Comparative Analyses of Clinical, Laboratory, and Radiological Findings between COVID-19 Deceased and Recovered Patients

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ABSTRACT

Background

Understanding the coronavirus disease 2019 (COVID-19)-specific indices has become important with increasing cases of COVID-related in-hospital mortality.

Objective

This case-control study compared clinical, laboratory, and radiological findings between deceased and recovered COVID-19 patients and identified the significant biomarkers associated with deceased patients.

Method

An analysis of clinical, laboratory, and radiological findings of COVID-19 patients admitted to the COVID-dedicated wards of Nepal Armed Police Force Hospital between March and December 2021 was performed using SPSS version 17.0, with statistical significance considered at $p < 0.05$.

Result

A total of 187 COVID-19 patients, comprising deceased [n=95, median (interquartile range, IQR) age: 66 (53–76) years, male: 61 (64.2%) (p=0.024)] and recovered [n=92, median (IQR) age: 51 (38–61) years, male: 44 (47.8%)], were included in the study. Compared to recovered COVID-19 patients, deceased patients had increased median respiratory (20 versus 29.5 breaths/minute) and pulse (83 vs. 86 beats/minute) rates; multiple co-morbidities (≥ 2) (11.9% vs. 32.6%) ($p < 0.001$); significantly ($p < 0.05$) lowered alkaline phosphatase (ALP), total protein (TP), albumin, lymphocytes, monocytes, eosinophil, hemoglobin and significantly ($p < 0.05$) elevated glucose, lactate dehydrogenase (LDH), alanine transaminase (ALT), aspartate aminotransferase (AST), leucocytes, neutrophils, D-dimer and C-reactive protein (CRP); and chest abnormalities including bilateral ($p < 0.001$), peripheral ($p < 0.001$) interstitial ($p < 0.001$) and ground glass opacity (GGO) (p=0.002).

Conclusion

Elderly, male sex, increased respiratory and pulse rate, presence of multiple co-morbidities, lowered levels of ALP, TP, albumin, lymphocytes, monocytes, eosinophils, hemoglobin, elevated levels of glucose, LDH, ALT, AST, leucocytes, neutrophils, D-dimer, CRP, and chest X-rays showing bilateral, peripheral interstitial and GGO abnormalities were the significant indices associated with deceased COVID-19 patients.

KEY WORDS

Biomarkers, Comorbidity, COVID-19, Laboratory, Radiology, Signs symptoms, Vitals

INTRODUCTION

In Nepal, the first case of coronavirus disease 2019 (COVID-19) was reported on January 13, 2020.[1] As of December 8, 2021, there are over 0.8 million confirmed cases of COVID-19, with over eleven thousand deaths in Nepal.[2]

With heterogeneous clinical presentations, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) mainly infects the lower respiratory tract and results in atopic pneumonia, with clinical manifestations ranging from asymptomatic or mild flu-like symptoms to severe disease that often requires intensive care.[3] Symptoms may even be multiple because of rapid disease progression involving multiple organs and systems, namely the cardiovascular system, the pulmonary system, and other systemic components, which cause complications such as acute respiratory distress syndrome, coagulation abnormalities, and kidney failure, ultimately causing death.[4] In-hospital mortality and clinical worsening can be associated with pathological immune responses induced by defective type I/III interferon responses.[3] Additionally, patients with chronic, non-communicable diseases such as diabetes, hypertension, obesity, asthma, malignancies, and others could also be predisposed to such an aftermath.[4]

The rate of COVID-associated mortality has increased in low- and middle-income countries like Nepal during the infection surge. A shortage of medical supplies, limited healthcare facilities to treat patients in a timely manner, and a lack of a method for categorizing patients for their likelihood of developing severe disease could explain this.[5] The clinical characteristics of the deceased COVID-19 patients in relation to the Nepalese population are still limited, posing a dilemma for clinicians. Hence, the goal of this study was to identify clinical, laboratory, and radiological biomarkers associated with deceased COVID-19 patients.

METHODS

A case-control study was conducted among COVID-19 deceased and recovered patients, who were admitted to the COVID-dedicated wards of Nepal Armed Police Force Hospital (NAPFH), Balambu, Kathmandu, Nepal, between March 2021 and December 2021. The Ethical Review Board, Ramshah path, Kathmandu, Nepal approved this study (Reference. Number: 310).

Data from the COVID-19-positive patients, confirmed by real-time reverse transcriptase-polymerase chain reaction (rtRT-PCR) were included in the study. Hospital-visiting patients without COVID-19 diagnoses and COVID-19 patients admitted before March 1, 2021, and after December 30, 2021, were excluded from the study.

Socio-demographic, clinical, laboratory and radiological data of both deceased and recovered patients were obtained from the electronic medical databases of the hospital. Any missing or uncertain records were collated and clarified through communication with involved healthcare providers or patients and their families.

Different clinical characteristics such as vitals, signs and symptoms, co-morbidities, and clinical outcomes were examined among the patients with COVID-19. We defined disease severity according to WHO guidelines.[6] Mild cases represented asymptomatic infection or mild clinical symptoms without abnormal chest imaging findings. Moderate cases were defined as having both clinical symptoms and abnormal chest imaging findings. Severe cases were defined when the disease progressed to significantly increased respiration rate of ≥ 30 breaths/min, oxygen saturation ≤ 93% in resting state, or PaO_2/FiO_2 ≤ 300 mmHg, or more than 50% lesion progression in lung imaging within 24-48 hours. Time of follow-up was defined as the duration from hospital admission to outcomes (recovered or deceased) of patients. Recovered were defined as patients who were discharged from the hospital, while deceased as those who succumb to the disease.

Several biochemical [glucose, urea, sodium, potassium, creatinine, alanine transaminase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total protein (TP), lactate dehydrogenase (LDH), and albumin], hematological (hemoglobin, leucocytes, erythrocytes, and platelets), coagulatory [prothrombin time (PT) and D-dimer], and inflammatory (CRP) biomarkers were also analyzed in patients. D-dimer and CRP were analyzed by Fine Care Fluorescence Analyzer (China). The rest of the biochemistry biomarkers were analyzed by Diatron Fully Automated Biochemistry Analyzer (Pictus 500, Hungary), except for sodium and potassium, which were measured by Medica EasyLyte Analyzer (United States). Hematological biomarkers were analyzed by Beckman Coulter (DxH 500, France). Radiological findings of the observation of different types of chest abnormalities and occurrence of laterality and centrality among COVID-19 patients were studied by the images of chest X-rays.

Initially, all requisite data for the study were extracted in Microsoft Excel version 10. The data was imported to the SPSS software version 17.0 (SPSS Inc., Chicago, IL, USA). The complete data sets for both survivors and deceased patients were evaluated for the removal of duplicate cases. The quantitative variables included in the study were calculated as mean ± standard deviation (SD) by using descriptive statistics. For the quantitative variables involving two groups, we tested the statistical significance by an independent student t-test, and for those involving more than two groups, we tested using one-way ANOVA. A Chi-square test was used for qualitative variables involving two groups, and a Kruskal-Wallis test for qualitative variables involving more than two groups. The analyses were performed at a 95% confidence interval and a p-value < 0.05 indicated there was a significant relationship between the variables.

Table 1. Age group and duration of hospitalization among deceased and recovered patients

Age Group (years)		Duration of Hospitalization (days)					
		≤ 5 (n=36)	6-10 (n=66)	11-15 (n=55)	16-20 (n=17)	21-25 (n=9)	≥ 31 (n=4)
21-30	Deceased (n=3)	1	1	0	1	0	0
	Recovered (n=14)	1	5	7	0	1	0
31-40	Deceased (n=10)	2	2	4	1	1	0
	Recovered (n=17)	2	10	5	0	0	0
41-50	Deceased (n=6)	0	2	1	0	3	0
	Recovered (n=14)	2	7	5	0	0	0
51-60	Deceased (n=18)	4	5	3	3	1	2
	Recovered (n=23)	2	9	10	1	1	0
61-70	Deceased (n=19)	2	6	5	4	1	1
	Recovered (n=15)	3	6	3	3	0	0
71-80	Deceased (n=25)	9	8	4	3	0	1
	Recovered (n=7)	2	2	2	0	1	0
81-90	Deceased (n=13)	4	3	5	1	0	0
	Recovered (n=2)	1	0	1	0	0	0
≥ 91	Deceased (n=1)	1	0	0	0	0	0
	Recovered (n=0)	0	0	0	0	0	0

RESULTS

Among the total 187 COVID-19 patients, there were 95 (50.8%) deceased patients and 92 (49.2%) recovered patients. The deceased patients had a median (interquartile range, IQR) age of 66 (53-76) years and were predominated by males (n=61, 64.2%) (p=0.024). On the other hand, recovered patients [median (IQR) age: 51 (38-61) years] were predominated by females (n=48, 52.2%). The median duration of hospitalization among both groups was 10 days (p=0.176).

Among the deceased patients, there were 25 (26.3%) patients belonging to the age group 71-80 years, followed by patients in the age group 61-70 years (n=19, 20.0%) and 51-60 years (n=18, 18.9%). Similarly, recovered patients belonging to the age group 51-60 years (n=23, 25.0%) predominated the group, followed by patients in the age group 31-40 years (n=17, 18.5%) and 61-70 years (n=15, 16.3%). There were 14 (14.7%) deceased and 2 (2.2%) recovered patients with the age ≥ 81 years. Nine (9.5%) patients died within five days of hospitalization and 8 (9.4%) patients died within 10 days of hospitalization. These patients belonged to the age group 71-80 years. There were 2 (2.1%) patients belonging to the age group 51-60 years and 1 (1.1%) patient belonging to the age group 51-60 years and 71-80 years each, who had died after 30th days of hospitalization (Table 1).

Among the total patients, deceased patients had median (IQR) respiration and pulse rate to be 29.5 (22.0-36.0) (p < 0.001) and 86.0 (75.0-103.0) (p=0.084), respectively. Both deceased and recovered patients had a normal median axillary temperature, varying from 97.4 to 98.0°F. Majority (n=23, 24.2%) of deceased patients were at

Table 2. Comparison of the vitals between deceased and recovered patients

Vitals	Deceased (n=95)	Recovered (n=92)	p-value
Temperature (°F) [Median (IQR)]	98.0 (97.3-98.6)	97.4 (97.0-98.0)	-
Respiration Rate (breaths/min) [Median (IQR)]	29.5 (22.0-36.0)	20.0 (20.0-22.0)	-
Pulse Rate (beats/min)			
[Median (IQR)]	86.0 (75.0-103.0)	83.0 (76.0-93.3)	-
Blood Pressure (mm Hg)			
≤90/≤60 (n=7)	7 (7.4)	0 (0)	0.999
<120/<80 (n=59)	26 (27.4)	33 (35.9)	0.342
≥120/<80 (n=33)	12 (12.6)	21 (22.8)	0.472
≥130/≥80 (n=36)	23 (24.2)	13 (14.1)	0.063
≥140/≥90 (n=43)	21 (22.1)	22 (23.9)	0.633
≥180/>120 (n=4)	4 (4.2)	0 (0)	0.999

hypertension stage 1 (≥130/≥80) (p=0.063), 21 (22.1%) patients at hypertension stage 2 (≥140/≥90) (p=0.633), and 4 patients at hypertension stage 3 or at hypertensive crisis (≥180/>120) (p=0.999). However, the majority of recovered patients had normal blood pressure (<120/<80) and did not have any patients with hypertensive crisis (Table 2).

Among 187 COVID-19 patients enrolled in the study, 178 (95.2%) patients were symptomatic. Eighty-one (43.3%) COVID-19 patients showed presence of ≥ 3 symptoms [deceased: 45 (47.4%), recovered: 36 (39.1%), (p=0.076)]. Fever [n=107 (57.2%), deceased: 61 (64.2%), recovered: 46 (50.0%), p=0.063] and cough [n=107 (57.2%), deceased: 54 (56.8%), recovered: 53 (57.6%), p=0.123] was the most

common symptom, followed by dyspnea [n=102 (54.6%), deceased: 72 (75.8%); recovered: 30 (32.6%), p=0.010] (Table 3).

Table 3. Comparison of the signs and symptoms between deceased and recovered patients

Signs and symptoms		Group				p-value
		Deceased (n=95)		Recovered (n=92)		
No of Symptoms	Asymptomatic (n=9)	2	2.1	7	7.6	0.186
	≤ 2 (n=97)	48	50.5	49	53.3	0.136
	≥ 3 (n=81)	45	47.4	36	39.1	0.076
Symptoms	Altered Consciousness (n=7)	5	5.3	2	2.2	0.061
	Anorexia (n=3)	1	1.1	2	2.2	0.702
	Asthenia (n=5)	2	2.1	3	3.3	0.486
	Dyspnea (n=102)	72	75.8	30	32.6	0.010
	Fever (n=107)	61	64.2	46	50.0	0.063
	Headache (n=18)	6	6.3	12	13.0	0.554
	Myalgia (n=30)	8	8.4	22	23.9	0.789
	Pharyngitis (n=21)	10	10.5	11	11.9	0.205
	Cough (n=107)	54	56.8	53	57.6	0.123
	Rhinorrhea (n=8)	5	5.3	3	3.3	0.104
	Nausea (n=6)	3	3.2	3	3.3	0.274
	Vomiting (n=5)	3	3.2	2	2.2	0.172
	Diarrhea (n=6)	2	2.1	4	4.4	0.635
	Others	1	1.1	2	2.2	-

Others include chest pain (n=1), dry mouth (n=1), epistaxis (n=1)

There were 36 (37.9%) deceased patients with one co-morbidity (p < 0.001) and 31 (32.6%) deceased patients with ≥ 2 co-morbidities (p<0.001). Hypertension [n=55 (29.4%), deceased: 34 (35.8%), recovered: 21 (22.8%), p < 0.001] was the most common comorbidity followed by diabetes [n=32 (17.1%), deceased: 23 (24.2%), recovered: 9 (9.8%), p < 0.001] and respiratory diseases [n=20 (10.7%), deceased: 17 (17.9%), recovered: 3 (3.3%), p < 0.001] such as asthma and chronic obstructive pulmonary disease (Table 4).

Various laboratory biomarkers were analyzed before 48 hours of clinical outcome. Deceased patients had significantly lowered mean±SD value of ALP (153.8U/L±95.4) (p=0.030), TP (5.9g/dL±1.4) (p=0.010), albumin (3.1g/dL±0.5) (p=0.002), lymphocytes (11.9%±6.6) (p<0.001), monocytes (1.9%±1.7) (p<0.001), eosinophils (1.2%±1.1) (p=0.013), hemoglobin (12.9g/dL±2.2) (p=0.002) as compared to ALP (184.5U/L±88.1), TP (6.8g/dL±0.5), albumin (3.6g/dL±0.5), lymphocytes (27.7%±12.3), monocytes (2.9%±1.5), eosinophils (1.7%±1.5), and hemoglobin (13.9g/dL±1.5) of the recovered patients. Additionally, deceased patients had significantly elevated mean±SD serum level of glucose (186.2mg/dL±82.7) (p<0.001), urea (66.8mg/dL±39.5) (p<0.001), sodium (138.9mEq/L±6.5) (p=0.034), creatinine (1.5mg/dL±1.3) (p=0.001), LDH (807.8U/L±460.7) (p=0.028), ALT (80.9U/L±110.4) (p=0.001), AST (93.7U/L±159.8) (p=0.004), leucocytes (14,954.5cmm±17,635.5) (p<0.001), neutrophils (85.2%±8.1) (p<0.001), D-dimer (183.5ng/mL±693.2) (p=0.047), and CRP (98.6mg/L±60.9) (p<0.001) as compared to glucose (130.0mg/dL±53.4), urea (30.0mg/dL±8.5), sodium (137.2mEq/L±3.3), creatinine (0.9mg/dL±0.7), LDH (592.3U/L±252.1), ALT (40.9U/L±23.7), AST (41.7U/L±20.8), leucocytes (7,021.7cmm±2,777.9), neutrophils (67.7%±13.2), D-dimer (0.4ng/mL±0.4), and CRP (37.9mg/L±39.6) of the recovered patients (Table 5).

Table 4. Comparison of the co-morbidity between deceased and recovered patients

Co-morbidities		Group				P-value
		Deceased (n=95)		Recovered (n=92)		
		n	%	n	%	
No. of Co-morbidities	None (n=94)	28	29.5	66	71.7	<0.001
	1 (n=51)	36	37.9	15	16.3	<0.001
	≥2 (n=42)	31	32.6	11	11.9	<0.001
Co-morbidities	Cancer (n=3)	3	3.2	0	0	0.999
	Diabetes (n=32)	23	24.2	9	9.8	<0.001
	Dyslipidemia (n=2)	0	0	2	2.2	0.999
	Heart Disease (n=8)	8	8.4	0	0	0.999
	Hypertension (n=55)	34	35.8	21	22.8	<0.001
	Hypothyroidism (n=7)	4	4.2	3	3.3	0.150
	Liver Disease (n=2)	2	2.1	0	0	0.999
	Neurological Disease (n=5)	5	5.3	0	0	0.999
	Organ Transplant (n=4)	4	4.2	0	0	0.999
	Renal disease (n=2)	1	1.1	1	1.1	0.549
	Respiratory disease (n=20)	17	17.9	3	3.3	<0.001
	Rheumatoid Arthritis (n=5)	4	4.2	1	1.1	0.049
	Others (n=3)	2	2.1	1	1.1	0.213

Others include hyperuricemia (n=1), neutrophilia (n=1), vascular disease (n=1)

There were 86 (45.9%) COVID-19 patients with moderate illness [deceased: 50 (52.6%), recovered: 36 (39.1%), p=0.012] and 25 (13.4%) patients with severe illness [deceased: 16 (16.8%), recovered: 9 (9.8%), p=0.027]. Thirty-three (34.7%) deceased COVID-19 patients had lung consolidation (p<0.001) and 22 (23.2%) had GGO chest abnormality (p=0.002). Majority of deceased COVID-19 patients also showed the presence of bilateral (n=41, 43.2%) (p<0.001), peripheral disease (n=52, 54.7%) (p<0.001) with interstitiality (n=34, 35.8%) (p<0.001) (Table 6).

Table 5. Analysis of the laboratory biomarkers for deceased and recovered patients

Biomarkers		Before 48 hours of clinical outcome		
		Deceased	Recovered	p-value
Biochemistry	Glucose(mg/dL)	186.2 ± 82.7	130.0 ± 53.4	< 0.001
	Urea(mg/dL)	66.8 ± 39.5	30.0 ± 8.5	< 0.001
	Sodium (mEq/L)	138.9 ± 6.5	137.2 ± 3.3	0.034
	Potassium (mmol/L)	4.0 ± 0.8	4.1 ± 0.6	0.244
	Creatinine(mg/dL)	1.5±1.3	0.9 ± 0.7	0.001
	LDH (U/L)	807.8±460.7	592.3±252.1	0.028
	ALT (U/L)	80.9 ± 110.4	40.9 ± 23.7	0.001
	AST (U/L)	93.7 ± 159.8	41.7 ± 20.8	0.004
	ALP (U/L)	153.8 ± 95.4	184.5 ± 88.1	0.030
	Total Protein(g/dL)	5.9 ± 1.4	6.8 ± 0.5	0.010
	Albumin(g/dL)	3.1 ± 0.5	3.6 ± 0.5	0.002
Hematology	WBC (cmm)	14,954.5 ± 17,635.5	7021.7 ± 2777.9	< 0.001
	Neutrophils (%)	85.2 ± 8.1	67.7 ± 13.2	< 0.001
	Lymphocytes (%)	11.9 ± 6.6	27.7 ± 12.3	< 0.001
	Monocytes (%)	1.9 ± 1.7	2.9 ± 1.53	< 0.001
	Eosinophils (%)	1.2 ± 1.1	1.7 ± 1.5	0.013
	Basophils (%)	0.0 ± 0.0	0.0 ± 0.1	0.32
	RBC (trillion cells/L)	3.8 ± 1.4	4.7 ± 0.4	0.073
	Hemoglobin (g/dL)	12.9 ± 2.2	13.9 ± 1.5	0.002
	Platelets (billion/L)	208.1 ± 89.3	228.8 ± 81.6	0.122
Coagulatory	D-dimer (ng/mL)	183.5±693.2	0.4 ± 0.4	0.047
	PT (sec)	14.6 ± 2.0	14.5 ± 1.9	0.772
Inflammatory	CRP (mg/L)	98.6 ± 60.9	37.9 ± 39.6	<0.001

LDH: lactate dehydrogenase, ALT: alanine transaminase, AST: aspartate aminotransferase, ALP: alkaline phosphatase, WBC: white blood cell, RBC: red blood cell, PT: prothrombin time, CRP: C-reactive protein

Table 6. Radiological findings amongst deceased and recovered patients

Radiological parameters		Group		p-value
		Deceased (n=95)	Recovered (n=92)	
Type of Abnormality	Interstitial	34 (35.8)	15 (16.3)	< 0.001
	Consolidation	33 (34.7)	5 (5.4)	< 0.001
	Ground Glass Opacity	22 (23.2)	11 (11.9)	0.002
Severity	Mild (n=76)	29 (30.5)	47 (51.1)	0.016
	Moderate (n=86)	50 (52.6)	36 (39.1)	0.012
	Severe (n=25)	16 (16.8)	9 (9.8)	0.027
Laterality	Bilateral (n=51)	41 (43.2)	10 (10.9)	< 0.001
	Unilateral (n=34)	19 (20.0)	15 (16.3)	0.028
Centrality	Central (n=11)	20 (21.1)	4 (4.3)	< 0.001
	Peripheral(n=61)	52 (54.7)	22 (23.9)	< 0.001

DISCUSSION

Studies have examined the importance of laboratory parameters as early COVID-19 diagnostic parameters; mostly independently.[7,8] However, COVID-associated in-hospital mortality is not well studied using clinical, laboratory, and radiological parameters. In this study, we compared the clinical characteristics, laboratory parameters, and radiological findings between deceased and recovered COVID-19 patients.

In this study, the median age of deceased (66 years) COVID-19 patients were higher than recovered (51 years) patients. Unlike the deceased patients, who were predominated by males (64.2%) ($p < 0.05$), recovered patients were predominated by females (52.2%). Chen et al. reported similar median ages for deceased (62 years) and recovered (51 years) COVID-19 patients, however, unlike this study with females (52.2%) being predominant in the recovered group, Chen et al. reported males (54.7%) as the predominant gender in the recovered group.[8] Nonetheless, our findings were consistent with the WHO advocacy brief report on "Gender and COVID-19", which shows a higher incidence of SARS-CoV-2 infection (51%) and COVID-associated mortality (58%) in men.[9] Furthermore, this study showed a higher number of deceased patients with an increased duration of hospitalization along with increased age (≥ 80 years) compared to recovered patients (Table 1). The Center for Disease Control and Prevention also highlights the fact of increased risk of severe COVID-19 illness among older people, especially with people aged higher than 80 years, often with the need for increased duration of hospitalization, ICU admission mostly with ventilator, and despite the facilities being more prone to death.[10]

In this study, deceased patients had higher median respiratory (29.5 versus 20 breaths/minute) and pulse (86 vs. 83 beats/minute) rates and arterial blood pressure ≥ 140 mmHg (26.3% vs. 23.9%) compared to recovered patients. WHO highlights a respiratory rate of > 30 breaths/minute as one of the significant attributes of severe COVID-19, which was almost similar to the respiratory rate of deceased patients in this study.[6] Similar to this study, Chen et al. reported a higher respiratory rate (≥ 30 breaths/minute) among deceased patients (27%) compared to recovered patients (3%).[8] In contrast to our findings on pulse rate, a similar study conducted in Nepal reported a higher median pulse rate (102 beats/minute) among the deceased patients, which could be due to severe inflammation, as indicated by substantially elevated median serum CRP (142 mg/L) and ferritin (1079 µg/L) levels.[11]

The majority of deceased COVID-19 patients in the current study had the presence of three or more symptoms ($p > 0.05$), with fever being the most prevalent (64.2%) ($p>0.05$) symptom, followed by cough (56.8%) ($p > 0.05$) and dyspnea (75.8%) ($p < 0.05$). Consistent with our findings, Badedi et al. reported dyspnea (91%), cough (80%), and fever (70%) as the commonest symptoms among deceased COVID-19 patients.[12] Several previously published literature have also indicated fever and dyspnea as the significant symptoms associated with COVID-associated mortality.[8,11] Furthermore, this study found that patients with two or more co-morbidities are nearly three times more vulnerable to death because of COVID-19 ($p < 0.05$). In this study, deceased patients were more likely to have hypertension (35.8% vs. 22.8%) ($p < 0.05$), diabetes (24.2% vs. 9.8%) ($p < 0.05$), and chronic respiratory illness (17.9% vs. 3.3%) ($p < 0.05$) as pre-existing health conditions compared to recovered patients. These findings were similar to the findings of several studies.[8,11,12] Patients with such chronic diseases have reduced immune function and are more vulnerable to the risk of complications, including clinical worsening of the underlying disease, multiple organ dysfunction, and eventually death.[13]

In the present study, deceased patients had two folds higher serum levels of ALT ($p < 0.05$) and AST ($p < 0.05$) and lower serum levels of ALP ($p < 0.05$), total protein ($p < 0.05$) and albumin ($p < 0.05$) compared to recovered patients. Elevation in transaminases has been reported by several published studies and is attributed to hepatic congestion due to right heart dysfunction in the setting of high pulmonary pressures in intubated ARDS patients.[12,14,15] In this study, deceased patients had elevated serum levels of glucose ($p < 0.05$), urea ($p < 0.05$), sodium ($p < 0.05$), and creatinine ($p < 0.05$). The findings of increased glucose levels were reported by several studies and inferred that SARS-CoV-2 infection induces blood glucose levels.[15,16] A study by Wang et al. reported varying levels of serum creatinine (0.6-0.7 mg/dL) and urea (66.6-135 mg/dL) levels in patients infected with SARS-CoV-2 Corresponding findings from the study of Henry et al. and Cheng et al. revealed the direct association of higher levels of serum urea and creatinine with severe forms of COVID-19 infection too.[15,17,18] While Cheng et al. revealed elevated serum creatinine levels to be significantly associated with abnormalities in the coagulation pathway; others reported such elevation with in-hospital mortality.[18] Similarly, deceased patients in this study had elevated WBC ($p < 0.05$) and neutrophils ($p < 0.05$) counts and lowered levels of lymphocytes ($p < 0.05$), monocytes ($p < 0.05$), and eosinophils ($p < 0.05$). An increase in WBC count (4.15-9.3×109/L) was reported in several published studies and was identified as a significant marker of the clinical worsening of COVID-19.[15-19] The reduction of platelet count in COVID-19 patients could be attributed to the activation, aggregation, and formation of the microthrombi, which leads to decreased platelet production and increased consumption.[20,21] In this study, deceased patients had a more than two-fold increase in the level of CRP (98.6 mg/L ± 60.9) ($p < 0.05$) compared to the recovered patients (37.9 mg/L ± 39.6). Several studies also reported significantly higher levels of CRP (2.1-126 mg/L) in COVID-19 patients, indicating CRP levels as a strong indicator to reflect the presence and severity of COVID-19 infection.[17,22,23] Such substantial elevation in serum CRP level was attributed to hyper inflammation phase indicated by systemic inflammation or cytokine storm that includes increased concentrations of different types of cytokines (IFN-γ, TNF-α, IL-2, IL-6, IL-7, IL-10, and others).[20,24] Deceased patients in this study were four times more likely to have the coagulatory disorder than recovered patients, as evident by elevated serum levels of D-dimer (1.8ng/mL±6.9) ($p < 0.05$) in deceased patients compared to D-dimer (0.4ng/mL±0.4) of recovered patients. Several studies discussed that the gradual increase in D-dimer levels and prothrombin time were significantly correlated with disease progression, and higher mortality rates, and could be used to triage patients into critical care.[25,26] This could be due to increased inflammation in patients, which may have resulted in systemic vasculitic processes and defects in the coagulation processes.[21]

In this study, deceased patients were twice as likely to have interstitial chest abnormalities ($p < 0.05$), six times as likely to have lung consolidation ($p < 0.05$), and twice as likely to have GGO ($p < 0.05$). In the current study, the majority of deceased COVID-19 patients had moderate disease severity (53.6%) ($p < 0.05$) and exhibited bilateral (43.2%) ($p < 0.05$), peripheral disease (54.7%) ($p < 0.05$) on chest radiographs. However, in contrast to our findings, deceased patients in a study by Zhou et al. showed lower occurrences of GGO (22-35%) and lung consolidation (25-54%) compared to the recovered group.[27] Several studies have discussed the significance of chest CT scores to find specific CT features such as peripheral distribution of lesions and crazy-paving patterns among COVID-19 patients and have positively concluded it is a good indicator to diagnose COVID-19 pneumonia.[28,29]

This study suffers from several limitations. Firstly, this was a single-center cross-sectional study comprising the Nepalese population only; hence the findings could not be generalizable for individuals throughout the world. Secondly, our findings were based on a limited number of observational studies; therefore, further well-designed studies with larger sample sizes are necessary to understand the significance of such medical indices in association with COVID-19-associated mortality. Nonetheless, these findings shed light on the true burden of COVID-19 deaths in a tertiary care hospital in Nepal, and can be used to reappraise the COVID-19-associated diagnostic and prognostic policy for the effective treatment of patients with COVID-19.

CONCLUSION

In patients with COVID-19, a combination of vitals, including respiration and pulse rate; symptoms, including dyspnea; co-morbidities, including hypertension, diabetes, and respiratory disease; laboratory biomarkers, including elevated levels of glucose, urea, sodium, creatinine, LDH, ALT, AST, WBC, D-dimer, CRP neutrophil and lowered levels of ALP, TP, albumin, lymphocytes, monocytes, and hemoglobin; and radiological findings, including moderate and severe pneumonia, lung consolidation and GGO chest abnormality with bilateral peripheral occurrences can be considered as significant risk stratifying factor of the severe form of disease and predictors of mortality during the stay in hospitals.

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