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Original Research Article

Epidemiological study of COVID-19 mortality in a tertiary care center of South India

Jayakrishnan Thayyil[1]*, Aparna Padmanabhan[2], Alan Gangadharan[3], Navya Annikady[2]

[1]Department of Community Medicine, KMCT Medical College, Calicut, Kerala, India
[2]Department of Community Medicine, Govt Medical College, Calicut, Kerala, India
[3]Directorate of Health Service, Govt of Kerala, Kerala, India

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***Correspondence:**
Dr. Jayakrishnan Thayyil,
E-mail: drjayakrishnanthayyil@gmail.com

ABSTRACT

Background: COVID-19 infection have taken a huge death toll across the globe since its emergence in 2019 in Wuhan, China. There have been inconsistencies related to many of the epidemiological features, which vary from country to country or are not known or explained properly. Therefore, there is an urgent need to generate epidemiological evidence of COVID-19 at the state level based on the data. Also, very limited published studies from India have analyzed the factors associated with death due to COVID-19. The objective of this study was to identify the epidemiological factors involved in COVID deaths in a tertiary care center of north Kerala, South India and to compare the trend of these factors affecting COVID-19 mortality in the consecutive years.
Methods: Descriptive study was conducted prospectively using secondary data extracted from the electronic surveillance records of the tertiary care center were analyzed using suitable software and presented.
Results: During the study period 1747 deaths due to COVID-19 was reported. The duration of hospital stay was 6.5+ 6.3 days. The median age was 67.5 years (IQR14) and males constitute 67.5% (95% CI: 64.8-69.3%). Among them 88.3% (95% CI:86.7-89.7%) have any of reported co morbidities which mainly diabetes and hypertension. Immediate cause of mortality mainly (73.6%) ARDS. Epidemiological factors related to mortality was similar during years.
Conclusions: Since COVID-19 deaths affect older age groups, and those with comorbidities, reverse isolation needs to be given more importance wherever possible and its high time to consider targeted COVID-19 vaccination among them.

Keywords: COVID-19, Mortality associated factors, Co-morbidities, Interval of death

INTRODUCTION

The World Health Organization declared a global pandemic on 11 March 2020 in response to the emergence and spread of Coronavirus disease 2019 (COVID-19).[1] Globally, it is found that there is not much difference between the age groups affected by this disease however when it comes to the mortality associated with the disease, its seen that elderly people are more vulnerable to death. In the United States, 82% of COVID-19 deaths had happened in people aged more than 65 years.[2] A peculiar tropism for the male gender by the COVID-19 virus have been noted since the emergence of the disease and it has been documented by global studies that males are more prone to succumbing to the illness.[3] Among the first reported patients in China, 56% were males.[4] Individuals with any co-morbidities like those affected by obesity, diabetes, asthma or are immunosuppressed owing to cancer and other conditions, are at a higher risk of hospitalization and of dying of

COVID-19. Healthy individuals younger than 40 years very rarely die of COVID-19.[5]

The recent record numbers of infections in the United States revealed that the fraction of people who died because of SARS-CoV-2 infection is 1% or less, much smaller than previous estimates that had placed it at about 5% to 10%, percentages largely on the basis of hospital testing.[6] Even though mortality rates calculated from a hospital setting will be an overestimation ,which are fraction of deaths among severely affected population it will give a picture for future course of action for policy makers to prevent mortality.

There have been inconsistencies related to many of the epidemiological features, which vary from country to country or are not known or explained properly. Therefore, there is an urgent need to generate epidemiological evidence of COVID-19 at the state level based on the data. Also, very limited published studies from India have analyzed the factors associated with death due to COVID-19. This study will be very helpful in analyzing the trends and risk factors of deaths due to COVID-19 and the results might help in health system planning, formulating guidelines, preventing future deaths, and further scientific researches. During second year of pandemic the infections were mainly due to variants of concern (VoC) like alpha and delta in this region. Hence in this paper, demographic and epidemiologic profile of patients who succumbed to infection in year 2020 and 2021 in tertiary care hospital in South India will be discussed with special emphasis to the notable differences in 2-year mortality patterns.

The objective of this study was to identify the epidemiological factors involved in COVID deaths in a tertiary care center of north Kerala, South India and to compare the trend of these factors affecting COVID-19 mortality in the two consecutive years.

METHODS

Present hospital-based study conducted at government medical college, Calicut a tertiary care center in North Kerala, South India during the period from March 2020 to May 2021. Regional prevention of epidemics and infectious diseases cell (R-PEID cell) under the department of community medicine collects details of COVID-19 cases and deaths on a daily basis from wards and intensive care units. Required information were extracted from this data using a structured format. Data such obtained were retrieved, coded, stratified and analyzed using suitable statistical software.

Study setting

The study was done on Government medical college, Calicut a tertiary care center, North Kerala, South India.

Study population

Patients who were admitted with a diagnosis of COVID-19 and later succumbed to the infection in the tertiary care center from March 2020 till May 2021. All adult patients who were diagnosed with COVID-19 according to ICMR guideline, who admitted and died between March 2020 to May 2021, were included in our study. The first confirmed case of COVID 19 infection was reported to the tertiary care center in March 22, 2020 and the first COVID-19 death happened in April 21, 2020

Study duration

During 1st March 2020 to 31st May 2021 (15 months) study was conducted.

Sampling technique

Universal sampling technique used in study.

Sample size

The 1747 (total COVID 19 deaths as of May 2021 reported to the RPEID cell).

Inclusion criteria

All the patients admitted with a lab confirmed diagnosis of COVID-19, who died and whose details have been entered into the RPEID cell COVID-19 mortality surveillance network included in the study.

Exclusion criteria

Patients admitted with suspected COVID-19 and not confirmed with lab diagnosis were excluded.

The study was approved by institutional ethics committee GMC Calicut.

Variables used in the study

Variables used in the study were age, gender, co-morbidities, duration of hospital stay and interval of death since admission.

Data collection

Epidemiological, demographic, clinical, laboratory, treatment, and outcome data were extracted from electronic records available using a standardized data collection format. The cause of death was listed immediate, antecedent, underlying and contributory according to WHO COVID-19 death audit form.[7] All data were checked by investigators (AP, AG) and a third investigator (JK) adjudicated any difference in interpretation between the two primary reviewers.

Analyzed data were represented in form of tables and figures. Qualitative variables were represented as frequencies and percentages with 95% CI and quantitative variables represented as mean and standard deviation. Mortality monthly trend was represented as line diagram. Mortality trends were compared for years 2020 and 2021.

RESULTS

During the study period of fifteen months, a total of 12609 patients were admitted with confirmed COVID-19 infections. The first patient was admitted on March 22nd and first death was reported on April 21st 2020. During this period 1747 deaths were reported with a case fatality ratio (CFR) of 13.9% (95% CI :13.2- 14.5%). The overall CFR remained without much difference in the two years (12.6% ,95% CI 11.7-13.5%) and (14.7%, 95% CI 13.9-15.5%) respectively). During 2020, COVID-19 cases and deaths peaked during the October of 2020 in the first wave with 1477 cases and 190 deaths (CFR: 12.8). During 2021 the second wave peaked in the month of May 2021 with a surge of 3024 cases and 580 deaths (CFR 19.2%) due to surge.

Place wise majority of deaths 780 (69.5%, 95% CI: 66.5-70.9%) among patients from native district Kozhikode followed by other neighboring districts Malappuram (23.7%, 95% CI 21.4-25.5%), and rest (7%, 95% 5.3-9.2%) from other districts Wayanad, Kannur, Palakkad.

The mean age of mortality was 65.9 years (Median 67.5, IQR 14) and with Mean age of 65.1, 6.8 years (Median 67 IQR 12, 68 IQR 18) in the two years. Age wise majority of COVID 19 deaths (74.5% in 2020 and 75.5% in 2021) happened in the age group above sixty of respectively. Death below 40 years was <5% and below 20 years was <1%.Overall, there was increased mortality among males than females (67.5%, 95% CI: 64.8-69.3%). However, while comparing 1st and 2nd years, there slight reduction in mortality among males from 69.8% to 65.8%.

There were not much difference between the age among different genders in respect to mortality. Overall age of males 65.9±14.2 years and that among females 66.3±16.1 years. Age also showed a slight increase between the 2 waves from 65.1±14.5 years to 66.7±15.4 years among males and from 65.5±16.7 years to 67.1±15.8 years among females which not significant (p=0.75)

Stratifying age and gender, it was seen that male gender constitute more deaths except in less than 20 years where females contributed 60%. In the age group of more than 80 years, there was a comparability between the gender with 53.2% contributed by males and 46.8% contributed by females (Table 1).

Co-morbidities

Majority (88.3%, 95% CI:86.7-89.7%) had one or the other comorbidities (multiple co-morbidities). Comparing the frequency of co-morbidities, it was found that 86%, (95% CI 83.1-88.6%) of those died of COVID-19 had co-morbidities in the year 2020 and this has increased to 89.6% (95% CI 86.7-89.7%) in the year 2021which was significant (p=0.03) (Table 2).

In 2020, hypertension and diabetes mellitus contributed majority with 46.8% and 44.8% and in 2021 they contributed 53.9% and 48.8% respectively. Coronary artery disease (CAD), chronic kidney disease (CKD) and cerebrovascular accident (CVA) together contributed around 60% of the co-morbidities (Table 2).

Gender wises it was found that females (90.2% ,95% CI 87.5-92.5%) had co-morbidities at a higher frequency than males (87.2, 95% CI:85.2-89.1%) (p=0.12). Out of 206 patients aged less than 50 years who died of COVID-19 infection, 163(79.1%) had co-morbidities and of the total 1526 patients aged more than 50 years, 1379 (90.4%) had co-morbidities (Table 3).

Interval of death since admission

The mean duration of hospitalization among the deceased was 6.5±6.3 days (Median: 5, IQR 5.5 days). After hospital admission 42% died within 3 days, more than 51% of patients died had an interval of more than 3 days to two weeks and very few (7%) had an interval of more than two weeks (Table 3). Majority of the people succumbed to the illness in the first 7 days of hospitalization and this proportion increased as the age advanced. Around 74% of people in the age group above 50-died within 7 days of hospitalization compared to 66% among those aged less than 50 years., There is a significant increase in the number of deaths among age >50 years in the year 2021 compared to 2020 (p=0.01).

Table 1: Age and gender wise distribution of deaths.

Age (Years)	Gender, n (%)				Total	
	2020		2021			
	Male	Female	Male	Female	Male	Female
≤20	3 (30)	7 (70)	3 (60)	2 (40)	6 (40)	9 (60)
21-40	17 (100)	0 (00)	29 (60.4)	19 (39.6)	46 (70.8)	19 (29.2)
41-60	103 (77.4)	30 (22.6)	153 (71.8)	60 (28.2)	256 (73.9)	90 (26.1)
61-80	272 (73)	101 (27)	413 (66.9)	204 (33.1)	685 (69.2)	305 (30.8)
>80	40 (43)	53 (57)	128 (57.4)	95 (42.6)	168 (53.2)	148 (46.8)
Total	435	191	726	380	1119	623

Table 2: Pre-existing co-morbidities among deceased patients.

Comorbidities	2020, n=547	2021, n=995	Total, n=1542
	N (%)	N (%)	N (%)
Hypertension	256 (46.8)	536 (53.9)	792 (51.4)
Diabetes mellitus	245 (44.8)	486 (48.8)	731 (47.4)
CAD	160 (29.3)	247 (24.8)	407 (26.4)
CKD	133 (24.3)	193 (19.4)	326 (21.1)
CVA	62 (11.3)	131 (13.2)	193 (12.5)
COPD/Br asthma	55 (10.1)	108 (10.9)	163 (10.6)
Malignancy	36 (6.6)	51 (5.1)	87 (5.6)
CLD	29 (5.3)	40 (4.0)	69 (4.5)
Others	79 (14.4)	95 (9.5)	174 (11.3)

*Multiple options allowed. CAD: Coronary artery diseases. CKD: Chronic kidney disease, CVA: Cerebrovascular accidents. CLD: Chronic liver disease.

Table 3: Interval of death since admission.

Duration (hours)	2020, n=614 (%)	2021, n=1111 (%)	Overall, n=1725 (%)
	N (%)	N (%)	N (%)
<24	76 (12.4)	181 (16.3)	257 (14.9)
24-48	86 (14.0)	162 (14.6)	248 (14.4)
48-72	109 (17.8)	109 (9.8)	218 (12.6)
72 to 1 week	124 (20.2)	289 (26.0)	413 (23.9)
1 to 2 weeks	170 (27.7)	298 (26.8)	468 (27.1)
> 2 weeks	49 (7.9)	72 (6.5)	121 (7.0)

Table 4: Death audit: cause of death.

Cause	2020	2021	Total
	N (%)	N (%)	N (%)
Immediate			
ARDS	453 (71.2)	833 (74.9)	1286 (73.6)
AKI	69 (10.8)	110 (9.9)	179 (10.2)
A/c pulmonary edema	49 (7.7)	57 (5.1)	106 (6.1)
MI (ACS)	39 (6.1)	47 (4.2)	86 (4.9)
Sepsis/MODS	26 (4.1)	64 (5.8)	90 (5.2)
Antecedent			
COVID pneumonia	590 (92.8)	1000 (90)	1590 (91)
Myocarditis	36 (5.6)	67 (6.0)	103 (5.9)
Others	10 (1.6)	44 (4.0)	54 (3.1)
Underlying cause			
COVID-19 infection	626 (98.4)	1067 (96)	1702 (97.4)
Indirect causes	10 (1.6)	44 (4)	54 (2.6)
Total	636 (100)	1111 (100)	1747 (100)

Out of the 1136 patients who died within 7 days of hospitalization, 776 (66.1%) were males. When comparing the two years, overall proportion of people surviving for more than 7 days after admission has increased from 33.9% in 2020 to 37.1% in 2021.

Cause of death

As per WHO criteria the cause of death was analysed as immediate, antecedent, underlying causes. a) Immediate cause of death: acute respiratory distress syndrome (ARDS) constituted 73.6% of the followed by acute kidney injury (10.2%), a/c pulmonary edema (6.1%), sepsis/MODS (5.2%) and myocardial infarction (MI) (4.9%) (Table 4). b) Antecedent cause: COVID pneumonia contributed 91% of the followed by myocarditis (5.9%) (Table 4). c) Underlying cause: Majority (97.4%) of deaths were directly attributed to COVID 19 infection. Indirect causes are contributory in those patients who died due to other diseases like head injury, road traffic accident but were COVID positive at the time of admission (Table 4).

DISCUSSION

We have conducted an epidemiological study on mortality among admitted patients in a tertiary care hospital for a period of fifteen months from the beginning of pandemic till May 31st 2021. During this period 12609 patients were admitted among whom 1747 died due to COVID-19. Our analyses provide a preliminary picture of how key demographic characteristics and a range of comorbidities which were primarily selected as being of interest and are jointly associated with poor outcomes in COVID-19.

Age

Majority of COVID 19 deaths (74.5% in 2020 and 75.5% in 2021) happened in the age group of more than 60 years with a mean age of 66 years. In a study conducted by Stokes et al in the United States, around 90% of the COVID-19 cases were in those aged more than 50 years.[8] A systematic review about Covid 19 deaths concluded that the estimated infection fatality (IFR)is close to zero for children and younger adults but rises exponentially

with age, reaching 0.4% at age 55, 1.3% at age 65, 4.5% at age 75, and 15% at age 85.[9] Another study reported similar fatality below 45, increasing to 3.1% for 65-74-year-olds and to 11.6% for anyone older above it.[10] In a study conducted in Pune, India, age more than 60 years was found to be an independent predictor of mortality associated with COVID-19.[11] Another study comparing transmission dynamics of COVID-19 in two states of India (Tamil Nadu and Kerala), concluded a higher age-specific case fatality ratio ranging from 0.05% (0.012 to 0.11%) at ages 5 to 17 years to 16.6% (13.4 to 19.9%) at ages ≥85 years. Higher mortality in older age groups and among males has similarly been observed in high-income settings.[12] Only less than 5% of COVID-19 deaths happened among patients less than 40 years were reported from a study from United states.[2] It has been explained by low levels of inflammation and ramped up immune system in them proportional to age.[13]

However, in a study conducted in a tertiary hospital New Delhi, it was found that the second wave affected more of younger people.[14] In our study, there is no difference in the age of the people who succumbed in the two corresponding years which may be attributed to flattening of the curve leading to large susceptible of older people during the second wave in the state.

Gender

Overall, COVID-19 caused increased mortality among males than females in all age groups, except below 20. As per the study from south India the risk overall of death was higher among male than among female , and the magnitude of this difference widened in the oldest age groups.[12] In another study from neighboring state also reported similarly with , 65% males and 35% females.[15] Another study from Tamil Nadu concluded that 78% (95% CI=75.4-80.8%) of the deceased without any comorbidities were male; which was similar in our study which gave the clue that male gender is an independent risk factor for COVID deaths.[16] There are many animal as well as human studies that have confirmed that angiotensin converting enzyme2 activity may be driven by estradiol.[17.] Compared to males the female immune system can detects the risks early and can react accordingly. These findings will explain the biological plausibility for the observed sex differences in COVID19 outcomes.[13]

Co-morbidities

Of the total deaths, majority (88.3%) had one or the other comorbidities. The major co-morbidities present were hypertension and Diabetes Mellitus each contributing 51.4% and 47.4% respectively. A study in USA reported that 95% of patients who died of COVID-19 had co-morbidities with diabetes mellitus and cerebrovascular accidents contributing to 30% and 32% respectively.[8] Another study in China documented that around 52% of COVID 19 deaths were associated with co-morbidities.[18] In UK up to 25% of people in are designated high risk with underlying health conditions such as respiratory and cardiovascular disease, and cancer along with all adults aged over 70.[19]

In our study majority of the people who died due to COVID-19 had multiple co-morbidities. CAD, CKD and CVA together contributed around 60% of the co-morbidities. When comparing co-morbidities within gender, it was found that females (90.2%) had co-morbidities at a higher frequency (NS) than males (87.2%). Similarly greater number of people had co-morbidities in 2021 as compared to 2020. Age wise of the total 206 patients aged less than 50 years who died, 163 (79.1%) and of the total 1526 patients aged more than 50 years, 1379 (90.4%) had any reported co-morbidities. In a study conducted In Tamil Nadu, India, around 85% reported having any one or more comorbidities; Diabetes (62%), hypertension (49.2%) and CAD (17.5%) were the commonly reported comorbidities.[15] Another study reported in Germany, hypertension was the most prevalent co morbidity (65.4%), followed by obesity (38.5%), chronic ischemic heart disease (34.6%), atrial fibrillation (26.9%), and chronic obstructive pulmonary disease (23.1%).[20] So along with age these co morbidities are to be considered important predictors of mortality. The reported hazard ratios (HR: 95% CI) of co morbidities in COVID mortality in a large cohort study was diabetes 1.95 (1.82-2.08), HT 1.09 (1.05-1.14), kidney disease 2.52 (2.33-2.72), liver disease 1.75 (1.51-2.03).[21]

Duration of hospitalization

The duration of stay or interval before death will indirectly reflect the seriousness of the condition when the patient is brought to the hospital either due delay in referral or seeking care. In our study the mean duration of hospitalization among the deceased was 6.5±6.3 days. A study in Tamil Nadu found out that the duration between admission and death was 4 days (IQR: 2, 7) which was less than our study.[15] In the United States, median time to death from the date of hospital admission was 13 days.[22] WHO estimated that time to death after onset of symptoms could range from 2 to 8 weeks on the basis of data from China.[23]Majority of the people succumbed to the illness in the first week of hospitalization and this proportion increased as the age advanced. Around 74% of people in the age group >50 died within 7 days of hospitalization compared to 66% among those aged less than 50 years. A meta-analysis reported that the mean time interval of symptom onset to death in those >65 years were less than those <64 years which were 12 days (IQR 7-9) and 15 days (IQR 9-24) respectively.[9]

Total 1136 patients died within 7 days of hospitalization. The death rate within 7 days of hospitalization was 776/1175 (66.1%) among males and 360/572 (62.9%) among females reflecting that the survival rate was less in males. Overall proportion of people surviving for more

than 7 days after admission has increased from 33.9% in 2020 to 37.1% in 2021. It may be attributed due to better medical care or due to early admission.

Cause of death

Since SARS Cov 2 is a respiratory virus it mainly affect lungs. Our death audit found that majority (97.4%) of deaths were directly attributed (Underlying cause) by COVID-19 infection. Very few were found to be indirectly attributed to COVID-19. COVID-19 is said to cause death by pneumonia/acute respiratory distress syndrome (ARDS)/cardiac injury/disseminated intravascular coagulation etc.[24]

Acute respiratory distress syndrome (ARDS) constituted 73.6% of the immediate cause of death followed by AKI (10.2%), A/c pulmonary edema (6.1%), sepsis/MODS (5.2%) and MI (4.9%). The antecedent causes were COVID pneumonia (91%) of followed by myocarditis (5.9%).

Study done in Tamil Nadu found that nearly 99% (95% CI: 97.9-99.5%) had died due to respiratory cause, among them, majority had bronchopneumonia (98.6%), acute respiratory distress syndrome (ARDS) and respiratory failure (68.9%). Cardiovascular cause accounts for about 12.3% (95% CI: 10.2-14.5%) with cardiorespiratory arrest (10.9%) being common.[16]

Similar to our study a study in Germany found out that ARDS, ACS, and Sepsis were the major cause of death in the hospitalized patients.[19] Data from the Houston fire department shows a 45% increase, in the number of cardiac arrest calls with patients deaths during this COVID-19 pandemic.[25] Hospital data from China revealed that 27.8% of admitted COVID-19 patients had myocardial injury.[26] Data from Italy suggests a significant positive association with spread of COVID-19 and an increase number of out of hospital cardiac arrest (OHCA).[27] Our study found that there is no difference between the cause of mortality between east or west, and SARS Cov2 virus mainly affecting the lungs.

Limitations

Our study was done in a tertiary care hospital so, selection bias is one of the limitations, which is inherent in this study as only patients with serious signs and symptoms come to tertiary level care hospital for treatment, hence, it lacks generalizability. Since our study was based on retrieved secondary data so many information may be under reported or missed. But due to COVID-19 restrictions most of the mortality studies are conducted based on secondary data. Strengths were due to its prospective nature, large sample size in a single centre with all patients were receiving same standard care there may not be any bias in outcome. we expect that our study could reflect the true epidemiological factors related to COVID deaths in this part of the country which can be considered for formulating future policies.

CONCLUSION

Our study provides evidence regarding the current trend of deaths due to COVID-19, demographic characteristics, their most common causes of death, time trends that had caused these deaths, and other factors. As reported elsewhere our study also found that the death tolls mainly in elderly above 60 age group and males. Majority died had multiple preexisting comorbidity like diabetes, hypertension and kidney disease. Though the infections were caused by different strains in two years there was not much difference in the epidemiological factors related to mortality like age, gender and severity. This information will help and guide the different management strategies, health system planning, and further research in the field of public health.

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