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Original Article

Clinical Features, Laboratory Parameters, Treatment and Outcome analysis of COVID-19 Patients admitted to a Referral Hospital at Nepalese Terai Region during Second Wave

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ABSTRACT

Background & Objective: COVID-19 pandemic has tested health care systems worldwide. The massive wave of infection in Nepal between March to April 2021 overwhelmed the health care institutions throughout the country. This study describes the demographic, clinical, laboratory parameters and outcome of patients hospitalized in a secondary level facility during second wave of infection.

Material and Methods: The data was extracted from admitted patients at Janaki Health Care and Teaching Hospital (JHCTH) with COVID-19, between 9th April to 14th June 2021. Demographic, clinical, laboratory parameters, treatment and outcome were recorded from the medical records and analyzed.

Results: Out of 122 admitted patients,11%, 18.03%, 33.60% and 35.24% presented with mild, moderate, severe and critical illnesses respectively, with the median saturation of peripheral oxygen (SPO_2) at admission was 89(34-99)% and 17 deaths were recorded a mortality rate of 20.4%.A significantly high mortality rate

was found among ventilated patients (73.3%), against non ventilated (7.2%). Mortality rates among critically and severely ill patients were 38.46 % and 6.9% respectively. Mean C reactive protein (CRP) was 51.13(±30.50)mg/dl. Statistically significant CRP levels were observed in patients who presented with mild illness (32.53±10.85 mg/dl) and those who died in hospital (61.08±30.00 mg/dl). Remdesivir use did not offer any mortality benefit.

Conclusion: A very high mortality rate (20.40%) observed in this study due to COVID-19 in hospitalized patients, may be associated with a high proportion of severe and critical cases (68.70%) admitted. Further upgrading of health resources should be prioritized to manage severe COVID-19 related mortalities, because of the possibility of a future waves.

Keywords: COVID-19, C- reactive protein, in-patient. Mortality, Remdesivir

INTRODUCTION

The first laboratory-confirmed case of COVID-19 in the Nepal was reported on 13th January, 2020 [1]. Fuelled by emergence of a new variant B.1.617.2 also called Delta, first reported from neighboring country India [2], the number of confirmed cases nearly tripled through the period from May to June 2021, overwhelming healthcare institutions. 275,402 cases, 5103 deaths, were reported during this peak, respectively. This proved to be the most devastating wave in terms of numbers as well as deaths [3].

There is limited data regarding clinical characteristics, treatment, laboratory parameters and outcomes of hospitalized adults with COVID-19 in Nepal [4]. Insights into above topics are imperative to improve therapeutic management of these high risk patients especially with the possibility of further peaks of infection in the future.

The objective of this study was to analyze the demographics, clinical characteristics, laboratory parameters, therapeutic management and outcomes of hospitalized COVID-19 patients in Nepal during this massive wave of infection.

MATERIAL AND METHODS

This was an observational study conducted at Janaki Health Care and Teaching Hospital (JHCTH), Janakpurdham, Madhesh province, Nepal. JHCTH is a 100 bedded private hospital, which cares to referred cases from surrounding 4 to 5 districts. COVID ward consisted of 35 beds along with 4 ventilators and BiPAP machines. It included all the patients admitted to COVID-19 designated ward of JHCTH from 9th April 2021 to 14th June 2021 with confirmed clinical and laboratory/radiological diagnosis of COVID-19.

Patients were included if they had at least 1 positive SARS-CoV-2 polymerase-chain-reaction (PCR) test of a nasopharyngeal or throat swab. In patients with clinical suspicion but negative PCR, High Resolution Computed Tomography (HRCT) chest was done and those having corona virus disease 2019 Reporting and Data System (CO-RADS) score of 4 or 5 were included in the study. CO-RADS is a categorical assessment scheme for pulmonary involvement of COVID-19 at unenhanced chest CT that performs very well in predicting COVID-19 in patients with moderate to severe symptoms and has substantial inter observer agreement, especially for categories 1 and 5 [5].

Study procedures and data collection

Data collection was done by reviewing medical records of individual patients obtained from medical record section of the hospital. Details regarding demographics,

clinical status, laboratory values, treatment and patients outcomes were retrieved. Based on these collected data, patients were classified in to mild, moderate, severe and critical as per National Institutes of Health (USA) COVID-19 treatment guidelines Panel, as presented on Table 1 [6].

previous history of hypersensitivity to Remdesivir or its component, elevated transaminase (ALT) >5 times of upper limit of normal range and impaired glomerular filtration rate <30ml/minute or End-Stage Renal Disease were not treated with Remdesivir.

Table 1: Classification of COVID-19 patients as per National Institures of Health (USA) COVID-19 treatment guidelines Panel [7]

Mild disease	Individuals who have any of the various signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but who do not have shortness of breath, dyspnea, or abnormal chest imaging.
Moderate disease (Pneumonia)	Individuals who show evidence of lower respiratory disease during clinical assessment or imaging and who have an oxygen saturation (SpO_2) ≥94% on room air at sea level
Severe disease (Severe pneumonia)	Individuals who have SpO_2 <94% on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO_2/FiO_2) <300 mm Hg, a respiratory rate >30 breaths/min, or lung infiltrates >50%.
Critical disease	Individuals who have respiratory failure, septic shock, and/or multiple organ dysfunction.

Treatment protocol

Steroid, Enoxaparin and supportive measures was used in the treatment of these patients as per the guidelines laid down by Nepal Medical Council and World Health Organization [8,9]. Those patients having severe or critical illness requiring oxygen supplementation or mechanical ventilation and having history of onset of disease ≤7 days were treated with Remdesivir, as per guidelines laid down by Nepal Health Research Council and Nepal Medical Council A 200mg intravenously stat dose was given on day 1, followed by 100mg once daily for 10 days to inpatients on mechanical ventilation and 5 days to other patients. However, cases not meeting criteria for sever or critical COVID-19 infection, duration of disease onset ≥ 8 days and had contraindication such as;

Criteria for discharge from hospital

Patients who had been afebrile for more than two days, had better respiratory symptoms, did not need additional oxygen, and had a clear absorption of inflammation on a chest x-ray were released from the hospital.

Study variables

Characterization of patients, including demographics, severity of disease, oxygen saturation at admission, laboratory parameters upon admission , respiratory support (oxygen or mechanical ventilation), use of Remdesivir, length of hospital stay and clinical outcome data (e.g. mortality)

Statistical analysis

The extracted data were entered into the Microsoft Excel sheet and then transferred to

IBM SPSS Statistics 23.0 version (Statistical Package for Social Science for Windows version: SPSS, Inc., Chicago, IL) for statistical analysis. No imputation of the missing data was done. In the descriptive analysis, age and length of hospital stay were expressed as median (range). The categorical variables were expressed as number (percentage). Association between the variables was analyzed using Chi-square test. T test was applied for continuous variables to differentiate by different parameters. P-values <0.05 were considered statistically significant.

Ethical considerations

Ethical approval for the study was obtained by the Nepal Health Research Council (NHRC), National Ethical Guidelines for Health Research in Nepal (Reg. no. 496/2021P). Patients' identity was anonymized, as this was an observational study by retrieving the information from medical records from hospital.

RESULTS

Table 2 depicts demographic and baseline characteristics of COVID-19 patients. Overall, 122 COVID-19 patients were admitted during the study period and were included in the analysis. Mean age of the patients was 51.40(±14.27) years and majority (74.6%) were male. Median length of hospital stay was 5 (range 1-87) days. Few (13.2%) patients were admitted with mild symptoms, whereas 18.0%, 33.6% and 35.2% had moderate, severe and critical illness at admission respectively.

Median SPO_2 was 89 (34-99) %. Out of 122 patients, 39 (31.96%) did not require oxygen support during their hospital stay. Respiratory support in the form of supplemental oxygen alone, ranging from low flow oxygen through nasal cannula to high flow oxygen through non rebreathing mask was required by 66 (54.1%) patients. Ventilator support was given to 17 (13.9%) patients in view of respiratory failure not

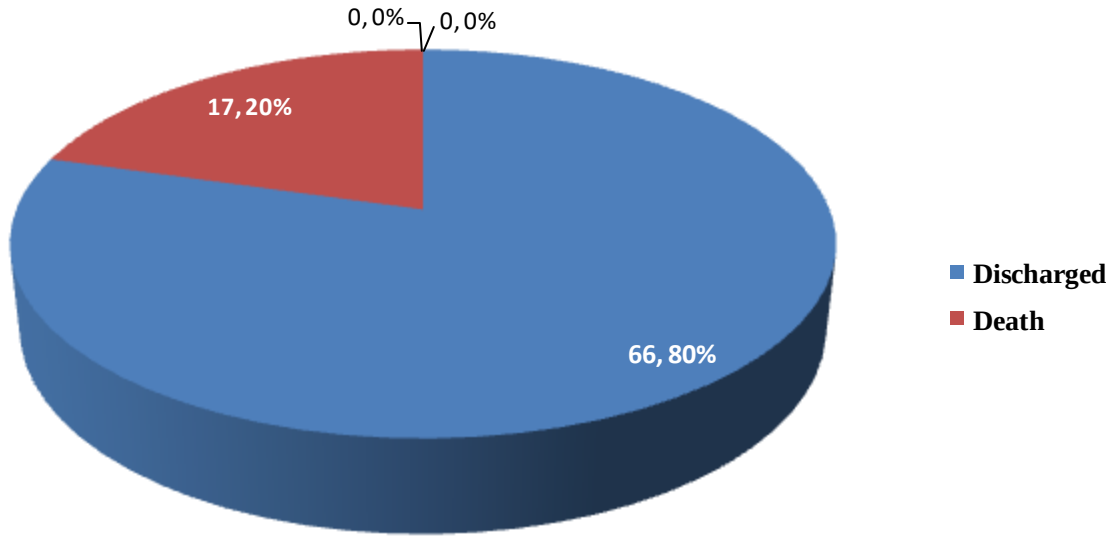
Table2: Demographic and baseline characteristics of COVID-19 patients

Characteristics	Category	Frequency	Percentage (%)
Age (years)	Mean (±SD)	51.40 (±14.27)	-
Age group	40 years & less	28	23.0
	41- 50 years	30	24.6
	51-60 years	31	25.4
	Greater than 60 years	33	27.0
Sex	Male	91	74.6
	Female	31	25.4
Severity on admission	Mild	16	13.2
	Moderate	22	18.0
	Severe	41	33.6
	Critical	43	35.2
Oxygenation modality	M. Ventilation	17	13.9
	Oxygen	66	54.1
	None	39	32.0
SPO_2 % at admission	[Median (Range)]	89 (34-99)	-
Length of hospital stay (days):	Median (Range)	5 (1-87)	-

corrected with supplemental oxygen alone. Non invasive mechanical ventilation with BiPAP (Bilevel Positive Airway Pressure) mask was the mode used for ventilatory support in all of them and no patient was intubated.

Fifteen patients (12.29%) were referred to higher center for further treatment. 24 patients (19.67%) got discharged on request (DOR) or left against medical advice(LAMA) from the hospital and hence the final outcome of these 39 patients could not be ascertained. Out of 83 patients included, 66 (79.51%) were discharged following satisfactory improvement in symptoms and clinical condition, whereas 17 (20.0%) died (Figure 1). Furthermore, age of patient was found to be differed significant for severity at admission (mild/moderate verus critical; p =0.04) as well as for status at discharge (improved versus death; p= 0.009) (Table 3)

Figure 1: Outcome of COVID-19 Patients



*Out of 122, 39 Patients were not included in outcome analysis

Table 3: Severity at admission and death by age

Characteristics	Total N=122	Age in years	p – value
Severity at admission		**[Mean ± SD]**	
Mild/Moderate	38	48.13±13.95*	**0.040**
Severe	41	50.14±14.56	
Critical	43	55.48±13.61*	
Status at discharge			
Death	17	60.29±14.11*	**0.009**
Improve	66	48.37±13.154*	
DOR	18	48.33±14.51	
LAMA	6	58.50±22.95	
Refer	15	55.46±9.80	

* Significant difference observed between categories.

In hospital, 17 people died, with a mortality rate of 20.4%.The mortality rates were 73.3% for ventilated patients and 7.2% for non-ventilated patients, respectively. Death rates among critically and severely ill patients were respectively 15/39 (38.46%) and 2/29 (6.9%), with no mortality in the mild or moderately ill category (Table 4). Remdesivir was administered to 31 (45.58%) of the 68 severely and critically ill patients who were found to be suitable for its usage. The mortality rate in this Remdesivir-treated subgroup was 6/31 (19.3%). In this sample of patients, there was no statistically significant change in mortality with Remdesivir usage (p=0.325). The average length of hospital stay was greater in those who got Remdesivir(13.35±14.81days)than in those who did not (6.78±7.15days), and this difference was found statistically significant (p= 0.020) (Table 5). Mean CRP among the patients was 51.13 (±30.50)mg/dl. CRP levels differed significantly between patients with mild illness (32.53±32.56 mg/dl) and those with critical disease (61.08±30.00 mg/dl) (p=0.013). Raised CRP at admission (>6 mg/dl) was seen in 78(83%) patients (Table 6).

Table 4: Mortality in COVID-19 patients

Characteristics	Total	Deaths (%)	p – value
Support during treatment			
Ventilated	15	11(73.3)	<0.0001
Non-ventilated	83	6(7.2)	
Severity at admission*			
Mild	13	0(0.0)	0.003
Moderate	17	0(0.0)	
Severe	29	2(6.9)	
Critical	39	15(38.5)	
**Compared between severe and critical cases*			

Table 5: Death and average length of stay (LoS) in patients by Remdisiver administration (n =68)

Injection Remdesiver	Total N=68	Deaths (%)	Length of stay	
			Mean ± SD	Median (Range)
Given	31	6(19.3%)	13.35±14.81days	10 days (1 to 87 days)
Not given	37	11(29.7)	6.78±7.15days	6 days (1 to 34 days)
p-value		0.325	0.001	

*Observed significant difference between categories

Table 6: CRP in patients by severity at admission (n=83)

Lab parameter	Severity at admission	Number	[Mean ± SD]	p – value
CRP	Mild*	9	32.53±32.56	0.013*
	Moderate	13	50.10±33.69	
	Severe	31	47.34±26.81	
	Critical*	30	61.08±30.00	
	Overall	83	51.13 ±30.50	
Raised CRP at admission	(>6 mg/dl))	78	-	

*p-value significant between mild and critical

DISCUSSION

In this study, males constituted almost three-fourth of population(72.4%) which is in congruence with other hospital based studies where higher rates of male admission were observed [10,11]. Almost equal distribution of COVID-19 among the various age groups was seen in this study. This uniform affliction across age groups could be due to the fact that this study was conducted at the peak of community transmission of COVID-19 in Nepal.

The mortality rate in this study was 20.4%. Mortality rate among ICU patients by Hamal et al. and another study conducted at the Institute of Medicine, Kathmandu, which is a tertiary care centre, was 35.91% and 39.47% respectively [10,11]. In the meta-analysis by Lin et al, Delta variant has been shown to be associated with greater risks of severe disease and mortality, compared to the wild type virus [12].The study conducted by GC et al. revealed that during the second wave in Nepal, there was 227% increase in CFR compared to the preceding wave (November 2020-October 2020) [3]. Outcome of COVID-19 is complex interplay between host factors (immunity status, age, co-morbidities etc), disease factors (virulence of the strain) and environmental factors (adequate availability of resources, overwhelming of healthcare system etc).

In the global analysis by Goel et al., in-hospital mortality was significantly higher in America (22.23%) and Europe (22.9%) compared to Asia (12.65%), but no difference was seen when compared with each other [13]. The relatively higher mortality rate in our study was driven by high proportion of severely and critically ill patients (68.80 % of total) patients and a more lethal variant of the virus. Lack of resources in terms of equipments, oxygen, logistics and trained manpower to manage the sickest of these patients also contributed to mortality. Advanced age has been established as a risk factor for severe disease and death in various studies across the globe as observed in the systematic review by Starke K et al. and this was seen in our study as well [14].

CRP has been studied as a biomarker of disease severity as well as prognostic marker in various studies [15]. In our study, the difference in CRP levels among those with mild and critical illness was statistically significant. Similar findings were seen in various studies which showed the increased CRP level with increased severity of infections as in systematic review by Yitbarek et al. [16].

Remdesivir is the only antiviral drug that is approved by the Food and Drug Administration (FDA) for the treatment of COVID-19 [17].Although it has shown clinical benefits such as shorter hospital stay and lower requirement of mechanical ventilation, whether it decreases mortality is unclear [18]. In our study, out of the total patients who were severely or critically ill, 45.85% were found eligible for and received Remdesivir under emergency use authorization. No significant difference in mortality was observed with Remdesivir use in this subset of patients. The average length of hospital stay was longer in those patients who received Remdesivir compared to those who did not receive it. This paradoxical finding has been seen in other studies as well [19,20]. As mentioned in these studies, possible explanation could be that these patients were kept in hospital to complete the course of Remdesivir injection leading to longer hospital stay. No major or minor

adverse effects were seen with Remdesivir and none of the patients required its discontinuation due to adverse effects.

This study was conducted during the second wave of COVID-19 in Nepal which examined complete spectrum of the disease as well as analyzed various laboratory parameters and treatment modalities. However, the study has several limitations. It was a single centre study with limited patients. Data was missing for many patients across different variables. Patients who were referred to higher centre, left without medical advice or got discharged on request were not followed up and hence their final outcome could not be ascertained. Data regarding comorbidities, temporal changes in lab parameters, symptomatology was not incorporated and the sample size for CRP was small.

CONCLUSION

COVID-19 had a very high mortality of nearly one in five which was driven by high proportion (nearly 68 % of total patients) of severe and critical illness. Severity of illness at admission, need for mechanical ventilation, advanced age, raised CRP level was associated with mortality. Use of Remdesivir did not show mortality benefit but was associated with longer hospitalization. This study emphasizes an urgent need to strengthen health care delivery across all levels to deal with high burden of severe cases in order to contain mortality in instances of future waves of infection.

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Conflict of interest

None

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None

Author's Contribution: *Conceptualized and designed the study, performed statistical analysis, and drafted the primary manuscript-* ***RM,JKS;*** *participated in the acquisition of data, developed methodology-* ***BKJ, KP, AK, AA, AKY;*** *carried out the analysis, and participated in the interpretation of results, drafting and subsequent revision of the contents of the manuscript-* ***RM, JKS, AA, AKY****. Finally, all authors read and approved the final version of the manuscript.*

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