensive Care Unit (ICU) admissions (Singh *et al*., 2020). Diabetic patients are more prone to the deleterious and severe effects of the Covid-19 which is due to the fact that the inflammatory processes are elevated because of constant glucose recognition by C-type lectin receptors and advanced glycation End Products (AGEs) that subsequently culminates into an uncontrollable proinflammatory response leading to ‘cytokine storms’ (de Lucena *et al*., 2020; Mitra *et al*., 2020). Despite having a huge number of COVID-19 patients, it is surprising that there are currently just a few sizable published studies available regarding the prevalence of comorbidities in patients with COVID-19 from India. The presence of comorbidities was reported in 14% (95% CI, 11.1-17.2) of the 522 confirmed COVID-19 patients from a large medical college and hospital in Jaipur, India. Of these, hypertension (42.5%), diabetes (39.7%), past history of tuberculosis (20.5%), COPD/asthma (16.4%), CAD and CKD (13.7%), and hypertension were the most common (Bhandari *et al*.,2020). Similarly, patients affected with hypertension are medicated with anti-hypertensive drugs that increase the expression of ACE2 receptors and release of proprotein convertase, which eventually aids the entry and multiplication of SARS-CoV-2 through these receptors, leading to a high risk of infections and other clinical complications in them. In Italy alone, the mortality associated with hypertension due to COVID-19 is 73.8 percent which is alarming (Ejaz *et al*., 2020). People with Chronic Obstructive Pulmonary Disease (COPD) or any other respiratory illness are more likely to develop severe SARS-CoV-2 illness (Zhao *et al*., 2020).

The severity of SARS-CoV-2 infection is more likely to be increased by four times in patients with COPD than in patients without COPD [45]. 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 and developing severe SARS-CoV-2, according to current research and clinical expertise (C.D.C., 2020). The poorly orchestrated immune response coupled with severely elevated ACE2 receptor and furin expression exacerbates the lung condition leading to COPD, hypoxemia, and mortality ((Ejaz *et al.*, 2020). 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 (B.C.C.D.C., 2020). People with uncontrolled medical conditions such as hypertension, diabetes, lung, liver, and kidney disease, pathogenic co-infections, smokers, transplant recipient's cancer patients on chemotherapy, and patients on long-term steroid therapy are more likely to contract and develop severe SARS-CoV-2 infection (C.D.C., 2020; B.C.C.D.C., 2020; Tiwari Pandey *et al.*, 2020). 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 (Zhao *et al.*, 2020). Similarly, obesity with a higher BMI predisposes to all the risks including hypertension, diabetes, and hypothyroidism all of which are excellent playgrounds for risk and associated severity of COVID-19-related complications and mortality (Joshi, 2020).

The influence of age on a number of positive cases and disease severity has also been analyzed in this study. The age criteria were classified into 4 different class intervals 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 the critical age groups that are most affected during the pandemic situation so that effective preventive measures can be undertaken for the high-risk group. It is shown that the CFR of SARS-CoV-2 increases with age (C.D.C., 2020; B.C.C.D.C., 2020; Tiwari Pandey *et al.*, 2020; Joshi, 2020; Meo *et al.*, 2020) across different countries. The Italian population (23%) was either 65 years of age or older (Zhou *et al.*, 2020). This would explain the higher mortality rates in Italy compared to other countries. A similar study was 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 contrasting findings in the children with mild symptoms and less positivity show the age-specific affection during the first wave of the pandemic (Russell *et al.*, 2020). Similarly, the CFR rate of SARS-CoV-2 is reported to be higher in older adults than younger individuals i.e., 42% for those <65 vs 65% >65 years; and the association of chronic conditions and risk of dying across different age groups follows the same trend (Tisminetzky *et al.*, 2022). This study also reported that the global mortality cases stood at 2.68 million. The mortality cases were higher in the United States (538 thousand) followed by Brazil (282 thousand) and India (157 thousand). This depicts that India has the third highest mortality rate globally during the reported period. In India, Maharashtra recorded high mortality followed by Tamil Nadu and others. Similarly, earlier studies reported that in Tamil Nadu, the crude death rate was 2.44 per lakh population; while the elderly (>75 years) showed a mortality of 22.72 percent. Also, the study pinpoints that around 85% of the affected were reported to have one or more comorbidities including a higher proportion of diabetes followed by hypertension and others (Asirvatham *et al.*, 2021). Whereas in one study conducted in Maharashtra, it was reported that the age group from 3-60 years was majorly affected due to COVID-19 during the first wave with the mean age being 45.8 years, while hypertension was the most common comorbidity followed by diabetes (Tambe *et al.*, 2020). The overall percentage of mortality due to SARS-CoV-2 cases was significantly higher in the 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 (Battegay *et al.*, 2020). 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 (Kang, 2020). 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 (Molenberghs *et al.*, 2022).

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 being the most visited, crowded place in India. Furthermore, countries like Iran began to report or test cases only after higher fatalities (Iype and Gulati, 2020). It is also to be noted that higher CFR values were reported at the initial stages of the pandemic.

There lies a relational trend between higher CFR rates and the 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 had non-immunization control, where vaccination was not practiced widely in the population. The pandemic dynamics of the first wave actually represent the Omicron BA.1 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 that was started at various stages of the second wave could provide a meaningful conclusion on the pandemic dynamics and herd immunity.

Conclusion

SARS-CoV-2 continues to pose a formidable global health threat, highlighted by India's substantial mortality burden, ranking third globally. During the peak period from April to June 2020, the Case Fatality Rate (CFR) was notably higher compared to other periods, underscoring the severity of the initial wave. Notably, the Western zone exhibited a significantly elevated mortality rate, possibly exacerbated by extensive population movement during lockdowns and its status as a major economic and transit hub. Hypertension emerged as the predominant comorbidity among severe cases, followed by diabetes and liver disease, underscoring the critical role of underlying health conditions in disease outcomes. Understanding these mortality patterns across age groups and comorbidities is crucial for targeted interventions, particularly in resource-constrained settings. This study provides essential insights for managing high-risk populations and guiding future pandemic preparedness strategies. Validation with additional data and consideration of other influencing factors will further enhance the study's robustness. Moving forward, these findings can inform proactive measures and resource allocation to mitigate the impact of future pandemics, leveraging existing healthcare systems effectively until new therapeutic breakthroughs emerge.

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Author's Contributions

Rakesh Kaushik: Conceptualization, data collection, formal analysis, investigation, methodology, software, validation, visualization, writing original draft, writing review and edited.

Nikita: Data collection, methodology, writing review and edited.

Yogita Lugani: Data compilation, writing review and edited.

Gururaj Kumaresan: Formal analysis, investigation, supervision, writing discussion draft, writing review and edited.

Saurabh Gupta: Writing draft review.

Aditya Arya: Data collection, formal analysis, investigation, methodology, visualization, writing review and edited.

Manish Kumar Chatli: Manuscript review, supervision.

Gopal Dass: Data interpretation, manuscript review.

Rishabh: Methodology design, map design.

Ethics

This study is review article and has not been published in any journals. The corresponding author acknowledges that other authors have reviewed and approved this manuscript; no ethical issues are involved.

Conflicts of Interest

The authors declared no conflict of interest.

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