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Descriptive analysis of COVID-19 death at Patan Academy of Health Sciences

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Abstract

Introduction: The Coronavirus Disease 2019 (COVID-19) pandemic has led to infection and deaths worldwide. The clinical and laboratory findings at presentation to emergency can provide clue for deaths. This study aims to analyze COVID-19 deaths, and clinical-laboratory findings at presentation.

Method: This is a retrospective cross-sectional study conducted at Patan Hospital, Patan Academy of Health Science, Lalitpur, Nepal to analyze mortality due to COVID-19 during the year 2020. The study describes the clinical presentation, laboratory parameters at the time of presentation to the emergency department and clinical course during hospital stay.

Result: Among 133 COVID-19 deaths analyzed, the median age was 61y (2d to 91y), males 73(54.9%), hypertension in 34(25.6%), 104(78.1%) had shortness of breath, 70(52.6%) fever and 34(25.6%) had cough on presentation. Median oxygen saturation on arrival was 77%, all 133(100%) required oxygen. Oxygen requirement at admission, ferritin (median 603 mcg/L), C- Reactive protein (median CRP 89.5 mg/) and lactate dehydrogenase (median LDH, 432 u/L) were not significantly correlated with duration of disease or hospital/ICU stay. Median duration of disease was 10d, hospital stay 8d and ICU stay 3d. COVID-19 deaths occurred due to respiratory failure in 105(78.9%).

Conclusion: COVID-19 deaths were due to respiratory failure in 2/3rd (78.9% of 133), more in middle age (>46y) males with comorbidities, commonly hypertension. Abnormal vital signs, elevated CRP, ferritin, LDH, were seen in COVID-19 deaths. Oxygen requirement at admission was not correlated with duration of disease, or hospital/ICU stay.

Keywords: COVID-19, death, mortality, Nepal

Introduction

The emergence of Coronavirus Disease 2019 (COVID-19) has led to many deaths associated with the infection worldwide, with a case fatality rate of 1-7%.[1] Predictor of high mortality in patients with COVID-19 is increasing age, concurrent cardiovascular, cerebrovascular disease, diabetes, chronic kidney diseases, and autoimmune diseases.[2,3]

The first reported death due to the coronavirus in Nepal was on May 14, 2020[4] and by February 2021 the total death toll is 2054 across the country.[5] There is limited published information on COVID-19 related deaths in Nepal. With the aim of analyzing COVID-19 deaths, this study is designed to evaluate the clinical and laboratory findings of those patients at presentation to the emergency department.

Method

This is a cross-sectional study conducted at Patan Hospital, Patan Academy of Health Science (PAHS), Lalitpur, Nepal in April 2021. This study includes a retrospective chart review of COVID-19 death from January to December 2020. Objectives of this study were to find the average age of the patient who died of COVID-19, the proportion of male and female and analysis of past illness and comorbidity (Diabetes, Hypertension, Chronic liver disease, Chronic neurological condition, pregnancy, post-partum less than 6 weeks, immunodeficiency, chronic renal disease, chronic lung disease, malignancy).[5] This study also analyzed symptoms at presentation to emergency (fever, cough, sore throat, running nose, shortness of breath, diarrhea, nausea/vomiting, headache, confusion, myalgia)[5], initial lab investigation at presentation to emergency (Total count, Differential count, Platelet, Ferritin, CRP) and average duration of stay, duration of symptom onset to death and duration from intubation to death and its relation.

Ethical approval for the study was taken from IRC-PAHS. Following the ethical approval, COVID-19 death reported from PAHS who had mortality while inside COVID-19 ward or Intensive Care Unit (ICU) during treatment for COVID-19 and has been issued death certificate indicating COVID-19 as the primary or secondary cause of death was included in this study. Records with incomplete data were excluded from the study. Continuous nominal variables like age gender, clinical parameter, lab investigation, and durations were analyzed as average values. Spearman correlation coefficient was calculated to find the correlation coefficient of clinical presentation, comorbid condition, and oxygen requirement at admission with the duration of disease, duration of hospital stays, and duration of ICU stay.

Result

We analyzed 133(85.4%) COVID-19 deaths in this study (after the exclusion of 24 cases due to incomplete information from among the total 157 deaths reported during 2020 from Patan Hospital, PAHS). The median age was 61 years (IQR1:46- IQR3:72 years). The minimum age of the patient was 2 d of life and the maximum was 91 years. Patients were categorized into those having and not having comorbid conditions. There were 79(59.3%) cases who comorbid conditions and the median age of this group was 68 years (IQR1: 51.75, IQR3:74.5). The median age of patients without comorbidities was 51 years (IQR1:51, IQR3:65). There were 73(54.9%) males and 60(45.1%) females, the median age of males was 60 years and that of females was 62 years. There were 49(62%) males and 30(38%) females who had comorbidity.

There were 104(78.1%) patients who presented to COVID-19 emergency with shortness of breath, 70(52.6%) with fever, and 34(25.6%) with cough.

One hundred and twenty-seven (95.4%) patients had at least one past illness. Out of the five most common past illnesses or

comorbidities, hypertension was the most common 34(25.6%), Table 1. Eleven (8.2%) patients were on angiotensin-converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB).

Table 1. Proportions of the comorbid condition of patients who were registered as COVID-19 death (N=133)

Comorbid condition	Yes	No
Hypertension	34(25.6%)	99(74.4%)
Diabetes	27(20.3%)	106(79.7%)
Chronic respiratory problem	26(19.5%)	107(80.5%)
CKD under dialysis	19(14.2%)	114(85.8%)
Malignancy	15(11.2%)	118(88.8%)

Table 2. The median value of clinical and laboratory variables in COVID-19 mortality patients (N=133)

Clinical and lab variables	N	IQR1	IDR2 (Median)	IQR3
Oxygen saturation on presentation (%)	133	68	77	86.5
Oxygen saturation on admission (%)	133	92	94	94
Pulse on admission (beats/min)	131	90.5	102.0	114.0
Systolic Blood pressure on admission(mmHg)	109	110	130	140
Diastolic blood pressure on admission(mmHg)	109	69	80	84.2
Temperature on admission (^{o}F)	133	97	98	99
Ferritin on admission (mcg/L)	89	375	603	1560
Highest recorded ferritin during stay(mcg/L)	62	544.5	1079.0	1632.5
CRP on admission (mg/L)	101	41.9	89.5	263.0
Highest recorded CRP during stay (mg/L)	34	54	142	365
LDH on admission (u/L)	45	299	432	807
Highest recorded LDH during admission (u/L)	21	355	867	1109
Total count on admission (cells/mm^{3})	130	6200	9150	14500
Highest total count recorded during stay (cells/mm^{3})	89	10500	14800	20800
Platelet on admission	130	140000	185000	248000
Highest platelet recorded during stay (cells/ mm^{3})	89	157500	224000	321000
Duration of disease(d)	121	5	10	13.5
Duration of hospital stay(d)	133	2	8	13.25
Duration of ICU stay(d)	133	1	3	9

Six(4.5%) patients had a history of hyperthyroidism, 3(2.3%) had a history of chronic liver disease, 2(1.5%) had a history of coronary artery disease and 3(2.3%) had a history of stroke. Two(1.5%) patients each had granulomatosis polyangiitis, rapidly

progressing glomerulonephritis (RPGN) and 1(0.75%) had systemic lupus erythematosus (SLE). This patient with SLE was under dialysis.

Median oxygen saturation at presentation to the emergency was 77%. All 133(100%) required oxygen, 79(59.4%) patient had oxygen requirement of <5 L/min , 11(8.3%) had oxygen requirement of 5-10 L/min, 43(32.3%) >10 L/min and 2(1.5%) were intubated.

Median ferritin on admission was 603 mcg/L, C- Reactive protein (CRP) was 89.5 mg/L and Lactate dehydrogenase (LDH) was 432 units/L, Table 2. Spearman correlation coefficient of clinical presentation, comorbid condition, and oxygen requirement at admission with the duration of symptom, duration of hospital stay, and duration of ICU stay was not statistically significant (p>0.05), Table 2.

Table 3. The median duration of disease, hospital stay, and ICU stay patient registered as COVID-19 death (N=133)

		Duration of disease, median d	Duration of hospital stay, median d	Duration of ICU stay, median d
Gender	Male	10.5	9.0	3.0
	Female	9.0	7.0	4.0
Shortness of breath	Yes	10.0	7.5	3.0
	No	10.0	10.5	3.5
Fever on admission	Yes	9.0	7.0	4.0
	No	10.0	9.0	3.0
Cough on admission	Yes	10.0	8.0	3.0
	No	10.0	8.0	3.0
Hypretension	Yes	9.0	10.0	7.0
	No	10.0	6.5	3.0
Diabetes	Yes	8.0	8.0	7.0$^{\sim}$
	No	11.0	7.0	3.0
Chronic respiratory condition	Yes	10.0	4.0	2.0
	No	9.5	8.0$^{\wedge}$	3.0
Chronic kidney disease under dialysis	Yes	8.5	13.0	2.0
	No	10.0	7.0	4.0
Malignancy	Yes	14.0	10.0	3.5
	No	10.0	7.0	3.0
Patient on ACEi or ARB	Yes	29.5	14	3.0
	No	9.5*	7.5	3.0
Oxygen requirement on admission	Intubated	6.0	11.0	11.0
	≤5 L/min	11.5	9.0	3.0
	>5-10 L/min	10.0	10.0	5.0
	>10 L/min	9.0	5.0	4.0

~p=0.024, ^p=0.019, *p=0.004

The mean duration of hospital stay before death was 7d in diabetic patients and 3d in non-diabetics, this finding was statistically significant (p=0.024). Duration of hospital stay before death was 4d for the patient with chronic respiratory condition and 8d for those who did not have chronic respiratory condition, this difference was statistically significant (p=0.019).
The average duration of symptoms at the time of presentation was 29.5 d in patients taking ACEi or ARB and 9.5 d in those who did not take

the medicine, the difference was statistically significant (p=0.004), Table 3.

Out of all 133 COVID-19 deaths, 105(78.9%) were due to respiratory failure secondary to acute respiratory distress syndrome (ARDS), Figure 1. Amongst those who died of ARDS, 2(1.5%) had undergone surgery; 1(0.75%) patient had a cholecystectomy and another 1(0.75%) patient had an abdominal hysterectomy with bilateral salpingo-oophorectomy for ovarian cancer.

Out of 11(8.2%) patients who had septic shock, 2(1.5%) patients were postoperative patients, Table 4.

Out of 5(3.8%) meningoencephalitis, 2(1.5%) had acute meningitis and 3(2.3%) had encephalitis. Out of three encephalitis, 1(0.75%) had Rabies. Out of 4(3%) cardiogenic shock, 2(1.5%) had acute ST-elevation myocardial infarction, one infraction also had diabetic ketoacidosis. Out of the rest two cardiogenic shocks, one had decompensated

liver disease and the other had obstructive jaundice.

In 4(3%) patient aspiration pneumonia was documented out of which two had alcohol withdrawal syndrome, one of whom was in delirium tremens; one had non-convulsive status epilepticus, and one was a case of organophosphorus poisoning. Out of 3(2.3%) pulmonary edema, 2(1.5%) were due to chronic kidney disease and 1(0.75%) had acute kidney injury.

Table 4. Diagnosis of the patient with septic shock who were registered as COVID-19 death (N=11)

S.N.	
1	The first postoperative day following Primary repair of perforation for Multiple enteric perforations with peritonitis with Sepsis and in Septic shock with Pneumonia
2	Left-sided Ischaemic CVA with Haemorrhagic Transformation with HTN with Post COVID Pneumonia
3	Second Day of Life, Silo Repair for Gastroschisis with Tension Pneumothorax with Sepsis
4	Seizure Disorder with Hospital-Acquired Pneumonia
5	Alcohol dependent syndrome with bilateral pneumonia
6	Right Hand Cellulitis
7	HTN with Type II diabetes with Severe B/L Pneumonia
8	Primigravida at 23 weeks of gestation with bilateral Pneumonia
9	Granulomatosis Polyangiitis
10	Multiorgan dysfunction syndrome
11	Exploratory laparotomy with Lt Salpingoophorectomy with Repair of Bowel Injury for Ruptured Lt Sided Chocolate cyst with Pyoperitoneum with multiorgan dysfunction syndrome
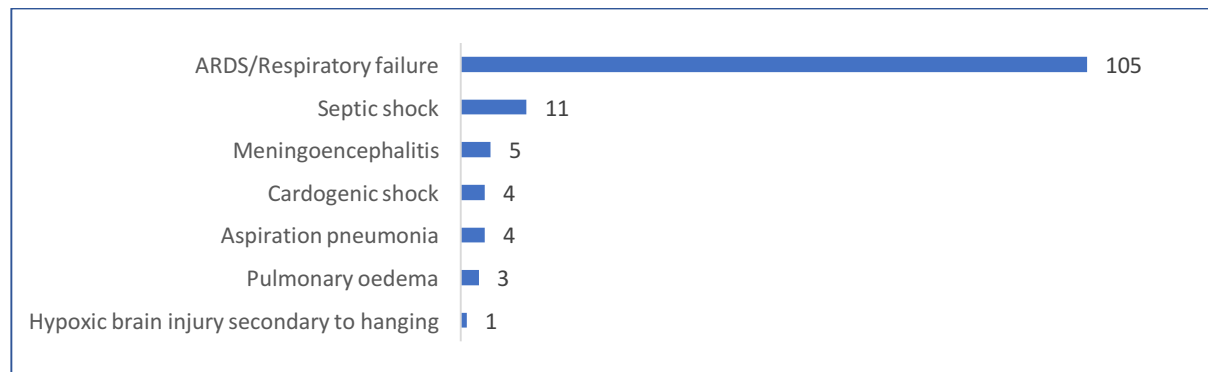
Figure 1. Cause of death inpatient registered as COVID-19 death (N=133)

Discussion

The median age of patients with COVID-19 death was 61 years and the first quartile was 46 years which means that the maximum COVID-19 death was above 46 years of age. Most of the COVID-19 deaths were male 73(54.9%) in our study. In another study where analysis of 178,568 COVID-19 death was done, older age and male sex were associated with

an increase in COVID-19 mortality. In the same study, mortality was 8.1 times higher among the age group of 55 to 64 years and 62 times higher in 65 years and older in comparison to those of less than 55 years.[6] Similarly, COVID-19 mortality in men aged 40–59 years was almost 2.5 times more than women of the same age.[7]

There were 79(59.3%) cases that had comorbidity and the median age of this group was 68 years. Likewise, the median age of the group without comorbidity was 51 years. Therefore, comorbidity and not age might be an important factor determining the rate of mortality in COVID-19. Had it been age only, the median age of the group of the population without comorbidity should have been in the elderly population but contrary to it the median age is below 65 years. The mortality of COVID-19 has a gender predominance as seen in our study also where it was predominantly seen in males and the median age of males was 60 years. However, this may not be due to increase virulence of disease towards male but due to various socio-cultural and their travel factors. It can also be due to comorbidities which were seen more (62%) in males.

Out of the top five comorbidities observed in this study, hypertension was the most common 34(25.6%), followed by diabetes, chronic respiratory problem, chronic kidney disease under dialysis, and malignancy 9(11%). In one of the studies, patients with hypertension (aOR, 3.576; 95% CI, 1.694–7.548) and diabetes mellitus (aOR, 12.234; 95% CI, 4.126–36.272) were two common comorbid conditions observed in COVID-19 patients.[8] Similarly a systemic review and meta-analysis showed that in the patients with severe/fatal COVID-19, the most prevalent chronic comorbidities were obesity (42%, 95% CI 34–49%) and hypertension (40%, 95% CI 35–45%), followed by diabetes (17%, 95% CI 15–20%), cardiovascular disease (13%, 95% CI 11–15%), respiratory disease (8%, 95% CI 6–10%), cerebrovascular disease (6%, 95% CI 4–8%), malignancy (4%, 95% CI 3–6%), kidney disease (3%, 95% CI 2–4%), and liver disease (2%, 95% CI 1–3%).[9] Hypertension is considered to be an important risk factor for COVID-19 mortality in various studies[10-13], and although the virus makes its access through angiotensin-converting enzyme 2 receptor[14], it is not clear whether hypertension is an independent risk factor for COVID-19 mortality or not.[15] Hypertension is one of the non-communicable diseases with high prevalence, its prevalence in Nepal is 23.0% (95% CI, 22.3%-23.7%)[16],

therefore hypertension may be observed as an important risk factor in COVID-19 mortality only due to its high prevalence. Out of these hypertensive patients, very few were in ACEi or ARB in our study, though there is no evidence to conclude the benefit or harm of angiotensin-converting enzyme inhibitor or angiotensin receptor blocker in COVID-19.[17] In our study duration of symptom at the time of presentation was longer (29.5 vs. 9.5 d) inpatient taking AECi or ARB compared to those who were not under those medicines.

Our study found no correlation of clinical presentation, comorbid condition, and oxygen requirement at admission with the duration of disease, duration of hospital stays, and duration of ICU stay. Though our study was not sufficiently powered to test the above-mentioned correlation, this leads to an important hypothesis that the death might be multi-factorial and may not be related to a single factor. The vulnerability of individuals, time to seek medical care are important factors that play role in such circumstances. Ferritin, CRP, LDH was higher in our study group upon their presentation to COVID-19 emergency, suggesting it to be an indicator of mortality. An analysis of 243 COVID-19 adult patients showed increased CRP, increased fibrinogen, and decreased FVIII/VWF:Ag ratio at admission was significantly associated with the risk of increased oxygen requirement during follow-up.[18]

In our study population, most of the patients 79(59.4%) had an oxygen requirement of <5 L/min, mortality of these patients suggests rapid progression of the disease process. We did not do multivariate regression analysis, however, there are several other studies where the following has been identified as risk factors for mortality; age, low oxygen saturation at admission, increase body temperature, differences in white blood cell counts, absolute values of lymphocytes, platelets, albumin, total bilirubin, blood urea nitrogen, blood creatinine, myoglobin, cardiac troponin, C-reactive protein (CRP) and interleukin-6 (IL-6).[19-21]

The ARDS was the commonest cause of death in our study, accounting for 87(65.4%) of total COVID-19 deaths in the hospital. In one of the studies, among hospitalized COVID-19 patients, approximately 33% developed ARDS, the mortality rate in COVID-19-associated ARDS was 45%, and the incidence of ARDS among non-survivors of COVID-19 was 90%.[22] Second common cause of death in our study was septic shock, 11(13.4%), it has been known that COVID-19 patients who are admitted to ICU showed a dysregulation host response characterized by hyper inflammation, alteration in coagulation, and dysregulation in the immune response that further contribute to multi-organ dysfunction syndrome (MODS), as in sepsis.[23,24] Sepsis and septic shock in our study were not primarily due to COVID-19 but it was due to complication of other medical and surgical conditions. So, the mortality in these eleven cases was not due to COVID-19 but with COVID-19.

This observational study generates an important hypothesis that it might be a comorbid condition that predicts mortality rather than age. Regarding comorbidity, it is necessary to evaluate it explicitly to determine whether it is a risk factor for death or is associated with death. The requirement of oxygen at admission and lab parameters can still be a strong predictor of severity and mortality but this is beyond the scope of this study.

Conclusion

Most of the COVID-19 deaths were in the age group more than 46 years and hypertension was the most common factor associated with mortality. Abnormal vital signs, elevated CRP, ferritin, LDH, were seen in these patients however there was no correlation between these parameters and duration of disease, duration of hospital stay, and duration of ICU stay.

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Author Contribution
Concept, design, planning- AS, SB, RS, AC; Literature review- AS, SB; Data collection/analysis: AS, SB, RS, AC; Draft manuscript: AS, SB, RS, AC; Revision of draft: AS, SB, RS, AC; Final manuscript: AS, SB, RS, AC; Accountability of the work: AS, SB, RS, AC.

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