Original Research Article

Factors affecting death due to COVID-19: an analytical study from a tertiary care hospital of Assam

Bipanchi Mahanta[1], Deepjyoti Saikia[2], Rana Doley[3], Jawgam Umbon[2], Purnima Barua[3]*

[1]Department of Microbiology, Nagaon Medical College, Nagaon, Assam, India
[2]Department of Medicine, Jorhat Medical College, Jorhat, Assam, India
[3]Department of Microbiology, Jorhat Medical College Jorhat, Assam, India

*Correspondence:
Dr. Purnima Barua,
E-mail: drpurnimabarua@gmail.com

ABSTRACT

Background: Globally, the Case Fatality Rate (CFR) due CoVID19 ranges from 0.1-4.7%. CoVID-19 death remained 0.5% till April 2021 in Assam as compared to India (1.3%). Though pre-existing diseases greatly contributes to CFR yet its association study from India is scarce. This study documents association of such death with comorbidities in a tertiary hospital of Assam.
Methods: Retrospective analysis of 234 COVID death from May 2020 to December 2020 in Jorhat Medical College (JMCH) were done. Demography, comorbidities at admission and blood parameters were analyzed in Epi-Info version7.2.4.0. Continuous variables were presented as mean±SD or median (interquartile ranges) and correlated with death.
Results: Out of 3781 confirmed cases admitted in JMCH, 234 died (72% male) with CFR of 0.06. Highest deaths occurred between 61 to 70 years. Median duration of disease was 4 days (IQR 2-8days). Acute respiratory distress or pneumonia was most common (53.1%) symptom followed by septicemia (24.6%) at admission. Diabetes mellitus (36.6%), hypertension (24.8%), diabetes with hypertension (11.4%) and chronic kidney diseases (22.4%) were common chronic comorbidities. About 64% cases had thrombocytopenia, and 66.9% had leukocytosis at admission. Many cases had coronary artery diseases, left ventricular failure, post-operative complications, post-partum complications, severe hemoptysis, severe anemia, metabolic encephalopathy, acute myocardial infarction, non-ketotic coma and acute gastroenteritis and SARS-COV2 infection.
Conclusions: CoVID19 associated mortality in Assam was low and mostly among elderly with chronic comorbidities. CKD was most significantly associated with mortality. Superimposed bacterial infection at admission contributed to many fatal outcomes in COVID19, thus warranting proper empirical antibiotic.

Keywords: Assam, Comorbidity, CoVID-19, CKD, Diabetes, Hypertension

INTRODUCTION

The disease COVID-19, caused by a Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), continues to be a global threat to mankind. The major route of transmission is through aerosol from an infected individual. Though most of the cases remain asymptomatic or present with mild symptoms, yet around 5-10% cases become severe and require intensive care with mechanical ventilation or extracorporeal membrane oxygenation.[1, 2]

With continuous evolution of the novel virus, we comprehend a huge lacuna in our knowledge about the population that get infected critically. Studies carried out across the globe showed that COVID-19 patients with pre-existing comorbidities had higher risk of developing serious disease symptoms.[3] Elderly patients with chronic

comorbidities like hypertension, diabetes, other cardio vascular diseases, chronic kidney diseases and pulmonary diseases were seen to be more vulnerable to have more ICU admissions contributing to COVID-19 fatality rates.[4,5] Evaluation of clinical records and autopsy findings of patients who died from COVID-19 found that the most common cause of death was suppurative pulmonary infection in patients with multiple comorbidities such as obesity, heart diseases, and hypertension.[6] A study carried out across mainland China among 1590 hospitalized COVID-19 patients found that patients with comorbidities showed poor clinical outcome than those without any comorbidity.[7]

Globally, the Case Fatality Rate (CFR) due to SARS CoV2 infection ranges from 0.1-4.7% excluding countries like Peru and Mexico where CFR is higher than 9%.[8] In India, the CFR was reported as approximately 1.3%.[8] In Assam, CoVID-19 death was consistently low compared to other states of India with a CFR of 0.5 during the COVID pandemic surge.[9] However, detailed information from the developing countries, on the association of pre-existing diseases with case fatality, time taken to seek a healthcare facility and other clinical conditions contributing to a fatal outcome are scarce.

Therefore, this study was carried out to estimate the CFR due to COVID19 among cases admitted in a tertiary care center of Assam and to find out the correlation of duration of survival from onset of symptoms with presence of comorbidities in SARS CoV2 infection.

METHODS

This was a retrospective analysis of registered death cases among the COVID19 patients admitted in JMCH, which is a tertiary care hospital of Assam, catering to the health care services of Middle and most of the areas of Upper Assam along with neighboring states like Arunachal Pradesh and Nagaland.

A total of 234 cases of death were reported among a total of 3780 COVID19 cases admitted in the year 2020. The study cohort included 211 death cases following SARS CoV2 infection at Jorhat Medical College and Hospital. A total of 23 cases were excluded due to incomplete data extraction.

The first confirmed case of COVID19 was admitted to the hospital on 8th May, 2020. Data was extracted from all cases of death due to COVID19 from 8th May 2020 to 31st December 2020.

Case definition

Confirmed SARS-CoV-2 infection was defined as Real-time Reverse-transcriptase PCR (RTPCR) assay for detection of RdRp, N and ORF1ab genes or Rapid Antigen test for detection of Standard Q Antigen positive from nasopharyngeal swab samples. All reagents, kits,

consumables and equipment used for detection were provided by National Health Mission (NHM), Government of Assam. All the admitted patients were primarily diagnosed and treated for COVID-19 as per guidelines laid down by Indian Council of Medical Research (ICMR), Ministry of Health& Family Welfare, Government of India (MHFoW) and NHM, Government of Assam. Any associated comorbidities were diagnosed by relevant diagnostic tests.

COVID19 mortality data was extracted and reviewed. From the records, data on demographic information, association of comorbidities with death, duration of symptoms, condition at the time of admission, duration of hospitalization till death along with blood parameters were noted.

Ethical clearance was obtained from Institutional Ethics Committee (human) and permission to publish the data was obtained from competent authority.

Statistical analysis

Data were analyzed in Epi Info version 7.2.4.0. No formal sample size estimation was made as the study was a full representation of total study population. Continuous variables were presented as mean ± SD or median [interquartile ranges (IQR)] as appropriate and correlation analysis was done to find any association. The categorical variables were presented as frequencies and percentages.

RESULTS

During the pandemic of CoVID-19, a total of 3781 confirmed cases were admitted in JMCH till 30.12.2020. Out of them, 234 cases died in the hospital accounting to a CFR of 0.06. A total of 162 cases succumbed even after intensive care.

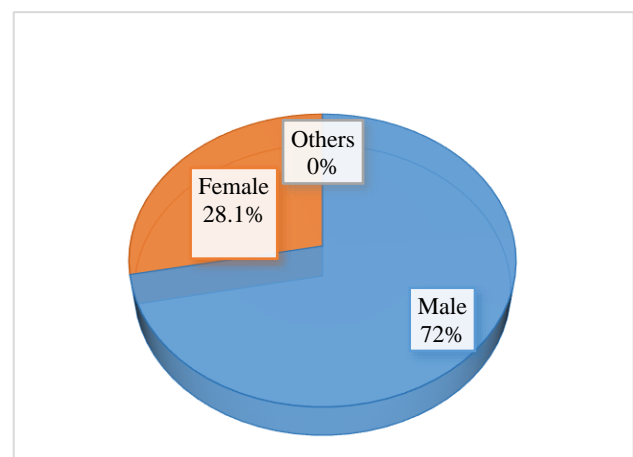Of the total deaths, 168 (72%) were male and 65 (28.1%) were female (Figure 1).

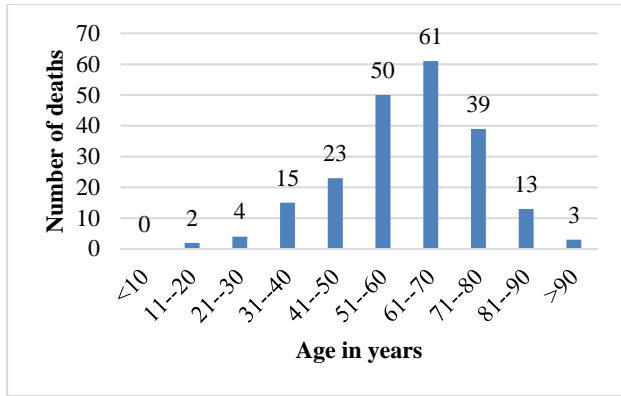**Figure 1: Gender wise distribution of deaths among the admitted cases.**
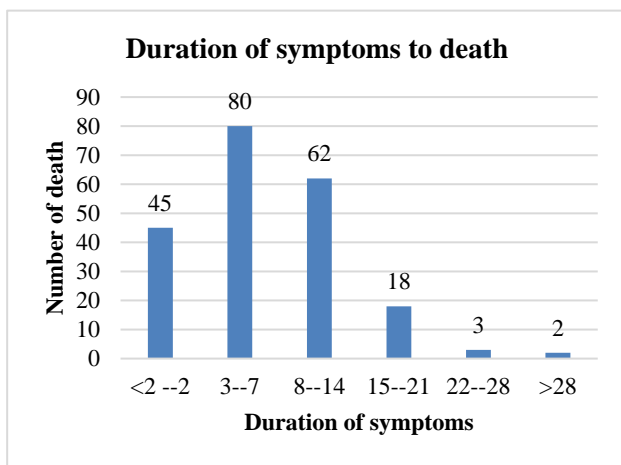
Figure 2: Age-wise number of death due to COVID-19.

Figure 3: Duration of onset of symptoms to death in COVID-19 cases.

Table 1: Distribution of cases presenting with different comorbidities.

Comorbidities	Number (%) with comorbidities
Diabetes mellitus (DM)	77 (36.6)
Hypertension (HTN)	52 (24.8)
Chronic kidney disease (CKD)	47 (22.4)
Electrolyte imbalance	26 (12.4)
Chronic liver disease (CLD)	20 (9.5)
Cardio vascular accident (CVA)	18 (8.6)
Severe anemia	7 (3.3)
Coronary Artery disease (CAD)	5 (2.4)
Myocardial infarction (MI)	3 (1.4)
Left ventricular failure (LVF)	3 (1.4)
DM+HTN	24 (11.4)
DM+CKD	10 (4.8)
DM+HTN+CKD	16 (7.6)
DM+HTN+CVA+CKD	2 (0.9)
DM+HTN+CVA	4 (1.9)
HTN+CVA	2 (0.9)
DM+HTN+CVA	2 (0.9)

Table 2: Correlation between duration of survival from onset of symptoms and presence of co-morbidity.

Co-morbidity	Pearson correlation	p-value
Diabetes mellitus	-0.034	0.621
Hypertension	-0.116	0.094
Chronic liver disease	-0.026	0.699
Chronic kidney disease	-0.171	**0.013**
Cardiac disease	-0.048	0.491

Table 3: TLC and platelet counts of cases of COVID-19 at admission.

Platelet counts (per mm³)	Number of cases (n=133)	TLC (per mm³)	Number of cases (n=148)
<20000	16	<1000	1
20000-50000	3	1000-5000	20
50000-100000	16	5000-10000	30
100000-150000	50	10000-15000	50
150000-200000	18	15000-20000	18
200000-250000	15	20000-30000	30
250000-300000	4	30000-50000	5
300000-500000	8	>50000	4
>500000	3	-	-

Highest number of COVID related deaths were recorded between the age group of 61 to 70 years. However, no fatality was recorded among the pediatric age group (Figure 2).

Highest no. of deaths occurred within 3-7 days of onset of symptom. (Figure 3). Median duration from onset of symptoms to death was 4 days (IQR 2-8days).

Acute comorbid conditions at the time of admission included lung involvement presenting with acute respiratory distress or pneumonia (n=112, 53.1%), septicemia (n=52, 24.6%), severe electrolyte imbalance (6.1%, n=13) and even cerebrovascular accident (5.6%, n=12).

Among the chronic pre-existing comorbidities at admission, Diabetes mellitus (DM) (36.6%, n=77) was frequent, followed by hypertension (HTN) (24.8%, n=52) and chronic kidney diseases (22.4%, n=47). Diabetes mellitus and hypertension were found to be co-existing in few cases (11.4%, n=24). Moreover, many patients came with multi-organ involvement (Table 1).

Out of the co-morbidities, presence of chronic kidney disease was significantly associated with reduced survival in CoVID-19 cases (p=0.013) (Table 2).

Other underlying conditions contributing to death were, coronary artery diseases (n=5), left ventricular failure (n=3), post hemi-colectomy complications, post-partum pulmonary edema, pulmonary tuberculosis, severe

anemia (n=7), metabolic encephalopathy (n=24), acute myocardial infarction (n=9), non-ketotic coma (n=2) and one with acute gastroenteritis.

On examining the blood parameters, Total Leucocyte counts (TLC) and platelet counts were available from 148 and 133 cases respectively. Most of the patients (63.9%, n=85) presented with thrombocytopenia, and 66.9% (n=89) had leukocytosis (Table 3).

DISCUSSION

Out of 211 cases, median age of COVID19 related deaths was 62.5 years (IQR 52-73 years), which is similar to studies reported from elsewhere.[7,10,11] Most countries with available data indicate a male to female case fatality ratio higher than 1·0, ranging up to 3·5 in some cases.[12] Our studies revealed data similar to global findings with male predominance among the death cases. However, in other parts of India, the COVID-19 case fatality rate among men was 2·9% and 3·3% among women.[13] Such differential findings might reflect incomplete COVID-19 data across different geographies, biases in case identification by sex or higher risks for a particular sex in certain regions due to demographic factors or lifestyle related behaviors.

Research presented at ESCMID Conference on Coronavirus Disease (ECCVID, held online) [14] shows that a shorter time from symptom onset to hospitalization is associated with more serious disease and death in patients with COVID-19 disease. This was similar to our findings that the median duration of days from onset of symptoms to death was 4 days (IQR 2-8days). Lung involvement with acute respiratory distress syndrome and septicemia were the predominant symptoms among the cases of death. Studies documenting post mortem finding also recorded suppurative pulmonary infections in 19.2%, including purulent pneumonia with or without abscess formation. Excess cytokine release might be contributed by bacterial infection.[7,15] This finding suggests that bacterial infection superimposed on SARS-CoV-2 infection might have contributed to death in majority of cases. Respiratory failure superimposed with septicemia has also been recorded in autopsy studies elsewhere.[6]

Studies in mainland China analyzing 1590 cases in hospital recorded that patients with hypertension, diabetes, obstructive pulmonary diseases or malignancy have poorer outcome from CoVID-19 compared to those without any comorbidity.[16] In the present series majority of the cases had diabetes mellitus followed by hypertension and chronic kidney diseases. A significant association (p=0.013) of CKD with death was noted in the present study. However, studies from Germany recorded much higher prevalence of hypertension among fatal cases of CoVID-19 infection but Type II Diabetes and CKD were low in their series.[6] People with diabetes are at higher risk of COVID-19-related mortality than people without diabetes. Studies across the globe also showed association of chronic life style related diseases with higher mortality from CoVID-19.[6,7] In a nationwide study from England showed that type 1 and type 2 DM were independently associated with a significant increase of death from COVID-19.[17] One study from India also observed non-significant association of case fatality with diabetes and hypertension[4]. Such lifestyle related comorbidities points to not only life style related non communicable diseases (NCDs), but also for the increase in susceptibility to infectious diseases involving vital organs like lung, heart etc. and calls for public health interventions for minimizing both NCD as well as infectious diseases.[6,18,19]

Present study suggested thrombocytopenia in most (63.7%) fatal cases. It has been observed that severe COVID-19 presents with abnormal platelet parameters, including decreased platelet counts.[20] Large-scale studies have revealed that 18.8% to 36.2% of patients present with thrombocytopenia on admission.[15,21]

Leukocytosis at admission was seen in majority (66.9%) of the cases having fatal outcome in the present analysis. Several studies observed that elevation of inflammatory markers is associated with severe disease including meta-analysis showing the association between severe COVID-19 and elevated markers of inflammation like fever and leukocytosis that concluded leukocytosis and elevated CRP on arrival as predictors of poorer outcome.[22]

CONCLUSION

Mortality following SARS CoV2 infection in our region was lower compared to the other parts of the country. The elderly age group with chronic comorbidities was found to be more prone to severe SARS CoV2 infection and mortality due to COVID19. Chronic kidney disease was significantly associated with death following SARS CoV2 infection. Acute involvement of lung with superimposed bacterial infection at admission, contributed hugely to a fatal outcome of COVID19 cases, thus warranting inclusion of proper empirical antibiotic therapy in COVID19 case management.

REFERENCES

1. Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, et al. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy Region, Italy. Jama. 2020;323(16):1574-81.
2. Bartlett RH, Ogino MT, Brodie D, McMullan DM, Lorusso R, MacLaren G, et al. Initial ELSO guidance document: ECMO for COVID-19 patients with severe cardiopulmonary failure. Asaio Journal. 2020;66(5):472.
3. Sanyaolu A, Okorie C, Marinkovic A, Patidar R, Younis K, Desai P, Hosein Z, Padda I, Mangat J, Altaf M. Comorbidity and its impact on patients with COVID-19. SN Comprehensive Clinical Medicine. 2020;2:1069-76.
4. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA. 2020 Apr 7;323(13):1239-42.
5. Mehra MR, Desai SS, Kuy S, Henry TD, Patel AN. Cardiovascular disease, drug therapy, and mortality in Covid-19. New England Journal of Medicine. 2020;382(25):e102.
6. Elezkurtaj S, Greuel S, Ihlow J, Michaelis EG, Bischoff P, Kunze CA, et al. Causes of death and comorbidities in hospitalized patients with COVID-19. Scientific Reports. 2021;11(1):1-9.
7. Guan WJ, Liang WH, Zhao Y, Liang HR, Chen ZS, Li YM, et al. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. European Respiratory Journal. 20201;55(5).
8. Johns Hopkins University of Medicine. New cases of COVID-19 in world countries. Available at: https://ccp.jhu.edu/kap-covid. Accessed on 16 July 2021.
9. Upadhyay AK, Shukla S. Correlation study to identify the factors affecting COVID-19 case fatality rates in India. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2021;15(3):993-9.
10. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. The lancet. 2020;395(10229):1054-62.
11. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China. JAMA. 2020;323(11):1061-9.
12. The Sex, Gender, and COVID-19 Project. The COVID-10 sex-disaggregated data tracker. Available at: https://globalhealth5050.org/covid19/. Accessed on 18 Sept 2020.
13. Joe W, Kumar A, Rajpal S, Mishra US, Subramanian SV. Equal risk, unequal burden? Gender differentials in COVID-19 mortality in India. J Glob Health Sci. 2020;14(2):1.
14. Dr Annie Wong-Beringer and colleagues, University of Southern California (USC) School of Pharmacy, Los Angeles, CA, USA. Shorter time from symptom onset to hospitalization is associated with worse outcome in patients with COVID-19. European Society of Clinical Microbiology and Infectious diseases, News release 25-Sep-2020. Available at: https://medicalxpress.com/news/2020-09-shorter-symptom-onset-hospitalization-worse.html. Accessed on 2 March 2023.
15. Zafer MM, El-Mahallawy HA, Ashour HM. Severe COVID-19 and sepsis: immune pathogenesis and laboratory markers. Microorganisms. 2021;9(1):159.
16. Wu C, Chen X, Cai Y, Zhou X, Xu S, Huang H, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA internal medicine. 2020;180(7):934-43.
17. Barron E, Bakhai C, Kar P, Weaver A, Bradley D, Ismail H, Knighton P, Holman N, Khunti K, Sattar N, Wareham NJ. Associations of type 1 and type 2 diabetes with COVID-19-related mortality in England: a whole-population study. The lancet Diabetes & endocrinology. 2020;8(10):813-22.
18. Petrilli CM, Jones SA, Yang J, Rajagopalan H, O'Donnell L, Chernyak Y, Tobin KA, Cerfolio RJ, Francois F, Horwitz LI. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. BMJ. 2020;369.
19. Covid C, Team R, Chow N, Fleming-Dutra K, Gierke R, Hall A, et al. Preliminary estimates of the prevalence of selected underlying health conditions among patients with coronavirus disease 2019-United States, February 12–March 28, 2020. Morbidity and Mortality Weekly Report. 2020;69(13):382.
20. Zhang S, Liu Y, Wang X, Yang L, Li H, Wang Y, et al. SARS-CoV-2 binds platelet ACE2 to enhance thrombosis in COVID-19. Journal of Hematology Oncology. 2020;13(1):1-22.
21. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. New England Journal of Medicine. 2020;382(18):1708-20.
22. Yamada T, Wakabayashi M, Yamaji T, Chopra N, Mikami T, Miyashita H, et al. Value of leukocytosis and elevated C-reactive protein in predicting severe coronavirus 2019 (COVID-19): A systematic review and meta-analysis. Clinica Chimica Acta. 2020;509:235-43.