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Original Article

Changing Pattern of Mortality in First and Second COVID-19 Waves: A Comparative Study From Kerala, India

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Abstract

Background and aims: India has seen a two-wave pattern of coronavirus disease 2019 (COVID-19) infections. The comparative characteristics of these two waves remain largely unknown. Changing trends in the demographic and clinical characteristics of the deceased COVID-19 patients in these two waves helped to identify the vulnerable population and guide public health interventions to decrease mortality.

Methods: We obtained COVID-19 death summaries from the medical records of a large tertiary healthcare centre in North Kerala, India. Two groups of COVID-19 deaths were selected: the first group included patients who died in the first wave between 1 July 2020 and 31 December 2020 (n = 311), and the second group included those who died in the second wave between 1 March 2021 and 30 June 2021 (n = 431).

Results: The mortality in the second wave in young patients (≤50 years) was 2.2% higher (11.8% vs. 9.6%, $P = 0.346$) and that in elderly patients (≥80 years) was 7.7% higher (19.95% vs. 12.2%, $P = 0.005$) compared to the first wave. The average duration from symptom onset to death also significantly decreased in the second wave. Further, there was an increased proportion of COVID-19-related deaths in patients with diabetes in the second wave (59.3% vs. 51.7%, $P = 0.025$). The main cause of death was respiratory failure due to COVID-19 pneumonia in both waves.

Conclusion: The second COVID-19 wave was different from the first wave with more deaths in the young and elderly, a shorter duration from symptom onset to death, and an increase in the proportion of deaths with diabetes, maternal deaths, and deaths in those without any pre-existing comorbidities.

Keywords: COVID-19, SARS-CoV-2, Pandemic, Mortality

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Introduction

The coronavirus disease 2019 (COVID-19) is highly infectious and has spread worldwide. India is one of the countries most affected by the COVID-19 pandemic. The first case in India was reported on 30 January 2020 in Kerala.

Pandemics occur in waves. The Spanish flu epidemic in 1918, the deadliest pandemic in the last 120 years, had multiple waves.[1] The first wave of COVID-19 in India was severe and lasted from July to December 2020. The second wave of COVID-19 hit India in the first week of March 2021 and continued to rage throughout India in the last week of July 2021. The second wave was much more severe than the first and coincided with shortages of vaccines, hospital beds, oxygen, and other medicines in some parts of the country due to excessive need.

Many countries such as Malaysia had multiple COVID-19 waves.[2] In Japan, the third wave was the most severe.[3] As observed in other countries, India is anticipating an impending third COVID-19 wave. The main cause of the rapid spread of the second wave in India is the new mutant strains of disease. Cases with these mutant strains have affected different age groups to different degrees compared to the wild type strain as reported in other countries, but the comparative characteristics of the fatalities of the two waves in India remain largely unknown.

It is necessary to know the pattern of these waves so that public health strategies can be developed to decrease the spread and mortality of the disease while optimizing resources. To the best of our knowledge, this is the first study from the state of Kerala to compare the nature of COVID-19 fatalities between the two waves, and such studies are very limited in developing countries like India.

Materials and Methods

Study Design and Objectives

We performed a retrospective analysis of mortality parameters of COVID-19 deaths during the two waves of the COVID-19 pandemic in Kerala, India.

The objective of this study was to assess and compare the demographic factors, clinical characteristics, associated comorbidities, and complications related to mortality in confirmed COVID-19 deaths during the first and second waves.

Settings and Sample

The study was conducted in a tertiary care teaching institute with 1300 beds in Kerala, India. According to the national records, the peak of the first wave of the COVID-19 pandemic in India was on 16 September 2020 with a gradual decline, and the nadir reached on 1 February 2021 after which cases again started increasing with the next peak on 8 May 2021.[4] Based on this, 2 groups of COVID-19 deaths were selected: the first group corresponded to the first COVID-19 wave with deaths of patients admitted between 1 July 2020 and 31 December 2020, while the second group corresponded to the second COVID-19 wave with deaths of patients admitted between 1 March 2021 and 30 June 2021. A gap of 2 months was maintained between groups to decrease overlap between waves. The dataset for the first wave was frozen on 31 December 2020 and on 30 June 2021 for the second wave. The included participants were all deceased patients with laboratory-confirmed COVID-19 infection during their hospital stay over the study period. Patients who died due to causes other than COVID-19 (e.g., suicide or accidents) and patients who were deceased upon arrival to the hospital were excluded.

All patients were confirmed for COVID-19 by real-time polymerase chain reaction, or a rapid antigen test was performed according to the World Health Organization guidelines. All patients received routine comprehensive treatments including intravenous antibiotics, assisted oxygenation, specific treatment for the underlying diseases, and supportive treatments as per the prevailing state government treatment guidelines.

The duration of illness was defined as the period from the first day of symptom onset to the day of death. All deaths from 50 years old or below were considered to be young deaths. The age distribution of COVID-19 deaths between waves was examined. Special categories such as maternal deaths, deaths without pre-existing comorbidities, young deaths, and deaths in elderly patients were identified and compared in both groups.

Data Extraction

Data abstraction forms included demographic data, clinical presentation, associated comorbidities, laboratory findings, chest X-ray and computed tomography findings, complications, and cause of death. Data were then reviewed and double-checked independently by two experienced physicians. For missing or vague data, direct communication was conducted with the attending doctors and other healthcare providers. Reports which could not be retrieved were excluded from mortality analysis.

Statistical Analysis

Categorical data were presented as frequency and proportions, while continuous data were represented as mean, median, and standard deviation as appropriate. Comparisons between the characteristics of the first and second waves were made using the Chi-squared test, student's t-test, and Mann-Whitney U test. A P value of less than 0.05 was used as a cut-off for statistical significance. Microsoft Excel (Microsoft, Redmond, and WA) and SPSS Statistics version 24 (IBM, Armonk, and NY) were used for analysis.

Results

A total of 768 COVID-19 deaths occurred during the study period, of which 742 met the inclusion criteria. This study included 311 and 431 COVID-19 deaths in the first wave and second waves, respectively. There were 3295 and 2722 hospital admissions during the first and second waves, respectively. The rates of in-hospital mortality for the first and second waves were 9.4% and 15.83%, respectively.

The demographic characteristics of deaths in the first and second waves are summarized in Table 1. The mean ages of both waves were similar (Table 1). Figure 1 presents the age distribution of deaths in which more deaths occurred proportionately in extremes of age in the second wave. There were more deaths on the first day of admission in the second wave (15.5% vs. 10.2%). Then, a steep decline in mortality was noticed as age decreased from 50 years in both waves. Among 742 deaths in the study group, there were only 3 deaths in those aged <10 years. The youngest death in the study group was a 7-month-old female without any comorbidity who developed severe COVID-19 pneumonia and septicaemia. Further, there was a significant decrease in the number of days from admission to death in the second wave (Mann-Whitney U test, $P<0.001$) and a significant decrease in the total duration of illness (Mann-Whitney U test, $P=0.036$).

Fourteen deceased patients in the second wave were vaccinated with one dose of a vaccine, and one deceased patient had taken both doses of the CoviShield vaccine.

Comorbidities of COVID-19 deaths for both waves are presented in Table 1. There were 4.27% more deaths in the second wave without any pre-existing comorbidities (93.6% vs. 89.33%). As results indicate, hypertension (53.6%) and diabetes (59.3%) were the most common comorbidity in the first and second waves, respectively. In addition, the presence of comorbidities increased with increasing age.

The symptoms on admission to our hospital are shown in Table 2 in which most deaths occurred due to respiratory failure. The other main causes of death were septicaemia, renal failure, and cardiac failure.

Mortalities in special categories are summarized in Table 3. Mortality in young patients (≤50 years) was 2.2% higher in the second wave. Even among the deceased young patients, most had comorbidities. Further, 24 out of 30 (80%) young patients had comorbidities in the first wave, while 37 out of 51 (72.5%) patients had comorbidities in the second wave. In other words, there were more deaths

Table 1. Demographic Characteristics and Comorbidities of the Deceased With COVID-19 in the First and Second Pandemic Waves

Characteristics	First Wave (1 July, 2020 to 31 December, 2020) (n=311)	Second Wave (1 March1, 2021 to 30 June, 2021) (n=431)	*P* Value
Age (year), mean±SD	65.02±13.21	65.64±14.62	0.549
Age categories (year)			0.250
0-9	1	2	
10-19	1	1	
20-29	3	5	
30-39	8	14	
40-49	17	29	
50-59	60	79	
60-69	100	117	
70-79	85	98	
≥ 80	38	86	
Gender			0.129
Male	223 (71.7%)	284 (65.8%)	
Female	88 (28.29%)	147 (34.1%)	
Duration (days)			
Symptom onset to admission	4.9 (IQR 5)	5.2 (IQR 4)	0.069
Admission to death	8.7 (IQR 8)	7 (IQR7)	<0.001
Total duration	13.6 (1QR 10)	12.2 (IQR 9)	0.036
Comorbidities, No. (%)			
Hypertension	167 (53.6%)	216 (50.1%)	0.381
Diabetes	161 (51.7%)	256 (59.3%)	0.025
Coronary artery disease	74 (23.7%)	83 (19.2%)	0.135
Chronic kidney disease	76 (24.4%)	68 (15.7%)	0.003
Chronic liver disease	19 (6.1%)	23 (5.3%)	0.791
Chronic respiratory illness, No. (%)	39 (12.54%)	44 (10.2%)	0.320
Stroke	30 (9.64%)	25 (5.8%)	0.068
Malignancy	20 (6.4%)	15 (3.4%)	0.060

Note. SD: Standard deviation; IQR: Interquartile range; COVID-19: Coronavirus disease 19.

in young people who were healthy in the second wave.

The mortality in the elderly age group (≥70 years) was 3.14% higher in the second wave. This difference became more marked (7.7%) with advanced age (≥80 years). Of the elderly patients, relatively healthy people (without pre-existing comorbidities) were more affected in the second wave (91.9% vs. 89.5%). There was one maternal death in the first wave and four maternal deaths in the second wave.

Of the total five maternal deaths, four were older than 35 years, had diabetes, and were multiparous, and only one 24-year-old maternal death had no comorbidities. On evaluation, there was more thrombocytopaenia in the second wave (47.2% vs. 43.7%). Inflammatory markers increased in the majority of deaths. C-reactive protein levels were elevated to be more than 100 mg/L in the first wave (48.9% vs. 37.6%, $P=0.010$). Serum ferritin > 500 mcg/dL was observed more frequently in the second wave (80.87% vs. 75.7%, $P=0.248$), and serum lactate dehydrogenase was elevated to be more than 1000 U/L in the first wave (69.9% vs. 64.1%, $P=0.169$).

Moreover, chest X-ray findings consistent with COVID pneumonia were found in 93.6% (236/252) and 95% (387/407) of deaths in the first and second waves, respectively ($P=0.563$).

Discussion

In the present study, there were 311 COVID-19 deaths

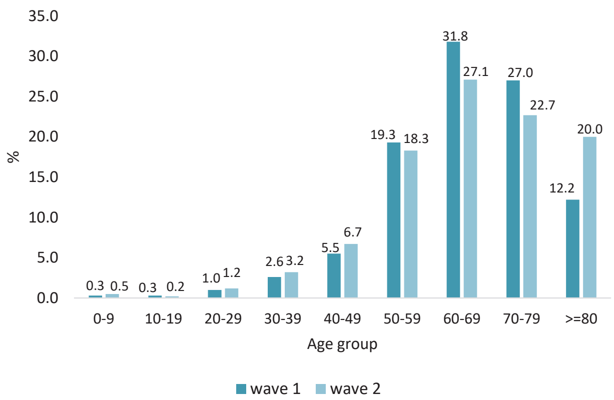

Figure 1. Age Distribution of COVID-19 Deaths in the First and Second Waves. *Note.* COVID-19: Coronavirus disease 19.

Table 2. Symptoms and Causes of Death Among the Deceased With COVID-19 in the First and Second Pandemic Waves

	First Wave (1 July, 2021 to 31 December, 2020)	Second Wave (1 March, 2021 to 30 June, 2021)	*P* Value
	n = 311 (%)	n = 431 (%)	
Clinical symptoms			
Fever	168 (54)	237 (55)	0.229
Cough	121 (38.9)	159 (36.9)	0.472
Breathlessness	193 (62)	295 (68.4)	0.933
Diarrhea	17 (5.4)	29 (6.7)	0.552
Cause of death			
Respiratory failure	275 (88.4)	368 (85.4)	0.229
Sepsis	50 (16.1)	78 (18.1)	0.472
Renal failure	121 (38.9)	169 (39.2)	0.933
Cardiac failure	81 (26)	104 (24.1)	0.552

Note. COVID-19: Coronavirus disease 19.

Table 3. Mortality in Special Categories Among the Deceased With COVID-19 in the First and Second Pandemic Waves

	First Wave (n = 311)	Second Wave (n = 431)	*P*
Mortality in young (< 50 years)	30 (9.6%)	51 (11.8%)	0.346
Mortality in very old (≥ 80 years)	38 (12.2%)	86 (19.95%)	0.005
Deaths with no pre-existing co morbidities	22 (7.1%)	46 (10.67%)	0.094
Maternal mortality	1 (0.32%)	4 (0.92%)	0.999
Mortality in children < 18 years	2 (0.64%)	3 (0.73%)	0.406

Note. COVID-19: Coronavirus disease 19.

over 6 months in the first wave and 431 COVID-19 deaths over 4 months in the second wave. Likewise, the number of deaths in the second wave was higher in India as shown by the daily positivity rate and steep rise in the absolute number of cases.[4] This pattern has been observed in most other countries,[5] which could be due to the increased transmission or virulence of mutant viruses. The circulating variants in the second wave of COVID-19 in India, B.1.1.7 and B.1.617, are considered more transmissible and more virulent.[6]

In the present study, the mean age of the deceased in both waves was similar but slightly older in the second wave (65.44 vs. 65.64 years). This similarity in mean age in the different waves of COVID-19 has been observed in studies from other countries.[7] However, age stratification of the deaths differed in both waves. COVID-19 underwent an extremely steep risk gradient for death across different age groups.[5,8] In the present study, 2.2% more young deaths (≤50 years) occurred in the second wave (11.8% vs. 9.6 %).

In comparison, young deaths were very low in high-income countries such as the United States (2.8%), the UK (1%), and France (0.7%). In contrast, middle- to low-income countries such as Colombia (8%), Chile (6%), Indonesia (20% deaths in those < 45 years), and India (14.4% deaths in those < 40 years) showed a higher proportion of young deaths among total COVID-19 deaths.[5] The second and subsequent waves in other countries such as Germany, Japan, South Korea, and Iran have also reported a shift towards younger demographics.[9-11] This slight increase in young deaths in the second wave is likely to increase further due to the prioritisation of vaccination in the elderly. Paradoxically, a larger share of young deaths may not necessarily be a sign that public health measures are not working but an indicator of better protection of vulnerable elderly individuals. However, if there are low vaccination rates in the elderly population or if the vaccine is less effective in the elderly population, the death rate can increase in this population.

There were 3.1% more deaths of elderly people (≥70 years) in the second wave. This increase was more marked in those aged ≥80 years. These rates are very low compared to elderly deaths among total COVID-19 deaths occurring in high-income countries.[5] This could be due to the predominantly younger population in India and higher life expectancy in high-income countries. The similar pattern of age distribution of COVID-19 deaths in the same country in both waves suggests that country-specific population demographics are a key factor in the age distribution of infections, which is also reflected in the age distribution of deaths.[12] One may expect shifts in the age distribution of COVID-19 deaths in the second wave if the epidemic within a country is spreading to new epicentres and populations with different demographics. Alternatively, documentation of COVID-19 may have become more aggressive in the second wave, with more testing conducted, especially among deceased elderly individuals.

The greatest and the fewest deaths in both waves occurred in the population aged 60-69 years, and in those aged < 20 years, respectively, which is consistent with most other studies.[13] In the present study, men were affected more than women during both waves (5.9% more in the first wave). Similar findings were observed in a study by the Indian Council of Medical Research, where 1.7% more men were affected in the first wave.[14] These gender differences could be due to immunological and lifestyle behaviours such as smoking, health-related self-care, or other factors that can potentially change the gendered impacts of the epidemic.[8,15]

The average duration of illness (symptom onset to death) was lower in the second wave (12 days vs. 13.5 days), indicating that there were relatively quicker deaths in the second wave. Better understanding of the disease, better treatment modalities, and increased vaccination should have prolonged the duration of illness in the second wave. However, the duration from onset to death can be shortened if mutant viruses are more virulent.

Mortality in COVID-19 is strongly influenced by pre-existing comorbidities. Hypertension was the leading comorbidity in the first wave and diabetes in the second wave. A very low number of deaths in those without coexisting comorbidities show that following a healthy lifestyle and preventing lifestyle diseases such as diabetes and hypertension can be an effective preventive strategy and drastically decrease the mortality.

There were more deaths without pre-existing comorbidities in the second wave in our study. Similar findings were noted in a study by the Indian Council of Medical Research, [15] suggesting that the mutant viruses in the second wave were more capable of producing negative outcomes in healthy people.

In the second wave, there was a 7.6% increase in the proportion of patients with diabetes (59.3% vs. 51.7%). Patients with diabetes were more likely to progress to a worse prognosis with COVID-19 infection due to increased inflammatory factors and hypercoagulability.[16] Further, the prevalence of diabetes among COVID-19 deaths in South India[17] was higher than that in the United States, China, and Pakistan.[18-20] This reflect the higher prevalence of diabetes in India. In addition, there is a need to further evaluate the relationship between the new mutant strains and diabetes.

Maternal mortality showed a mild increase of 0.6% in the second wave (0.92% vs. 0.32%). It should be noted that four of the five maternal mortalities in our study had diabetes. The association between diabetes and COVID-19 deaths in pregnancy needs further evaluation. Only one patient was younger than 35 years. This may indicate that age and diabetes are significant risk factors for COVID-19 mortality during pregnancy. Furthermore, mortality in children was very low in both waves without a significant difference between waves.

The clinical presentation was similar in both waves. Breathlessness was the most common presentation followed by fever. Our findings were inconsistent with those of population-based studies where fever is the most common symptom. This may be due to the preferential referral of dyspnoeic patients from first- and second-line COVID-19 treatment centres to our centre. Our centre is the only major public tertiary healthcare centre for a large geographic area, has strict admission criteria, and caters mostly to patients requiring advanced care.

None of the deceased in the first wave were vaccinated as the vaccination drive in India started in January 2021. Fourteen deceased patients in the second wave were vaccinated with one dose of vaccine, and 1 deceased patient took both doses of the CoviShield vaccine. The double-vaccinated deceased patient was 85 years old with diabetes and hypertension and was presented with acute myocardial infarction without any respiratory symptoms. A part of the population in Kerala was vaccinated during the study period of the second wave, which might have decreased the mortality in that group. Of those eligible for vaccination (> 18 years old), 41% received one dose, and 12% were fully vaccinated with two doses by the end of the study period (30 June 2021) in the state of Kerala.[21]

The strengths of our study lie in its single-centre design with similar types of patients, admission criteria, and management by the same team during both waves, making the comparison relevant. The novelty of this study is the comparison of the demography and clinical aspects of COVID-19 deaths in two waves in India, which is very limited at the time this study was undertaken.

Limitations of the Study

Kerala differs from other parts of the country due to its high population density, larger geriatric population, higher burden of lifestyle diseases, increased literacy, and better health infrastructure. Hence, the present study may not be a true national representation of COVID-19 mortality as the demographic and clinical characteristics show marked geographical variation. Further, many known risk factors for COVID-19 mortality such as obesity, socioeconomic status, and behavioural risk factors (e.g., smoking and alcohol addiction) could not be analyzed due to logistic difficulties.

Conclusion

The present comparative study indicated that the second wave of COVID-19 differed from the first wave in the age distribution of COVID-19 deaths with more deaths occurring in young (≤50 years) and elderly (≥70 years) people. In addition, the duration of disease from symptom onset to death was shorter in the second wave, leading to relatively quicker deaths in the second wave. Further, maternal mortality and mortality in those without any pre-existing comorbidities were higher in the second wave. Identifying those at higher risk for mortality, enhancing the vaccination drive, immunizing vulnerable populations quickly, and promoting healthy lifestyles to decrease comorbidities would be the most important strategies to prevent further deadly waves of COVID-19.

Conflict of Interest Disclosures

The authors declare that there is no conflict of interests.

Ethical Approval

Approval was obtained from the Institutional Ethics Committee. A waiver of written informed consent was obtained owing to the rapid emergence and highly infectious nature of the disease as well as being a record-based study with anonymized data.

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