Original Research Article

Demographic and clinical characteristics of COVID-19 mortality in Southern India-A single centre observational study

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Abstract

Background: COVID-19 pandemic has spread worldwide with new variants of viruses and reinfections. As we have to live with COVID-19, public health efforts should focus on preventing avoidable mortalities. The mortality with COVID 19 shows marked regional variation; hence regional studies are needed. **Objectives**: Our study analyses the demographic and clinical characteristics of deceased COVID-19 patients, which are critical for developing geographic-specific public health interventions to reduce mortality. **Materials and methods**: We conducted a retrospective observational study from 1 April 2020 to 31 August 2021 in Kerala, India. We analysed 1201 death summaries of laboratory-confirmed COVID-19 deaths and included 1076 cases for the study. **Results**: Mean age of the deceased was 65.7 years (SD: 14 years). Of the total deaths, 65.9% were males. The mean duration between the onset of symptoms to admission in our hospital was 4.9 days (SD 3.7 days, IQR 5 days). The most frequent presenting symptoms were breathlessness (68.2%) and fever (57.3%). 90.1% in the study group had at least one comorbidity. Diabetes (53.5%) was the most common comorbidity, followed by hypertension (52.3%). Diabetes was also the most frequent comorbidity reported in COVID-19 deaths among young (≤40 years), pregnant and vaccinated groups. **Conclusion**: The elderly, males and patients with underlying comorbidities, especially diabetes, die disproportionately due to COVID-19. Health intervention strategies like vaccination, promotion of healthy lifestyle to control comorbidities and awareness programmes for COVID appropriate behaviour should be prioritised in these vulnerable populations.

Keywords: Covid 19, mortality, comorbidities, SARS-CoV2, India.

Introduction

Covid -19 caused by the novel SARS CoV2 is a devastating pandemic of the twenty-first century. As early as 2019, with the first case reports from Wuhan, China, it was found that the mortality parameters varied from region to region and was influenced by geographical and ethnic factors.

Age, comorbidities, cultural and socio-economic factors influenced the outcome in severe COVID-19 infection. Earlier reported studies showed wide variability in the mortality rate across regions, and it varied from 1% to 12% in different geographical areas[1]. Studies have shown that elderly patients and those with comorbidities like diabetes and hypertension had higher mortality[2]. India, which has the second-highest population in the world, was one of the countries badly affected with 3.43 crores infected cases and 4.5 lakhs deaths by the first week of November 2021 [3].Kerala, situated in the southernmost part of India, is the fourth densely populated state in India, with a high population density of 859 per square km[4].

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It also witnessed an increased incidence of COVID-19 infection. In addition, the state of Kerala has a high prevalence of non-communicable diseases like diabetes mellitus, hypertension and coronary artery disease; even in the young population[5]. Also, Kerala and its neighbouring states in South India have a high proportion of geriatric population. There is a need for a better understanding of the demographic and clinical characteristics of deceased COVID-19 patients in this part of India, which could inform public health interventions focusing on preventing mortality. This study was conducted in our centre to fill this knowledge gap.

Materials and methods

We performed a retrospective analysis of the mortality characteristics of COVID-19 deaths during the COVID-19 pandemic in Kerala, South India. The objectives of the study were to assess the demographic factors, clinical characteristics, associated comorbidities, and complications related to mortality in confirmed COVID-19 deaths and estimate the time interval between the symptom onset, hospital admission, and death.

Ethics

After obtaining approval from the Institutional Ethics Committee, the study was registered with the Clinical Trials Registry-India. A waiver of written informed consent was obtained due to the rapid emergence and highly infectious nature of the disease and being a record-based study with anonymised data.

Settings and sample

The study was conducted in a large tertiary care teaching institute with 1300 beds in Kerala, India. The study period was 17 months, from 1 April 2020 to 31 August 2021.All deceased patients with laboratory-confirmed COVID-19 infection admitted to the hospital during the study period were included. Patients who died due to causes other than COVID-19, such as suicide or accidents, were excluded. Patients who were deceased upon arrival to the hospital were also excluded. According to the World Health Organization guidelines, all patients were confirmed for COVID-19 by real-time polymerase chain reaction or a rapid antigen test. All patients received routine comprehensive treatments, including intravenous antibiotics, assisted oxygenation, specific treatment for the underlying diseases and supportive therapies 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 40 years of age and below were considered to be young deaths. Special categories such as maternal deaths, deaths without pre-existing comorbidities, young deaths, and deaths in elderly patients were identified and analysed.

Data extraction

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

Statistical analysis

Qualitative variables were represented in the form of frequency and percentages. Quantitative variables were represented using mean, standard deviation (SD), median and Interquartile range (IQR) as appropriate. The proportions for categorical variables were analysed using the Chi-squared test. A p-value of less than 0.05 was used as a cut-off for statistical significance. Microsoft Excel (Microsoft, Redmond, WA) and SPSS Statistics version 24 (IBM, Armonk, NY) was used for analysis. Graphical representation was done in the MS Excel package included in Microsoft office365.

Results

A total of 1201 COVID-19 deaths were reported during the study period, of which 1076 cases of deaths that met the inclusion criteria were taken up for analysis. Total admissions during the study period were 6770. The case fatality rate was 17.74 %. The first death occurred on 11 April 2020.

Demographic characteristics

The age of the patients who died ranged from 2 months to 96 years. The mean age was 65.7 years (standard deviation 14 years). 65.9 % of deaths were among males. The age and sex-wise distribution of deaths are shown in Figure 1 below

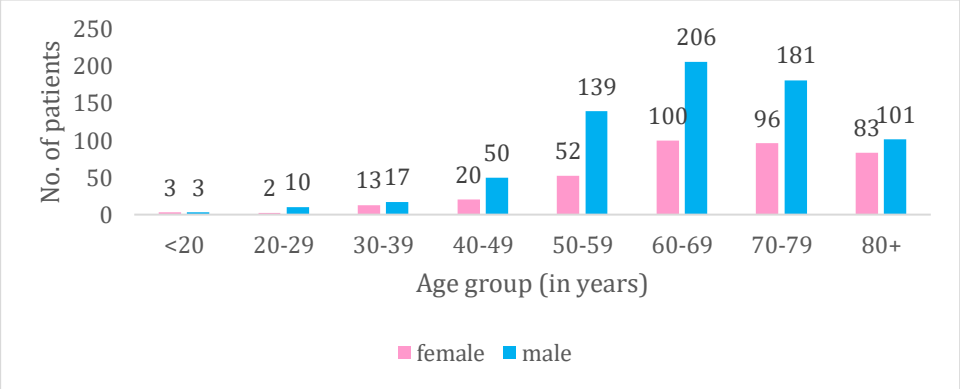

Fig 1: Age and sex-wise distribution of deaths

There is a significant association between age group and sex (p=0.01, using Chi-square test of association). From Figure 1 above, it is evident that in both males and females, the age group of 60 to 69 years had the maximum deaths (29% for males and 27% for females).

Clinical characteristics

The mean duration between the onset of symptoms to admission in our hospital was 4.9 days with a standard deviation of 3.7 days (median was four days with an inter-quartile range of 5 days). The mean duration of hospital stay was 7.4 days with a standard deviation of 5.8 days (median was six days with an interquartile range of 7 days). The onset of symptom to death ranged from 2 to 39 days, with a mean of 12.3 days and a standard deviation of 6.7 days (median was 11 days with an interquartile range of 9 days).

157 patients (14.5%) died within 24 hours of admission. 180 patients (16.72%) died >24 hours but < 72 hours of admission.

Breathlessness was the most common symptom reported among the deaths studied (68.2%, n = 734) followed by fever (57.3%, n = 617), cough (36.6%, n = 394) and diarrhea (4.8%, n=52)

Comorbidities

Comorbidities were reported in 969 (90.1%) of the patients who died due to COVID 19. The distribution of the number of comorbidities is shown in Figure 2 below.

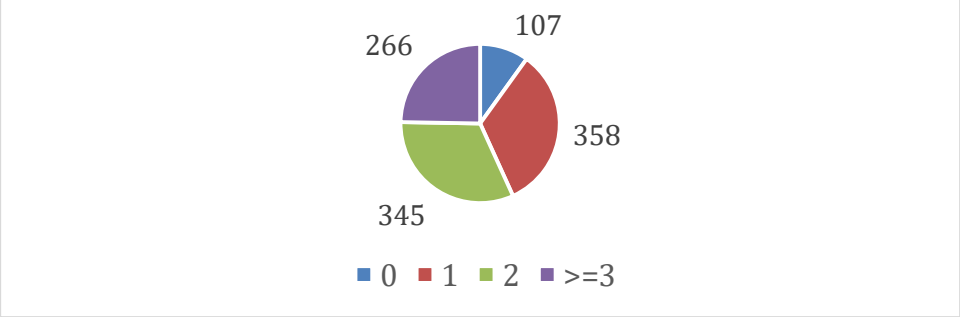

Fig 2: Distribution of the number of co-morbidities

From Fig. 2, it is seen that the majority (33.3%) had only one comorbidity. Also, 107 (9.9%) patients who died had no comorbidities. Among the comorbidities, diabetes mellitus was the highest (53.5%), followed by hypertension (52.3%).
The age-wise distribution of comorbidities is shown in Table 1 below.

Table 1: The age-wise distribution of comorbidities

Co-morbidity	Age group (in years)								Total	P
	<20 (n=6)	20-29 (n=12)	30-39 (n=30)	40-49 (n=70)	50-59 (n=191)	60-69 (n=306)	70-79 (n=277)	80+ (n=184)		
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	
Diabetes	0 (0)	1 (8.3)	18 (60)	39 (55.7)	112 (58.6)	189 (61.8)	134 (48.4)	83 (45.1)	576 (53.5)	<0.001
Hypertension	0 (0)	2 (16.7)	4 (13.3)	25 (35.7)	93 (48.7)	157 (51.3)	171 (61.7)	111 (60.3)	563 (52.3)	<0.001
Cardiovascular diseases	0 (0)	0 (0)	0 (0)	5 (7.1)	30 (15.7)	77 (25.2)	80 (28.9)	44 (23.9)	236 (21.9)	<0.001
Chronic renal disease	0 (0)	3 (25)	5 (16.7)	13 (18.6)	47 (24.6)	70 (22.9)	52 (18.8)	20 (10.9)	210 (19.5)	0.024
Chronic liver diseases	0 (0)	1 (8.3)	3 (10)	8 (11.4)	13 (6.8)	22 (7.2)	5 (1.8)	3 (1.6)	55 (5.1)	0.001
Chronic respiratory diseases	0 (0)	0 (0)	2 (6.7)	2 (2.9)	13 (6.8)	37 (12.1)	41 (14.8)	30 (16.3)	125 (11.6)	0.007
Cerebro vascular stroke	1(16.7)	0 (0)	3 (10)	3 (4.3)	11 (5.8)	25 (8.2)	29 (10.5)	21 (11.4)	93 (8.6)	0.283
Malignancy	0 (0)	0 (0)	1 (3.3)	2 (2.9)	6 (3.1)	19 (6.2)	17 (6.1)	5 (2.7)	50 (4.6)	0.513
Diabetes + Hypertension	0 (0)	0 (0)	3 (10)	20 (28.6)	67 (35.1)	114 (37.3)	98 (35.4)	59 (32.1)	361 (33.6)	0.006
Diabetes + Hypertension + Cardiovascular diseases	0 (0)	0 (0)	0 (0)	2 (2.9)	13 (6.8)	35 (11.4)	32 (11.6)	15 (8.2)	97 (9)	0.058

From Table 1 above, it is seen that hypertension, diabetes and cardiovascular diseases were individually having a significant association with age group, with 61 to 80 age group accounting for the maximum proportion of patients who had hypertension as well as those patients who had cardiovascular diseases. In contrast, in diabetes, the highest proportion was observed in the 41 to 60 age group. The combination of hypertension and diabetes was also significantly associated with the age group, and the most significant proportion was observed in the 61 to 80 age group.
The sex-wise distribution of comorbidities was also looked into and is depicted in Figure 3 below.

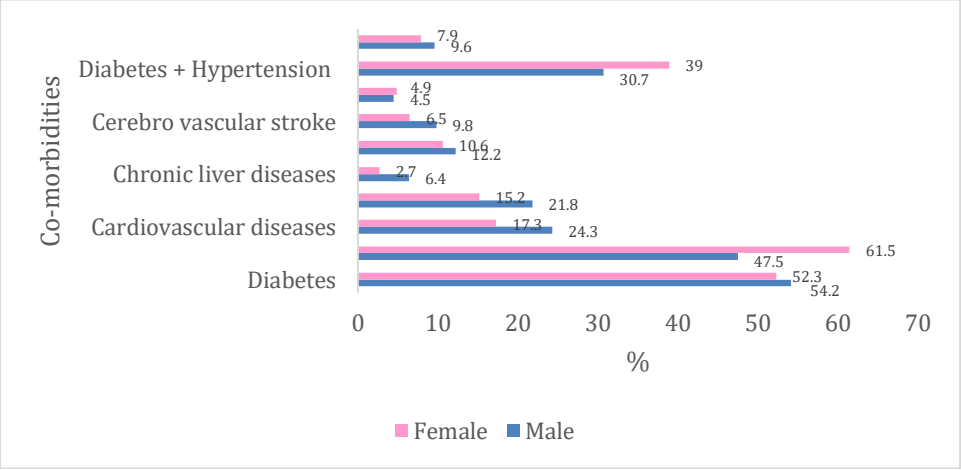

Fig 3: Sex-wise distribution of comorbidities

It was found that females had a significantly higher proportion of hypertension (p<0.001) as well as the combination of diabetes and hypertension (p=0.006). In contrast, males had a more significant proportion of cardiovascular diseases (p=0.009), chronic renal diseases (p=0.009) and chronic liver diseases (p=0.01), using the Chi-square test.

Young deaths

58 patients (5.39%) in the study group were ≤ 40 years of age. The mean age was 32.28 years. The average duration of illness from onset of symptoms to death was 13.53 days. Commonest associated comorbidity was diabetes (41.37 % ,n=24/58) followed by chronic kidney disease (17.24%,n= 10/58), hypertension(13.79% ,n=8/58), chronic liver disease(6.89%,n=4/58) and stroke(6.89%,n=4/58).14 deceased had no comorbidities .Respiratory failure was the main cause of death (82.75%,n= 48/58). Among the deceased, four were below 18 years.

Maternal mortality

There were nine maternal deaths during the study period. One death occurred during the first wave of COVID-19 and eight during the second wave. Six deceased out of the nine were diabetic. Among

them, three had pre-gestational diabetes. Five of the deceased pregnant women were above 35 years. Death was due to severe COVID pneumonia in all the cases

Death among vaccinated

41 patients had taken vaccination.29 patients took the first dose, and 12 took two doses. Among the vaccinated who died , the most common comorbidity was diabetes (53.65%,n=22/41) followed by hypertension (1.46%,n=17/41), coronary artery disease(17.07%,n= 7/41) and chronic kidney disease(17.07%,n=7/41). Seven of the vaccinated deceased were not having any comorbidity.

Discussion

The case fatality rate in our hospital during the study period was 17.74%. The mortality rate in India is 1.33%. [5] Our centre is the only tertiary care centre for a large geographic area, mainly admitted sick patients requiring advanced respiratory support referred from peripheral centres. Hence the hospital case fatality rate was high. The case fatality rate was 13.2% in a study done in Mumbai in a tertiary care centre by Vikram Londhey et al[6]. In a retrospective cohort study from China, a mortality of 28% was reported[7]. In a survey by Safiya Richardson from the US, the death rate reported was 21%[8].

The mean age in our study group was 65.7 years which showed that it primarily affected the elderly population. Different studies conducted in Indian subcontinent also showed a similar mean age between 60-70 years[9,10]. Studies from western countries show a higher mean age[11,12]. Countries with a significant elderly population and a longer life expectancy tends to offer a higher mean age.

There were 58 young deaths(5.39%) in our study (age ≤ 40 years). The younger age group was less affected than the middle age group. This finding is consistent with the observations from other studies, which suggest a decreased case fatality rate with decreasing age[9,12,13].

It may be noted that there is a sharp rise in mortality from the 50-59 age group to the 60-69 age group in our study. A similar increase in age group-specific death rate was shown in other studies on the age distribution in COVID -19 deaths[10,13].

71.28 %(n = 767) COVID-19 deaths in the present study occurred above 60 years of age, similar to the observation of studies in other centres[11,12]. This finding clearly shows that the elderly are more affected than the young, and they should be prioritised in preventive measures. The pathophysiology of why Covid 19 predominantly affects the elderly is not fully known. Possible reasons are the poor immune status and comorbidities like cardiovascular disease, diabetes and hypertension in the elderly age group that contribute to a decrease in functional reserve and thus hinder the fight against infections[14]. Literature shows that SARS COV2 infections among older individuals result in robust immune responses than younger adults[15].65.9 % of the deceased were males in the present study. Males have comprised a disproportionately high number of deaths in cohorts in most studies[8-15]. Less mortality among women has been reported in many studies, which could be due to the protection of the X chromosome and sex hormones, which play an essential role in providing innate and adaptive immunity. The higher mortality among men could be due to behavioural risk factors such as smoking, and alcohol consumption, which are relatively higher among men in India.The predominant symptom in our patients was breathlessness (68.2%), unlike the population-based studies where fever and cough were the main complaints. In our study, breathlessness was more than fever because patients with respiratory failure were selectively referred to our tertiary care hospital from peripheral hospitals for advanced respiratory support. Symptoms in Covid 19 are not specific for COVID 19, and the predictive value of a single symptom in the diagnosis of Covid 19 is uncertain[14]. 90.1 % of the patients had some form of significant comorbidities in our study, which is high compared to similar studies done in Tamilnadu (85%)in South India, Pakistan (71%), China (70%) and South Korea(83%)[9,10,19,20]. Our study's high prevalence of pre-existing comorbidities in COVID-19 deaths could be due to the high prevalence of lifestyle diseases, especially diabetes, in Kerala. Diabetes (53.5%) was the most frequent pre-existing comorbidity in our study, followed by hypertension (52.3%). This was unlike most of the mortality studies worldwide, where hypertension was more common than diabetes. Our finding is consistent with the study done by Asirvatham et al. from Tamilnadu, a neighbouring state of Kerala, where diabetes was the most frequent associated comorbidity (61.9%,n=1038/1678) followed by hypertension (49.2%, n=825/1678)[9]. The prevalence of diabetes in COVID-19 deaths in South Indian studies was higher than in other countries, which reflect the higher prevalence of diabetes in these regions[11,19,10].In Kerala, the prevalence of diabetes is very high compared to the national average. Genetic predisposition, dietary habits and sedentary lifestyle are considered to be the reason for this phenomenon. In Kerala, the prevalence of hypertension, obesity, hyperlipidaemia, heart attack, stroke, and cancers is also high, which may account for the very high prevalence of comorbidity among the fatalities in our study. Many of the patients in our study presented without any history of comorbidities. Later they were found to have comorbidities on evaluation. There were only 9.9 % COVID-19 deaths with no pre-existing comorbidities in our study.

Among the host factors, age and gender are non-modifiable, but comorbidities are modifiable and risk reduction strategies can minimise or prevent comorbidities.Most of the comorbidities can be controlled with adequate public awareness campaigns, promoting a healthy lifestyle with a balanced diet, good exercise, and reducing smoking and alcohol intake.

5.39 %(n=58) Covid deaths were below 40 years of age. Out of which, 75% (44 cases) were with pre-existing comorbidities. This finding shows that most of those who die with COVID-19 have pre-existing comorbidities even at a young age. They should be prioritised in public health intervention strategies. There were only 13 female non-pregnant covid-19 deaths below 40 years, making them one of the least vulnerable subgroups in our cohort. Among the deceased ≤ 40 years of age, 41.37 % had diabetes, which shows that even in young; Covid-19 mortality is strongly linked to diabetes.

Out of the nine maternal deaths, six (66%) were having diabetes. Three among them had pre-gestational diabetes. The majority were above 35 years. This finding suggests that maternal deaths with COVID-19 are strongly linked with diabetes and maternal age and needs further evaluation.The leading cause of death in our study was respiratory failure (88.66%), followed by renal failure (33.64%), cardiovascular diseases (17%) and sepsis (19.8%). The most common organ damaged other than the lung is the kidney in our study. Renal complications were more in our study, unlike the cardiac complications in most other studies[9,10,11]. High prevalence of renal failure in our study may be due to the increased prevalence of pre-existing renal disease and coexisting comorbidities like hypertension and diabetes. Hence, early recognition of acute kidney injury and providing appropriate interventions are essential to avoid further renal injury, which may be helpful to improve the prognosis of patients with COVID-19.There was a resource crunch in many parts of the world and in India, especially during the second pandemic wave, contributing to the mortality in COVID-19. However, this overwhelming of health care facilities worldwide was less felt in Kerala as there was less peaking of cases during the pandemic, as evidenced by the lowest seroprevalence rate in Kerala for COVID-19 infection among the Indian states, in the fourth seroprevalence survey report by ICMR in May 2021.Limitations of the study are that the parameters related to COVID-19 mortality like obesity, smoking and alcohol addiction could not be included due to logistic difficulty, which could have given further insight into COVID-19 fatalities. A comparative study is suggested to assess the risk factors associated with COVID -19 deaths. The present study provides evidence from Kerala, South India, that the elderly, males and patients with underlying comorbidities die disproportionately due to COVID-19. Diabetes was the most common associated comorbidity with COVID-19 deaths, especially among the young (less than 40 years), pregnant women, and the COVID-19 vaccinated group. Other than the lungs, the most common organ involved was the kidneys.

Low fatalities among those without any significant comorbidities show that risk reduction strategies for lifestyle diseases like diabetes,

hypertension and cardiac diseases with lifestyle modifications should be actively promoted to bring down the mortality, especially in areas with a high prevalence of these diseases as in South India. Health intervention strategies like vaccination, promotion of healthy lifestyle to control comorbidities and awareness programmes for COVID appropriate behaviour should be prioritised in these identified vulnerable populations.

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